Universidad Europea

TRABAJO DE FIN DE GRADO

Grado en Odontología

ATTITUDE OF THE DENTIST TOWARDS THE ANTI-AGGREGATE PATIENT IN ORAL SURGERY

Madrid, curso 2020/2021

Número identificativo **148**

ABSTRACT

This paper aimed to provide information to clinicians regarding the approach to adopt towards patients who were undergoing some type of oral surgery and who were taking antiplatelet drugs at the same time.

In the introduction, a documented overview was given regarding the fact that cardiovascular disease is on the rise in much of the developed and developing world, and it was explained how one tool available to clinicians to combat these diseases are antiplatelet drugs. Furthermore, the mechanisms of actions and the uses of the most widespread and most important antiplatelet drugs were described, and after it was analyzed what are, according to the scientific literature, the treatments and oral surgeries performed in the dentist's clinic more likely to cause bleeding, and which ones instead were less likely to have it.

Regarding the objectives: this paper had a primary objective, namely to demonstrate based on the most recent scientific literature that it is not necessary to stop taking antiplatelet drugs in patients who had to undergo oral surgery, and two secondary objectives, namely to demonstrate that to stop antiplatelet therapy worsened the general clinical situation of the patients and that postoperative hemostasis measures were a valid help to combat bleeding.

As regards the materials and methods, some of keywords used were “antiplatelet therapy”, “dental surgery”, “dental extractions”, and only articles in English and from the last 10 years were considered.

In the discussion, through a bibliographic review, several articles were analyzed, and the authors' opinions on this important issue were compared.

In the conclusion it was noticed that the vast majority of the scientific articles analyzed agreed on the fact that it is neither advantageous for the clinician nor beneficial for the patient to suspend antiplatelet therapy before undergoing oral surgery, and that hemostatic measures were a valid help to keep bleeding under control.

SUMMARY

Con la realización de ese trabajo se pretende brindar información a los clínicos sobre la actitud a adoptar con los pacientes que estaban siendo sometidos a algún tipo de cirugía oral y que estaban tomando antiagregantes plaquetarios al mismo tiempo.

En la introducción, se dio una información documentada de que las enfermedades cardiovasculares están aumentando en gran parte del mundo desarrollado y en desarrollo, y se explicó cómo una herramienta disponible para contrastar estas enfermedades son los medicamentos antiplaquetarios. Además se describieron los mecanismos de acción y los usos de los antiagregantes plaquetarios más utilizados y más importantes, y luego se analizó cuáles eran, según la literatura científica, los tratamientos y cirugías bucales que se realizan en la clínica del odontólogo susceptibles de causar sangrado y cuáles eran menos propensos a tener sangrado postoperatorio.

Respecto a los objetivos: este trabajo tenía un objetivo principal, a saber, demostrar con base en la literatura científica más reciente, que no es necesario dejar de tomar antiagregantes plaquetarios en pacientes que deben someterse a cirugía oral, y dos objetivos secundarios, a saber, demostrar que detener la terapia antiplaquetaria empeoraba la situación clínica general de los pacientes y que las medidas de hemostasia postoperatoria eran una ayuda válida para bloquear el sangrado.

En cuanto a los materiales y métodos, se utilizaron algunas palabras clave como “terapia antiplaquetaria”, “cirugía dental”, “extracciones dentales” y solo se consideraron artículos en inglés y de los últimos 10 años.

En la discusión, a través de una revisión bibliográfica, se analizaron varios artículos y se compararon las opiniones de los autores sobre este importante tema.

En la conclusión se constató que la gran mayoría de los artículos científicos analizados coincidían en que no es ventajoso para el clínico ni beneficioso para el paciente suspender la terapia antiagregante antes de la cirugía oral, y que las medidas hemostáticas eran una ayuda válida para mantener el sangrado postoperatorio bajo de control.

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INTRODUCTION

It is possible to state that nowadays, especially in the Western world, more and more people are suffering from **cardiovascular problems**. This, rather than being due to a single factor, is due to a series of causes that together have led a continuing increasing number of individuals to suffer from this type of disease. One of the factors to consider is that from the second post-war period to today, over time, the jobs and occupations carried out by most individuals have gradually contemplated less and less physical effort, with the consequence that people have adopted lifestyles always more sedentary. Simultaneously with this, life expectancy has considerably lengthened in the last 50-60 years in the developed Western countries. (1)

This has led many people to reach old age, which is exactly the period of life in which one is more prone to suffer from diseases concerning the circulating system. Other risk factors that undoubtedly increase the chances of suffering from cardiovascular diseases are not quitting smoking, the easy availability of cheap junk food (and the consequent obesity that can derive from the constant intake of these foods assisted from lack of physical activity) and diabetes. (2)

Smoking, in particular, is believed to be responsible for over 30% of mortality related to coronary heart problems. The specific causes of cardiovascular injury are not fully understood, but what it has long been accepted is that smoking has damaging consequences on endothelial function. In addition, the fact that in correlation with smoking, the female gender is more likely to develop cardiovascular disease than the male gender is quite interesting. In fact, it has been found that, for the same consumption of tobacco cigarettes, women smokers are more likely than men smokers to have a risk of developing cardiovascular problems equal to 25%. It seems

that this susceptibility of the female gender is linked to genes that deal with signaling of thrombin. (3)

Excessive body weight is also a cause of cardiovascular disease, and the same is true for diabetes, a disease which over the years has also been affecting an increasing number of people. (4)

By now, cardiovascular diseases find fertile ground not only in the developed Western world, but also in developing countries, so we can speak of a global increase of these diseases. In these developing countries, among which China and India stand out, early diagnosis must become a widespread tool in order to predict the development of these pathologies. (5)

There is, therefore, a general picture of an *increase in cardiovascular diseases* that goes hand in hand with the increase in the general well-being of a society (in most cases). In this respect, one tool that clinicians have to combat and treat this kind of cardiovascular disease is the prescription of *antithrombotic drugs*. It's important to say that in much of the scientific literature, the term "antithrombotic drugs" refers to both anticoagulant and **antiplatelet drugs**. In this regard, it is important to underline the difference that exists between these two types of drugs. Commonly called "blood thinners", the anticoagulants inhibit the clotting factors. In other words, they interfere with the coagulation process (also called coagulation cascade) by acting on the cofactors and on the coagulation factors, that when activated lead to the formation of a fibrin network that acts by trapping the blood cells and giving rise to the clot (Fig. 1). (6)

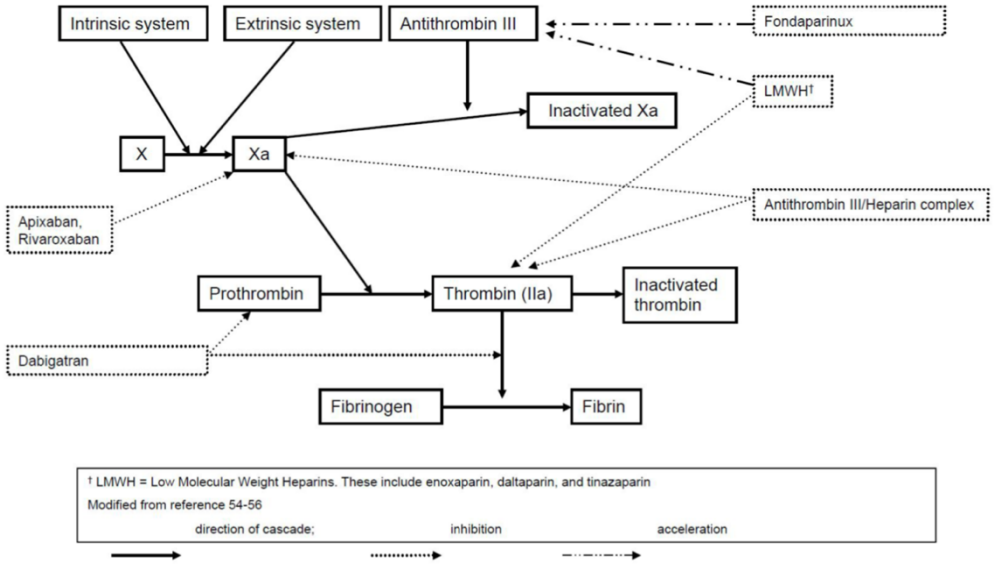

Figure 1 – Site of action of anticoagulants drugs (6)

The focus of this paper, as it's possible to guess from the title, are the antiplatelet drugs. Below, in this paper, the mechanism of action of the most relevant antiplatelet drugs will be thoroughly analyzed.

Antiplatelet drugs are administered both for the prevention and treatment of arterial thrombosis and after cardiovascular diseases (such as ischemic events affecting the coronary arteries), after diseases of the cerebral vessels and peripheral arteries, after myocardial infarction and after angioplasty with the installation of a "stent". These drugs are also dispensed after coronary artery bypass surgery. So, antiplatelet therapy is a very good tool to prevent acute thrombotic occlusions in arteries. That's because the activity of circulating platelets increases, together with the deliverance of platelet-derived vasoactive mediators. (7)

In the field of dentistry, it is important to keep in mind what a dentist must ensure when a patient who takes antiplatelet drugs is in his or her dental office. It is important to have clear the level of risk the patient is about to undergo, and to make sure to be prepared to take

appropriate action in the event of a medical emergency. Furthermore, the clinician should always have clear whether the patient can be treated in the dental office or whether it is better to have him or her undergo dental treatment in a hospital setting. Given that frequently in the professional life of a clinical dentist there is the need to practice dental extractions or other oral surgeries in the dental office, usually (especially in the past) there was a tendency to suspend antiplatelet therapy by replacing it with other medicines that had a similar effect, for example with anticoagulant drugs. (8)

In order to proceed orderly, below is present a listing of the different anti-aggregation drugs, their pharmacology and uses.

Nowadays, the antiplatelet agents most used are:

- **acetylsalicylic acid** (systematic chemical name for aspirin)
- **non-selective NSAIDs**
- **thienopyridines** (that include **clopidogrel**, **ticlopidine**)
- **dipyridamole**

(9)

The *mechanism of action* of **acetylsalicylic acid (ASA)** acid consists in the deactivation of cyclooxygenase (COX-1 and COX-2) in an irreversible way. The duration corresponds to the life of the platelets (7-10 days). This very widespread antiplatelet drug is indicated in the avoidance of myocardial infarction, in some forms of cerebrovascular accidents and in peripheral arterial disease. It can be also prescribed in patients suffering from degenerative inflammation of the joints (arthritis) or chronic moderate pain (interfering significantly with their daily living activities). (9) (10)

So acetylsalicylic acid is used a lot as an antiaggregant agent (in low dose), in many cases in patients who suffer from myocardial ischemia or who are at risk of stroke. Studies show that the incidence of spontaneous bleeding is very rare, but it can occur. After oral surgery, bleeding problems are infrequent, with the exception of a few cases where platelet transfusions are required. (11)

Another effect that aspirin (ASA) has is to suppress the action of lipid mediators that are released by activated platelets via mechanism that are dependent by COX, and this can alter the development of the normal colonic mucosa to adenoma and, subsequently, to carcinoma. Taking the USA as an example, cardiovascular diseases remain, together with cancer and malignant neoplasia, one of the two main causes of mortality in 2015 (45.4%). This means that using acetylsalicylic acid in order to reduce the incidence of cardiovascular events can be of great help in reducing mortality and morbidity rates. (12)

A side effect of taking aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs) inhibiting cyclooxygenase 1 (COX-1) is to aggravate the condition in a number of asthmatic individuals. This clinical disorder is well defined and is called aspirin-induced asthma (AIA), and its clinical appearance is signalized by the presence of asthma, sensitivity to the aspirin, nasal polyposis and eosinophilic rhinosinusitis. (13)

As for the **non-selective NSAIDs**, these medications *act* by inactivating (in a reversible way, unlike ASA) the cyclooxygenase (COX-1 AND COX-2). Their duration depends on the half-life of the drugs. (14)

Prescribing occurs in those patients with mild to moderate pain, or when a patient has inflammatory and degenerative arthritis. (9) (14)

Hence, one of the most common uses for NSAIDs is to relieve pain, even in diseases such as osteoarthritis (15).

Some authors have investigated the role that prostaglandins play in regulating blood pressure and have provided interesting diagrams on how NSAIDs work (Fig. 2) . (16)

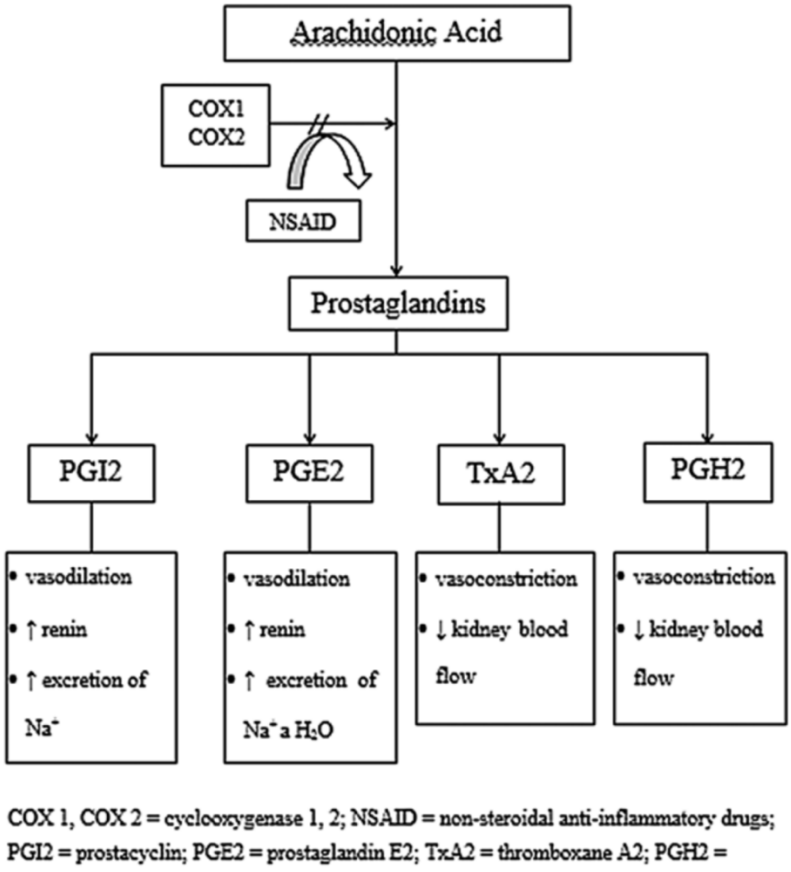

Figure 2 – NSAID, site of action (16)

There are several side effects that can arise regarding the use of these drugs, on different systems of the body. Specifically, there may be side effects regarding the gastrointestinal system (especially in the case in which elderly patients suffering from osteoarthritis are treated), renal (possibility to cause acute kidney injury) and cardiovascular (specific risk for pharmacotherapy). (15)

Scientific literature usually classifies NSAIDs into groups according to their chemical structure and to their selectivity: acetylated salicylates (which we have discussed separately in this paper), non-acetylated salicylates (diflunisal, salsalate), propionic acids (naproxen, ibuprofen, acetic acids), enolic acids (meloxicam, piroxicam), anthranilic acids (meclofenamate, mefenamic acid), naphthylalanine (nabumetone), and selective COX-2 inhibitors (celecoxib, etoricoxib).

As for **Ticlopidine (Clopidogrel)**, the *mechanism of action* of the medicine in this case is to act on the adenosine diphosphate (ADP) receptors on the platelets, which are blocked. The effective antiplatelet duration corresponds to 7-14 days, and the indications for prescribing this drug are not dissimilar to ASA (regarding secondary prevention of myocardial infarction and CVA and secondary prevention of peripheral arterial disease). Only clopidogrel is prescribed in the last described indication. (9) (10)

Ticlopidine is a first generation thienopyridine that has been mostly substituted by Clopidogrel (second generation thienopyridine). This has happened because Clopidogrel has kindred efficacy but better tolerability, diminished incidence of side effects of hematologic origin and a more suitable dosing regimen (17).

And finally, as regards **Dipyridamole**, its *mechanism of action* consists in the increase in contraction of cAMP and in hindering the enzyme phospho-diesterase due to inhibition of the adenosine transporter (18).

Furthemore, also platelet inhibitory actions of prostacyclin (PGI2) is influenced by dipyridamole, and cellular uptake and metabolism of adenosine are inhibited because of

potential stimulation of the adenylyl cyclase in platelets: this ensues in elevated cAMP. Sometimes this drug is used in combination with acetylsalicylic acid. (18)

Its duration of the antiplatelet effect is 24 hours, with a half-life of 12 hours.

This medicine is prescribed to ensure secondary prevention in patients at risk of cerebrovascular accidents. (9) (10)

Although most clinicians use dipyridamole mainly for problems related to thromboembolism prevention after surgery, it is important to remember that there are some consequences derived by its use such as the increase in cAMP and cGMP levels, vasodilatation and tissue perfusion that are relevant in ocular diseases. That's why it's also a drug of interest in the treatment of different disorders involving the eye and its structures. (18)

Given that this paper aims (as it is specified in the "Objectives section") precisely to provide indications to clinicians regarding whether or not to suspend their drug therapy in patients who are taking antiplatelet drugs in case of oral surgery, it is interesting to investigate more about which are the treatments performed by the dentist that most often could cause oral bleeding.

Among the *odontologic treatments that almost never or rarely involve gingival bleeding* we can include small fillings and restorative dentistry treatments that are not particularly invasive and that do not have subgingival margins. Other treatments that do not cause oral bleeding with a few exceptions are intraoral or extraoral radiographs (used by the dentist to perform a more proper oral diagnosis, to discover oral injuries of hard and soft tissues, to detect the presence of impacted third molar, to analyze the maxillary sinuses, the maxillary bones, the bone structure of the temporomandibular joints etcetera) and the placement or the removal of prosthetic devices. (19)

Therefore, with some treatments there is low probability that bleeding will be caused. In particular, according to the Scottish Dental Clinical Effectiveness Program (SDCEP), these treatments are (in addition to those that have already been mentioned); the mental, infiltrative, intraligamentary and troncular nerve technique for anesthesia; basic periodontal evaluations; the elimination of hardened dental plaque (tartar) at a supragingival level; endodontic procedures with orthograde filling; the adaptation and the try-in of most of the orthodontic appliances . (20)

Among the *treatments that instead could cause bleeding* and that are most frequently carried out in the dental office, there are certainly dental **extractions**. Regarding this, it is interesting to say that the scientific literature has introduced a differentiation regarding the various types of bleeding that could follow an extraction, based on timing with which they appear. This was done in order to facilitate clinical work and the treatment of postoperative hemostasis. According to this classification, it's possible to distinguish a *primary hemorrhage*, a *reactionary hemorrhage* and a *secondary hemorrhage*. (21)

The following table explains these three concepts (Tab 1.)

TYPE	**Description**
Primary hemorrhage	When the patient begins to bleed during oral surgery
Reactionary hemorrhage	When, due to the end of the vasoconstriction effect, bleeding begins 2-3 hours after oral surgery

Secondary hemorrhage	When, presumably due to an infection, bleeding occurs until 14 days after the surgical procedure.

Table 1. Description of the 3 types of hemorrhage

Another way to classify the post-extraction hemorrhage is to do it in line with the site affected. Bleeding can indeed occur in the soft tissue (for example in the gum), in the alveolar bone or at a vascular level. (21)

It is very important to take into consideration, after a dental extraction (surgical or not), the fact that the patient may not know what behaviors to adopt and which ones not to adopt in order to keep bleeding under control and not negatively affect coagulation. Actions *to avoid* in the post extraction phase are to rinse the oral cavity the same day of the surgery, to consume alcoholic or hot beverages, to inhale cigarette and tobacco smoke (for a minimum of one full day), to masticate hard meals for the following 24 hours and to engage in any form of physical exercise. Smoking, in particular, could decrease vasodilation and increase the chances of having alveolar osteitis, while engaging in exercising would cause an increase in blood pressure which instead would be desirable to be kept under control during the day in which the extraction is carried out. Some behaviors and actions are instead to be encouraged, in order, among other things, that the clot in the dental socket is not removed and in order not to negatively affect coagulation. These actions include drinking tepid beverages carefully and biting a non-cotton gauze or tissue on the extraction area for the first 15 minutes to facilitate clotting. As for brushing the teeth and rinsing the mouth, chlorhexidine should be used in the mouthwash (or water with salt), and brushing should avoid affecting the extraction area for the first 24 hours (21).

An interesting distinction regarding the possibility of bleeding in case of extractions was introduced by Dr. Dezsi et al. (2017). In their paper, always referring to the classification made by SDCEP, it is highlighted how the extractions that are less likely to bleed are those characterized by a low level of surgical complexity and a relatively small number of teeth to be extracted (maximum 3). An additional feature that classifies an extraction as low-risk for bleeding is the limited lesion dimensions obtained after the procedure. Instead, extractions that are more likely to bleed are those who require a more complicated surgical approach, that have a number of contiguous teeth to be extracted higher than three and that will produce big injuries. (20)

Another class of treatments that could cause bleeding in the clinic (and therefore worth mentioning, as this paper deals with the attitude of the dentist towards the anti-aggregate patient in oral surgeries and treatments that could cause bleeding in the mouth of the patient) is the one of **periodontal treatments**. Periodontal treatments can be performed by both the general dentist and the periodontist, based on the degree of complexity of each treatment and on the experience and preparation of the clinician who is going to treat the patient. Periodontal treatments can be surgical or non-surgical: in the case of non-surgical treatments we find scaling and root planning, the use of an ultrasonic laser to keep the gum healthy and oral irrigation whose purpose is to remove the bacterial plaque underneath the gum. Some examples of the most common surgical periodontal treatments are flap surgery, regeneration technique and soft tissue graft. (22)

According to SDCEP the possibility of bleeding is low in case of instrumentation of the root surface and in the event of complete periodontal check in six points, while procedures that are more likely to bleed are the treatments that involve the raising of a flap (surgeries whose purpose is to ensure a good fit of a prosthesis and invasive periodontal treatments). (20)

The incisions made with the purpose of draining bulges, or excrescences or abscesses are considered at low possibility of generating intraoral bleeding, again according to the "SDCEP". The treatments we haven't mentioned yet that have a high chance of causing bleeding in the dentist's office are the procedures of crown lengthening, placement of titanium implants, the redesigning of the gingival tissue called gum recontouring, surgeries in the peri-radicular region and *biopsies*. It's important to say that biopsy is a procedure that is often practiced for diagnostic purposes, and that it can be of two types: excisional and incisional. We are talking about excisional biopsy when the lesion is removed entirely (therefore advantages are obtained both at a therapeutic and diagnostic level), while we are talking about incisional biopsy when one or more representative fragments of the lesion are taken, together with the adjacent tissues, and only after the histological examination, the treatment of the residual lesion can be established. The clinician must pay particular attention to any bleeding especially if the biopsy is performed on the tongue or in the sublingual area, which are regions of the mouth richly supplied with blood vessels. (20) (23)

The following table schematize all these procedures (Tab 2).

	Dental procedures that are likely to cause bleeding	
Dental procedures that are unlikely to cause bleeding	Low bleeding risk procedures	High bleeding risk procedures
• Local anaesthesia by infiltration, intraligamentary or mental nerve block • Local anaesthesia by inferior dental block or other regional nerve blocks • Basic periodontal examination (BPE) • Supragingival removal of plaque, calculus, and stain • Direct or indirect restorations with supragingival margins • Endodontics (orthograde) • Impressions and other prosthetic procedures • Fitting and adjustment of orthodontic appliances	• Simple extractions (1–3, with restricted wound size) • Incision and drainage of intraoral swellings • Detailed six-point full periodontal examination • Root surface instrumentation (RSI) • Direct or indirect restorations with subgingival margins	• Complex extractions, adjacent extractions that will cause a large wound, or more than three extractions at once • Flap raising procedures ○ Elective surgical extractions ○ Periodontal surgery ○ Preprosthetic surgery ○ Periradicular surgery ○ Crown lengthening ○ Dental implant surgery • Gingival recontouring • Biopsies

Table 2. Dental treatments classified on the basis of their possibility of causing bleeding (20)

OBJECTIVES

1) Primary objective: demonstrate through a bibliographic review that it is not necessary for the dentist to interrupt the antiplatelet treatment when performing oral surgery.

2) The secondary objective is to demonstrate that suspending antiaggregant drugs could increase cardiovascular risks

3) The other important secondary objective: to establish whether post-extraction measures of local hemostasis are of proven utility in reducing the bleeding in the patient who did not interrupt the intake of antiplatelet drugs.

MATERIALS AND METHODS

As information sources basically online medical databases were used, in particular Pubmed, and also MDPI (Multidisciplinary Digital Publishing Institute) was used to access valid scientific journals.

English-language scientific articles and journals were preferred.

The key words that have been used were the following: “antiplatelet therapy”, “dental surgery”, “oral surgery “, “dental extractions”, “post-operative bleeding”, “cardiovascular risk”, “anti-aggregate patient”.

Revised papers were 60, and 22 were excluded for the criteria that are explained here.

Speaking of the inclusion and exclusion criteria, as regards the former, the following have been taken into consideration and used to continue the work.

- Studies of patients undergoing antiplatelet therapy
- Studies about patients who have undergone oral surgery (include clinical data about the post-operatory bleeding after surgery)
- Studies about patients who need dental extractions that could be performed without resorting to the hospital setting
- Papers of the last 10 years. Three articles used were from 2002, 2003 and 2005, and they’ve been included because of their relevance. In total, 37 articles and one book were selected for writing this project
- Only journals and books in English

Instead, the following exclusion criteria were applied:

- Lack of information on the patient's oral health
- Lack of information on the patient's drug therapy status
- Studies conducted on animals
- Studies missing parts necessary for the overall understanding of the articles (i.e. incomplete articles, articles without the full text)
- Editorials, letters and articles not written in English.
- Studies of dubious scientific reliability

DISCUSSION

By researching the scientific literature it is possible to find a lot of material on this topic.

The *primary objective* of this paper is to demonstrate that it is not necessary for the dentist to interrupt the antiplatelet treatment when performing oral and/or dental surgery.

Precisely in this regard, in the article of Cervino et al. (2019) it is stated that for less invasive dental surgeries it is not necessary to suspend the administration of antiplatelet drugs. (8)

Reading the article of Sheeraz Badal et al. (2012), the authors also comes to the conclusion that the most recently documented scientific research affirms that, according to latest scientific evidence, the most suitable indication is to not block the intake of antiplatelet drugs. An additional indication is given: in case the patient is not at high cardiac risk and is taking clopidogrel in combination with antiplatelet therapy, the clopidogrel can be suspended, better for 10 days, before the surgery. Contrariwise it is more convenient to carry on with the administration of the clopidogrel in case of high cardiac risk. (10)

The study conducted in the article of Dr. Sajid Hasan et al. (2019) focuses on analyzing the need to interrupt or not the administration of aspirin prior to dental surgery, specifically extractions. Also in this case, the conclusion reached by its authors is that, although it is necessary to evaluate each time on a case-by-case basis to establish the pros and cons of discontinuing antiplatelet therapy, in general it can be observed that before extractions it is better not to change the patient's dressing. (11)

Several other articles give scientific confirmation of the fact that subjecting the patient to risk of thrombosis (suspending the intake of antiplatelet drugs before oral surgery) is not at all a

justified clinical attitude, as the bleeding following surgery is in the vast most cases mild and can be easily controlled. Specifically, the study conducted in 2018 by Reza Tabrizi et al. (2018) focuses in particular on the placement of dental implants in anti-aggregate patients. The study refers to two groups: twenty-two patients in group 1 (13 men and 9 women) and 20 patients in group 2 (10 men and 10 women). Their mean age is 60.50 ± 7.94 years (group 1) and 61.90 ± 7.62 years (group 2). The authors' paragon between the continuation of administration and the suspending of ASA or clopidogrel in the course of placement of dental implant shows irrelevant increase of postoperative bleeding in those patients not stopping drugs' assumption (24).

A team of Taiwanese scientific investigators have carried out a study analyzing a group of patients regarding the need to suspend antiplatelet therapy and warfarin therapy (if INR<4) before tooth extractions, and has reached the same results. (25)

Similar results are also obtained by the authors of the article by Gröbe et al. (2015). In this case the focus is on a slightly more invasive surgical procedure than a simple extraction, i.e. osteotomy, and the study proves how it is possible to carry out this surgical procedure by continuing the administration of clopidogrel or the double administration of clopidogrel / aspirin. (26)

An interesting narrative review is conducted in the article by Carrizo et al (2015), about antithrombotic drugs. The paper is not specifically about antiplatelet drugs, but it has been decided to include it in this paper as it contains also interesting information about the management of this kind of patient. The authors argue that, as amply demonstrated by oral and maxillofacial surgeons who are dedicated to the publication of scientific articles, cases of particularly serious and difficult to manage postoperative problems do not arise in patients who are taking antiplatelet drugs (after oral surgeries). However, the authors warns about the fact

that particular attention must be paid and medical inter-consultation requested in cases where the patient has concomitant disorders, or uses the latest generation anticoagulant drugs, or there are interactions with the medicines prescribed during dental procedures. (27)

The article by Michael J. Wahl (2014) raises the question of whether or not to suspend antiplatelet therapy with a very evocative title: "Bleed or Die", precisely. The author concludes his article with a statement as straightforward as it is simple: clinicians today should stop withholding antiplatelet therapy before oral surgery (28).

A work group from the “Oral Medicine and Oral Surgery Francophone Society” provides an interesting digression on the clinical behaviors that were adopted in the past regarding the management of patients on antiplatelet therapy when they had to undergo an oral surgery in the dental office. In fact, what was done until relatively recently, that is to say suspend the antiplatelet treatment, is no longer considered appropriate. Antiplatelet therapy was suspended not only for oral and/or periodontal surgery, but also for conservative dental treatments. This paper affirms that the impropriety of continuing to administer antiplatelet drugs has never been proven in any recent accredited study. Nowadays, therefore, the general trend supported by the scientific literature is not to suspend antiplatelet therapy in patients who need to undergo oral surgery. The Oral Medicine and Oral Surgery Francophone Society also insist on another important aspect: the postoperative risk must be assessed globally and in a multidisciplinary manner. Only this can allow to properly manage patients treated with antiplatelet therapy in odontostomatological surgery. (29)

Many other researchers from Saudi Arabia and Asia dedicated themselves in producing scientific literature on this topic , and basically they have come to conclusions very similar to those of their European and American colleagues. (30) (31) (32)

In this regard, a study conducted by Dr. Santhosh Kumar also shows that it's not necessary to suspend antiplatelet therapy, and that the risk of postoperative bleeding is statistically higher in patients who undergo both antiplatelet therapy and anticoagulant therapy, or in patients who are undergoing dual antiplatelet therapy. (30)

In the article by Dr. Altaf Hussain Shah et al. (2015) published on The Saudi Journal for Dental Research a really interesting bar chart is provided about the opinion of the practitioners regarding the most concerned medicine (Fig. 3). From the evaluation of the responses that the authors of this study obtains regarding which is the most concerned medicine, it has been found that it is statistically significant ($p < 0.001$) that most dentists have concerns about aspirin (53,3 %) while in the case of doctors it is warfarin (59.3%) the most concerned drug. A really consistent part of dental and medical practitioners (77.9%) decide to interrupt antiplatelet or anticoagulant drugs before any dental surgery such as tooth extraction.

More dental practitioners ($n = 84$) as compared to medical practitioners ($n = 50$) want to stop aspirin prior to any dental surgery and there is a statistically significant difference in opinion (Chi-square test, $p = 0.001$). In total, 84 (15.4%) dental and medical practitioners want to carry on with the anti- platelet or anticoagulant treatment without making any alteration, while 6.6% are insecure whether to interrupt the medication or carry on its use (Fig. 3) (Fig. 4). (31)

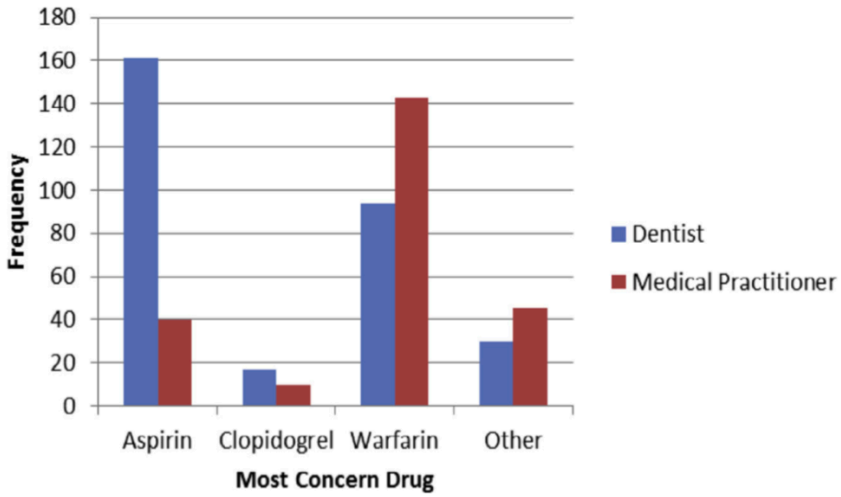

Figure 3 – Opinion of the clinicians about the drug they have more concerns about. (31)

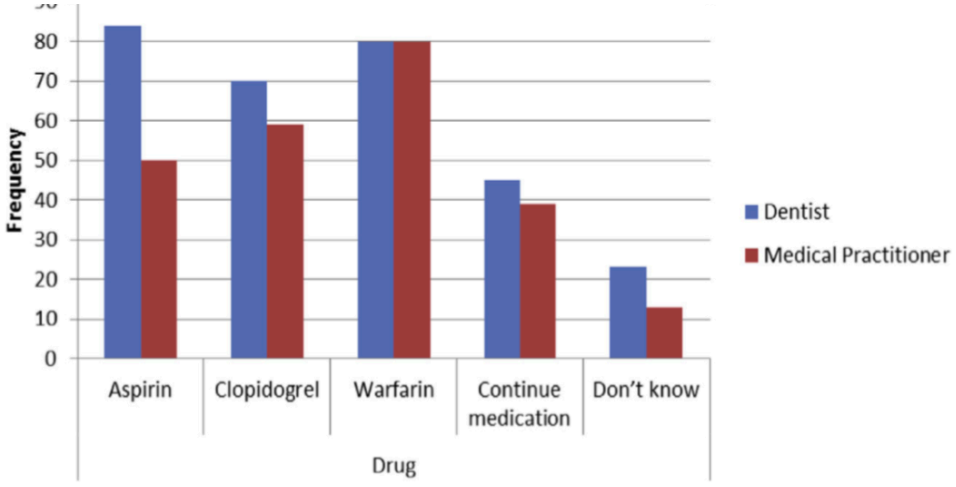

Figure 4 – Opinion of the clinicians about the drug to be interrupted prior to dental treatment (31)

The conclusions reached by the authors of this paper are that both dental and medical practitioners in most cases base their clinical approach both with patients who are taking antiplatelet drugs and with patients who are taking anticoagulant drugs on experience. The authors also add that in this regard it is very important to sensitize and educate both medical and dental practitioners to always act relying on updated scientific literature, rather than on

personal clinical experience. Clinical experience can help, but the medical or dental professional approach cannot be based on this alone, completely ignoring the guidelines dictated by the updated scientific literature. (31)

Another interesting study is conducted by Dr Mahn-Won Park et al (2011). In this case the patients analyzed are not only undergoing antiplatelet dentistry, but they also have DES (drug-eluting stents). Out of 100 patients who are examined (72 men and 238 women), only two percent of them (i.e. 2 patients) have problems in the postoperative phase (i.e. after tooth extractions), i.e. show some level of severe bleeding or thrombo-encephalic events of greater entity. In the vast majority of cases, however, it is not contraindicated to suspend antiplatelet therapy as excessive bleeding or serious cardiovascular events does not occur in the experiment conducted in this paper. Therefore, for patients who have DES and who are undergoing dental extractions, it is possible to continue to administer antiplatelet therapy, even triple antiplatelet therapy. (32)

Dr Saez-Alcaide et al. have worked at the realization of an article containing a systematic review that is included in an article (2017). The authors provide, with their paper, some important information regarding this issue. Two important considerations are affirmed: first of all it is said that it is always necessary to give more importance to the patient's medical/systemic condition than to his dental care needs, and secondly it is also stated that with regard to the new antiplatelet drugs, it is not yet possible to state with certainty what the clinical attitude to follow is, as yet 100 percent secure and reliable protocols haven't been drawn up. In this regard it is necessary to continue the studies in this verse in order to have better and more precise information in the future. (33)

Two papers respectively by Dr. Malik et al (2020) and by Dr. Ockerman et al. (2019) both reiterate the fact that the suspension of administration of antiplatelet agents due to minor oral surgery is completely unjustified. (34)(35)(36)

In the second of the two aforementioned articles an analysis is conducted in order to introduce an interesting distinction: the difference between dual antiplatelet therapy, single antiplatelet therapy and the lack of antiplatelet therapy in a patient. Two studies are analyzed and it is noted that bleeding in dual antiplatelet therapy (DAPT) patients is greater than in single antiplatelet therapy (SAPT) and no antiplatelet therapy patients (no APT). So the conclusion drawn at the end of this review is that there are differences, albeit not significant, in the risk of bleeding a patient with DAPT faces compared to a patient with SAPT or a patient with no APT. In the end, therefore, the suspension of the antiplatelet drug in antiplatelet therapy (dual or single) is not recommended in any case, as it is reiterated that the differences in perioperative bleeding are irrelevant, and that this bleeding can be kept under control . (35)

In another revised paper by Cupp et al. (2011) aims to evaluate the risks of discontinuing antiplatelet and anticoagulant therapy in patients who are about to undergo dental surgery. This article warns that in case there is a patient who is taking an anticoagulant agent (such as warfarin), before subjecting him to an extraction, his INR should be checked and made sure that it is within the parameters considered acceptable. Furthermore, according to the guidelines dictated by the authors of this article, the possibility of suspending unnecessary antiplatelet drugs in this type of patient should be considered and also the prescription of antibiotics that could amplify the effect of warfarin should be avoided (such as example metronidazole, clarithromycin, erythromycin) . The last important consideration made in the conclusions of

this article by its authors is that of considering the hospital-based treatment with this type of patient. (37)

Dr José A Cedeño et al., in their article (2013) underline how important it is, in patients under antiplatelet therapy who must undergo oral surgeries such as extractions, to create their own medical history that also involves an inter-consultation with the patient's doctor (specialist or general practitioner). It is also important for the dentist to gather information on the patient's disease and also to carry out all the necessary biological laboratory tests. (38)

With regard to the primary objective that this paper sets itself, after having analyzed the revised scientific articles in the discussion section, it is possible to state that almost all the authors of the articles that have been analyzed agree on the fact that it is neither necessary, nor desirable, nor justifiable to suspend antiplatelet therapy in patients who have to undergo oral surgery.

Only in the article of the author Cupp (2011), there's a slight deviation from this guideline, and it's stated that patients who are already taking anticoagulant medications may need to stop administering "unnecessary" antiplatelet drugs before oral surgery (37).

The *secondary objective* of this paper is to demonstrate that suspending antiaggregant drugs could increase cardiovascular risks.

About this, in the article of Cervino et al. (2019) it is asserted that in the event that the patient on antiplatelet drugs has to undergo more complex oral surgeries (such as the placement of dental implants), today's protocols suggest that postoperative bleeding levels are considered controllable and manageable without the need to resort to suspension of the antiplatelet drugs, always after a detailed medical history . Indeed, in the event that it is decided to suspend the

antiplatelet therapy, the clinician could even expose the patient to some risks related to his pathology. (8)

In their paper, Sheeraz Badal et al. (2012) also came to the conclusion that the most recent documented scientific research affirms that, in order to avoid running the antiplatelet patient the risk of having a cerebrovascular problem or a myocardial infarction, the most suitable indication is to not block the intake of antiplatelet drugs. (10)

In the article by Michael J. Wahl (2014) it is stated that, according to the study conducted in the paper, there is a rather negligible 0.2% chance that surgery in an antiplatelet patient will cause non-fatal postoperative bleeding, against a greater risk of thrombo-encephalic complications. (28)

In the work group from the "Oral Medicine and Oral Surgery Francophone Society" it's stated that in the past, it was common to suspend antiplatelet therapy not only for oral surgery, but also for conservative dental treatments. This way of proceeding in many cases caused thrombo-encephalic consequences in the period following the interruption of antiplatelet therapy (1-3 weeks), even when flurbiprofen was administered in place of common antiplatelet drugs. (29)

This paper has *another important secondary objective*: to establish if post-extraction measures of local hemostasis are of proven utility in reducing the bleeding in the patient who do not interrupt the intake of antiplatelet drugs.

Regarding this, in the article of Cervino et al. (2019) is stated by the authors that in less invasive dental surgeries, it is not necessary to suspend the administration of antiplatelet drugs, and in these cases, if good hemostasis is provided after dental surgery (through measures such as the

application of sutures, tranexamic acid, ice and compression) there are no particular post-operative problems and the surgery can be completed without previous laboratory tests. (8)

Also in the article by Dr. Sajid Hasan et al. (2019) is recommended to use good local hemostasis measures after the oral surgery in antiaggregated patients. (11)

The results obtained in the paper by Dr Shin-Yu Lu et al. (2018) tend towards obtaining a good hemostasis rather than towards the suspension of the patient's pharmacological antiplatelet therapies (25) .

Always in this regard, the studies conducted by Dr. Santhosh Kumar (2016) and Dr Saez-Alcaide (2017) et al. show that, in addition to stating that it's not necessary to suspend antiplatelet therapy, it's sufficient (in order to control bleeding) to perform hemostatic measures. (30)(33) .

The two articles respectively by Dr. Malik et al (2020) and by Dr. Ockerman et al. (2019) reiterate the fact that in the perioperative it is important to act with hemostatic agents such as tranexamic acid, sutures or collagen sponges in order to control the eventual bleeding. (34)(35).

CONCLUSION

The purpose of this paper was to be able to provide a guide to clinicians who are faced with the doubt as to whether or not to suspend antiplatelet therapy in patients who have to undergo oral surgery.

Indeed, the primary objective of the paper was to demonstrate that it is not necessary to stop antiplatelet therapy.

The bibliographic review conducted in this work confirmed this.

After having gone through the bibliographic review, it's possible to state that the totality of the authors of the articles examined have repeatedly confirmed the onset of thrombo-encephalic complications following the suspension of the antiplatelet therapy (secondary objective).

From the analysis of scientifically reviewed articles on this topic it emerged that post-surgical measures of hemostasis are an excellent ally in reducing post-operative bleeding in patients who do not interrupt antiplatelet therapy (secondary objective).

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ANNEXES

Published by Oxford University Press on behalf of the International Epidemiological Association
International Journal of Epidemiology 2011;**40**:271–277
doi:10.1093/ije/dyr061

EDITORIAL

Trends in European life expectancy: a salutary view

David A Leon

London School of Hygiene & Tropical Medicine, Keppel Street, London WC1E 7HT, UK. E-mail: david.leon@lshtm.ac.uk

Making a difference to the health of populations, however small, is what most people in public health hope they are doing. Epidemiologists are no exception. But often caught up in the minutiae of our day-to-day work, it is easy to lose sight of the bigger picture. Is health improving, mortality declining, are things moving in a positive direction? Getting out and taking in the view (metaphorically as well as literally) can have a salutary effect. It broadens our perspectives and challenges our assumptions. Looking at recent trends in European life expectancy is a case in point.

Since 1950 estimated life expectancy at birth of the world's population has been increasing. Initially, this was accompanied by a convergence in mortality experience across the globe—with gains in all regions. However, in the final 15 years of the 20th century, convergence was replaced with divergence, in part due to declines in life expectancy in sub-Saharan Africa.[1] However, this global divergence was also the result of declining life expectancy in Europe.[2,3] Home to 1 in 10 of the world's population,[4] and mainly comprised of industrialized, high-income countries, Europe has over 50 states. These include Sweden and Iceland that have consistently been ranked among the countries with the highest life expectancies in the world. But while for the past 60 years all Western European countries have shown increases in life expectancy, the countries of Central and Eastern Europe (CEE), Russia and other parts of the former Soviet Union have had a very different, and altogether more negative experience.

Trends in life expectancy between 1970 and the latest year available are shown in the Figure 1 for an illustrative selection of countries. These data were taken from one of two open sources : (i) the WHO Health for All Database[5] or (ii) the Human Mortality Database,[6] depending on which one had the longest time series. Differences between the sources are minimal for the purposes of this editorial. It is important to emphasize at the outset, that with one exception (discussed below), the trends shown in the Figure 1 are overwhelmingly driven by changes in mortality in adult life, not in infancy or childhood and are not the result of artefact.

Former communist countries of Eastern Europe

Between 1970 and the end of the 1980s, life expectancy at birth in the former communist countries of CEE (Czech Republic, Hungary, Poland and Slovakia), Russia and the Baltic states (Estonia, Latvia and Lithuania) stagnated or declined (Figure 1). This led to an increasing gap between them and Western European countries as the latter steadily improved. However, within a few years of the collapse of the Berlin wall in 1989, life expectancy started to steadily increase in the countries of CEE. This vividly illustrates that mortality can decline rapidly in response to political, social and economic change. Interestingly, once underway, the post-1989 increase in life expectancy in these countries has continued at a steady rate that is very similar to Western Europe. These parallel trajectories mean that the East–West gap, measured in terms of absolute differences in years of life expectancy, is proving very difficult to eliminate, despite earnest hopes to the contrary.[7]

The trajectories of Russia and other Soviet countries, including the three Baltic States in the Figure 1, were strikingly different to those of the CEE countries. The anti-alcohol campaign introduced in 1985 by the last Soviet President, Mikhail Gorbachev,[8] was accompanied by a brief increase in life expectancy.[9] Soon afterwards there was a precipitate decline, induced by the collapse of the Soviet Union in 1991. This was particularly dramatic in Russia: between 1990 and 1994 male life expectancy fell by 6 years to a low of 57 years.[10] There was then a short-lived period of recovery until 1998 at which point Russia once more declined.[11,12] In the Baltic states, which by then were independent countries looking westwards for membership of the European Union, life expectancy improvements flattened out and for Lithuanian and Latvian men even reversed. In the most recent period, improvements have at last been seen in all the former Soviet countries of Europe, with the possible exception of Ukraine. But it will take a longer period of improvement to be convinced that Russia, Latvia and Lithuania have embarked upon a sustainable upward trajectory given their recent history.

Article 1

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European Journal of Cardiovascular Nursing 10 Suppl 2 (2011) S5–S13

European Journal of Cardiovascular Nursing

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The global burden of cardiovascular disease

Christi Deaton[a,*], Erika Sivarajan Froelicher[b], Lai Har Wu[c], Camille Ho[d], Kawkab Shishani[e], Tiny Jaarsma[f]

[a] *Professor of Nursing, School of Nursing, Midwifery and Social Work, University of Manchester and Central Manchester Foundation Trust; Manchester Academic Health Sciences Centre, Manchester, United Kingdom*
[b] *Professor, School of Nursing and Epidemiology and Biostatistics, School of Medicine, University of California, San Francisco, California, United States*
[c] *Assistant Professor, The Hong Kong Polytechnic University, Hong Kong*
[d] *Heart Program Manager, Hong Kong Adventist Hospital, Hong Kong*
[e] *Assistant Professor, College of Nursing, Washington State University, Spokane, Washington, United States*
[f] *Professor, Department of Social and Welfare Studies, Linköpings University, Norrköping, Sweden*

Abstract

Cardiovascular disease (CVD) today is responsible for approximately one-third of deaths worldwide, and that figure will surely increase in both developing and developed countries as risk factors for the disease – primarily dyslipidemia, hypertension, obesity, diabetes, physical inactivity, poor diet, and smoking – continue to increase. Although these risk factors are modifiable, to date there is a relative paucity of measures to prevent or control them, particularly in developing countries. A population strategy combined with a high-risk strategy for CVD prevention could greatly reduce the burden of disease in the coming decades. Many initiatives are working, but many more are needed. This chapter provides background on the global burden of CVD and provides the context for the subsequent chapters addressing nurses' roles in reversing the bleak predictions for the ravages of CVD if risk factors are left unchecked in the coming decades.

Keywords: Cardiovascular disease; Developing countries, Prevention

1. The need for global cardiovascular disease prevention

Cardiovascular disease (CVD) is a major health problem across the world, accounting for 30% of all deaths (Figure) [1,2]. Of the 58 million deaths from all causes worldwide in 2005, an estimated 17.5 million were due to CVD, 3 times more deaths than are caused by infectious diseases including HIV/AIDS, tuberculosis, and malaria combined [2,3]. It is estimated that noncommunicable conditions will account for more than three-fourths of all deaths in 2030, and deaths from CVD will rise to 23.4 million, an approximately 37% increase from 2004 rates. Furthermore, the leading causes of death in the world in 2030 are predicted to be ischemic heart disease (IHD) and cerebrovascular disease (stroke), both components of CVD [2].

The World Health Organization (WHO) noted that CVD has no geographic, socioeconomic, or sex boundaries. It is estimated that, far from being confined to the most developed countries, CVD is the leading cause of death in developing countries as well. Low- and middle-income countries contribute to about 80% of CVD deaths [3]. Stroke deaths in low- and middle-income countries were 5 times more likely than in high-income countries [4]. In developed countries, lower socioeconomic groups have a higher prevalence of risk factors, higher incidence of disease, and higher mortality. As the CVD epidemic matures in developing countries, the greater disease burden will shift to lower socioeconomic groups [3]. Among women across the world, heart disease is the also the most common cause of death [5]. Tables 1 and 2 provide the prevalence of IHD across the world [6].

* Correspondence: Christi Deaton, PhD, RN, University of Manchester, Jean McFarlane Bldg, Oxford Rd, Manchester, UK M20 3RA.
E-mail address: mcdeaton@manchester.ac.uk (C. Deaton).

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DOI: **10.1016/S1474-5151(11)00111-3**

Article 2

Review Article on Improving Outcomes in Lung Cancer Through Early Diagnosis and Smoking Cessation

Cardiovascular risk of smoking and benefits of smoking cessation

Giuseppina Gallucci[1], Alfredo Tartarone[2], Rosa Lerose[3], Anna Vittoria Lalinga[4], Alba Maria Capobianco[2]

[1]Cardiology Unit, [2]Department of Onco-Hematology, Division of Medical Oncology, [3]Hospital Pharmacy, [4]Pathology Unit, IRCCS-CROB Referral Cancer Center of Basilicata, Rionero in Vulture (PZ), Italy

Contributions: (I) Conception and design: G Gallucci, A Tartarone; (II) Administrative support: None; (III) Provision of study materials or patients: None; (IV) Collection and assembly of data: None; (V) Data analysis and interpretation: None; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Dr. Alfredo Tartarone. Department of Onco-Hematology, Division of Medical Oncology, IRCCS-CROB Referral Cancer Center of Basilicata via Padre Pio 1, 85028 Rionero in Vulture (PZ), Italy. Email: tarta1@virgilio.it.

Abstract: Smoking increases mortality from all causes and has a crucial role in atherosclerotic cardiovascular disease (ASCVD). Active smoking and secondhand smoke exposure determine more than 30% of coronary heart disease (CHD) mortality. The exact mechanisms of cardiovascular damages are not well known, but the detrimental effect of smoking on endothelial function has long been recognized. Smoking elicits oxidative processes, negatively affects platelet function, fibrinolysis, inflammation and vasomotor function; all these proatherogenic effects double the 10-year risk of fatal events in smokers compared to non smokers. An intriguing issue about smoking is the vulnerability of female gender. The mortality from cardiovascular diseases (CVDs) is higher in female than male smokers and female smokers show a 25% higher risk of developing CHD than men with the same exposure to tobacco smoke. This female vulnerability seems to be related to genes involved in thrombin signaling. The effects of smoking cessation have also been extensively studied. Cessation at an early age (40 years) has an impressive 90% reduction in the excess risk of death. In this review we report recent data about the causal link between smoking and CVDs and about the benefits of smoking cessation.

Keywords: Cardiovascular diseases (CVDs); tobacco smoking; secondhand smoke

Submitted Feb 05, 2020. Accepted for publication Feb 28, 2020.
doi: 10.21037/jtd.2020.02.47
View this article at: http://dx.doi.org/10.21037/jtd.2020.02.47

Introduction: the causal link

Cardiovascular diseases (CVDs) are a major cause of morbidity and mortality throughout the world. In the United States, CVDs affect many racial or ethnic groups, and this fact has an extremely high cost that is estimated around $200 billion annually in healthcare services, drugs, and loss of productivity. Much of this burden is due to insufficient implementation of prevention strategies and poor control of atherosclerotic cardiovascular disease (ASCVD) risk factors in many adults (1,2). According to World Health Organization data, smoking determines 10% of all CVDs (3). Tobacco smoking usage causes approximately 6 million death per year throughout the world, in the United States almost 500,000 deaths can be attributed to smoking and about 10% of these deaths are caused from second-hand smoke exposure. Epidemiologic studies have supported the assumption that cigarette smoking increases the incidence of myocardial infarction and fatal coronary artery diseases (4). The increased risk of cardiovascular events has also been shown for low-tar cigarettes and smokeless tobacco. Even passive smoking is responsible for a 30% increased risk of ASCVD, a little less than half of the risk increase in active smokers that is around 80% (5,6). Ever since the Framingham study, the epidemiologic investigations have tried to identify people with a high likelihood for a future cardiovascular events in order to make actionable interventions to reduce the risk. The concept of "risk factors" was made popular by Kannel *et*

Article 3

Editorial

***Circulation Research* Compendium on Obesity, Diabetes, and Cardiovascular Diseases**

Philipp E. Scherer and Joseph A. Hill, Editors

Obesity, Diabetes, and Cardiovascular Diseases
A Compendium

Philipp E. Scherer, Joseph A. Hill

Excess body weight, a burgeoning problem worldwide, is a major risk factor for cardiovascular disease. Diabetes affects >180 million people around the world, and the number of patients is anticipated to increase to 300 million by 2025.[1] Recent data indicate that diabetes prevalence in adults has increased since 1980 virtually in every country of the world; the end-result is a near quadrupling of the number of adults worldwide with diabetes.[2]

Within this escalating healthcare problem of monumental proportions, obesity-associated type 2 diabetes accounts for 90% to 95% of all diagnosed diabetes cases in adults.[1] In fact, diabetes and insulin resistance are powerful predictors of cardiovascular morbidity and mortality, and each is an independent risk factor for death in patients with heart failure. Yet, the complex mechanisms underlying the deleterious impact of diabetes on the heart and the vasculature are poorly characterized.

Diabetes-associated cardiovascular diseases arise by a variety of mechanisms. Atherosclerotic disease often emerges in multiple vascular beds. Also, patients with diabetes are often hypertensive. Obesity is associated with a proinflammatory state marked by chronic elevations of systemic adrenergic activity, dyslipidemia, and hyperglycemia. Circulating levels of a variety of bioactive molecules are perturbed. Clearly, the underlying pathophysiology is complex.

Constant and unremitting metabolic stress on the heart leads over time to progressive deterioration of myocardial structure and function, and heart failure is a typical end-result. Sadly, current therapies are insufficient to arrest the progression of heart failure, and developing new therapies will require greater understanding of molecular mechanisms underlying pathological cardiac remodeling. This suggests that therapeutic interventions early in the disease, targeting specific metabolic and structural derangements, may be required. This is especially relevant as rigid control of hyperglycemia, however central to treatment, has not fulfilled hopes of meaningful morbidity and mortality benefit.[3] Recent and ongoing research into mechanisms of metabolic control, insulin resistance, and diabetes-associated derangements portend novel therapies designed to benefit the rapidly expanding cohort of patients with diabetes, a benefit with tremendous societal impact.

In light of these realities, we have assembled thought leaders from around the world to review recent developments in the complex biology of obesity-associated diabetes and cardiovascular disease. In so doing, we present a compendium of 10 articles that touch on all critical aspects of this complex and fascinating biology.

In an article entitled "Epigenetic Changes in Diabetes and Cardiovascular Risk," Keating et al[4] provide an overview

The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.

From the Touchstone Diabetes Center (P.E.S.), Departments of Internal Medicine (P.E.S., J.A.H.), Cell Biology (P.E.S.), and Cardiology and Molecular Biology (J.A.H.), University of Texas Southwestern Medical Center, Dallas.

Correspondence to Philipp E. Scherer, PhD, Touchstone Diabetes Center, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd, Dallas, TX 75390. E-mail philipp.scherer@utsouthwestern.edu or Joseph A. Hill, MD, PhD, Division of Cardiology, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd, Dallas, TX 75390. E-mail Joseph.Hill@UTSouthwestern.edu

(*Circ Res*. 2016;118:1703-1705.
DOI: 10.1161/CIRCRESAHA.116.308999.)

***Circulation Research* is available at http://circres.ahajournals.org**
DOI: 10.1161/CIRCRESAHA.116.308999

Article 4

Journal of the American College of Cardiology
© 2012 by the American College of Cardiology Foundation
Published by Elsevier Inc.

Vol. 60, No. 14, 2012
ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2012.03.074

STATE-OF-THE-ART PAPER

Cardiovascular Disease in the Developing World

Prevalences, Patterns, and the Potential of Early Disease Detection

David S. Celermajer, MBBS, PHD,*† Clara K. Chow, MBBS, PHD,*‡§ Eloi Marijon, MD,‖ Nicholas M. Anstey, MBBS, PHD,¶# Kam S. Woo, MBBS, MD**

Sydney and Darwin, Australia; Paris, France; Hong Kong, China

Over the past decade or more, the prevalence of traditional risk factors for atherosclerotic cardiovascular diseases has been increasing in the major populous countries of the developing world, including China and India, with consequent increases in the rates of coronary and cerebrovascular events. Indeed, by 2020, cardiovascular diseases are predicted to be the major causes of morbidity and mortality in most developing nations around the world. Techniques for the early detection of arterial damage have provided important insights into disease patterns and pathogenesis and especially the effects of progressive urbanization on cardiovascular risk in these populations. Furthermore, certain other diseases affecting the cardiovascular system remain prevalent and important causes of cardiovascular morbidity and mortality in developing countries, including the cardiac effects of rheumatic heart disease and the vascular effects of malaria. Imaging and functional studies of early cardiovascular changes in those disease processes have also recently been published by various groups, allowing consideration of screening and early treatment opportunities. In this report, the authors review the prevalences and patterns of major cardiovascular diseases in the developing world, as well as potential opportunities provided by early disease detection. (J Am Coll Cardiol 2012;60:1207–16) © 2012 by the American College of Cardiology Foundation

Globally, cardiovascular diseases (CVDs), which include coronary heart disease (CHD), strokes, rheumatic heart disease (RHD), cardiomyopathy, and other heart diseases, represent the leading cause of death (1). In 2001, it was estimated that there were 16 million deaths from CVD, but somewhat surprisingly (given that the vast majority of studies concerning CVD are carried out in "developed" regions such as the United States and Western Europe), 13 million of these CVD deaths occurred in low-income and middle-income countries, compared with 3 million in high-income countries (1). Although CVDs have previously been characterized as affecting "rich" countries, age-specific rates of CVD have declined in these areas, while they are increasing rapidly in many middle-income and low-income countries. In low-income and middle-income countries, the proportion of all deaths due to CVD in 2001 was 28%, compared with 23% in 1990; the corresponding proportions in developed countries were 39% and 48% (1,2).

Although most CVDs in the world are due to atherosclerosis (CHD and ischemic strokes), other CVDs due to infection (e.g., RHD, Chagas' heart disease, cardiomyopathy from human immunodeficiency virus (HIV) infection, cerebrovascular complications of malaria) remain common in many regions of the developing world (Fig. 1). Early functional and structural changes of the vessels and/or heart (before the onset of symptoms and/or advanced disease) are now detectable in some of these diseases (particularly but not exclusively by ultrasound) (3,4), and recent studies of early detection using these modalities have been published and have provided insights into the early stages of these disease processes.

Particular challenges in addressing the increasing burden of CVD in developing countries include low budgets for health (including for screening, prevention, and treatment), as well as the education and skill mix of the health workforce.

From *The University of Sydney, Sydney, Australia; the †Department of Cardiology, Royal Prince Alfred Hospital, Sydney, Australia; ‡The George Institute for Global Health, Sydney Australia; §Department of Cardiology, Westmead Hospital, Sydney, Australia; ‖Paris Cardiovascular Research Center, European Georges Pompidou Hospital, Paris, France; ¶Global Health Division, Menzies School of Health Research and Charles Darwin University, Darwin, Australia; #Department of Infectious Diseases, Division of Medicine, Royal Darwin Hospital, Darwin, Australia; and the **School of Life Sciences, The Chinese University of Hong Kong, Hong Kong, China. Dr. Celermajer's work is supported by a National Health and Medical Research Council Program Grant. Dr. Chow's work in India was supported by a National Health and Medical Research Council (Australia)/National Heart Foundation (Australia) cofunded fellowship, and she is funded by a Sydney Medical School Foundation Chapman Fellowship. Dr. Anstey is supported by a National Health and Medical Research Council of Australia Practitioner Fellowship and Program Grant. Studies carried out with the Maputo Heart Institute were supported in part by the Magdi Yacoub Institute and Chain of Hope (United Kingdom), by Chaîne de l'Espoir (France), and by Cadeia de Esperança (Portugal). Aspects of our work in China were supported by the Dr. Leung Kit Wah Project Fund. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Manuscript received January 31, 2012; revised manuscript received February 29, 2012, accepted March 6, 2012.

Article 5

Anticoagulation Drug Therapy: A Review

Katherine Harter, MD
Michael Levine, MD
Sean O. Henderson, MD

University of Southern California, LA+USC Medical Center, Department of Emergency Medicine, Los Angeles, California

Supervising Section Editor: Michael Abraham, MD
Submission history: Submitted June 23, 2014; Revision received December 23, 2014; Accepted December 23, 2014
Electronically published January 12, 2015
Full text available through open access at http://escholarship.org/uc/uciem_westjem
DOI: 10.5811/westjem.2014.12.22933

Historically, most patients who required parenteral anticoagulation received heparin, whereas those patients requiring oral anticoagulation received warfarin. Due to the narrow therapeutic index and need for frequent laboratory monitoring associated with warfarin, there has been a desire to develop newer, more effective anticoagulants. Consequently, in recent years many novel anticoagulants have been developed.

The emergency physician may institute anticoagulation therapy in the short term (e.g. heparin) for a patient being admitted, or may start a novel anticoagulation for a patient being discharged. Similarly, a patient on a novel anticoagulant may present to the emergency department due to a hemorrhagic complication. Consequently, the emergency physician should be familiar with the newer and older anticoagulants. This review emphasizes the indication, mechanism of action, adverse effects, and potential reversal strategies for various anticoagulants that the emergency physician will likely encounter. [West J Emerg Med. 2015;16(1):11–17.]

INTRODUCTION

During routine homeostatic conditions, the human body maintains a constant balance between thrombus formation and destruction. This equilibrium is maintained by a complex interaction between platelets and the vascular endothelium, the coagulation cascade, and the fibrinolytic system. The coagulation cascade (Figure 1) involves an interaction between the contact activation pathway (previously called the intrinsic system), and the tissue factor pathway (previously the extrinsic system). These two seemingly independent pathways lead to the conversion of factor X to Xa, which is the start of the common pathway. This common pathway converts prothrombin to thrombin, which subsequently catalyzes the formation of fibrin and ultimately leads to the stabilization of aggregated platelets to form a stable clot.[1,2]

Historically, vitamin K antagonists, such as warfarin, were the only anticoagulants widely available for human use. It has been estimated that more than 65,000 patients are treated in U.S. emergency departments (ED) annually for warfarin-related hemorrhage.[3] Because of this high rate of bleeding, along with the drug's narrow therapeutic index and the need for frequent monitoring, there has been a desire to create safer anticoagulants without such strict drug monitoring. Consequently, there have been several novel anticoagulants (NACs) developed, including direct thrombin inhibitors (e.g. dabigatran), and factor Xa inhibitors (e.g. rivaroxaban, apixaban), designed to target different points of the coagulation cascade (Figure 2).[4,5]

As NACs become more pervasive in the clinical setting, used for both therapeutic and prophylactic purposes, it will become essential for the emergency physician to become aware of the indications to start specific drugs, as well as unique complications and recommended reversal methods for such agents. An intimate knowledge of these drugs will be required for the ideal management. Unfortunately, while the clinical efficacy of NACs has been established, much less is known about the risks of adverse reactions as well as the ability to reverse these agents.[6] Figure 3 below summarizes the most widely-used anticoagulants; they will be discussed in this article. This article provides a review of the literature as it focuses on both the risks associated with anticoagulants, as well as reversal agents of the most commonly used NACs to help guide management in the emergency setting.

Vitamin K antagonists

Vitamin K antagonists (VKAs) such as warfarin function by blocking the vitamin K-epoxide reductase, thereby preventing

Article 6

Journal section: Oral Surgery
Publication Types: Review

doi:10.4317/medoral.22708
http://dx.doi.org/doi:10.4317/medoral.22708

Antiplatelet therapy in patients undergoing oral surgery: A systematic review and meta-analysis

Julio Villanueva [1], Josefina Salazar [1], Ana Alarcón [1], Ignacio Araya [1], Nicolás Yanine [1], Stefan Domancic [1], Alonso Carrasco-Labra [1,2]

[1] Oral & Maxillofacial Department. Cochrane Associated Center at School of Dentistry. University of Chile
[2] Department of Health Research methodology, Evidence and Impact. Mc Master University, Hamilton, Ontario, Canada

Correspondence:
Sergio Livingstone P 943
Independencia. Santiago de Chile
javm@uchile.cl

Received: 15/08/2018
Accepted: 12/11/2018

Villanueva J, Salazar J, Alarcón A, Araya I, Yanine N, Domancic S, Carrasco-Labra A. Antiplatelet therapy in patients undergoing oral surgery: A systematic review and meta-analysis. Med Oral Patol Oral Cir Bucal. 2019 Jan 1;24 (1):e103-13.
http://www.medicinaoral.com/medoralfree01/v24i1/medoralv24i1p103.pdf

Article Number: 22708 http://www.medicinaoral.com/
© Medicina Oral S. L. C.I.F. B 96689336 - pISSN 1698-4447 - eISSN: 1698-6946
eMail: medicina@medicinaoral.com
Indexed in:
Science Citation Index Expanded
Journal Citation Reports
Index Medicus, MEDLINE, PubMed
Scopus, Embase and Emcare
Indice Médico Español

Abstract

Background: The number of patients under antiplatelet therapy (APT) continues to raise as current recommendations foster this practice. Although some recommendations to manage this treatment during oral surgery procedures exist, these have methodological shortcomings that preclude them from being conclusive.

Material and Methods: A systematic review and meta-analysis of the best current evidence was carried out; The Cochrane Library, EMBASE and MEDLINE databases were searched for Randomized Controlled Trials (RCT) concerning patients undergoing oral surgery with APT, other relevant sources were searched manually.

Results: 5 RCTs met the Inclusion criteria. No clear tendency was observed (RR= 0.97 CI 95%: 0,41–2,34; p=0,09; I2= 51%), moreover, they weren't clinically significant.

Conclusions: According to these findings and as bleeding is a manageable complication it seems unreasonable to undermine the APT, putting the patient in danger of a thrombotic event and its high inherent morbidity, which isn't comparable in severity and manageability to the former."

Key words: *Antiplatelet therapy, aspirin, oral surgery, platelet aggregation inhibitors, oral surgical procedures, systematic reviews.*

Introduction

Blood flow obstruction by a clot may cause ischemia and organ infarction. Thrombus formation is produced as consequence of vascular injuries, activation of the clotting process and blood flow disruption, this can happen at venous or arterial level. In arterial thrombosis the main etiologic factors are platelet activation and injuries to the arterial wall such as atheromatous plaques producing platelet rich thrombi. Blood Stasis and clotting are the main factors in venous thrombosis, producing thrombi rich in fibrin and erythrocytes (1).

Atherothrombosis, i.e., thrombus formation over an

Article 7

materials

MDPI

Article

Advances in Antiplatelet Therapy for Dentofacial Surgery Patients: Focus on Past and Present Strategies

Gabriele Cervino [1], Luca Fiorillo [1,2], Ines Paola Monte [3], Rosa De Stefano [1], Luigi Laino [2], Salvatore Crimi [3], Alberto Bianchi [3], Alan Scott Herford [4], Antonio Biondi [3] and Marco Cicciù [1,*]

1 Department of Biomedical and Dental Sciences and Morphological and Functional Imaging, Messina University, 98100 Messina ME, Italy; gcervino@unime.it (G.C.); lfiorillo@unime.it (L.F.); rsdestefano@libero.it (R.D.S.)
2 Multidisciplinary Department of Medical-Surgical and Odontostomatological Specialties, University of Campania "Luigi Vanvitelli", 80121 Naples, Italy; luigi.laino@unicampania.it
3 Department of General Surgery and Medical-Surgery Specialities, University of Catania, 95100 Catania CT, Italy; inemonte@unict.it (I.P.M.); torecrimi@gmail.com (S.C.); alberto.bianchi@unict.it (A.B.); antonio.biondi@unict.it (A.B.)
4 Department of Maxillofacial Surgery, Loma Linda University, Loma Linda, CA 92354, USA; aherford@llu.edu
* Correspondence: mcicciu@unime.it or acromarco@yahoo.it; Tel.: +390902216920; Fax: +390902216921

Received: 10 April 2019; Accepted: 7 May 2019; Published: 9 May 2019

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Abstract: Background: Nowadays, patients involved in antiplatelet therapy required special attention during oral surgery procedures, due to the antiplatelet drugs assumption. The motivations of the assumption may be different and related to the patient's different systemic condition. For this reason, accordingly to the current international guidelines, different protocols can be followed. The aim of this work is to analyze how the dentist's approach to these patients has changed from the past to the present, evaluating the risk exposure for the patients. Methods: This review paper considered different published papers in literature through quoted scientific channels, going in search of "ancient" works in such a way as to highlight the differences in the protocols undertaken. The analyzed manuscripts are in the English language, taking into consideration reviews, case reports, and case series in such a way as to extrapolate a sufficient amount of data and for evaluating the past therapeutic approaches compared to those of today. Results: Colleagues in the past preferred to subject patients to substitution therapy with low molecular weight anticoagulants, by suspending antiplatelet agents to treatment patients, often for an arbitrary number of days. The new guidelines clarify everything, without highlighting an increased risk of bleeding during simple oral surgery in patients undergoing antiplatelet therapy. Conclusion: Either patients take these medications for different reasons, because of cardiovascular pathologies, recent cardiovascular events, or even for simple prevention, although the latest research shows that there is no decrease of cardiovascular accidents in patients who carry out preventive therapy. Surely, it will be at the expense of the doctor to assess the patient's situation and risk according to the guidelines. For simple oral surgery, it is not necessary to stop therapy with antiplatelet agents because the risk of bleeding has not increased, and is localized to a post-extraction alveolus or to an implant preparation, compared to patients who do not carry out this therapy. From an analysis of the results it emerges that the substitutive therapy should no longer be performed and that it is possible to perform oral surgery safely in patients who take antiplatelet drugs, after a thorough medical history. Furthermore, by suspending therapy, we expose our patients to more serious risks, concerning their main pathology, where present.

Keywords: antiplatelet drugs; oral surgery; dental extraction; cardiovascular risk; dentofacial surgery

Antiplatelet Drugs : Is There a Surgical Risk?

• Nach G. Daniel, DMD, BSc, MSc •
• Jacques Goulet, DMD •
• Marc Bergeron, MD, FRCPC •
• Robert Paquin, DMD, FRCD(C) •
• Pierre-Éric Landry, DMD, FRCD(C) •

Abstract

Acetylsalicylic acid has long been the only nonsteroidal anti-inflammatory drug recommended for the treatment and prevention of thromboembolic diseases. More recently, new compounds have been used in patients with vascular diseases. However, these drugs are often associated with longer bleeding times and greater operative risk. In most surgical specialties, the question always arises as to whether antiplatelet therapy should be stopped before elective surgery. If so, for how long? If not, what are the risks? This article reviews the various antiplatelet drugs in use today, focusing on their mode of action, their effects on platelet function and the associated operative risks. It also proposes an algorithm for decision making in this setting, based on the literature and an understanding of the mechanisms of action of this class of drugs.

MeSH Key Words: *hemorrhage/chemically induced; platelet aggregation inhibitors/adverse effects; perioperative care*

© J Can Dent Assoc 2002; 68(11):683–7
This article has been peer reviewed.

Hemostasis is a process encompassing the various mechanisms that stop the bleeding when the vascular wall is ruptured. A number of factors, including the endothelial wall, the platelets, and the proteins of the coagulation cascade and of fibrinolysis, play essential roles in this function. A congenital or acquired anomaly involving one or more of these factors predisposes a patient to hemorrhagic accidents[1] (Table 1).

Hemostasis consists of a vascular phase, a platelet phase and a coagulation phase. The first 2 phases constitute primary hemostasis, in which the vessel wall, platelets and plasma proteins, including von Willebrand factor and fibrinogen, participate. Reflex vasoconstriction of the blood vessel facilitates platelet adhesion and aggregation needed for formation of the hemostatic clot (see Fig. 1, Platelet activation and aggregation mechanisms, at the end of the article. The coagulation phase, also known as secondary hemostasis, allows consolidation of the platelet clot by formation of a fibrin clot. Finally, fibrinolysi rids the organism of fibrinous deposits.

Abnormal platelet aggregation plays an important role in the pathogenesis of thromboembolic diseases such as myocardial infarction, cerebral ischemia and peripheral arterial insufficiency.[3] Although several antiplatelet agents have been developed in recent years, acetylsalicylic acid (ASA) is still the standard for preventing vascular diseases.[4–6] Of the newer agents, ticlopidine,[7] clopidogrel[8] and dipyridamole[9] have an effectiveness comparable to that of ASA. Each of these drugs has its own mechanism of action and pharmacokinetics (Table 2). Their effects on primary hemostasis also differ. This article reviews the various drugs in use today, focusing on their mode of action, their effects on platelet function and the associated operative risks.

Evaluation of Platelet Function

The preoperative assessment of all dental patients should include a targeted medical questionnaire aimed at identifying any personal or family history of hemostatic anomalies. It is important to note the circumstances (traumatic vs. spontaneous), duration (a few minutes vs. several hours or days), severity (whether a blood transfusion was needed) and type of bleeding reported. Platelet disorders are evidenced mainly by epistaxis, bleeding gums or mucocutaneous bleeding in the form of ecchymoses or petechiae, whereas coagulopathies are associated more with deep

Article 9

Review Article

Continuing antiplatelet therapy throughout dental procedures: A clinical dilemma

Sheeraz Badal, Syed Ahmed, Rohit Shrikanthan[1], Afreen Badal[2]

Department of Oral & Maxillofacial Surgery, MIDSR Dental College and Hospital, Latur, [1]Raja Rajeshwari Dental College, Bangalore, [2]MIDSR Dental College and Hospital, Latur, India

Address for correspondence: *Dr. Sheeraz Badal, E-mail: sheeraz77@yahoo.com*

ABSTRACT

Antiplatelet therapy is commonly recommended for the prevention of the thromboembolic events, including the myocardial infarction and stroke. It has reduced the mortality and morbidity of cardiovascular diseases remarkably. A considerable number of patients presenting before a dentist give a history of antiplatelet therapy. A clinical dilemma exists whether to discontinue the antiplatelet therapy or to continue during the routine and invasive dental procedures. Continuing antiplatelet therapy during surgery minimizes the risk of thromboembolic complications but theoretically increases the risk of hemorrhage. Discontinuing antiplatelet therapy may expose patients to life-threatening thromboembolic events, while presumably reducing the risk of hemorrhagic complications. Diverse opinions exist regarding the management of such patients. Some advice continuation of the antiplatelet therapy rather than inviting possible thromboembolic event, while others encourages its discontinuation.

Key words: Antiplatelet therapy, cardiovascular diseases, hemorrhagic complications, thromboembolic events

INTRODUCTION

Antiplatelet drugs are used in clinical practice to prevent the adverse sequelae of thrombosis in atherosclerotic arteries of the heart, brain, and limbs. Cardiovascular diseases account for the highest mortality and morbidity worldwide.[1] With increasing awareness and health consciousness, there is a striking decrease of cardiovascular mortality with the Introduction of preventive and maintenance antiplatelet therapy.[1] Antiplatelets are commonly recommended for the prevention of thromboembolic events including myocardial infarction and stroke,[2] and are recommended for individuals with diabetes, who are at risk of cardiovascular disease.[3] But it is often discontinued prior to routine and invasive dental procedures because of concern for bleeding complications. Discontinuing therapy may expose patients to life-threatening thromboembolic events. The aim of this manuscript is to evaluate the need of stopping antiplatelet drugs before extended oral or dental surgeries.

Access this article online

Quick Response Code:

Website: www.jidonline.com

DOI: 10.4103/2229-5194.94186

DISCUSSION

Platelets are small disk-shaped cells without a nucleus, derived from bone marrow, and when released into the blood have a life span of 10 days. They provide the initial haemostatic plug at the site of a vascular injury. They are also involved in pathological processes and are an important contributor to arterial thrombosis leading to myocardial infarction and ischemic stroke in patients with cardiovascular diseases. Patients with such diseases are treated with antiplatelet therapy to reduce the risk of thromboembolic events. Antiplatelet therapy has been reported to have reduced the overall mortality of vascular disease by 15% and non-fatal vascular complications by 30%.[1]

A considerable number of patients presenting before a dentist give a history of antiplatelet therapy. A clinical dilemma whether to discontinue the antiplatelet therapy or continue the same always confronts the practitioner. Diverse opinions exist regarding the management of such patients. While one group of researchers advice continuation of antiplatelet therapy rather than invite remote, but possible,

Article 10

Original Research Article

OPEN ACCESS

Evaluation of post-extraction bleeding in patients taking low dose aspirin

Dr. Sajid Hasan[1], Dr. Mahmuda Akhter[2], Dr. Saeed Hossain Khan[3], Dr. Dilruba Sharmin[4], Dr. Md. Manjurul Karim[5], Dr. Rifat Rahman[6]

AFFILIATION:

1. **Dr. Sajid Hasan**
BDS, FCPS (Oral & Maxillofacial Surgery)
Assistant Professor, Ibrahim Medical College
Junior Consultant, Department of Dental Surgery, BIRDEM General Hospital
2. **Dr. Mahmuda Akhter**
BDS, MS, FCPS (Oral & Maxillofacial surgery)
Associate Professor
Department of Oral & Maxillofacial surgery, BSMMU
3. **Dr. Saeed Hossain Khan**
BDS, FCPS (Orthodontics)
Associate Professor, Ibrahim Medical College
Consultant, Department of Dental Surgery, BIRDEM General Hospital
4. **Dr. Dilruba Sharmin**
BDS, MPH (NIPSOM)
5. **Dr. Md. Manjurul Karim**
BDS, MPH
Lecturer, Department of Oral & Maxillofacial surgery
Marks Medical College (Dental Unit)
6. **Dr. Rifat Rahman**
BDS, MPH, MSc Oral Medicine
Senior Lecturer, Department of Periodontology, Oral Pathology & Oral Medicine, Update dental college & hospital, Dhaka, Bangladesh

Article info.

Received: 17th January, 2019
Accepted: 2nd February, 2019

Volume: 9, Issue-1 April, 2019

DOI: https://doi.org/10.3329/updcj.v9i1.41204

Publisher: Update Dental College, Dhaka, Bangladesh
Web: www.updatedentalcollege.edu.bd
E-mail: updcj@hotmail.com

*** Corresponding Author**
Dr. Sajid Hasan
BDS, FCPS (Oral & Maxillofacial Surgery)
Assistant Professor, Ibrahim Medical College
Junior Consultant, Dept. of Dental Surgery, BIRDEM General Hospital
Ph: 01717054471, E-mail: dr. sazidhasan@gmail.com

Citation
Dr. Sajid Hasan, Dr. Mahmuda Akhter, Dr. Saeed Hossain Khan, Dr. Dilruba Sharmin, Dr. Md. Manjurul Karim, Dr. Rifat Rahman. Evaluation of post-extraction bleeding in patients taking low dose aspirin.Update Dental College Journal. 2019 April; 9(1): 32-36. DOI: https://doi.org/10.3329/updcj.v9i1.41204

ABSTRACT

Background: Acetylsalicylic acid (ASA) generically known as Aspirin is an analgesic, antipyretic, anti-inflammatory and also an antiplatelet drug. In order to avoid excessive bleeding and to be on the safer side, dentists have traditionally advised their patients to stop taking aspirin before extraction of teeth although this surgical procedure can be done without cessation of aspirin intake.

Objective: The purpose of the study was to assess the necessity of interrupting aspirin therapy prior to dental extraction.

Materials and Methods: A cross sectional study was conducted in November 2015 at outpatient department of dentistry, BIRDEM Hospital, Dhaka. Sample of 50 patients who took low dose aspirin (75mg) once daily were purposely selected for this study. The blood pressure of all the subjects was recorded preoperatively. The extractions were done atraumatically under local anesthesia using 2% lidocaine with 1:100,000 epinephrine. A gelatin sponge piece was placed in socket and closed by atraumatic silk. The subjects were instructed to apply pressure pack with sterile gauze for 30 min. Evaluation was done in every 10 minutes for 30 minutes.

Results: Among 50 patients, 82.0% patients were suffering from IHD. Simple extraction was done in 92.0% of patients while the remaining extractions were done surgically. 68% was managed by pressure pack and gelatin sponge while 26.0% were managed by pressure pack only. According to Post-extraction bleeding, it was found that the bleeding time was 10 min in case of 94% patients while only 2% showed 30 minutes of bleeding time.

Conclusion: The study revealed that it is not necessary to alter or stop aspirin therapy and local hemostatic measures are sufficient to control bleeding. Therefore it can be assumed that extraction can be done without cessation of low dose aspirin and avoiding the life threatening issues.

Key words:

Acetylsalicylic acid (ASA), Aspirin, Dental Extraction, Bleeding, IHD (Ischemic Heart Disease) Thromboembolism.

Introduction:

Cardiac patients on aspirin therapy may require extractions for their diseased teeth. It is a common practice among physicians and treating surgeons to stop aspirin prior to tooth extraction because of fear of bleeding complications. This practice often predisposes the patient to adverse thromboembolic events. This practice is based on theoretical risk of bleeding and on isolated case reports of excessive bleeding with aspirin therapy. The current consensus and recommendations are in favor of continuing aspirin therapy during simple tooth extraction as the bleeding complication incidence is very less and if it occurs can be controlled efficiently with local hemostasis measures.[1]

In recent years, most studies do not recommend reducing or interrupting anticoagulation,or replacing it with heparin, prior to tooth extraction - provided therapeutic international normalized ration (INR) levels are maintained, with emphasis on the application of local measures such as antifibrinolytic agents, for the control of hemostasia.[2]

Article 11

8th Annual Women's Heart & Vascular Symposium

What Do the Guidelines Really Say About Aspirin?

Michael A. Millard, MD
Eduardo A. Hernandez-Vila, MD

★ ***CME Credit***

Presented at the 8th Annual Women's Heart & Vascular Symposium, Texas Heart Institute; Houston, 20 January 2018.

Section Editor: *Stephanie A. Coulter, MD*

Key words: *Anticarcinogenic agents/therapeutic use; aspirin/administration & dosage/adverse effects/therapeutic use; cardiovascular diseases/prevention & control; colorectal neoplasms/prevention & control; hemorrhage/chemically induced; practice guidelines as topic; primary prevention/methods/standards*

From: *Departments of Cardiology, Texas Heart Institute and CHI St. Luke's Health–Baylor St. Luke's Medical Center; Houston, Texas 77030*

Address for reprints: *Eduardo Hernandez-Vila, MD, Department of Cardiology, CHI St. Luke's Health–Baylor St. Luke's Medical Center, 6624 Fannin St., Suite 2780, Houston, TX 77030*

E-mail: *eduardohernandezmd@gmail.com*

According to the latest available national mortality data, cardiovascular disease (CVD) and malignant neoplasm remain the 2 leading causes of death in the United States, accounting for 45.4% of all deaths in 2015. Among the malignant neoplasms, colorectal cancer (CRC) was the second leading cause of death, behind only lung cancer.[1] Aspirin has reduced the incidence of both cardiovascular (CV) events and CRC, and thus taking aspirin may have a substantial epidemiologic effect on morbidity and mortality rates.[2,3] However, to determine aspirin's role in primary and secondary prevention of CVD, the beneficial effects on CVD and CRC prevention must be weighed against the bleeding risks associated with its use.

Aspirin irreversibly inactivates cyclooxygenase-1 (COX-1), leading to decreases in the biosynthesis of prostaglandin H_2 and thromboxane A_2.[4] Suppression of thromboxane A_2 production inhibits platelet aggregation, a key event in coronary thrombosis and acute myocardial infarction. As a result of COX-1 inactivation, complete suppression of thromboxane A_2 can be achieved through the cumulative effects of a daily regimen of low-dose (<100 mg) aspirin. As one of several postulated mechanisms for reducing CRC risk, aspirin suppresses numerous lipid mediators released by activated platelets via COX-dependent mechanisms that alter the progression of normal colonic mucosa to adenoma and, subsequently, to carcinoma.[5] However, aspirin-mediated COX-1 inhibition also leads to mucosal damage in the gastrointestinal tract, and, in conjunction with aspirin's antiplatelet effect, increases gastrointestinal and nongastrointestinal bleeding, including intracranial hemorrhage and hemorrhagic stroke.

In patients with known CVD, the benefits of taking aspirin to reduce CV events outweigh the risks of bleeding. A collaborative meta-analysis conducted by the Antithrombotic Trialists' Collaboration showed a statistically significant reduction in severe vascular events (nonfatal myocardial infarction, nonfatal stroke, or vascular death) in patients with acute or prior vascular disease who were taking low-dose aspirin.[6] The reduction in vascular events substantially outweighed the absolute risks of major extracranial bleeding. These findings led to the 2012 American College of Cardiology/American Heart Association (ACC/AHA) recommendation that "treatment with aspirin 75 to 162 mg daily should be continued indefinitely in the absence of contraindications in patients with stable ischemic heart disease."[7]

In patients who have no known CVD, the net clinical benefit obtained from aspirin use is less clear when weighing the associated reduction in the incidence of CV events and CRC against increased bleeding in this population. In 2016, the U.S. Preventive Services Task Force (USPSTF) issued updated recommendations for the use of low-dose aspirin for primary prevention of CVD and CRC.[8] In separate meta-analyses of primary prevention trials, the USPSTF found that aspirin use reduced the incidence of nonfatal myocardial infarction by 22%, had no effect on the incidence of stroke or cardiovascular death, and reduced 20-year CRC mortality rates by 33%. Aspirin therapy had little or no effect on all-cause death; it increased the risk of major gastrointestinal bleeding by 58% and that of hemorrhagic stroke by 27%.[2,3,9] The data also suggested that the CV benefits of aspirin began within the first 5 years of therapy, whereas the decrease in CRC mortality rates was not seen until after 10 years of therapy. After performing a decision analysis with use of a microsimulation model, the USPSTF made a class B recommendation to initiate "low-dose aspirin use for the primary prevention of CVD and CRC in adults aged 50 to 59 years who have a 10% or greater 10-year CVD risk, are not at increased risk for bleeding, have a life expectancy of at least 10 years, and are willing to take low-dose aspirin daily for at least 10 years."[8] An individualized approach was recommended for patients 60 to

Article 12

Current reviews of allergy and clinical immunology
(Supported by a grant from GlaxoSmithKline, Research Triangle Park, NC)

Series editor: Harold S. Nelson, MD

Aspirin-induced asthma: Advances in pathogenesis, diagnosis, and management

Andrew Szczeklik, MD, PhD,[a] and Donald D. Stevenson, MD[b] *Krakow, Poland, and La Jolla, Calif*

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In some asthmatic individuals, aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs) that inhibit cyclooxygenase 1 (COX-1) exacerbate the condition. This distinct clinical syndrome, called *aspirin-induced asthma* (AIA), is characterized by an eosinophilic rhinosinusitis, nasal polyposis, aspirin sensitivity, and asthma. There is no in vitro test for the disorder, and diagnosis can be established only by provocation challenges with aspirin or NSAIDs. Recent major advances in the molecular biology of eicosanoids, exemplified by the cloning of 2 cysteinyl leukotriene receptors and the discovery of a whole family of cyclooxygenase enzymes, offer new insights into mechanisms operating in AIA. The disease runs a protracted course even if COX-1 inhibitors are avoided, and the course is often severe, many patients requiring systemic corticosteroids to control their sinusitis and asthma. Aspirin and NSAIDs should be avoided, but highly specific COX-2 inhibitors, known as *coxibs*, are well tolerated and can be safely used. Aspirin desensitization, followed by daily aspirin treatment, is a valuable therapeutic option in most patients with AIA, particularly those with recurrent nasal polyposis or overdependence on systemic corticosteroids. (J Allergy Clin Immunol 2003;111:913-21.)

Key words: *Aspirin-induced asthma, nasal polyposis, chronic sinusitis, COX-1 and 2 inhibitors, aspirin desensitization*

Shortly after introduction of aspirin (ASA) therapy 100 years ago, violent episodes of bronchospasm were reported after ASA ingestion. The association of ASA sensitivity, asthma, and nasal polyps was described in 1922 by Widal et al,[1] and this clinical entity, renamed the "aspirin triad," was subsequently popularized by the studies of Samter and Beers[2] in the late 1960s. A distinct clinical syndrome emerged. Here we discuss developments in the pathogenesis and management, concentrating on the insights and discoveries that have evolved over the last 4 years, since publication of our review[3] on the same topic.

Abbreviations used

AIA:	Aspirin-induced asthma
ASA:	Aspirin
COX:	Cyclooxygenase
Cys-LT:	Cysteinyl leukotriene
FLAP:	5-lipoxygenase–activating protein
LO:	Lipoxygenase
LT:	Leukotriene
LTC_4S:	Leukotriene C_4 synthase
NSAID:	Nonsteroidal anti-inflammatory drug
PGD_2:	Prostaglandin D_2
PGE_2:	Prostaglandin E_2

DEFINITION

The term *ASA-exacerbated respiratory disease*[4] is the best description of the aggressive and continuous inflammatory disease of the airways, combined with exacerbation of asthma and rhinitis attacks, after ingestion of ASA and most nonsteroidal anti-inflammatory drugs (NSAIDs). However, most physicians refer to this condition as *ASA-induced asthma* (AIA), *the aspirin triad*, *ASA sensitivity*, or *ASA-intolerant asthma*. We will use the term *ASA-induced asthma* because of its widespread use and acceptance in clinical medicine.

PREVALENCE

Based on patients' histories alone, the incidence of ASA sensitivity in asthmatic adults is 3% to 5%, but this percentage doubles or triples when adult asthmatic patients are prospectively challenged with ASA. Three large population-based sampling studies, using specifically designed questionnaires, were recently concluded.

From [a]the Department of Medicine, Jagellonian University School of Medicine, Krakow, and [b]the Division of Allergy, Asthma and Immunology, Department of Medicine, Scripps Clinic and The Scripps Research Institute, La Jolla.

Received for publication February 4, 2003; revised February 18, 2003; accepted for publication February 21, 2003.

Reprint requests: Donald D. Stevenson, MD, Division of Allergy, Asthma and Immunology, Department of Medicine, Scripps Clinic and The Scripps Research Institute, 10066 N Torrey Pines Road, La Jolla, CA 92037.

0091-6749/2003 $30.00 + 0
doi:10.1067/mai.2003.1487

Article 13

Review

Nonsteroidal Anti-inflammatory Drugs (NSAIDs)

Ida Ghlichloo [1], Valerie Gerriets [2]

In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan.
2020 May 18.

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PMID: 31613522 Bookshelf ID: NBK547742

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Excerpt

NSAIDs are a class of medications used to treat pain, fever, and other inflammatory processes. This activity describes the indications, mechanism of action, administration, adverse effects, contraindications, monitoring, and important points for providers regarding NSAIDs.

Sections

Article 14

Drugs & Aging (2019) 36 (Suppl 1):S15–S24
https://doi.org/10.1007/s40266-019-00660-1

REVIEW ARTICLE

Safety of Oral Non-Selective Non-Steroidal Anti-Inflammatory Drugs in Osteoarthritis: What Does the Literature Say?

Cyrus Cooper[1,2,3] · Roland Chapurlat[4] · Nasser Al-Daghri[5] · Gabriel Herrero-Beaumont[6] · Olivier Bruyère[3,7] · François Rannou[8] · Roland Roth[9] · Daniel Uebelhart[10] · Jean-Yves Reginster[3,5,7]

Abstract
Non-steroidal anti-inflammatory drugs (NSAIDs) are widely recommended and prescribed to treat pain in osteoarthritis. While measured to have a moderate effect on pain in osteoarthritis, NSAIDs have been associated with wide-ranging adverse events affecting the gastrointestinal, cardiovascular, and renal systems. Gastrointestinal toxicity is found with all NSAIDs, which may be of particular concern when treating older patients with osteoarthritis, and gastric adverse events may be reduced by taking a concomitant gastroprotective agent, although intestinal adverse events are not ameliorated. Cardiovascular toxicity is associated with all NSAIDs to some extent and the degree of risk appears to be pharmacotherapy specific. An increased risk of acute myocardial infarction and heart failure is observed with all NSAIDs, while an elevated risk of hemorrhagic stroke appears to be restricted to the use of diclofenac and meloxicam. All NSAIDs have the potential to induce acute kidney injury, and patients with osteoarthritis with co-morbid conditions including hypertension, heart failure, and diabetes mellitus are at increased risk. Osteoarthritis is associated with excess mortality, which may be explained by reduced levels of physical activity owing to lower limb pain, presence of comorbid conditions, and the adverse effects of anti-osteoarthritis medications especially NSAIDs. This narrative review of recent literature identifies data on the safety of non-selective NSAIDs to better understand the risk:benefit of using NSAIDs to manage pain in osteoarthritis.

Key Points

Although effective against inflammatory-mediated pain, non-steroidal anti-inflammatory drugs are associated with multiple class-specific toxicities affecting the gastrointestinal, cardiovascular, and renal systems. Some adverse effects are related to the class mechanism of action, while others appear to be pharmacotherapy specific.

The choice of any agent should be considered on an individual patient basis in osteoarthritis to provide adequate symptom relief while minimizing unwanted side effects.

✉ Cyrus Cooper
cc@mrc.soton.ac.uk

Extended author information available on the last page of the article

1 Introduction

Oral non-steroidal anti-inflammatory drugs (NSAIDs) are universally recommended in international and national guidelines for the management of pain in osteoarthritis (OA) in patients presenting with severe pain and musculoskeletal pain, and those who are unresponsive to merely paracetamol (acetaminophen) [1–5]. Non-steroidal anti-inflammatory drugs are one of the most widely used drugs in OA: over 50% of patients with OA in USA are prescribed NSAIDs, and among patients with OA across Europe using prescription medications (47%), 60% of those received NSAIDs [6, 7]. Non-prescription NSAIDs were the most frequently reported medications (27%) used by participants in the Osteoarthritis Initiative with symptomatic radiographic knee OA, even for those aged > 75 years [8]. While there was a reduction in prescription NSAID use in the older population, in line with recommendations that oral NSAIDs should not be prescribed to those aged older than 75 years [9], the use of over-the-counter NSAIDs remained worryingly high in this age group [8].

REVIEWS

Adv Clin Exp Med 2014, **23**, 6, 993–1000
ISSN 1899–5276

Stanislava Kalafutova[1, A–D, F], Bozena Juraskova[2, 3, E, F], Jiri Vlcek[1, E, F]

The Impact of Combinations of Non-Steroidal Anti-Inflammatory Drugs and Anti-Hypertensive Agents on Blood Pressure*

[1] Department of Social and Clinical Pharmacy, Faculty of Pharmacy in Hradec Kralove, Charles University in Prague, The Czech Republic
[2] Sub-Department of Gerontology, Faculty of Medicine in Hradec Kralove, Charles University in Prague, The Czech Republic
[3] 3rd Clinic of Internal Medicine, Metabolism and Gerontology, University Hospital Hradec Kralove, The Czech Republic

A – research concept and design; **B** – collection and/or assembly of data; **C** – data analysis and interpretation; **D** – writing the article; **E** – critical revision of the article; **F** – final approval of article; **G** – other

Abstract

Nowadays NSAIDs are the most frequently used groups of drugs, especially because of their availability. Their consumption is high among older people, who are much more sensitive to the side effects, and who are often also taking other drugs which can interact with them. Moreover, the majority of the older population is suffering from hypertension. This could well explain the commonly encountered experience of drug interaction between NSAIDs and antihypertensive drugs, which is very common in clinical practice. The severity of this drug interaction is classified as class C, with a recommendation to monitor therapy. However, even a minor long-term increase in blood pressure can significantly increase the risk of cardiovascular mortality, while mortality rates can possibly be reduced by sufficiently effective treatment of hypertension. Therefore, in clinical practice, this type of interaction should not be overlooked as a major cause of failure of hypertension treatment in older patients, as well in many cases in general. The present article focusses on the mechanism and the degree of influence on the blood pressure of particular types of antihypertensive agents used in combination with NSAID. Not all groups of antihypertensive drugs are affected to the same degree; some are more affected, and others, such as calcium channel blockers, are not affected at all. Similarly, not every NSAID increases blood pressure. Many studies, some of which are analyzed in this article, present evidence of the degree of the influence NSAIDs have on blood pressure (**Adv Clin Exp Med 2014, 23, 6, 993–1000**).

Key words: antihypertensive drugs, non-steroidal anti-inflammatory drugs, blood pressure, hypertension.

Hypertension is well known as one of the most common cardiovascular diseases. Approximately 690 m people around the world suffer from hypertension. It is one of the major risk factors causing arteriosclerosis, including atherogenic coronary artery disease in the form of ischemic heart disease [1]. Hypertension affects the majority of people over 65 years of age, occurring in up to 60% of this population [2]. In most cases, it accounts for subsequent organ damage or many other manifestations of cardiovascular diseases [2, 3]. Adequate treatment of hypertension is important especially in older populations, as has been confirmed by the HYVET study [4]. Moreover, older populations often experience pain, both chronic and acute. The use of different analgesics therefore becomes a regular part of their lives. It should therefore be borne in mind that the treatment of hypertension may be significantly influenced by the concomitant use of other therapeutic classes.

The authors of this article focused on clarifying the mechanisms of the influence on blood

* This study was supported by grant SVV 260 066 from Charles University in Prague.

Article 16

Clin Pharmacokinet
DOI 10.1007/s40262-014-0230-6

REVIEW ARTICLE

Clinical Pharmacokinetics and Pharmacodynamics of Clopidogrel

Xi-Ling Jiang · Snehal Samant · Lawrence J. Lesko · Stephan Schmidt

Abstract Acute coronary syndromes (ACS) remain life-threatening disorders, which are associated with high morbidity and mortality. Dual antiplatelet therapy with aspirin and clopidogrel has been shown to reduce cardiovascular events in patients with ACS. However, there is substantial inter-individual variability in the response to clopidogrel treatment, in addition to prolonged recovery of platelet reactivity as a result of irreversible binding to $P2Y_{12}$ receptors. This high inter-individual variability in treatment response has primarily been associated with genetic polymorphisms in the genes encoding for cytochrome (CYP) 2C19, which affect the pharmacokinetics of clopidogrel. While the US Food and Drug Administration has issued a boxed warning for CYP2C19 poor metabolizers because of potentially reduced efficacy in these patients, results from multivariate analyses suggest that additional factors, including age, sex, obesity, concurrent diseases and drug–drug interactions, may all contribute to the overall between-subject variability in treatment response. However, the extent to which each of these factors contributes to the overall variability, and how they are interrelated, is currently unclear. The objective of this review article is to provide a comprehensive update on the different factors that influence the pharmacokinetics and pharmacodynamics of clopidogrel and how they mechanistically contribute to inter-individual differences in the response to clopidogrel treatment.

Key Points

Multiple genetic and non-genetic factors contribute to the high inter-individual variability in the dose–concentration–response relationship following oral administration of the standard clopidogrel dosing regimen (300 mg loading dose, 75 mg maintenance dose).

In order to understand the relative contribution of each of these factors to the overall variability in treatment response, sufficient understanding of the underlying pharmacokinetics and pharmacodynamics is needed.

An understanding of the variability in pharmacokinetics and pharmacodynamics requires a mechanistic-based, quantitative analysis approach that integrates available information on the clinically relevant factors that impact the pharmacokinetics and pharmacodynamics of clopidogrel.

Once established and qualified, this qualitative and quantitative link can then be used to translate genetic and clinical information into actionable dosing recommendations and thus help to personalize clopidogrel therapy on a patient-by-patient basis.

X.-L. Jiang · S. Samant · L. J. Lesko · S. Schmidt (✉)
Department of Pharmaceutics, Center for Pharmacometrics and Systems Pharmacology, University of Florida at Lake Nona (Orlando), 6550 Sanger Road, Room 467, Orlando, FL 32827, USA
e-mail: sschmidt@cop.ufl.edu

Published online: 06 January 2015

1 Introduction

Cardiovascular disease (CVD) is currently the leading cause of death worldwide [1]. Many CVD patients develop an acute coronary syndrome (ACS), a life-threatening

Article 17

JOURNAL OF OCULAR PHARMACOLOGY AND THERAPEUTICS
Volume 32, Number 2, 2016
Mary Ann Liebert, Inc.
DOI: 10.1089/jop.2015.0128

Ocular Applications of Dipyridamole: A Review of Indications and Routes of Administration

Moshe Rogosnitzky,[1,2] Itzhak Isakov,[1] Wjatschesslaw Wlassoff,[2] April Ingram,[2] and Y. Robert Barishak[1]

Abstract

Dipyridamole was introduced decades ago as a treatment for angina, subsequently found to inhibit platelet aggregation. It is most commonly used, and approved for use in thromboembolism prevention, following surgery. Some of its recognized effects such as adenosine uptake inhibition, elevation of cAMP and cGMP levels, vasodilation, and tissue perfusion are important in various ocular disorders. For this reason, dipyridamole represents an interesting candidate as a therapeutic target for the treatment of eye disorders affecting different ocular structures. The aim of this article is to review the evidence and current understanding of the mechanisms by which dipyridamole exerts its effects on different ocular tissues, discuss the role of dipyridamole in clinical practice, and highlight areas of use and routes of administration.

Introduction

Dipyridamole was introduced in the early 1960s as a coronary vasodilator, most often administered orally, and is currently approved in the United States for prophylactic thromboembolism prevention following surgery.[1] As a platelet inhibitor, indicated for the secondary prevention of transient ischemic attack, it inhibits the enzyme phosphodiesterase due to inhibition of the adenosine transporter and elevates cAMP and cGMP levels, preventing platelet aggregation.[2,3] Moreover, dipyridamole plays a role in the platelet inhibitory actions of prostacyclin (PGI2) and inhibits cellular uptake and metabolism of adenosine, also related to platelet aggregation, through potential stimulation of the adenylyl cyclase in platelets, resulting in elevated cAMP.[2] Used in combination with aspirin, it prevents the reoccurrence of myocardial infarctions.[4]

In addition to the established antithrombotic activity, studies suggest that dipyridamole provides beneficial properties to the vasculature, including both direct and indirect effects to the endothelium. Endothelial effects include inhibition of proliferation, antioxidant, and anti-inflammatory properties, as well as their subsequent effect on cell signaling.[5] The inhibition of the reuptake of adenosine into platelets, endothelial cells and red blood cells by dipyridamole results in increased extracellular concentrations of adenosine into the cytosol and subsequent vasodilation.[6] This combination of the antiplatelet and vasodilator activity of dipyridamole leads to improved tissue perfusion.[7]

Although much of the research conducted with dipyridamole is related to its coronary and thrombolytic mechanisms of action, adenosine inhibition, elevation of cAMP and cGMP levels, vasodilation and tissue perfusion are closely associated with many ocular disorders. As an example, cGMP levels are related to the production and drainage of aqueous humor. Artherosclerosis, vasculitis, and similar vascular dysregulations have been shown to play a role in the pathogenesis of normal-tension glaucoma.[8,9] The Egna-Neumarkt study compared patients with diastolic perfusion pressures <50 mmHg to those with 65 mmHg or higher, demonstrating a 4.5-fold increase in glaucoma prevalence in the group in the lower range.[10] Retinal capillary nonperfusion or retinal ischemia is associated with branch or central vein occlusions in some patients and disc hemorrhages are a classic vascular manifestation of a change in perfusion of the tissue. Also, impaired ocular circulation can be prompted by numerous vascular diseases and has been treated with calcium channel blockers, serotonin antagonists, and platelet inhibitors.

Because of these types of associations, in addition to currently approved uses, dipyridamole has been used in the treatment of various ocular conditions and disorders. These

[1]Ocular Research Department, Center for Drug Repurposing, Ariel University, Ariel, Israel.
[2]Eye Research Program, MedInsight Research Institute, Hampshire, United Kingdom.

Article 18

Dental radiographs
Benefits and safety

Dental radiographs (often called x-rays) are an important part of your dental care. Along with an oral examination, they provide your dentist with a more complete view of what's happening in your mouth.

BENEFITS OF DENTAL RADIOGRAPHS

A dental radiograph gives your dentist a picture of your hard tissues (teeth and bones) and the soft tissues that surround your teeth and jawbones. For example, dental radiographs may help your dentist see

- caries (tooth decay) that develops between the teeth or under restorations (fillings);
- diseases in the bone;
- periodontal (gum) disease;
- infections that develop under your gums;
- some types of tumors.

Dental radiographs can alert your dentist to changes in your hard and soft tissues. In children, radiographs allow the dentist to see how their teeth and jawbones are developing. Like medical radiographs, dental radiographs allow your dentist to evaluate any injuries to your face and mouth.

Dental radiographs can help your dentist identify diseases and developmental problems before they become serious health issues. Early detection of an infection or injury also can limit or prevent further damage to other areas of the mouth.

SAFETY OF DENTAL RADIOGRAPHS

Some people wonder if dental radiographs are safe because they expose the patient to radiation. Several factors and practices work together to make dental radiography safe.

The amount of radiation used to obtain dental radiographs is very small. For example, bitewing radiographs—two to four images of the back teeth—expose a patient to about 0.005 millisieverts (mSv) of radiation (a millisievert is a unit of measure).[1] By comparison, because radiation is part of our environment, people in the United States are exposed, on average, to 3.2 mSv every year from background sources of radiation.[1]

Dentists follow the ALARA principle, which stands for "As Low As Reasonably Achievable," when obtaining radiographs. This radiation safety principle limits your exposure by incorporating the following techniques:

- use of the fastest image receptor (that is, the fastest film speed or digital speed);
- reduction in the size of the x-ray beam to the size of the image receptor whenever possible;
- use of proper exposure and processing techniques;
- use of leaded aprons and, whenever possible, thyroid collars.

If you are seeing a new dentist, be sure to provide him or her with copies of your existing radiographs to avoid duplicating them. This also will help limit your exposure to radiation.

Your dentist will decide when radiographs are needed on the basis of your oral examination findings, any symptoms you report, a review of your health history, your risk of experiencing oral disease, your age, or any combination of the preceding. A dental staff member will place a leaded apron on your body during the procedure. He or she also may place a leaded collar around your neck to shield your thyroid gland (located in your neck) but only if its use does not interfere with the procedure. The lead in the apron and collar shields your organs from radiation exposure.

Because of the low radiation dose associated with dental radiographs, people who have received radiation treatment for head and neck cancer can undergo dental radiography safely. In fact, head and neck radiation treatment can increase the risk of developing tooth decay, making the radiographs all the more important for these patients.

If you are pregnant, tell your dentist. During your pregnancy, you may need to have radiographs taken as part of your treatment plan for a dental disease that requires immediate attention. Use of the leaded apron and collar will protect you and your fetus from radiation exposure.

To learn more about the benefits and safety of dental radiographs, talk with your dentist. ■

"For the Dental Patient" provides general information on dental treatments to dental patients. It is designed to prompt discussion between dentist and patient about treatment options and does not substitute for the dentist's professional assessment based on the individual patient's needs and desires.

1. American Nuclear Society. Radiation dose chart. "www.new.ans.org/pi/resources/dosechart/msv.php". Accessed Aug. 2, 2011.

Article 19

EUROPEAN JOURNAL OF GENERAL PRACTICE, 2017
VOL. 23, NO. 1, 196–201
https://doi.org/10.1080/13814788.2017.1350645

REVIEW ARTICLE

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Management of dental patients receiving antiplatelet therapy or chronic oral anticoagulation: A review of the latest evidence

Csaba András Dézsi[a], Balázs Bence Dézsi[b] and András Döme Dézsi[c]

[a]Department of Cardiology, Petz Aladár County Teaching Hospital, Győr, Hungary; [b]Private Practice, SolyDent Dentist's Office, Győr, Hungary; [c]Department of Cardiology, State Hospital for Cardiology, Balatonfüred, Hungary

KEY MESSAGES

- Most dental interventions can be safely performed without the alteration of antiplatelet therapy or anticoagulant therapy in patients taking direct oral anticoagulants or vitamin K antagonists.
- Before high bleeding risk procedures, missing one dose of direct oral anticoagulants on the morning of the intervention may be recommended.

ABSTRACT

The perioperative management of patients treated with antithrombotic medications who undergo surgical procedures represents a common clinical problem. Dental interventions are usually associated with a low risk of bleeding; however, the dental implications of new antithrombotic agents are not yet fully understood. The present review is based on the latest evidence and recommendations published on the periprocedural management of dental patients treated with single or dual antiplatelet therapy, vitamin K antagonists, or direct oral anticoagulants for a variety of indications.

Abbreviations: ACCP: American College of Chest Physicians; ACS: acute coronary syndrome; ADP: adenosine diphosphate; BPE: basic periodontal examination; CrCl: creatinine clearance; DAPT: dual antiplatelet therapy; DVT: deep vein thrombosis; DOAC: direct oral anticoagulant; ICD: implantable cardioverter defibrillator; INR: international normalized ratio; NOAC: novel oral anticoagulant; NVAF: non-valvular atrial fibrillation; PCI: percutaneous coronary intervention; PE: pulmonary embolism; RSI: root surface instrumentation; SDCEP: The Scottish Dental Clinical Effectiveness Programme; TURP: transurethral resection of the prostate; VKA: vitamin K antagonist; VTE: venous thromboembolism

ARTICLE HISTORY
Received 14 May 2016
Revised 11 May 2017
Accepted 25 May 2017

KEYWORDS
Antiplatelet therapy; vitamin K antagonists; direct oral anticoagulant; dental interventions; periprocedural management

Introduction

Most practical recommendations consider dental procedures as minor interventions associated with a low risk of bleeding and self-limited blood loss that can be managed with local haemostatic agents [1–3]. However, certain interventions, such as dental reconstruction surgery, may require the temporary discontinuation of antithrombotic therapy. Therefore, it may not be appropriate to handle dental procedures as a homogeneous group when it comes to assessing the risk of bleeding. The Scottish Dental Clinical Effectiveness Programme (SDCEP) guidance provides a comprehensive classification of dental interventions based on the associated bleeding risks (Table 1) [2].

Due to the increasing life expectancy and the ageing of the population, the periprocedural management of patients receiving oral anticoagulant or antiplatelet therapy for the primary or secondary prevention of cardiovascular disease is an increasingly common clinical problem [4,5]. The management of these patients represents a challenge for physicians as they should carefully balance the risk of bleeding with the risk of thromboembolic complications resulting from the temporary interruption of antithrombotic therapy. Previous

CONTACT Csaba András Dézsi dcsa62@gmail.com FESC, Petz Aladár County Teaching Hospital, Department of Cardiology, 2–4 Vasvári P. str., 9024, Győr, Hungary.
The authors contributed equally to the manuscript.

Neal J McCormick

Undrell J Moore and John G Meechan

Haemostasis Part 1: The Management of Post-Extraction Haemorrhage

Abstract: The management of bleeding complications following a dental extraction is an essential skill for the dental practitioner. Extractions are often carried out on patients with complex medical histories and a long list of medications. This paper aims to help the clinician manage post-extraction haemorrhage. A review of the management of patients on anti-thrombotic medications will be covered in a subsequent paper.

Clinical Relevance: This article reviews the management of haemorrhage following tooth extraction; from the risk assessment of any underlying medical conditions and medications, to the clinical techniques used to control bleeding following an extraction.

Dent Update 2014; 41: 290–296

Haemostasis at the site of a dental extraction is considered to be a prerequisite before the patient leaves the clinic. Failure of haemostasis could occur in any patient; however, a number of different medical conditions and medications may interfere with this process.

The most recent Adult Dental Survey (2009) has shown a growing number of our patients are remaining dentate.[1] People are living longer as a result of increasing health awareness and the success of medical treatments. The concept of 'polypharmacy' management requires dental clinicians to have an increased knowledge of the drugs that may affect dental treatment and their potential for drug interactions. Some drug therapies can increase the potential for bleeding post-operatively.

Risk assessment prior to embarking on a tooth extraction can allow the operator to foresee complications such as a haemorrhage. This involves careful planning and a thorough analysis of the medical history.[2] Table 1 shows the haemorrhage risk factors surrounding a dental extraction.

Neal J McCormick, BDS(Lpool), MFDS RCPS(Glasg), General Professional Trainee (GPT), Health Education North East, **Undrell J Moore**, BDS, PhD, FDS RCS(Eng), Senior Lecturer in Oral Surgery and **John G Meechan**, BSc, BDS, PhD, FDS RCS(Eng), FDS RCS(Ed), FDS RCPS, Honorary Consultant/Senior Lecturer in Oral Surgery, Newcastle Dental Hospital, Richardson Road, Newcastle Upon Tyne, NE2 4AZ, UK.

Overview of haemostasis

A sound knowledge of the physiology of haemostasis is important in understanding how haemorrhage may occur. A full description of the process is outside the remit of this paper; however, several key points are worth noting.

The process of haemostasis involves:

- Vasoconstriction – vascular spasm in smooth muscle in the walls of blood vessels;
- Platelet plug formation – adhesion, interaction and aggregation of platelets;
- Coagulation cascade/network – clotting factors in the extrinsic, intrinsic and common pathways lead to the formation of fibrin.

Clot formation is a dynamic process, involving a balance between the haemostatic and the fibrinolytic systems. The involvement of numerous cells, chemicals and plasma proteins are all required for successful haemostasis. Fibrinolysis occurs when the plasma enzyme plasminogen activates plasmin, which digests the fibrin threads in the clot. In health, this will occur once the site is repaired. Figure 1 outlines the timeline of clot formation.

Consideration of the normal mechanism allows the clinician to interpret which patients may be at high risk of poor haemostasis. This may be the result of underactive clotting or overactive

Soft Tissue Grafting Around Teeth and Implants

George R. Deeb, DDS, MD[a,*], Janina Golob Deeb, DDS, MS[b]

KEYWORDS

• Free gingival graft • Subepithelial connective tissue graft • Recession • Soft tissue defect • Allograft • Xenograft

KEY POINTS

- Esthetic appearance and functional longevity for teeth and implants often requires conversion of unfavorable soft tissue traits to more favorable ones.
- Improvement of tissue quality and quantity can be accomplished with many different techniques and materials, and largely depends on clinical presentation of the case and the familiarity of the clinician with the procedures and materials available.
- Identification of causal factors, selection of appropriate surgical technique, and evidence-based material selection lead to predictable success when improving soft tissue characteristics around teeth or implants.

THE IDEAL CHARACTERISTICS OF THE SOFT TISSUE TOOTH/IMPLANT INTERFACE

The presence of healthy attached tissue at the tooth and implant soft tissue interface correlates with long-term success and stability in function and esthetics. Not only can a lack of keratinized tissue facilitate plaque aggregation around teeth and implants but it can also lead to recession of free soft tissue margin in the esthetic zone. The thicker periodontium is less prone to recession, because of the thickness of the cortical bone as well as the thickness of the surrounding gingiva.

Treatment of mucogingival deficiencies has become a large part of practices involving teeth and implants. The ramifications of not having an adequate keratinized tissue surrounding teeth have been studied extensively for decades,[1,2] and have also extended into implantology. The presence of gingiva is strongly correlated with optimal soft and hard tissue health.[3] However, in patients maintaining proper plaque control, the absence of attached gingiva around teeth does not result in an increased incidence of soft tissue recession.[1,4] It has been shown in long-term studies that even minimal amounts of keratinized tissue can provide long-term stability of soft tissue margin in the presence of good plaque control.[1]

Early studies suggested that the recession of soft tissue margin around implants may be the result of the remodeling of the periimplant soft tissue barrier. Lack of masticatory mucosa and the mobility of periimplant soft tissue were related to more pronounced soft tissue recession around implants.[5] Plaque-induced inflammation has been shown to cause recession when mucosal margins, rather than gingiva, are surrounding implants.[6] Thicker keratinized tissue facilitates plaque removal around implants. Plaque has been found as the causal factor in periodontal diseases[7] as

[a] Department of Oral and Maxillofacial Surgery, School of Dentistry, Virginia Commonwealth University, 521 North 11th Street, Richmond, VA 23298, USA; [b] Departments of Periodontics and General Practice, School of Dentistry, Virginia Commonwealth University, 521 North 11th Street, Richmond, VA 23298, USA
* Corresponding author.
E-mail address: gdeeb@vcu.edu

Oral Maxillofacial Surg Clin N Am 27 (2015) 425–448
http://dx.doi.org/10.1016/j.coms.2015.04.010
1042-3699/15/$ – see front matter

Journal of Advanced Medical and Dental Sciences Research

Journal home page: www.jamdsr.com doi: 10.21276/jamdsr

(e) ISSN Online: 2321-9599; (p) ISSN Print: 2348-6805 SJIF (Impact factor) 2017= 6.261; Index Copernicus value 2016 = 76.77

Review Article

Biopsy of Oral Lesion -A Review Article

Tarun Vyas

Assistant Professor, Department of Oral Medicine and Radiology, R R Dental College & Hospital, Umarda, Udaipur, Rajasthan

ABSTRACT:

Biopsy is the removal of tissue from a living person for microscopic examination to confirm or to establish the diagnosis of a disease The purpose of this article is to review those skills, to discuss new developments in this area, and to highlight some of the potential pitfalls that may occur in taking a biopsy and methods available to avoid them. We feel it will be of value to both general dental practitioners and junior hospital staff. Problems related to specific areas will be covered including apical lesions and those associated with the dental hard tissues.

Key words: Biopsy , Dental hard tissues, FNAC

Corresponding author: Dr. Tarun Vyas, Assistant Professor, Department of Oral Medicine and Radiology, R R Dental College & Hospital, Umarda, Udaipur, Rajasthan

This article may be cited as: Vyas T. Biopsy of Oral Lesion -A Review Article. J Adv Med Dent Scie Res 2018;6(1):27-35.

INTRODUCTION:

Biopsy is the removal of tissue from a living person for microscopic examination to confirm or to establish the diagnosis of a disease.

The term was coined by Ernst Henry, a French dermatologist in 1879. This approach is used for all tissues of the body, including those of the oral cavity, where a wide spectrum of disease processes may present. Proper management of an oral mucosal lesion begins with diagnosis, and the gold standard for diagnosing disease, oral or otherwise, is tissue biopsy[2]. The oral environment, which is moist and confined, poses challenges for collecting a viable tissue sample that will be suitable for diagnosis. These challenges are further compounded by the myriad of biopsy techniques and devices now available. The dental clinician should be aware of the various biopsy techniques that are available for the oral tissues, as well as the challenges specific to these tissue. Whatever the method used, however, the aim is to provide a suitably representative sample for the clinician to interpret, while minimising preoperative discomfort for the patient. An unsuitable, unrepresentative sample is of no use to the clinician or most importantly the patient who would be ill served by an unnecessary repeat procedure (fig 1)[1].

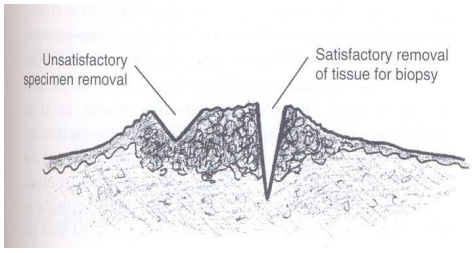

Figure 1

Rovin has made several observations on biopsy decisions.[3]

1. Any lesion that persists for more than two weeks with no apparent etiological basis.
2. Any inflammatory lesion that does not respond to local treatment after 10 to 14 days that is, after removing local irritant.
3. Persistent hyperkeratotic changes in surface tissues.
4. Any persistent tumescence either visible or palpable beneath relatively normal tissue.
5. Inflammatory changes of unknown cause, that persists for long periods.
6. Lesions that interfere with local function. Eg. Fibroma.
7. Bone lesion not superficially identified by clinical and radiographic findings.
8. Any lesion that has characteristics of malignancy.
   - Erythroplasia: Lesion is totally red or has a speckled red and white appearance.
   - Ulceration: an ulcerated lesion
   - Duration: Lesion has persisted more than 2 weeks.
   - Growth rate: Lesion exhibits rapid growth.
   - Bleeding: Lesion bleed on gentle manipulation.
   - Induration: Lesion and surrounding tissue is firm to touch.

Do Antiplatelet Drugs Increase the Risk of Bleeding After Dental Implant Surgery? A Case-and-Crossover Study

Reza Tabrizi, DMD, [*] *Isa Khaheshi, MD,* [†] *Afshin Hoseinzadeh,* [‡] *Babak Rezvanpour,* [§] *and Shervin Shafie* [‖]

Purpose: Cessation versus continuation of antiplatelet drugs in patients undergoing dental implant surgery is a controversial issue. The present study evaluated postoperative bleeding during and after dental implant surgery in patients taking aspirin (ASA) or clopidogrel.

Material and Methods: The present study is a case-and-crossover study. Patients who were using antiplatelet drugs and receiving 2 bilateral dental implants in the posterior region of the mandible were studied. During session 1, dental implants were placed without stopping the intake of antiplatelet drugs. During session 2, antiplatelet drugs were stopped for 5 days. In group 1, platelet activity was measured by an assay based on flow cytometry and represented the platelet reactivity index. In group 2, platelet function analysis was used to monitor the antiplatelet effect of ASA. Bleeding severity was assessed using a visual analog scale for 72 hours after dental implant placement during sessions 1 and 2. Use of antiplatelet drugs was the predictive factor of the study and bleeding severity and platelet function were the outcomes of the study.

Results: Twenty-two patients composed group 1 (clopidogrel 75 mg) and 20 composed group 2 (ASA 80 mg). In group 1, bleeding severity was 4.86 ± 0.77 during session 1 and 4.59 ± 0.66 during session 2. Data analysis showed no difference in bleeding severity between sessions 1 and 2 in group 1 (P = .72). In group 2, bleeding severity was 4.05 ± 0.94 during session 1 and 3.9 ± 0.85 during session 2. There was no difference in bleeding severity between sessions 1 and 2 in patients taking ASA (P = .19).

Conclusion: The results suggest that continuing the intake of antiplatelet drugs did not increase bleeding after placement of dental implants.

J Oral Maxillofac Surg 76:2092-2096, 2018

The withdrawal of anticoagulation medications in patients undergoing dental surgeries is a controversial subject among clinicians. Thrombocyte aggregation inhibitors, such as cyclooxygenase-1 inhibitors (aspirin [ASA]), and adenosine diphosphate (ADP) receptor antagonists, such as clopidogrel, are the most common medications used to prevent thrombosis in patients with ischemic heart disease or a history of coronary angina, myocardial infarction, or stent implantation. Because these medications are commonly prescribed for such patients and they undergo dental procedures, suitable consideration should be given to all dental interventions.[1]

Most recent studies have suggested that single- or dual-antiplatelet therapy should not be stopped before dental surgeries after comparing the risk of

Received from the Shahid Beheshti University of Medical Sciences, Tehran, Iran.

[*]Associate Professor of Oral and Maxillofacial Surgery, Shahid Beheshti Dental School.

[†]Assistant Professor of Cardiology, Cardiovascular Research Centre, Modarres Hospital.

[‡]Student of Dentistry, Shahid Beheshti Dental School.

[§]Student of Dentistry, Shahid Beheshti Dental School.

[‖]Student of Dentistry, Shahid Beheshti Dental School.

Conflict of Interest Disclosures: None of the authors have a relevant financial relationship(s) with a commercial interest.

Address correspondence and reprint requests to Dr Tabrizi: OMFS Department, Shahid Beheshti Dental School, Velenjak, Tehran; e-mail: tabmed@hotmail.com

Received January 21 2018

Accepted April 30 2018

0278-2391/18/30423-3

https://doi.org/10.1016/j.joms.2018.04.036

Journal of the Formosan Medical Association (2018) 117, 979–986

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.jfma-online.com

Original Article

Management of dental extractions in patients on warfarin and antiplatelet therapy

Shin-Yu Lu*, **Liang-Ho Lin**, **Shui-Sang Hsue**

Oral Pathology and Family Dentistry Section, Department of Dentistry, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung, Taiwan

Received 5 August 2018; received in revised form 14 August 2018; accepted 20 August 2018

KEYWORDS
Dental extractions;
Warfarin;
Aspirin;
Clopidogrel

Background/Purpose: Planning dental extractions for Taiwanese patients on antithrombotic therapy remains controversial. This study aimed to examine management of dental extraction in patients on warfarin and antiplatelet therapy.
Methods: Subjects comprised 1331 patients, with (1) 60 on warfarin with intentional normalized ratio (INR) below 4.0 (warfarin continued: 28 patients/33 occasions; warfarin stopped and switched to heparin under hospitalization: 32 patients/37 occasions); (2) 183 on antiplatelet therapy (aspirin: 125 patients/185 occasions; clopidogrel: 42 patients/65 occasions; dual therapy: 16 patients/24 occasions); and (3) a control group of 1088 patients/1472 occasions without any antithrombotic therapy. The patient's clinico-demographic parameters, warfarin effectiveness (dose and INR levels) and antiplatelet therapy, number and type of dental extraction and incidence of postoperative bleeding were investigated.
Results: Incidence of postoperative bleeding in the warfarinized group (warfarin continued: 9.1%; warfarin stopped: 8.1%) was higher than in the antiplatelet group (aspirin: 1.1%; clopidogrel: 3.1%; dual antiplatelet: 4.2%), and the control group (0.7%), but these differences were not significant and unrelated to INR or number and type of dental extraction. Postoperative hemorrhage was managed successfully by repacking with Gelfoam impregnated with tranexamic acid powder in most patients.
Conclusion: The study indicated that there is no need to interrupt warfarin (INR<4.0) and antiplatelet therapy before dental extractions in Taiwanese patients. A sufficient hemostasis could be obtained using local measures. This approach can save these individuals from becoming exposed to the risk of thromboembolism and the inconvenience of bridging anticoagulation with heparin.

* Corresponding author. Kaohsiung Chang Gung Memorial Hospital, 123 Dapi Road, Niaosong, Kaohsiung, 833, Taiwan, ROC. Fax: +886 7317123 x8288.
E-mail address: jasminelu@adm.cgmh.org.tw (S.-Y. Lu).

https://doi.org/10.1016/j.jfma.2018.08.019

Article 25

Hindawi Publishing Corporation
BioMed Research International
Volume 2015, Article ID 823651, 4 pages
http://dx.doi.org/10.1155/2015/823651

Clinical Study

Postoperative Bleeding Risk for Oral Surgery under Continued Clopidogrel Antiplatelet Therapy

Alexander Gröbe,[1] Meike Fraederich,[1] Ralf Smeets,[1] Max Heiland,[1] Lan Kluwe,[1] Jürgen Zeuch,[2] Martina Haase,[2] Johannes Wikner,[1] Henning Hanken,[1] Jan Semmusch,[1] Ahmed Al-Dam,[1] and Wolfgang Eichhorn[1,2]

[1]*Department of Oral and Maxillofacial Surgery, University Medical Center Hamburg-Eppendorf, Martinistraße 52, 20246 Hamburg, Germany*
[2]*Department of Oral and Maxillofacial Surgery, General Hospital Balingen, Tuebinger Straße 30, 72336 Balingen, Germany*

Correspondence should be addressed to Wolfgang Eichhorn; w.eichhorn@uke.de

Received 20 July 2014; Revised 8 October 2014; Accepted 22 October 2014

Academic Editor: Betti Giusti

Object. To determine the incidence of postoperative bleeding for oral osteotomy carried out under continued monoantiplatelet therapy with clopidogrel and dual therapy with clopidogrel/aspirin. *Design.* Retrospective single center observatory study of two study groups and a control group. *Methods.* A total of 64 and 60 oral osteotomy procedures carried out under continued monoclopidogrel therapy and dual clopidogrel/aspirin therapy, respectively, were followed for two weeks for postoperative bleeding. Another 281 similar procedures were also followed as a control group. All oral osteotomy procedures were carried out on an outpatient basis. *Results.* We observed postoperative bleeding in 2/281 (0.7%) cases in the control group, in 1/64 (1.6%) cases in the clopidogrel group, and in 2/60 (3.3%) cases in the dual clopidogrel/aspirin group. The corresponding 95% confidence intervals are 0–1.7%, 0–4.7%, and 0–7.8%, respectively, and the incidences did not differ significantly among the three groups ($P > 0.09$). Postoperative hemorrhage was treated successfully in all cases with local measures. No changes of antiplatelet medication, transfusion, nor hospitalisation were necessary. No major cardiovascular events were recorded. *Conclusions.* Our results indicate that minor oral surgery can be performed safely under continued monoantiplatelet medication with clopidogrel or dual antiplatelet medication with clopidogrel/aspirin.

1. Introduction

Clopidogrel is a common antiplatelet agent used as an alternative for aspirin or in dual antiplatelet therapy with aspirin [1–3]. Clopidogrel irreversibly inhibits adenosine diphosphate, which is necessary for platelet aggregation while aspirin works through inactivation of the enzyme cyclooxygenase. Both drugs prevent clot formation for the lifetime of the platelet, which is 9–11 days [4, 5].

When patients under such antiplatelet therapy need surgery, the surgeon is confronted with the choice of interrupting the therapy, which increases the risks of thrombosis, or continuing the medication, which on the other hand increases the risk of hemorrhage. Published studies commonly recommended continuation of antiplatelet drugs for minor oral surgery [3, 6, 7]. However, a perioperative interruption of antiplatelet medication is still frequently practiced for dental procedures [8]. In particular, clopidogrel, either for single or dual therapy, is feared for exposing patients to a high risk of bleeding [9] since it takes 5–10 days for full recovery of platelet activity after withdrawal.

The purpose of this study is to evaluate the postoperative bleeding rate for oral osteotomy and other invasive oral procedures under continued monoclopidogrel therapy or dual clopidogrel/aspirin therapy. We focus on oral osteotomy because this procedure involves invading the bone and

Journal of Oral Research

REVIEW

Oral surgery in patients under antithrombotic therapy. Narrative review.

Anggelo Carrizo[1].
David Carrasco[2].

1. CESFAM Boca Sur, San Pedro de la Paz. Chile.
2. Práctica Privada. Chile.

Corresponding author: Anggelo Carrizo. 2° Transversal N° 457, Boca Sur. San Pedro de la Paz. Chile. Phone: +56 800500818. E-mail: anggelocarrizo@gmail.com

Receipt: 12/30/2014 **Revised:** 01/15/2014
Acceptance: 02/13/2015 **Online:** 02/13/2015

Abstract: Population aging and the increasing rates of cardiovascular diseases have raised the number of patients receiving antithrombotic therapy in elective or emergency dental care, including surgical procedures. The aim of this article is to review the evidence and clinical guidelines for management of patients on antithrombotic therapy published in the past five years. The American Antithrombotic Therapy Guideline - 2012 - generally recommends not to suspend antiplatelet or anticoagulant treatment in dental procedures since they are considered to have low bleeding risk and easy resolution. In the dental field, there is ample published evidence regarding oral surgical procedure management, especially by maxillofacial surgeons, showing a low number of complications associated with extractions or other minor oral surgical procedures without suspending antithrombotic drugs and only taking some minimum safeguards, such as healing by first intention or the use of some local hemostatic agents. In general, patients under chronic antithrombotic therapy should keep their medication when undergoing low and medium complexity dental procedures, since complications are minor and easy to handle. Due to interactions between them, particular care should be taken with patients using more than one drug.

Keywords: *Antithrombotic, coagulation, exodontia, oral surgery, hemorrhage, aspirin.*

DOI: *10.17126/joralres.2015.012*

Cite as: *Carrizo A & Carrasco D. Oral surgery in patients under antithrombotic therapy. Narrative review. J Oral Res 2015;4(1):58-64.*

INTRODUCTION.

Population aging and the increasing prevalence of chronic diseases, especially the cardiovascular ones, make cardiac events the main cause of death in developed countries and this is also happening in Chile[1]. Although there are several ways to intervene and prevent cardiovascular diseases (CVD), the pharmacological treatment is the most important. Prescribing antithrombotic drugs is currently the most used strategy to prevent the development of a major cardiac event[2,3].

Given that, it is becoming more and more frequent to find patients with CVD treated with antithrombotic therapy in the dental office[2]. This makes it necessary for the dentist to consider certain handling guidelines to avoid triggering a cardiac event and allow relevant and efficient care for these patients, especially in emergency situations involving routine and low complexity surgical procedures.

The objective of this article is to review the evidence and international clinical guidelines with regard to the management of dental patients treated with antithrombotic therapy published in the last 5 years. This is intended to generate recommendations for the national context according to today's patients' risk level.

Antithrombotic drugs.

Currently, in Chile, the most commonly used antithrombotic drugs are acetylsalicylic acid (aspirin), ace-

Article 27

REVIEW

THE AMERICAN JOURNAL of MEDICINE®

Dental Surgery and Antiplatelet Agents: Bleed or Die

Michael J. Wahl, DDS

Wahl Family Dentistry, Wilmington, Del.

ABSTRACT

In patients taking antiplatelet medications who are undergoing dental surgery, physicians and dentists must weigh the bleeding risks in continuing antiplatelet medications versus the thrombotic risks in interrupting antiplatelet medications. Bleeding complications requiring more than local measures for hemostasis are rare after dental surgery in patients taking antiplatelet medications. Conversely, the risk for thrombotic complications after interruption of antiplatelet therapy for dental procedures apparently is significant, although small. When a clinician is faced with a decision to continue or interrupt antiplatelet therapy for a dental surgical patient, the decision comes down to "bleed or die." That is, there is a remote chance that continuing antiplatelet therapy will result in a (nonfatal) bleeding problem requiring more than local measures for hemostasis versus a small but significant chance that interrupting antiplatelet therapy will result in a (possibly fatal) thromboembolic complication. The decision is simple: It is time to stop interrupting antiplatelet therapy for dental surgery.
 • The American Journal of Medicine (2014) 127, 260-267

KEYWORDS: Antiplatelet agents; Aspirin; Dental; Dental surgery; Stroke

The history of aspirin (acetylsalicylic acid) dates back more than 2000 years ago, when Hippocrates recommended chewing on willow leaves (which contain salicylic acid) during childbirth for analgesia. In 1899, the chemist Felix Hoffman of Bayer AG (Leverkusen, Germany) was the first to isolate pure acetylsalicylic acid, later calling it "Aspirin" for commercial manufacture and sale. Since then, Bayer AG lost or sold its rights to the trademark, and the "wonder drug" aspirin is widely used for its analgesic, antipyretic, anti-inflammatory, and anti-thrombotic effects.

Aspirin's antithrombotic indications include atrial fibrillation, history of angina or myocardial infarction, coronary artery disease prevention, history of coronary bypass surgery, and percutaneous coronary intervention and stent implantation. Newer antiplatelet medications include clopidogrel (Plavix; Bristol-Myers Squibb, New York, NY), ticlopidine (Ticlid; Roche Laboratories, Basel, Switzerland), cilostazol (Pletal; Otsuka America Pharmaceuticals Inc, Rockville, Md), dipyridamole (Persantine; Boehringer Ingelheim Pharmaceuticals, Inc, Ridgefield, Conn), ticagrelor (Brilinta; AstraZeneca, Paddington, London), and prasugrel (Effient; Ube Industries, Ube, Japan). Some of these newer agents are associated with greater antithrombotic efficacy but also higher bleeding risks than aspirin. When dental surgery is contemplated in patients taking 1 or more of these medications, dentists and physicians must weigh the potential bleeding risks in continuing the medications versus the thromboembolic risks in interrupting them before dental surgery.

Dentists frequently recommend aspirin withdrawal before dental surgery, even without consulting the patient's physician.[1] Both physicians and dentists frequently overestimate the bleeding risks of dental surgery in patients continuing antiplatelet medications and underestimate the thrombotic risks of interrupting antiplatelet therapy for dental procedures.[2-5] Dental surgery is unlike other types of surgery: Major vessels are unlikely to be encountered, and the perioperative and postoperative surgical sites are easily accessible to local measures for hemostasis, such as biting on gauze, absorbable gelatin sponges, and sutures. As early as 1987, Salzman[6] stated, "The hemostatic defect induced by aspirin in patients with otherwise normal hemostasis is usually minor…."

DENTAL SURGERY IN PATIENTS TAKING ANTIPLATELET MEDICATIONS

There have been many reports of patients continuing antiplatelet agents while undergoing dental surgery. Of at least

Funding: None.

Conflict of Interest: None.

Authorship: The author is solely responsible for the content of this manuscript.

Requests for reprints should be addressed to Michael J. Wahl, DDS, Wahl Family Dentistry, 2003 Concord Pike, Wilmington, DE 19803.

E-mail address: WahlDentistry@aol.com

0002-9343/$ -see front matter
http://dx.doi.org/10.1016/j.amjmed.2013.11.013

MANAGEMENT OF PATIENTS UNDER ANTI-PLATELET AGENTS' TREATMENT IN ODONTOSTOMATOLOGY

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Article 29

ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 9, Issue 3, 2016

Online - 2455-3891
Print - 0974-2441

Review Article

DENTAL MANAGEMENT OF PATIENTS ON ANTIPLATELET THERAPY: LITERATURE UPDATE

SANTHOSH KUMAR MP*

Department of Oral and Maxillofacial Surgery, Saveetha Dental College, Velappanchavadi, Chennai - 600 077, Tamil Nadu, India.
Email: santhoshsurgeon@gmail.com

Received: 03 March 2016, Revised and Accepted: 13 March 2016

ABSTRACT

Antiplatelet drugs are used in the prevention and management of arterial and venous thrombi. These drugs are associated with an increase in bleeding time and risk of post-operative hemorrhage. Because of this, dental surgeons recommend their patients to stop the therapy before surgical procedures which may in turn cause fatal thromboembolic complications. This article reviews the commonly used antiplatelet drugs, dental management of patients on these drugs when subjected to minor oral surgical procedures. The objective of this article is to review various literature, whether to discontinue or continue antiplatelet therapy during dental surgical procedures, and current consensus and recommendations have been established. It is concluded that antiplatelet monotherapy and even antiplatelet dual therapy can be safely continued on patients during dental surgical procedures, and there is no need for altering or discontinuing the drugs. Post-operative bleeding can be managed by local hemostatic measures.

Keywords: Aspirin, Antiplatelet therapy, Bleeding, Thromboembolism, Dental extraction.

INTRODUCTION

Thrombogenesis (clot formation) includes 2 principal processes: platelet aggregation and coagulation. Platelet aggregation consists of activated platelets attaching to strands of fibrinogen, whereas coagulation is a complex cascade of enzymatic events, leading to the formation of fibrin strands. Antithrombotic drugs include those that inhibit platelet aggregation (antiplatelet drugs), inhibit formation of fibrin strands (anticoagulants), and dissolve existing clots (fibrinolytics) [1].

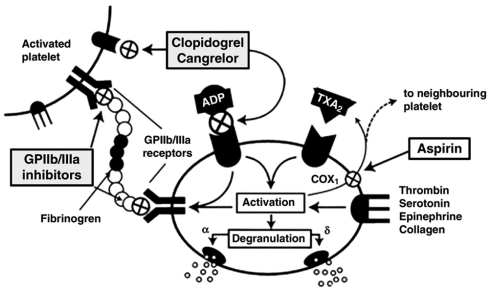
Platelets provide the initial hemostatic plug at the site of vascular injury, and they are involved in pathological processes and are an important contributor to arterial thrombosis, leading to myocardial infarction and ischemic stroke. Antiplatelet agents are widely used in prevention and treatment of various ischemic cardiovascular and cerebrovascular conditions [2], and the common indications for their long-term use are arterial thrombosis, ischemic heart disease, myocardial infarction, both stable and unstable angina, coronary artery bypass and placement of a stent, non-hemorrhagic stroke, transient ischemic attacks (ischemic stroke), peripheral arterial disease, atrial fibrillation.

Despite the benefits of antiplatelet drugs, they are not without the risks of bleeding during oral surgical procedures. Hence, dentists while treating patients on antiplatelet therapy advise them to stop drugs before extractions which may predispose them to thromboembolic complications. Hence, dental surgeons are in a dilemma whether to stop or continue antiplatelet drugs during extractions. Various studies have been conducted worldwide to address this issue. The rationale of this article is to review the present literature on this topic and to obtain the updated and recent consensus and recommendations made while treating patients on antiplatelet therapy undergoing oral surgical procedures.

ANTIPLATELET DRUGS

Drug	Mechanism of action
Aspirin	COX 1 inhibitor
Clopidogrel	ADP receptor inhibitors
Prasugrel	
Ticlopidine	
Dipyridamole	Adenosine reuptake inhibitor and phosphodiesterase inhibitor
Triflusal	COX and phosphodiesterase inhibitor
Abciximab	Glycoprotein IIb/IIIa inhibitor
Eptifibatide Tirofiban	

COX: Cyclooxygenase, ADP: Adenosine diphosphate



Mechanism of action – antiplatelet drugs

ASPIRIN

Aspirin, acetylsalicylic acid (ASA), is a non-steroidal anti-inflammatory drug that exhibits analgesic, antipyretic, anti-inflammatory, and antiplatelet properties. It is the most commonly used drug in the prevention and treatment of thromboembolic diseases because of its antiplatelet action. Aspirin has been shown to be a powerful secondary prevention agent, reducing the risk of myocardial infarction and ischemic stroke by up to 20% in patients diagnosed with cardiovascular disease [3]. Its mechanism of action involves an irreversible inhibition of the activity of cyclooxygenase-1 (COX-1) and a modification of the enzymatic activity of COX-2. COX is an enzyme responsible for the conversion of arachidonic acid to prostaglandins, prostacyclin, and thromboxane. Thromboxane-A2, a strong platelet agonist, is a specific eicosanoid lipid found in platelets important in promoting platelet aggregation over-damaged endothelium in blood vessels. The irreversible nature of the inhibition of COX is unique to aspirin among its counterparts [3,4]. Platelets are affected for the life of the cell, and complete reversal of antiplatelet activity might not occur until

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The Saudi Journal for Dental Research (2015) **xxx**, xxx–xxx

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ORIGINAL ARTICLE

Knowledge of medical and dental practitioners towards dental management of patients on anticoagulant and/or anti-platelet therapy

Altaf Hussain Shah [a,*], Hesham Saleh Khalil [b], Faleh Ali Alshahrani [c,1], Soban Qadir Khan [d], Nasser Raqe AlQthani [c,2], Ishfaq Ali Bukhari [e], Mohammed Zaheer Kola [f]

[a] *Department of Preventive Dental Sciences, College of Dentistry, Salman bin Abdulaziz University, P.O. Box 153, AlKharj, 11942, Saudi Arabia*
[b] *Department of Maxillofacial Surgery, College of Dentistry, King Saud University, Saudi Arabia*
[c] *Department of Oral and Maxillofacial Surgery and Diagnostic Sciences, College of Dentistry, Salman bin Abdulaziz University, AlKharj, Saudi Arabia*
[d] *College of Dentistry, University of Dammam, Saudi Arabia*
[e] *Department of Physiology and Pharmacology, College of Medicine, King Saud University, Saudi Arabia*
[f] *Department of Prosthetic Dental Sciences, College of Dentistry, Salman bin Abdulaziz University, AlKharj, Saudi Arabia*

Received 31 August 2014; revised 24 September 2014; accepted 20 October 2014

KEYWORDS

Anticoagulants;
Anti platelet therapy;
Patient management;
Practitioners

Abstract *Objective:* The purpose of this study was to evaluate the knowledge of medical and dental practitioners towards the dental management of patients who are on anti-coagulant and/or anti platelet agents.
Methods: This study was conducted in different hospitals/health centers of Riyadh and AlKharj cities, Saudi Arabia. Participants included practitioners working in government and private medical centers/hospitals. A self-administered questionnaire including details about the practitioners' level of education and work experience was used. Participants were asked questions regarding dental management of patients on anticoagulant therapy and/or antiplatelet therapy. *Result:* A total of 650 self-administered questionnaires were distributed among dental and medical practitioners, of which, 543 were returned complete. Most of the participants were general

* Corresponding author. Tel.: +966 115886237.
E-mail address: a.shah@sau.edu.sa (A.H. Shah).
[1] Current Address: Saudi Board Resident, Maxillofacial Surgery, King Fahad Medical City, Riyadh.
[2] Current Address: University College London (UCL), UK.

Peer review under responsibility of King Saud University.

Production and hosting by Elsevier

http://dx.doi.org/10.1016/j.sjdr.2014.10.002

Article 31

Clinical Investigations

Safety of Dental Extractions in Coronary Drug-Eluting Stenting Patients Without Stopping Multiple Antiplatelet Agents

Mahn-Won Park, MD; Sung-Ho Her, MD; Jong Bum Kwon, MD; Jae Beom Lee, MD; Min-Seok Choi, MD; Jung Sun Cho, MD; Dong-Bin Kim, MD; Wook-Sung Chung, MD; Ki-Bae Seung, MD; Keon-Yeop Kim, MD

Division of Cardiology, Department of Internal Medicine (Park, Her, Lee, Choi, Cho, D.-B. Kim, Chung, Seung), Department of Thoracic and Cardiovascular Surgery (Kwon), The Catholic University of Korea College of Medicine, Seoul, South Korea; Division of Preventive Medicine (K.-Y. Kim), Kyungpook National University College of Medicine, Daegu, South Korea

Address for correspondence:
Sung-Ho Her, MD
Daejeon St. Mary's Hospital
520-2, Daeheung-dong, Jung-gu
Daejeon-city,
South Korea 301-723
hhhsungho@naver.com

ABSTRACT

Background: The risk of excessive bleeding prompts physicians to stop multiple antiplatelet agents before minor surgery, which puts coronary stenting patients at risk for adverse thrombotic events.

Hypothesis: We hypothesized that most dental extractions can be carried out safely without stopping multiple antiplatelet agents.

Methods: All dental extraction patients who had undergone coronary stenting and who were also on oral multiple antiplatelet agents therapy were enrolled. One hundred patients underwent dental procedures without stopping antiplatelet agents. All wounds were sutured and followed up at 24 hours, 1 week, and 1 month after the procedure. There were 2233 patients who had not taken oral antiplatelet agents from a health promotion center and had teeth extracted by the same method. After performing propensity-score matching for the entire population, a total of 100 matched pairs of patients were created. The primary outcome was a composite of excessive intraextraction blood loss, transfusion, and rehospitalization for bleeding, and the secondary outcome was a composite of death, nonfatal myocardial infarction, target lesion revascularization, and stent thrombosis within 1 month after the procedure.

Results: There were 2 excessive intraextraction bleeding cases that continued at the extraction site for 4 and 5 hours, respectively, in the coronary stenting patients, and 1 excessive intraextraction bleeding case that continued for 3 hours in the control patients. There were no cases of transfusion, rehospitalization for bleeding, or major cardiovascular events for the 2 propensity-matched groups.

Conclusions: We found that most dental extractions in coronary stenting patients can be carried out safely without stopping multiple antiplatelet agents.

Introduction

Aspirin and clopidogrel (or ticlopidine) are widely used for their antiplatelet function effects, and although low-dose aspirin (75–100 mg daily) and clopidogrel (75 mg daily) or ticlopidine (250 mg twice daily) are generally indicated in cases of angina and ischemic heart disease, especially after coronary stenting following myocardial infarction (MI) and stroke,[1,2] the fear of uncontrolled bleeding prompts physicians to recommend stopping aspirin and thienopyridine intake before surgical procedures, including dental extractions.[3–5] This puts the patients at risk of developing thromboembolism, MI, or a cardiovascular accident.[6,7]

We conducted a study of 100 consecutive patients on long-term oral multiple antiplatelet-agent therapy scheduled for dental extractions. We did not stop antiplatelet agents and did not face any major untoward sequelae. We present our results of 100 matched pairs of patients who were compared and propose that most dental extractions can be carried out safely without stopping multiple antiplatelet-agent therapy.

Methods

Study Group Population

One hundred patients who fulfilled all inclusion criteria were enrolled in this study. They included patients on long-term (at least 7 days), oral, multiple antiplatelet agents,

The authors have no conflicts of interest to disclose.
This study was supported in part by a grant from Yuhan Corporation, Ltd., Seoul, The Republic of Korea.

Received: July 20, 2011
Accepted with revision: November 22, 2011

Published online in Wiley Online Library (wileyonlinelibrary.com)
DOI:10.1002/clc.21960

Article 32

Journal section: Odontostomatology for the disabled or special patients
Publication Types: Review

doi:10.4317/jced.54079
http://dx.doi.org/10.4317/jced.54079

Dental management in patients with antiplatelet therapy: A systematic review

Luis-Miguel Sáez-Alcaide [1], Cristina Sola-Martín [2], Pedro Molinero-Mourelle [1], Victor Paredes-Rodríguez [3], Carmen Zarrias-Caballero [3], Gonzalo Hernández-Vallejo [4]

[1] DDS. Postgraduate student. Department of Medicine and Oral Surgery, Faculty of Dentistry, Complutense University of Madrid
[2] DDS. Graduate student. Department of Medicine and Oral Surgery, Faculty of Dentistry, Complutense University of Madrid
[3] DDS, PhD. Assistant Professor. Department of Medicine and Oral Surgery, Faculty of Dentistry, Complutense University of Madrid
[4] DDS, MD, PhD. Associate Professor, Department of Medicine and Oral Surgery, Faculty of Dentistry, Complutense University of Madrid

Correspondence:
Department of Medicine and Oral Surgery (Dpto. Estomatología III)
Faculty of Dentistry
Complutense University of Madrid
Address: Pza Ramón y Cajal S/N
lsaez@ucm.es

Received: 24/05/2017
Accepted: 28/06/2017

Please cite this article in press as: **Sáez-Alcaide LM, Sola Martín C,** Molinero Mourelle P, Paredes-Rodríguez V, Zarrias-Caballero C, Hernández-Vallejo G. Dental management in patients with antiplatelet therapy: A systematic review. J Clin Exp Dent. (2017), *doi:10.4317/jced.54079*

Abstract

Background: Cardiovascular diseases are the most frequent cause of death in the Western world. Its treatment frequently needs therapy with antiplatelet agents, which increases the haemorrhage risk after oral surgical procedures. The aim of this study is to present a review on the dental management of the patients under antiplatelet treatment.
Material and Methods: A systematic review was carried out following PRISMA recommendations including studies searched in Pubmed-Medline, Embase and Cochrane databases.
Results: The current trend is to maintain the treatment during the surgical procedure, assuring a good control of the haemorrhage with local haemostatic measures. However, new antiplatelet drugs protocols are not firmly established.
Conclusions: In spite of the existing recommendations, it is always advisable to consult with the internist or cardiologist of every patient before any intervention.

Key words: *Antiplatelet, Oral Surgery, Exodontia, Dental Management.*

Introduction

Cardiovascular diseases were the main cause of mortality in USA in 2014 according to the National Institute of Statistics, being responsible of 167 deaths per 100.000 inhabitants. Among cardiovascular diseases, the ischemic ones (myocardial infarction, angina pectoris) were the first cause of death, followed by cerebrovascular accidents (CVA) (1). CVA represent the third cause of death in developed countries and they are one of the pathologies with major morbidity. About 85 % of the CVA are ischemic and, among these, 60 % have an atherothrombotic cause. Nowadays, the atheroesclerosis of the

Article 33

Original Article

Effect of antiplatelet therapy on minor dental procedures

ABSTRACT

Introduction: Minor oral surgical procedures are very common. Acetylsalicylic acid generically known as aspirin is used clinically as an analgesic, antipyretic, anti-inflammatory, and as a medication to prevent platelet aggregation.

Objective: The aim of this study was to determine if aspirin or clopidogrel was associated with bleeding after minor oral surgical procedures.

Materials and Methods: One hundred patients who were planned for extraction of the third molar were divided into two groups. In Group A, patients on antiplatelets were included and in Group B, patients who discontinued the drug before 5 days of procedure were included. The bleeding time of all patients was checked before extraction. The surgical procedure involved simple extraction of a single third molar tooth under local anesthesia. The extraction socket was sutured with 3–0 silk. A pressure pack of gauze was given for 1 h. Bleeding after 1 h and 24 h was compared between two groups. A Chi-square test was used to compare the variables.

Results: None of the patients showed active bleeding in the postoperative period. The results for postsurgical bleeding were statistically insignificant with $P = 0.05$.

Conclusion: Minor surgical procedures such as single-tooth extraction can be carried out without discontinuation of the antiplatelet therapy.

Keywords: Antiplatelet, aspirin, oral surgical

INTRODUCTION

Platelet function is important for platelet aggregation, and antiplatelet drugs are used to interfere with this function for prophylactic or therapeutic uses. Thromboembolic disorders such as coronary artery diseases and cerebrovascular diseases are very common these days due to change in lifestyle and increased life span. Commonly used oral antiplatelet drugs include aspirin and thienopyridines (e.g., clopidogrel). The enzyme cyclooxygenase-1 (COX-1) that produces thromboxane A2 is essential for platelet aggregation, aspirin irreversibly inhibits COX-1, thus preventing platelet aggregation and consequently increasing the bleeding time. At low doses such as 75 mg/day, the complete inhibition of the COX-1 enzyme and hence the maximal antiplatelet effect may take several days. At a dose of 160–325 mg/day, the maximal antiplatelet effect of aspirin occurs within 30 min.[1] Aspirin in low doses (75–150 mg/day) is used for the long-term prevention of heart attacks and strokes, whereas moderate doses (160–325 mg/day) of aspirin are given in situations where immediate anticlotting effects are needed (such as in the treatment of acute heart attacks and unstable angina). The other drug clopidogrel, commonly used nowadays, is a prodrug that alters adenosine diphosphate receptors on platelets and inhibits platelet aggregation.[2] The onset of action of clopidogrel is also dose related. Maximal antiplatelet effect occurs several days after the initiation of clopidogrel (75 mg/day). It is still a common practice among dentists and medical practitioners to discontinue aspirin therapy before any surgical procedure due to fear of excessive postoperative bleeding in patients on antiplatelet

Altaf Hussain Malik, Shabnum Majeed[1]
Department of Oral and Maxillofacial Surgery, Govt. Dental College, [1]Department of Health and Medical Education, Srinagar, Jammu and Kashmir, India

Address for correspondence: Dr. Altaf Hussain Malik, Govt. Dental College, Srinagar - 190 010, Jammu and Kashmir, India.
E-mail: drmalikaltaf@gmail.com

Received: 20 May 2019, **Revised:** 09 August 2019, **Accepted:** 26 February 2020, **Published:** 18 June 2020

Access this article online	
Website: www.njms.in	Quick Response Code
DOI: 10.4103/njms.NJMS_30_19	

How to cite this article: Malik AH, Majeed S. Effect of antiplatelet therapy on minor dental procedures. Natl J Maxillofac Surg 2020;11:64-6.

Article 34

Int. J. Oral Maxillofac. Surg. 2019; xxx: xxx–xxx
https://doi.org/10.1016/j.ijom.2019.06.002, available online at https://www.sciencedirect.com

International Journal of Oral & Maxillofacial Surgery

Systematic Review and Meta-Analysis
Oral Surgery

Incidence of bleeding after minor oral surgery in patients on dual antiplatelet therapy: a systematic review and meta-analysis

A. Ockerman[1], M. M. Bornstein[2], Y. Y. Leung[3], S. K. Y. Li[4], C. Politis[1], R. Jacobs[1,5]

[1]Oral and Maxillofacial Surgery — Imaging and Pathology Research Group, Department of Imaging and Pathology, Faculty of Medicine, University of Leuven and Department of Oral and Maxillofacial Surgery, University of Leuven, Leuven, Belgium; [2]Applied Oral Sciences, Faculty of Dentistry, The University of Hong Kong, Hong Kong, China; [3]Oral and Maxillofacial Surgery, Faculty of Dentistry, The University of Hong Kong, Hong Kong, China; [4]Centralized Research Laboratory, Faculty of Dentistry, The University of Hong Kong, Hong Kong, China; [5]Department of Dental Medicine, Karolinska Institutet, Stockholm, Sweden

A. Ockerman, M. M. Bornstein, Y. Y. Leung, S. K. Y. Li, C. Politis, R. Jacobs: Incidence of bleeding after minor oral surgery in patients on dual antiplatelet therapy: a systematic review and meta-analysis. Int. J. Oral Maxillofac. Surg. 2019; xxx: xxx–xxx.

Abstract. Bleeding is a feared complication of minor oral surgery in patients on treatment with antiplatelet agents and there is no agreed strategy regarding the cessation or not of antiplatelet treatment. The aim of this systematic review was to evaluate bleeding with minor oral surgery in patients on dual antiplatelet therapy (DAPT), single antiplatelet therapy (SAPT), or no antiplatelet therapy (no APT). The PubMed, Embase, Web of Science, and Cochrane Library databases were screened. Sixteen studies were included. DAPT was continued in all studies. The perioperative bleeding risk was significantly higher for DAPT than for SAPT (risk ratio (RR) 10.16, $P = 0.010$; risk difference (RD) 0.35, $P = 0.269$), but not higher compared to no APT (RR 6.50, $P = 0.057$; RD 0.19, $P = 0.060$). The postoperative bleeding risk was significantly elevated for DAPT compared to SAPT (RR 2.61, $P = 0.010$) and no APT (RR 3.63, $P = 0.035$), but only by 1% (RD 0.01, $P = 0.103$) and 1% (RD 0.01, $P = 0.421$), respectively. Clinically, this may be considered quite similar. Additionally, local haemostatic measures could control all reported bleeding and no lethal events occurred. Therefore, DAPT interruption is not advised before minor oral surgery.

Key words: dual antiplatelet therapy; minor oral surgery; bleeding; haemostatic measures.

Accepted for publication

0901-5027/000001+09

Please cite this article in press as: Ockerman A, et al. Incidence of bleeding after minor oral surgery in patients on dual antiplatelet therapy: a systematic review and meta-analysis, *Int J Oral Maxillofac Surg* (2019), https://doi.org/10.1016/j.ijom.2019.06.002

Article 35

J. Maxillofac. Oral Surg.
https://doi.org/10.1007/s12663-019-01315-9

ORIGINAL ARTICLE

Prospective Comparative Evaluation of Post-extraction Bleeding in Cardiovascular-Compromised Patients with and without Antiplatelet Medications

Archana Shenoy[1] · Prasanth Panicker[2,3] · Ajoy Vijayan[4] · Ashford Lidiya George[2]

Received: 23 September 2019 / Accepted: 30 November 2019

Abstract

Background and Objective A considerable number of patients consulting a dental surgeon are on antiplatelet therapy, and an interruption of these agents for 3 to 7 days has been practised by majority of them prior to dental surgical intervention fearing excessive bleeding, risking the patient for the occurrence of adverse thrombotic events. The dental and medical literature shows a very low risk of excessive bleeding associated on the continuation of antiplatelet therapy. The objective of this study is to compare the bleeding following single-firm molar tooth extraction in patients who interrupt and those who continue antiplatelet therapy perioperatively.

Methodology This is a prospective descriptive study on 170 patients on long-term low-dose antiplatelet therapy with 2 groups, each containing 85 patients—Group 1 with patients who interrupted antiplatelet therapy for 5 days before extraction and Group 2, patients who continued it perioperatively. A single molar tooth extraction was done under local anaesthesia with a vasoconstrictor. Gauze pressure pack was placed for 60 min. Socket was observed every 15 min for 1 h to look for excessive post-extraction bleeding.

Results No statistically significant differences were found in post-extraction bleeding between the patients who stopped antiplatelet therapy and those who continued it.

Conclusion The bleeding risk when continuing long-term low-dose antiplatelet therapy following a single molar tooth extraction is minimal. Bleeding, if excessive, can be easily controlled by gauze pressure pack or other local haemostatic agents. Thus, dental extractions can be performed on these patients without interrupting the antiplatelet drug pre-operatively provided a thorough medical history, physician's consent and coagulation profile have been obtained prior to the procedure.

Keywords Aspirin · Coronary artery disease · Tooth extraction · Thromboembolism

✉ Archana Shenoy
archana95shenoy@gmail.com

Prasanth Panicker
drprasanthpanicker555@gmail.com

Ajoy Vijayan
vjynjy@gmail.com

Ashford Lidiya George
drlidiyamaxfac@gmail.com

[1] Victoria Dental Centre, No. 201, 2nd Floor Divya Deepa Towers, Mangalore, Karnataka, India

[2] Department of Oral and Maxillofacial Surgery, Sree Anjaneya Institute of Dental Sciences, Calicut, Kerala, India

[3] Indira Gandhi Hospital, Ernakulam, Kochi, Kerala, India

[4] Department of Oral and Maxillofacial Surgery, Mahe Institute of Health Sciences, Mahé, Kerala, India

Introduction

Cardiovascular diseases are one of the primary causes of mortality and morbidity worldwide. Antiplatelet therapy is routinely used in these patients for primary and secondary prevention of adverse cardiovascular thromboembolic events like myocardial infarction, stroke and death [1]. Myocardial infarction is the most common perioperative complication in patients with coronary artery disease associated with a mortality rate of around 15 to 25% [2].

Aspirin, due to its ability to inhibit aggregation of platelets and prevent thrombosis, is by far the most extensively studied and widely used antiplatelet agent. It has been

Published online: 07 December 2019

PL Detail-Document **#270503**
–This PL Detail-Document gives subscribers additional insight related to the Recommendations published in–
PHARMACIST'S LETTER / PRESCRIBER'S LETTER
May 2011

Managing Anticoagulant and Antiplatelet Drugs Before Dental Procedures

Background

Patients taking warfarin or antiplatelet agents face an increased risk of bleeding due to dental procedures. But stopping these medications may put the patient at risk of a thrombotic event (e.g., DVT, stroke). Therefore, the risk of bleeding must be weighed against the risk and consequences of thrombosis. This article reviews recommendations for managing these medications in patients requiring a dental procedure.

Recommendations and Rationale

Warfarin or aspirin can be continued with local hemostatic measures (see below) provided the INR is less than 4 during most dental procedures.[1,2] These include crowns, bridges, root canals, simple extraction of a limited number of teeth, implants, surgical tooth removal, supragingival scaling, and gingival surgery.[3,4] These recommendations are based on studies of patients taking warfarin or low-dose aspirin undergoing simple extractions as well as oral surgery.[3] There is less data pertaining to bleeding risk with clopidogrel, prasugrel (*Effient*), or dipyridamole, either alone or with aspirin.[1,3,5] The risk of bleeding with dipyridamole/aspirin is similar to that of aspirin alone.[5] Clopidogrel and prasugrel should be handled like aspirin monotherapy (i.e., they should not be stopped).[3,5] However, patients taking clopidogrel or prasugrel (and by extension ticlopidine) plus aspirin are at higher risk of bleeding.[5] Patients taking such combinations could be considered for inpatient management by a dentist or oral surgeon familiar with these patients. Alteration of antiplatelet therapy is not recommended.[3,5] At this time, there is no data about the bleeding risk with dabigatran.

Life-threatening bleeding after dental surgery is rare.[1] The risk of thromboembolism off warfarin for as little as two days may be as high as 0.02% to 1%. The risk of death or disability due to holding warfarin is higher than the risk of death or disability due to continuing it during most dental procedures.[2]

Managing Bleeding

It is recommended that patients taking warfarin or antiplatelet agents be scheduled early in the day, and early in the week, to facilitate optimal management of both early and late re-bleeding.[3] For patients taking warfarin, the INR should be checked within 24 hours before the procedure. But within 72 hours prior is acceptable if the patient's INR is generally stable.[2] For help if the INR is out of range, get our *PL Chart, How to Manage High INRs in Warfarin Patients*.

Hemostatic measures include use of a gelatin sponge sutured within the socket, vasoconstrictor/anesthetic combinations, and atraumatic surgical techniques.[1,3] Having the patient bite down on gauze sponge/pad for 15 to 30 minutes after closure is suggested too.[3] Observe for hemostasis before the patient leaves. A thrombin solution-soaked gel sponge can be used for persistent bleeding.[6] Instruct patients to:[3,7]

- Rest for two or three hours.
- Not disturb the clot with the tongue or any object, or by sucking on straws, cigarettes, etc.
- Avoid hot foods/liquids and hard foods for the first day.
- Do not rinse for 24 hours.
- Avoid chewing on the affected side for at least a day or two.
- If bleeding starts, hold pressure with gauze or a slightly moistened tea bag (black tea) for 20 minutes, and call the dentist if it does not stop.
- Avoid NSAIDs for at least 24 hours post procedure.

In addition to these general measures, aminocaproic acid solutions have been recommended for use in warfarin-treated patients. Aminocaproic acid solution is easier to make and

More. . .

Revista Odontológica Mexicana
Facultad de Odontología
Vol. 17, No. 4 ● October-December 2013
pp 251-255
LITERATURE REVIEW

Dental treatment in patients with anti-platelet (anti-aggregating) therapy

Manejo odontológico en pacientes con terapia antiagregante plaquetaria

José A Cedeño M,* Neyla Rivas R,§ Rodolfo A Tuliano C||

ABSTRACT

Anti-platelet therapy is nowadays considered essential for those patients who are at risk to sustain strokes (cerebro-vascular events), thrombus formation, as well as in cases of coronary valvular prostheses (stents). This therapy allows prophylaxis before any possible thrombo-embolic event. Tendency to bleeding is doubtlessly one of its secondary effects. It therefore becomes relevant to be knowledgeable with consequences that might be encountered in common dental practice so as to avoid accidents and prevent post-operative bleeding (hemorrhage). The aim of the present study was to present drugs most used in this therapy, discuss their mechanism of action and to develop a defined protocol for the proper care of these patients.

RESUMEN

La terapia antiagregante plaquetaria se considera hoy en día esencial en aquellos pacientes que poseen riesgo de presentar accidentes cerebrovasculares, formación de trombos y en la colocación prótesis valvular o stents coronarios, esta permite la profilaxis ante cualquier evento tromboembólico que se pueda presentar; indiscutiblemente uno de sus efectos secundarios es la tendencia al sangrado, por lo tanto esto hace relevante conocer las consecuencias en la práctica odontológica habitual para evitar accidentes y prevenir hemorragias postoperatorias. El objetivo de este trabajo es presentar los fármacos más usados dentro de esta terapia, su mecanismo de acción y la elaboración de un protocolo definido para la atención adecuada de este tipo de pacientes.

Key words: Anti-platelet therapy, dental management.
Palabras clave: Terapia antiagregante plaquetaria, manejo odontológico.

INTRODUCTION

Hemostasis is a physiological process which consists in the combination of biochemical and cellular events which act jointly to preserve blood in a liquid state within veins and arteries. Through the mechanism of clot formation it prevents blood exit when a vessel is damaged. Hemostasis can be achieved with different mechanisms: vascular reaction, platelet response or primary hemostasis, coagulation activation and fibrinolysis. When the process is altered, significant blood loss can occur, even in very small lesions.[1]

Under physiological conditions, platelets do not interact with blood vessel walls. Nevertheless, platelet adhesion and thrombi formation can occur as response to vascular damage when the endothelium of the extracellular matrix results exposed. Platelets come into contact with exposed collagen and other adhesive proteins and this elicits a change in the platelet shape, passing from being disk-shaped to becoming spherically shaped. They thus emit pseudopods which can duplicate cellular diameter. At that point, they secrete the content of their granules, attracting thus other platelets to the damaged site to then form a primary hemostatic plug. These metabolic and morphological changes are called platelet reactions. These reactions entail adhesion, activation, degranulation and aggregation.[1]

Certain drugs interfere with normal platelet function. In recent years, indications and number of patients subjected to platelet therapy (PT) have increased. When these patients must be subjected to a surgical intervention, there is a need to discontinue PT and subject the patients to a possible risk increase to thrombo-embolic-cardiovascular complications. On the other hand, if treatment remains unaltered, the

* Professor and General Coordinator, Oral Surgery Graduate Program, School of Dentistry, Venezuela Central University, Los Chaguaramos, Av. Los Ilustres, Caracas Venezuela.
§ Public Health Ministry, Dental Section, Parroquia Altagracia, El Silencio, Caracas, Venezuela.
|| Venezuelian Institute of Social Security, Dental Section, Parroquia Altagracia, Av. Urdaneta, Caracas, Venezuela.

Environmental sustainability

The task of every good clinician is to improve the patient's health by trying to avoid unnecessary or superfluous procedures, especially if these can cause harm to the patient. This paper aims precisely to provide professionals who work in contact with patients with guidance to shed light on the usefulness of discontinuing antiplatelet drugs, and whether this can actually benefit the patient's health. The general trend in this regard is not to suspend therapy except in exceptional cases, and this work also confirms this. It is important in this field to always be up-to-date, and to train always bearing in mind the ultimate goal, that is to do what is best in order to obtain an improvement in the patient's health.