

Anti-Thrombotic Therapy: Implications for Invasive Outpatient Procedures in Dentistry

Hong CH^{1*} and Islam Intekhab²¹Discipline of Orthodontics and Pediatric Dentistry, Faculty of Dentistry, National University of Singapore, Singapore²Discipline of Oral and Maxillofacial Surgery, Faculty of Dentistry, National University of Singapore, Singapore

Abstract

This article reviews the implications of traditional and novel anti-thrombotic medications in dentistry, focusing on areas relating to the prevalence of significant post procedure bleeding, measures that should be taken to minimize and manage bleeding; and current opinions regarding need for alteration of anti-thrombotic regimens prior to dental procedures in dentistry. Based on the current literature, discontinuation of anti-platelet medications, warfarin therapy, dabigatran and Factor Xa inhibitors is not needed in majority of in office dental procedures. However, it is important that treating clinician must use discretion based on the patient's risk profile (e.g. presence of comorbidities) and extensiveness of planned dental procedures to assess each patient's risk for significant bleeding.

Keywords: Hemorrhage; Oral surgical procedures; Blood coagulation disorders

Introduction

Cardiovascular disease is the leading cause of death in the United States and is the primary cause of adult disability [1]. Given the high prevalence of this disease, it is not unexpected that there are many patients on anti-coagulant and anti-platelet medications to prevent complications from this disease. These medications are also used in a variety of other clinical settings such as in anti-phospholipid syndrome. Aside from these anti-thrombotic agents, there are other substances that can directly affect clotting and/or interact with anti-thrombotic medications; these include non-steroidal anti-inflammatory drugs (NSAIDs), selective serotonin reuptake inhibitors (SSRIs), and certain herbal and dietary supplements.

Despite, the rarity of life threatening bleeding events caused by traditional anti-thrombotic agents in the dental office, confusion persist among both dentists and physicians as to whether these medications put patients at risk for significant persistent post-operative bleeding following invasive dental procedures [2]. This article reviews the implications of traditional and newer anti-thrombotic medications in dentistry, focusing on areas relating to the prevalence of significant post procedure bleeding, measures that should be taken to minimize and manage bleeding; and current opinions regarding need for alteration of anti-thrombotic regimens prior to dental procedures in dentistry.

Anti-platelet agents

There are several classes of anti-platelet agents and they are broadly categorized based on their mechanism of action; 1. Cyclo-oxygenase inhibitors (e.g. aspirin); 2. Thienopyridines (e.g. clopidogrel); 3. Phosphodiesterase inhibitors (e.g. cilostazol, dipyridamole) and 4. Glycoprotein IIb/IIIa inhibitors. Though not considered to be in the anti-platelet category per se, NSAIDs exert a reversible inhibitory effect on platelet function and thus may pose a potential risk for bleeding complications.

Aspirin is the most ubiquitous of all the anti-platelet agents used today and expectedly the most studied. Aspirin irreversibly inhibits cyclooxygenase 1 which in turn blocks thromboxane A2 synthesis from arachidonic acid; an important agent required for platelet aggregation and blood clotting [3]. In patients who are unable to tolerate

aspirin therapy or for a variety of other reasons; thienopyridines, phosphodiesterase inhibitors and glycoprotein IIb/IIIa inhibitors may be suitable alternatives.

Since platelet function is an important component in the clotting cascade, it is not a stretch to suggest that patients on aspirin and other anti-platelet agents would be at risk for bleeding complications from invasive dental procedures. In a survey of various physician specialists (hematologists, cardiologists, internist, family/general practitioners), the authors concluded that there was no consensus among physicians as to whether aspirin should be discontinued and many physicians suggested alteration (reduction or discontinuation) of anti-thrombotic regimens before dental procedures [2]. Recent evidence contradicts this practice and recommends that alteration or discontinuation of anti-platelet medications prior to invasive dental procedures is unnecessary. Napenas et al. reviewed the literature for bleeding complications after dental procedures in patients on anti-platelet therapy and found 15 studies involving 2,428 patients who were either on aspirin, clopidogrel, cilostazol, dipyridamole, ticlopidine, and/or triflusal [4]. Based on the data reviewed, Napenas et al. concluded that although there appeared to be an increased occurrence of minor immediate postoperative bleeding, there were no clinically significant increase in the frequency and degree of intra- or late post-operative bleeding complications. For immediate post-operative bleeding, and in the rare event of prolonged post-operative bleeding, local hemostatic measures were sufficient to address the problem [4]. The dental procedures evaluated in Napenas' review included simple and surgical extractions, deep (subgingival) scaling, endodontic surgeries, small biopsies, periodontal surgery and

***Corresponding author:** Hong CH, Discipline of Orthodontics and Pediatric Dentistry, Faculty of Dentistry, National University of Singapore, 5 Lower Kent Ridge Road 119074, Singapore, Tel: +65-779-5555; Fax: +65 6773 2602; E-mail: chhong@umich.edu

Received August 03, 2013; **Accepted** October 16, 2013; **Published** October 22, 2013

Citation: Hong CH, Islam I (2013) Anti-Thrombotic Therapy: Implications for Invasive Outpatient Procedures in Dentistry. J Blood Disorders Transf 4: 166. doi: [10.4172/2155-9864.1000166](https://doi.org/10.4172/2155-9864.1000166)

Copyright: © 2013 Hong CH, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

placement of dental implants [4]. The support for continuation and maintenance of anti-platelet therapy during dental procedures is further reinforced by the widely accepted opinion that the cardioprotective benefit of anti-platelet therapy far outweighs the potential for bleeding complications [5]. Non-selective NSAIDs were not covered by Napenas et al. [4] review; however these drugs are similar to aspirin in that they inhibit cyclooxygenase 1 and 2, but unlike aspirin their effects are reversible; as such recommendations for aspirin are likely applicable to patients on non-selective NSAIDs.

Anti-coagulants

Vitamin K antagonists: Warfarin is the most frequently prescribed anti-coagulant in this group and works by inhibiting vitamin K dependent coagulation factors (i.e. factors 2,7,9,10) as well as proteins C and S. It is metabolized in the liver and excreted through the kidney, as such any substance with similar metabolism pathway can potentiate (e.g., ciprofloxacin, metronidazole, macrolide antibiotics, phenytoin, sulfamethoxazole, ginkgo biloba and ginseng) or decrease (barbiturates, carbamazepine, rifampin, thiazide diuretics) the effect of warfarin. The World Health Organization introduced the International Normalized ratio (INR) in the 1980s and since then INR has been used widely for warfarin therapy monitoring as well as by clinicians to assess the patients' potential for post-operative bleeding and the need for warfarin dose adjustment prior to a surgical procedure.

There has been an extensive volume of dental literature on warfarin and majority have concluded that the risk of clinically significant persistent bleeding post dental procedures is low (4-8%) in patients on therapeutic levels of warfarin therapy [6-8]. A meta-analysis by Nematullah et al. concluded that significant bleeding occurred in only 5.5% of patients whose warfarin therapy were not altered prior to dental procedures [9]. Based on their findings, the authors recommend that reduction or discontinuation of warfarin dose was not necessary in patients undergoing minor dental procedures [9]. In addition, any prolonged or significant bleeding in the oral cavity is easily detected and institution of local hemostatic measures is relatively straight forward [10]. Based on the current literature, guidelines recommend that in office dental procedures can be carried out for patients whose INR ≤ 4 with no other significant risk factors or comorbidities [11-15].

Standard heparin and its analogues: Standard unfractionated heparin and Low Molecular Weight Heparins (LMWH) are commonly used for the prevention of venous thromboembolism and deep vein thrombosis as well as in patients undergoing hemodialysis [16]. In recent years, the use of LMWH has become increasingly more popular than standard unfractionated heparin as they possess greater bioavailability, allow for fixed dosed administration due to their good correlation of anti-coagulant response with weight, have longer and more predictable anti-coagulant effect and have lower risk for thrombocytopenia immune mediated. Similar to standard unfractionated heparin, LMWH also inactivate factor Xa but they have a lesser effect on thrombin, as such they do not prolong activated partial thromboplastin time (aPTT) [17].

In dentistry, standard unfractionated heparin is used as a bridging therapy for warfarinized patients who are at high risk of developing thromboembolic events and who are undergoing oral surgical procedures where significant bleeding is anticipated (e.g., jaw surgery, multiple surgical extractions). This usually involves admission of patient to the hospital a few days prior to the planned procedure so that patients can be transitioned from warfarin to heparin therapy. The anti-coagulation is maintained with standard unfractionated heparin till a few hours (usually 6 hours) before surgery and resumed once hemostasis

is adequately achieved. The patient is then gradually switched back to warfarin and titrated back to their pre-surgical therapeutic levels [10]. Bridging therapy with standard unfractionated heparin has become unpopular as the same goals can now be achieved with subcutaneous LMWH injections on an outpatient basis.

At the time of the write up of this manuscript, there were only 3 studies that had reported the incidence of bleeding from the use of standard heparin or its analogues. Morimoto et al evaluated patients on continuous infusion of unfractionated heparin and found that 28.6% of extraction visits resulted in significant post dental extraction hemorrhage. The management of the bleeding episodes included one of the following measures; gauze and digital compression, hematoma removal, use of oxidized cellulose, re-suturing, electrocautery, and use of splint therapy. The only risk factor associated with post-operative hemorrhage was prolonged aPTT (i.e. 57 seconds or greater) [18]. The other study was carried out on patients receiving LMWH (enoxaparin). In this study, 3 patients (7%) presented with post-operative bleeding complications after dental procedures. However, all 3 were on LMWH and warfarin therapy concurrently. There were no bleeding episodes in patients who were only on LMWH [19]. The remaining study was by Bajkin et al. who conducted a randomized prospective trial comparing the post-extraction bleeding in patients who underwent bridging therapy with LMWH with those on oral anti-coagulation. Only 5% of LMWH patients exhibited significant post-operative bleeding on the day of the intervention; all were easily resolved with local hemostatic measures [20].

Novel Anticoagulants

Direct thrombin inhibitors: Vitamin K antagonists and standard unfractionated heparin had traditionally been the treatment of choice for the prevention of thromboembolic events; however these products have major limitations in that they either have narrow therapeutic indexes, highly variable dose responses requiring constant and frequent dose adjustments and/or are notorious for their interactions with a wide spectrum of drugs and dietary foods [21].

In 2010, dabigatran etexilate mesylate (Pradaxa®; Boehringer Ingelheim Pharma GmbH & Co.KG) was approved by the Food and Drug Administration (FDA) after trials demonstrated that its use in patients with atrial fibrillation (AF) was associated with a lower incidence of thromboembolic and bleeding events compared to warfarin [22,23]. Dabigatran directly inhibits both free and bounded thrombin and has a rapid onset of action of about 1-3 hours [24]. It is excreted via the kidneys and thus its half-life is prolonged from 12-14 hours to 18-24 hours in patients with significant renal impairment [25]. Currently, dabigatran is the only drug in its class that has been approved for use in humans.

Many have postulated that dabigatran will likely replace warfarin as it has a more predictable pharmacokinetic profile. However, dabigatran is similar to warfarin in that it also interacts with certain drug and food products, though to a lesser extent [21]. Ecarin Clotting Time (ECT) is the best method to assess bleeding risk in patients on dabigatran but this test is not readily available clinically. A comparison between PT, aPTT and thrombin time (TT) concluded that TT was the most sensitive test for detecting low levels of dabigatran but tended to be overly sensitive [26]. The lack of a definitive universal method for monitoring therapeutic levels of dabigatran is a concern; as unlike in warfarin monitoring, there is no clinically meaningful index that can be used to assess patients' risk for persistent bleeding from a surgical procedure.

To the authors' knowledge, the RELY (Randomized evaluation of Long Term Anticoagulation Therapy) trial was the only study that had evaluated bleeding risk from dental procedures in patients on dabigatran. The authors found no significant difference in peri-procedural bleeding risk in 4,591 patients treated with either warfarin or dabigatran [22]. Dental procedures were included in this analysis but the study did not provide any further details about the types of dental procedure performed.

Factor Xa inhibitors: Direct factor Xa inhibitors which as its namesake suggest act directly on factor Xa to exert their anti-coagulant effect. Currently, Rivaroxaban (Xarelto®; Janssen Pharmaceuticals, Inc.) and Apixaban (Eliquis®; Bristol Myers Squibb/Pfizer) are the only drugs approved by the FDA for use in humans. In general, medications in this class demonstrate rapid onset of action and can achieve peak anticoagulant effect within 2-4 hours of administration. Another major advantage is the negation for routine monitoring in most patients due to their relatively stable pharmacodynamics. In selected patients when monitoring is indicated, drug levels can be measured using aPTT [27].

There is currently no data in the literature on the prevalence of adverse bleeding events following dental procedures in patients on Factor Xa inhibitors; as such management of such patients in dentistry is largely based on expert opinions and extrapolation from the medical literature. Discontinuation of factor Xa inhibitor approximately two days before elective surgery without the need for bridging anti-coagulation and resumption of the medication 6 to 10 hours after surgery with attainment of adequate hemostasis have been suggested in the medical literature [28,29].

Others

Concomitant use of anti-thrombotic medications: Patients reporting the use of combination anti-thrombotic therapies (e.g. aspirin and clopidogrel) are not unusual; as it is considered to be the cornerstone of therapy after drug-eluting stent implantation [30]. Current guidelines recommend that non-emergent surgical procedures requiring cessation of anti-platelet therapy should be postponed until an appropriate duration of therapy has been completed, usually for 1 year [31]. This recommendation is based on data demonstrating that premature discontinuation of anti-platelet therapy could potentially result in devastating complications such as stent thrombosis, acute myocardial infarction and death [32]. Unfortunately, delaying treatment to after the year of mandatory dual anti-platelet therapy may not always be possible, as certain dental situations such as acute dental pain with or without swelling require immediate attention.

The risk of bleeding in patients on dual anti-platelet therapy after dental procedures has been evaluated by several groups. The largest prospective study was by Lillis et al. who compared the risk of immediate and delayed post dental extraction bleeding incidents in 643 patients who were on either aspirin or clopidogrel or a combination of both. The authors found that significantly more patients on dual anti-platelet therapy had prolonged immediate bleeding compared to patients on single anti-platelet therapy. However, all bleeding episodes were successfully controlled with local hemostatic measures [33]. In a recent comprehensive review by Napenas et al. [4]. A trend towards increased occurrence of immediate post-operative bleeding (<60 minutes) for patients on dual anti-platelet therapy (aspirin/clopidogrel, aspirin/α-tocopherol, aspirin/ ticlopidine and aspirin/cilostazol) was also observed but this was not clinically significant. Majority of the studies included in the review involved dental extractions; only 3 evaluated bleeding from other procedures e.g., periodontal procedures

including deep (subgingival) scaling and root planning (cleaning), gingival surgery [4].

Combination anti-thrombotic regimens have traditionally been limited to the aspirin/clopidogrel combination; however in recent years, combination of aspirin with newer anti-thrombotic agents and the use of triple anti-thrombotic therapy have been explored [34]. These combinations are thought to have superior anti-thrombotic protection, albeit at an increased, though not tremendously higher risk for bleeding complications. Presently, there is no data on clinically significant bleeding in dental procedures in patients on these new anti-thrombotic therapies other than those regimens covered in the review by Napenas et al. [4].

Based on our review of the literature, it appears that invasive dental procedures on patients on dual anti-thrombotic therapies are unlikely to cause bleeding that cannot be controlled by local hemostatic measures. However, for triple anti-thrombotic regimens, it is prudent to weigh the risks and benefits of modifying regimens against the bleeding potential of the planned procedure, in consultation with the physician.

Selective serotonin reuptake inhibitors (SSRIs): SSRIs inhibit the reuptake of serotonin into platelets; which is important in platelet aggregation promotion. In addition, they potentiate bleeding risk when prescribed in combination with anti-thrombotics [35,36] Of the various SSRIs, fluoxetine, paroxetine and setraline are most frequently associated with abnormal bleeding due to their potent inhibitory effect on serotonin reuptake [37-39]. The only study in the dental literature that evaluated bleeding in patients on SSRIs was by Napenas et al. [40]. This retrospective study evaluated 92 patients who were taking at least one SSRI (i.e. citalopram, escitalopram oxalate, fluoxetine, fluvoxamine maleate, paroxetine, setraline and dapoxetine) and also received an invasive dental procedure. Of 145 invasive procedure visits, there was only 1 return visit to the clinic and 1 telephone call with a chief complaint of oral bleeding. Hemostasis was easily achieved with placement of gelatin compressed sponge in the extraction socket at the follow up visit for one patient. In the other patient who made the telephone call, proper home care instructions were reinforced and this was sufficient to control the bleeding complaint [40]. To the authors' knowledge, there had only been one case of abnormal bleeding reported in the dental literature in a patient on SSRI [41]. In this report, the oral surgical procedure performed involved a wide resection of a squamous cell carcinoma in a patient whose history was also positive for chronic use of naproxen and alcohol abuse, in addition to the use of SSRI. The presence of other comorbidities (e.g., liver disease, NSAIDs use) likely compounded patient's risk for bleeding and it is unlikely that the use of SSRI alone was responsible for the bleeding episode. Based on the limited evidence, it appears that the risk of prolonged post dental procedure bleeding is low in patients who are only taking SSRI medications.

Herbal supplements: Several herbs contain substances that have coumarin, salicylate or anti-platelet properties (e.g., garlic, ginkgo

Alfafa	Evening Primrose	Green tea	Reishi
Anise	Fenugreek	Guarana	St John's wort
Bilberry	Feverfew	Guggul	Sweet clover
Bladderwrack	Garlic	Horse chestnut seed	Tumeric
Cat's Claws	Ginger	Horse radish	White willow
Celery	Ginkgo Biloba	Licorice	
Cordyceps	Ginseng	Prickly Ash	
Dong Quai	Grape Seed	Red clover	

Table 1: Herbs with anti-thrombotic properties [56].

and ginseng); some containing more than one active ingredient. In addition, some herbs namely feverfew, grapefruit, ginkgo biloba, ginger, garlic and ginseng have been frequently reported to interact with anti-thrombotic agents [42]. There has been no published study on the association between intake of herbal supplements and clinically significant oral bleeding. However, case reports and pharmacological studies suggest that ingesting herbs with anti-thrombotic drugs will likely result in over-coagulation [43-47]. Based on the current literature, it is reasonable to recommend that patients on anti-thrombotic therapy should discontinue their herbal intake prior to invasive dental procedures (Table 1).

Dental Management

The literature has unequivocally shown that patients on anti-platelet medications and warfarin therapy with INR levels ≤ 4 need not discontinue or reduce their medications for majority of in office dental

procedures. Based on the limited literature on dental procedures for patients on LMWH, it appears that the same can be applied to LMWH [10].

There are currently no definitive dental management recommendations for patients on dabigatran due to lack of data in the literature. Dabigatran's pharmacologic profile suggests that the drug need not be discontinued for most dental procedures (Table 2). However, in patients with comorbidities or in high risk dental procedures where significant bleeding is expected (e.g., facial trauma, jaw surgery or resection of head and neck tumor), dabigatran may be discontinued 24-48 hours pre-operatively (and restarted 24 hours post-operatively), in consultation with the patient's physician [48]. There is no specific reversal agent for dabigatran; however because of its short duration of action, drug withdrawal and local hemostatic measures (Table 3) are likely sufficient to reverse any excessive or prolonged bleeding associated with its use [49,50]. For life threatening bleeding, prothrombin complex

	Very Low Risk	Low Risk Procedures	Medium Risk Procedures	High Risk Procedures
GENERAL PROCEDURES	<ul style="list-style-type: none"> Examination Radiography 	<ul style="list-style-type: none"> Local anesthetic infiltration 	<ul style="list-style-type: none"> Local anesthesia nerve block 	
ORAL SURGERY		<ul style="list-style-type: none"> Simple single dental extractions Soft tissue biopsy ≤ 1 cm in size 	<ul style="list-style-type: none"> Simple extractions ≤ 5 teeth Soft tissue biopsy 1-2.5 cm in size Placement of single implants 	<ul style="list-style-type: none"> Multiple extractions > 5 teeth Surgical extractions requiring raising of periosteal flap and bone removal e.g., wisdom teeth removal Soft tissue biopsy > 2.5cm Osseous biopsy Removal of torus Placement of multiple implants
PERIODONTOLOGY	<ul style="list-style-type: none"> Periodontal Probing 	<ul style="list-style-type: none"> Superficial (supragingival) prophylaxis 	<ul style="list-style-type: none"> Ultrasonic scaling One to two quadrants (6-12 teeth) deep (subgingival) cleaning Localized gingival surgery ≤ 5 teeth 	<ul style="list-style-type: none"> Full mouth (3 or 4 quadrants) deep (subgingival) cleaning Generalized gingival surgery of >5 teeth
RESTORATIVE DENTISTRY	<ul style="list-style-type: none"> Certain orthodontic procedures e.g., wire adjustments Denture fabrication and repair 	<ul style="list-style-type: none"> Placement of rubber dam Restorations (fillings) Crown preparation Root canal therapy Prosthetic rehabilitation of implant Certain orthodontic procedures e.g. band and bracket removal, wire insertion 		<ul style="list-style-type: none"> Endodontic surgery which involve osseous manipulation

Table 2: Risk of common in office dental procedures.

	ANTI-PLATELETS	VITAMIN K ANTAGONIST	NOVEL ANTICOAGULANTS	LMWH	COMBINATION ANTI-THROMBOTIC THERAPY
LOW RISK PROCEDURES	<ul style="list-style-type: none"> No change 	<ul style="list-style-type: none"> No change 	<ul style="list-style-type: none"> No change 	<ul style="list-style-type: none"> No change 	<ul style="list-style-type: none"> No change
MEDIUM RISK PROCEDURES	<ul style="list-style-type: none"> No change Local hemostatic measures 	<ul style="list-style-type: none"> For INR ≤ 4 No change Local hemostatic measures 	<ul style="list-style-type: none"> No change Local hemostatic measures 	<ul style="list-style-type: none"> No change Local hemostatic measures 	<ul style="list-style-type: none"> Consider withdrawal of one of the drugs prior to procedure* Restart after hemostasis is achieved
HIGH RISK PROCEDURES	<ul style="list-style-type: none"> No change Local hemostatic measures 	<ul style="list-style-type: none"> For INR ≤ 3 no change For INR > 3 consider <ol style="list-style-type: none"> Low risk for thromboembolism: Withdraw drug or reduce dose to allow INR To fall High risk for thromboembolism: withhold warfarin, convert to LMWH. Withhold LMWH on the morning of the procedure 	<ul style="list-style-type: none"> Withhold 24 hours prior to procedure Local hemostatic measures Restart after hemostasis is achieved 	<ul style="list-style-type: none"> Withhold 6 hours prior to procedure Local Hemostatic measures Restart after hemostasis is achieved 	<ul style="list-style-type: none"> Withhold one of the drugs prior to procedure* Restart after hemostasis is achieved

* The decision of the number of days for drug withdrawal prior to procedure depends on the medication involved. For example, the typical recommendation for aspirin is discontinuation 3-5 days prior to planned procedure.

Table 3: Risk of procedures with regards to type of anti-thrombotic agents.

Atraumatic surgical procedure
Local pressure with gauze packs
Use of local anesthetic with adrenaline
Approximate soft tissues without dead spaces and suture
Avoid drugs that causes potentiation of anti-platelet or anti-coagulation actions
Implementation of any of the following as deemed necessary: <ol style="list-style-type: none">1. Oxidized cellulose or Gelatin sponge2. Anti-fibrinolytic topical agents e.g., 4.8% tranexamic acid mouthwash, 25% epsilon-aminocaproic acid elixir3. Topical thrombin4. Fibrin sealants and analogues

Table 4: Local hemostatic measures to be instituted routinely for patients on anti-thrombotic therapy.

concentrates (PCC) and/or fresh frozen plasma (FFP) transfusions and hemodialysis to aid renal clearance may be considered [51]. Activated charcoal has shown promise in preclinical studies but requires administration within 2 hours of taking dabigatran [49].

For Factor Xa inhibitors, most expert opinions propose that similar recommendations for dabigatran are likely applicable to this class of drugs.

The spectrum of dental procedures ranges from simple superficial (supragingival) cleaning to more extensive procedures such as deep (subgingival) cleaning and dental extractions. Furthermore, within each procedure type, the invasiveness may vary depending on the complexity of the case (Table 2). For example, the bleeding risk from an extraction of a mobile tooth is very different from the bleeding potential from an extraction of an impacted third molar (wisdom tooth). As such, we proposed a set of dental management guidelines illustrated in Table 3 with consideration on the type of in office dental procedures performed. These guidelines are strictly for patients without other comorbidities that may compound their bleeding risk e.g., multiple coagulopathies. Such patients are best managed in a hospital setting by a team of specialists.

In addition to the recommendations made in Table 3, the following should be undertaken for all patients on anti-thrombotic medications; 1. Appropriate laboratory tests at baseline and day of procedure e.g., INR, PT, aPTT; 2. Communication between the dentist and physician if alteration of anti-thrombotic therapy is necessary; 3. Institution of appropriate local hemostatic measures (Table 4) and 4. Review appointment; 2-3 days for patients on anti-platelet therapy, 5-7 days for patients on warfarin therapy and on the newer drugs such as dabigatran and Factor Xa inhibitors.

Conclusion

Discontinuation of conventional anti-thrombotic medications for most dental in-office procedures has largely been discarded with the exception of certain extenuating circumstances (e.g., multiple coagulopathies, extensive dental or oral maxillo-facial surgery). In the past, the rationale for reducing or discontinuing anti-coagulant and/or anti-platelet medications prior to an invasive dental procedure appear to stem from a handful of case reports reporting excessive bleeding post dental procedures [52-54]. A review of these cases revealed the presence of other comorbidities that could have contributed to the bleeding events. Another probable reason for the practice of altering anti-thrombotic regimens could also be attributed to the perception that prolonged bleeding from a dental procedure is similar to a general surgical procedure. The oral cavity however, differs from other sites in that persistent bleeding can be easily detected by both patients and health care providers. Furthermore, the anatomy of the oral cavity

allows the oral mucosa to be easily adapted against bone and often allows for effective hemostasis even with pressure alone. Monitoring of adequate hemostasis is also easily carried out due to the accessibility of the oral cavity. Even in situations whereby prolonged bleeding was reported, these episodes were rarely clinically significant. In a review of the literature by Wahl, the author suggests that all but 2% of bleeding events from dental surgical procedures could be controlled by local hemostatic measures [55,56].

In recent years, newer anti-thrombotic agents have been introduced to the market and many demonstrate superior pharmacokinetics with fewer drug and food interactions compared to their traditional counterparts. These are desirable properties and could potentially translate to the complete eradication for frequent coagulation monitoring and possibly even the need for bridging therapy. Despite their advantages, the lack of data with regards to risk for post procedure bleeding is still a concern amongst clinicians. Studies evaluating the risk of post-operative bleeding associated with these agents are urgently needed in dentistry such that a definitive evidence based management guideline can be developed and established.

Key Points

1. There is no need to discontinue or reduce the dose of single anti-platelet medication in majority of in office dental procedures.
2. There is no need to discontinue or reduce the dose of warfarin prior to majority of in office dental procedures for patients with INR \leq 4.
3. There is no need to discontinue or reduce the dose of dabigatran and Factor Xa inhibitors prior to majority of in office dental procedures.
4. For patients on combination anti-thrombotic therapy or with comorbidities that may potentiate bleeding, the clinician must use discretion to whether there is a need to adjust the patients anti-thrombotic regimen based on based on the patient's overall risk profile and invasiveness of planned dental procedures.
5. Local hemostatic measures with appropriate recall appointments should be instituted for all patients on anti-thrombotic medications.

References

1. Hoyert DL, Heron MP, Murphy SL, Kung HC (2006) Deaths: final data for 2003. *Natl Vital Stat Rep* 54: 1-120.
2. Wahl MJ, Howell J (1996) Altering anticoagulation therapy: a survey of physicians. *J Am Dent Assoc* 127: 625-626, 629-630, 633-634 passim.
3. George JN, Shattil SJ (1991) The clinical importance of acquired abnormalities of platelet function. *N Engl J Med* 324: 27-39.
4. Napeñas JJ, Oost FC, DeGroot A, Loven B, Hong CH, et al. (2013) Review of postoperative bleeding risk in dental patients on antiplatelet therapy. *Oral Surg Oral Med Oral Pathol Oral Radiol* 115: 491-499.
5. Antithrombotic Trialists' Collaboration (2002) Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. *BMJ* 324: 71-86.
6. Blinder D, Manor Y, Martinowitz U, Taicher S, Hashomer T (1999) Dental extractions in patients maintained on continued oral anticoagulant: comparison of local hemostatic modalities. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 88: 137-140.
7. Carter G, Goss AN, Lloyd J, Tocchetti R (2003) Current concepts of the management of dental extractions for patients taking warfarin. *Aust Dent J* 48: 89-96.
8. Zanon E, Martinelli F, Bacci C, Cordioli G, Girolami A (2003) Safety of dental extraction among consecutive patients on oral anticoagulant treatment managed using a specific dental management protocol. *Blood Coagul Fibrinolysis* 14: 27-30.

9. Nematullah A, Alabousi A, Blanas N, Douketis JD, Sutherland SE (2009) Dental surgery for patients on anticoagulant therapy with warfarin: a systematic review and meta-analysis. *Tex Dent J* 126: 1183-1193.
10. Doonquah L, Mitchell AD (2012) Oral surgery for patients on anticoagulant therapy: current thoughts on patient management. *Dent Clin North Am* 56: 25-41.
11. Karsli ED, Erdogan O, Esen E, Acarturk E (2011) Comparison of the effects of warfarin and heparin on bleeding caused by dental extraction: a clinical study. *J Oral Maxillofac Surg* 69: 2500-2507.
12. Devani P, Lavery KM, Howell CJ (1998) Dental extractions in patients on warfarin: is alteration of anticoagulant regime necessary? *Br J Oral Maxillofac Surg* 36: 107-111.
13. Campbell JH, Alvarado F, Murray RA (2000) Anticoagulation and minor oral surgery: should the anticoagulation regimen be altered? *J Oral Maxillofac Surg* 58: 131-135.
14. Salam S, Yusuf H, Milosevic A (2007) Bleeding after dental extractions in patients taking warfarin. *Br J Oral Maxillofac Surg* 45: 463-466.
15. Hong C, Napenas JJ, Brennan M, Furney S, Lockhart P (2012) Risk of postoperative bleeding after dental procedures in patients on warfarin: a retrospective study. *Oral Surg Oral Med Oral Pathol Oral Radiol* 114: 464-468.
16. Fareed J, Adiguzel C, Thethi I (2011) Differentiation of parenteral anticoagulants in the prevention and treatment of venous thromboembolism. *Thromb J* 9: 5.
17. Hirsh J, Levine MN (1992) Low molecular weight heparin. *Blood* 79: 1-17.
18. Morimoto Y, Niwa H, Minematsu K (2012) Risk factors affecting hemorrhage after tooth extraction in patients undergoing continuous infusion with unfractionated heparin. *J Oral Maxillofac Surg* 70: 521-526.
19. Hong CH, Napeñas JJ, Brennan MT, Furney SL, Lockhart PB (2010) Frequency of bleeding following invasive dental procedures in patients on low-molecular-weight heparin therapy. *J Oral Maxillofac Surg* 68: 975-979.
20. Bajkin BV, Popovic SL, Selakovic SD (2009) Randomized, prospective trial comparing bridging therapy using low-molecular-weight heparin with maintenance of oral anticoagulation during extraction of teeth. *J Oral Maxillofac Surg* 67: 990-995.
21. Little JW (2012) New oral anticoagulants: will they replace warfarin? *Oral Surg Oral Med Oral Pathol Oral Radiol* 113: 575-580.
22. Connolly SJ, Wallentin L, Ezekowitz MD, Eikelboom J, Oldgren J, et al. (2013) The Long-Term Multicenter Observational Study of Dabigatran Treatment in Patients With Atrial Fibrillation (RELY-ABLE) Study. *Circulation* 128: 237-243.
23. Schulman S, Kearon C, Kakkar AK, Schellong S, Eriksson H, et al. (2013) Extended use of dabigatran, warfarin, or placebo in venous thromboembolism. *N Engl J Med* 368: 709-718.
24. Douketis JD (2010) Pharmacologic properties of the new oral anticoagulants: a clinician-oriented review with a focus on perioperative management. *Curr Pharm Des* 16: 3436-3441.
25. Morales-Vidal S, Schneck MJ, Flaster M, Biller J (2012) Direct thrombin inhibitors and factor Xa inhibitors in patients with cerebrovascular disease. *Expert Rev Neurother* 12: 179-189.
26. Dager WE, Gosselin RC, Kitchen S, Dwyre D (2012) Dabigatran effects on the international normalized ratio, activated partial thromboplastin time, thrombin time, and fibrinogen: a multicenter, in vitro study. *Ann Pharmacother* 46: 1627-1636.
27. Eriksson BI, Quinlan DJ, Weitz JI (2009) Comparative pharmacodynamics and pharmacokinetics of oral direct thrombin and factor xa inhibitors in development. *Clin Pharmacokinet* 48: 1-22.
28. Schulman S, Crowther MA (2012) How I treat with anticoagulants in 2012: new and old anticoagulants, and when and how to switch. *Blood* 119: 3016-3023.
29. Turpie AG, Kreutz R, Llau J, Norrving B, Haas S (2012) Management consensus guidance for the use of rivaroxaban—an oral, direct factor Xa inhibitor. *Thromb Haemost* 108: 876-886.
30. Rossini R, Baroni M, Musumeci G, Gavazzi A (2013) Oral antiplatelet therapy after drug-eluting stent implantation: adherence and side-effects. *J Cardiovasc Med (Hagerstown)* 14: 81-90.
31. Grines CL, Bonow RO, Casey DE, Gardner TJ, Lockhart PB, et al. (2007) Prevention of premature discontinuation of dual antiplatelet therapy in patients with coronary artery stents: a science advisory from the American Heart Association, American College of Cardiology, Society for Cardiovascular Angiography and Interventions, American College of Surgeons, and American Dental Association, with representation from the American College of Physicians. *Circulation* 115: 813-818.
32. Rossini R, Capodanno D, Lettieri C, Musumeci G, Nijaradze T, et al. (2011) Prevalence, predictors, and long-term prognosis of premature discontinuation of oral antiplatelet therapy after drug eluting stent implantation. *Am J Cardiol* 107: 186-194.
33. Lillis T, Ziakas A, Koskinas K, Tsirlis A, Giannoglou G (2011) Safety of dental extractions during uninterrupted single or dual antiplatelet treatment. *Am J Cardiol* 108: 964-967.
34. Van de Werf F (2009) New antithrombotic agents: are they needed and what can they offer to patients with a non-ST-elevation acute coronary syndrome? *Eur Heart J* 30: 1695-1702.
35. Hackam DG, Mrkobrada M (2012) Selective serotonin reuptake inhibitors and brain hemorrhage: a meta-analysis. *Neurology* 79: 1862-1865.
36. Labos C, Dasgupta K, Nedjar H, Turecki G, Rahme E (2011) Risk of bleeding associated with combined use of selective serotonin reuptake inhibitors and antiplatelet therapy following acute myocardial infarction. *CMAJ* 183: 1835-1843.
37. Turner MS, May DB, Arthur RR, Xiong GL (2007) Clinical impact of selective serotonin reuptake inhibitors therapy with bleeding risks. *J Intern Med* 261: 205-213.
38. Weinrieb RM, Auriacombe M, Lynch KG, Lewis JD (2005) Selective serotonin re-uptake inhibitors and the risk of bleeding. *Expert Opin Drug Saf* 4: 337-344.
39. Andrade C, Sandarsh S, Chethan KB, Nagesh KS (2010) Serotonin reuptake inhibitor antidepressants and abnormal bleeding: a review for clinicians and a reconsideration of mechanisms. *J Clin Psychiatry* 71: 1565-1575.
40. Napeñas JJ, Hong CH, Kempter E, Brennan MT, Furney SL, et al. (2011) Selective serotonin reuptake inhibitors and oral bleeding complications after invasive dental treatment. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 112: 463-467.
41. Van Cann EM, Koole R (2008) Abnormal bleeding after an oral surgical procedure leading to airway compromise in a patient taking a selective serotonin reuptake inhibitor and a nonsteroidal antiinflammatory drug. *Anesthesiology* 109: 568-569.
42. Ulbricht C, Chao W, Costa D, Rusie-Seamon E, Weissner W, et al. (2008) Clinical evidence of herb-drug interactions: a systematic review by the natural standard research collaboration. *Curr Drug Metab* 9: 1063-1120.
43. Spolarich AE, Andrews L (2007) An examination of the bleeding complications associated with herbal supplements, antiplatelet and anticoagulant medications. *J Dent Hyg* 81: 67.
44. Ciocon JO, Ciocon DG, Galindo DJ (2004) Dietary supplements in primary care. Botanicals can affect surgical outcomes and follow-up. *Geriatrics* 59: 20-24.
45. Izzo AA (2012) Interactions between herbs and conventional drugs: overview of the clinical data. *Med Princ Pract* 21: 404-428.
46. Vale S (1998) Subarachnoid haemorrhage associated with Ginkgo biloba. *Lancet* 352: 36.
47. Vaes LP, Chyka PA (2000) Interactions of warfarin with garlic, ginger, ginkgo, or ginseng: nature of the evidence. *Ann Pharmacother* 34: 1478-1482.
48. Firriolo FJ, Hupp WS (2012) Beyond warfarin: the new generation of oral anticoagulants and their implications for the management of dental patients. *Oral Surg Oral Med Oral Pathol Oral Radiol* 113: 431-441.
49. van Ryn J, Stangier J, Haertter S, Liesenfeld KH, Wienen W, et al. (2010) Dabigatran etexilate—a novel, reversible, oral direct thrombin inhibitor: interpretation of coagulation assays and reversal of anticoagulant activity. *Thromb Haemost* 103: 1116-1127.
50. Pollack CV Jr (2013) Managing bleeding in anticoagulated patients in the emergency care setting. *J Emerg Med* 45: 467-477.
51. Fuster V, Ryden LE, Cannon DS, Crijns HJ, Curtis AB, et al. (2011) ACCF/AHA/HRS focused updates incorporated into the ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation: a report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. *Circulation* 123: e269-367.

52. Thomason JM, Seymour RA, Murphy P, Brigham KM, Jones P (1997) Aspirin-induced post-gingivectomy haemorrhage: a timely reminder. J Clin Periodontol 24: 136-138.
53. Lieberman BL, Kennedy MK, Lorenzo DR, Reed LJ, Adamo AK, et al. (2010) Control of life-threatening head and neck hemorrhage after dental extractions: a case report. J Oral Maxillofac Surg 68: 2311-2319.
54. Bloomer CR (2004) Excessive hemorrhage after dental extractions using low-molecular-weight heparin (Lovenox) anticoagulation therapy. J Oral Maxillofac Surg 62: 101-103.
55. Wahl MJ (1998) Dental surgery in anticoagulated patients. Arch Intern Med 158: 1610-1616.
56. Richard LW, Timothy FM, Harold LC (2005) Drug information handbook for dentistry (10thedn), Hudson: Lexi-Comp.

Citation: Hong CH, Islam I (2013) Anti-Thrombotic Therapy: Implications for Invasive Outpatient Procedures in Dentistry. J Blood Disorders Transf 4: 166. doi: [10.4172/2155-9864.1000166](https://doi.org/10.4172/2155-9864.1000166)

Submit your next manuscript and get advantages of OMICS Group submissions

Unique features:

- User friendly/feasible website-translation of your paper to 50 world's leading languages
- Audio Version of published paper
- Digital articles to share and explore

Special features:

- 250 Open Access Journals
- 20,000 editorial team
- 21 days rapid review process
- Quality and quick editorial, review and publication processing
- Indexing at PubMed (partial), Scopus, EBSCO, Index Copernicus and Google Scholar etc
- Sharing Option: Social Networking Enabled
- Authors, Reviewers and Editors rewarded with online Scientific Credits
- Better discount for your subsequent articles

Submit your manuscript at: <http://www.omicsonline.org/submission>

