

# Perspective of cardiologists on the continuation or discontinuation of antiplatelet therapy before dental treatment: a questionnaire-based study

Ruchi Banthia, MDS ▪ Pallavi Singh ▪ Priyank Banthia, MDS ▪ Rajbhan Singh, MBBS, DMD ▪ Santosh Gupta ▪ Sapna Raj

Antiplatelet and anticoagulant agents have been extensively researched and developed as potential therapies in the prevention and management of arterial and venous thrombi. These medications are associated with an increase in bleeding time and risk of intraoperative and postoperative hemorrhage in the dental office. There is some controversy regarding whether these agents should be temporarily discontinued before dental procedures. In order to gain insight into this controversy, a survey of 50

cardiologists was conducted regarding suggested guidelines for dentists in the management of patients who are taking anticoagulant medication.

Received: March 14, 2013

Accepted: June 13, 2013

Key words: antiplatelet therapy, bleeding risk, thromboembolic events, dental treatment

Platelets provide the initial hemostatic plug at the site of vascular injury. They are also involved in pathological processes and serve as an important contributor to arterial thrombosis possibly leading to myocardial infarction and cerebrovascular stroke.<sup>1</sup> Various antiplatelet and anticoagulant agents are used for the prevention and management of arterial thrombi.<sup>2</sup> The most common of these are low-dose aspirin (75-300 mg daily), clopidogrel, dipyridamole, and warfarin.<sup>3,4</sup> Antiplatelet therapy is associated with the inhibition of platelet aggregation. When platelets are inhibited, it takes longer for primary hemostasis to occur, hence bleeding time is prolonged, leading to an increased risk of intraoperative and postoperative hemorrhage during dental procedures.<sup>3,5,6</sup> Dental practitioners are encountering more and more cardiac patients taking antiplatelet medications in their routine practice. A decision needs to be made whether to temporarily discontinue antiplatelet therapy before performing any dental procedure on a patient with this medical history. The dilemma lies in the fact that although these medications increase the risk of hemorrhage during dental procedures, temporarily stopping them can put the patients at risk of thromboembolic events, such as stroke.<sup>6</sup> Therefore, a medical opinion and consent is mandatory for the management of cardiac patients in the dental office, and the risk of occurrence of thromboembolic event must be weighed against the risk of hemorrhage. Previously, discontinuation of antiplatelet therapy for either 3 or 7 days

was recommended prior to dental procedures to avoid excessive bleeding, but with increasing concern over the thromboembolic risk, this is no longer recommended.<sup>7</sup> There is a great deal of confusion and controversy among dental surgeons regarding this issue. This study sought to obtain evidence-based results by conducting a survey on 50 cardiologists with the goal of helping to resolve the controversy.

## Materials and methods

A structured questionnaire consisting of 7 questions was prepared by 2 of the study's coauthors (R. Banthia and P. Banthia). Verbal consent was obtained over the telephone from 72 cardiologists and the questionnaires were distributed by 2 different coauthors (P. Singh and R. Singh). The physicians were asked to respond in 2-3 days. The first 50 responses received were accepted for use in the study. The data was collected and the responses analyzed (Table).

## Discussion

Antiplatelet therapy agents (also known as *blood thinners*) are used mainly for the inhibition of platelet activation or aggregation. They are effective in arterial circulation where anticoagulants have little effect.<sup>7</sup> Aspirin irreversibly acetylates cyclooxygenase, inhibiting the production of thromboxane A<sub>2</sub>, resulting in decreased platelet aggregation.<sup>8</sup> Clopidogrel selectively inhibits ADP-induced platelet aggregation. Dipyridamole is an adenosine reuptake inhibitor and

phosphodiesterase inhibitor with antiplatelet and vasodilating activity.<sup>9</sup>

Most of the cardiologists surveyed use either aspirin as monotherapy, or aspirin and clopidogrel as dual therapy. Aspirin and clopidogrel have synergistic antiplatelet effects that block complementary pathways in a platelet aggregation cascade.<sup>10,11</sup>

Dipyridamole is another antiplatelet therapeutic agent. Oral antiplatelet regimens vary in different institutions, but the recommendations of the *American College of Chest Physicians* in 2006 were that aspirin (75-162 mg) should be prescribed and continued indefinitely for all patients with stable coronary artery disease (CAD), and clopidogrel in combination with aspirin is advised for all stable CAD patients with a risk profile that indicates a high likelihood of developing acute myocardial infarction.<sup>12</sup>

The effect on primary hemostasis is minimal when antiplatelet agents are used as monotherapy in patients, with no additional risk factors for impaired clotting.<sup>13</sup> The risk of bleeding may increase in combination therapy cases.<sup>14</sup> While aspirin can double the bleeding time, this may still be in normal range. Only 20%-25% of patients on aspirin were reported to have abnormal bleeding times. Burger et al observed that patients on an aspirin regimen have, on average, an increased (1.5-fold) risk of intraoperative hemorrhagic risk, without an increase in surgical morbidity and mortality.<sup>15</sup> Clopidogrel, being a more potent antiplatelet agent, can cause a 1.5 to 3-fold increase in bleeding times.<sup>16,17</sup>

**Table. Survey results**

Questions	Responses				
1. Which antiplatelet agent do you most frequently prescribe?	Ninety percent of the doctors prescribed either aspirin as a monotherapy, or aspirin and clopidogrel as a dual therapy. The remaining 10% used other antiplatelet agents such as dipyridole.				
2. Do you recommend stopping antiplatelet therapy before dental procedures?	<table border="0"> <tr> <td style="vertical-align: top;"> <b>A. Before minor dental procedures (such as scaling and extractions)?</b>                      Eighty percent of the doctors were in favor of not stopping the antiplatelet therapy before minor dental procedures. Twenty percent recommended the discontinuation of antiplatelet therapy.                 </td> <td style="vertical-align: top;"> <b>B. Before surgical procedures?</b>                      All the doctors were in favor of stopping antiplatelet therapy before surgical procedures.                 </td> <td style="vertical-align: top;"> <b>C. If 'yes', why?</b>                      Discontinuation of antiplatelet therapy was recommended to avoid the risk of postoperative and intraoperative bleeding and risk of haemorrhage.                 </td> <td style="vertical-align: top;"> <b>D. If 'yes', for how many days?</b>                      Sixty percent of the doctors were in favor of stopping antiplatelet therapy 5 days prior to the dental procedure. Thirty percent recommended the discontinuation of antiplatelet therapy 7 days prior to the procedure. Ten percent recommended discontinuation starting 3 days prior, and continuing 2 days postoperatively.                 </td> </tr> </table>	<b>A. Before minor dental procedures (such as scaling and extractions)?</b> Eighty percent of the doctors were in favor of not stopping the antiplatelet therapy before minor dental procedures. Twenty percent recommended the discontinuation of antiplatelet therapy.	<b>B. Before surgical procedures?</b> All the doctors were in favor of stopping antiplatelet therapy before surgical procedures.	<b>C. If 'yes', why?</b> Discontinuation of antiplatelet therapy was recommended to avoid the risk of postoperative and intraoperative bleeding and risk of haemorrhage.	<b>D. If 'yes', for how many days?</b> Sixty percent of the doctors were in favor of stopping antiplatelet therapy 5 days prior to the dental procedure. Thirty percent recommended the discontinuation of antiplatelet therapy 7 days prior to the procedure. Ten percent recommended discontinuation starting 3 days prior, and continuing 2 days postoperatively.
<b>A. Before minor dental procedures (such as scaling and extractions)?</b> Eighty percent of the doctors were in favor of not stopping the antiplatelet therapy before minor dental procedures. Twenty percent recommended the discontinuation of antiplatelet therapy.	<b>B. Before surgical procedures?</b> All the doctors were in favor of stopping antiplatelet therapy before surgical procedures.	<b>C. If 'yes', why?</b> Discontinuation of antiplatelet therapy was recommended to avoid the risk of postoperative and intraoperative bleeding and risk of haemorrhage.	<b>D. If 'yes', for how many days?</b> Sixty percent of the doctors were in favor of stopping antiplatelet therapy 5 days prior to the dental procedure. Thirty percent recommended the discontinuation of antiplatelet therapy 7 days prior to the procedure. Ten percent recommended discontinuation starting 3 days prior, and continuing 2 days postoperatively.		
3. On which criteria did you base your decision to continue or discontinue the antiplatelet therapy?	Fifty percent of the doctors based their decision on both clinical experience and evidence-based research. Twenty-five percent of the doctors based their decision solely on evidence-based research, and 25% based their decisions predominantly on their clinical experience.				
4. When 'written medical consent' is required by a dental practitioner, what protocol do you follow?	<table border="0"> <tr> <td style="vertical-align: top;"> <b>A. What investigations do you recommend?</b>                      All of the doctors recommend bleeding time, clotting time, ECG, routine investigations, and blood sugar level tests. Ten percent of the doctors request a chest X-ray and an international normalized ratio (INR) blood test, as well.                 </td> <td style="vertical-align: top;"> <b>B. Do you advise an INR?</b>                      Ten percent of the doctors advised INR routinely; 90% advised it only when the patient is on an oral anticoagulant, such as low molecular weight heparin or warfarin.                 </td> <td style="vertical-align: top;"> <b>C. Do you have printed consent forms in your clinic?</b>                      Eighty percent of the doctors did not have printed consent forms.                 </td> </tr> </table>	<b>A. What investigations do you recommend?</b> All of the doctors recommend bleeding time, clotting time, ECG, routine investigations, and blood sugar level tests. Ten percent of the doctors request a chest X-ray and an international normalized ratio (INR) blood test, as well.	<b>B. Do you advise an INR?</b> Ten percent of the doctors advised INR routinely; 90% advised it only when the patient is on an oral anticoagulant, such as low molecular weight heparin or warfarin.	<b>C. Do you have printed consent forms in your clinic?</b> Eighty percent of the doctors did not have printed consent forms.	
<b>A. What investigations do you recommend?</b> All of the doctors recommend bleeding time, clotting time, ECG, routine investigations, and blood sugar level tests. Ten percent of the doctors request a chest X-ray and an international normalized ratio (INR) blood test, as well.	<b>B. Do you advise an INR?</b> Ten percent of the doctors advised INR routinely; 90% advised it only when the patient is on an oral anticoagulant, such as low molecular weight heparin or warfarin.	<b>C. Do you have printed consent forms in your clinic?</b> Eighty percent of the doctors did not have printed consent forms.			
5. Have you ever been consulted for a bleeding episode—in a patient on antiplatelet therapy—by a dental office?	Five percent of the doctors had been consulted for the management of 1 or 2 bleeding episodes.				
6. How many episodes of thromboembolic events have been reported to you in cases where discontinuation of antiplatelet therapy was recommended?	All of the doctors encountered 1 or 2 cases of thromboembolic events after discontinuation of antiplatelet therapy.				
7. What is your final recommendation?	All of the doctors recommended discontinuation of the antiplatelet therapy before surgical procedures. Eighty percent recommended continuation of antiplatelet therapy before minor dental procedures, while 20% advised discontinuation of these agents before minor procedures.				

Eighty percent of the cardiologists surveyed were not in favor of discontinuing antiplatelet therapy before minor dental procedures. However, all of the doctors surveyed were in favor of stopping antiplatelet therapy for surgical procedures. This discontinuation was recommended to avoid the risk of postoperative and intraoperative bleeding.

Ardekian et al investigated the effect of aspirin on the hemorrhagic risk in patients undergoing dental extractions.<sup>18</sup> None of the patients reported any episode of uncontrolled bleeding immediately after the procedure or in the following week.<sup>18</sup> Intraoperative bleeding was managed either by suturing, gauze packs, and/or use of tranexamic acid in local packing.<sup>18</sup>

The pharmacological actions of clopidogrel and dipyridamole suggest that patients taking these medications will be at no greater risk of excessive bleeding than those taking aspirin. While clopidogrel has shown an increased bleeding time compared to aspirin, it has proved to be clinically more potent; and it has been established that there is no risk of

excessive bleeding when using clopidogrel during dental procedures.<sup>15-19</sup> If a patient is on a dual therapy of aspirin and clopidogrel, it is recommended that the dental procedure be performed in a hospital setting, in order to more proactively manage any severe bleeding episode, as such patients are at a higher risk of hemorrhage. Patients with underlying hepatic, renal, or bone marrow disorders often have disease-related bleeding disorders. Bleeding risk also increases with age and with heavy alcohol consumption.<sup>4</sup>

Sixty percent of the cardiologists surveyed were in favor of stopping antiplatelet therapy 5 days prior to the dental procedure. Thirty percent recommended the discontinuation of antiplatelet therapy 7 days prior to the procedures. Ten percent recommended discontinuation starting 3 days prior, continuing 2 days postoperative.

All patients on antiplatelet therapy may have drug-induced alterations of platelets, the degree of which varies from person to person. Aspirin irreversibly inhibits platelet aggregation within 1 hour of ingestion, and clopidogrel does so within 2 hours. This inhibition lasts for the lifetime of platelets, approximately 7-10 days. This effect is only overcome by the production of new platelets.<sup>20</sup> Complete recovery of platelet aggregation may occur in 50% of cases by Day 3, and in 80% of cases by Day 4 postoperative.<sup>21</sup> Ferrari et al concluded that when aspirin (either 75 or 300 mg) was stopped in healthy patients after 2 weeks of therapy, all bleeding times returned to normal after 6 days.<sup>22</sup> The action of dipyridamole is reversible and ceases about 24 hours after the drug is discontinued.<sup>16</sup>

Only 5% of the medical practitioners surveyed had been consulted for the management of 1 or 2 bleeding episodes. Lockhart et al suggested that postoperative bleeding is considered significant if the bleeding continues beyond 12 hours, causes the patient to call or return to the dental office or emergency department, results in the development of a large hematoma or ecchymosis within oral soft tissues, or requires a blood transfusion.<sup>23</sup>

Life-threatening bleeding after dental surgery is rare.<sup>24</sup> According to Matocha, the incidence of postextraction hemorrhagic complications is 0.2%-2.3%.<sup>25</sup> McGaul reported a case of sublingual hematoma in mandibular anterior teeth

following periodontal flap surgery in a patient on long-term antiplatelet therapy which resolved on its own.<sup>26</sup> Thomason et al reported severe bleeding following a gingivectomy in a patient taking 150 mg aspirin qd, which was resolved by platelet transfusion.<sup>27</sup>

Napenas et al found no differences in hemorrhages following dental treatments such as extractions, periodontal surgery, subgingival scaling, and root planing between patients receiving single or dual antiplatelet therapy.<sup>28</sup> In a study by Partridge et al, the amount of blood loss was found to be similar in patients on antiplatelet therapy and healthy patients (controls) during dentoalveolar surgery.<sup>29</sup> The Antiplatelet Trialists' Collaboration concluded that long-term antiplatelet therapy caused reductions in mortality, relative risk of myocardial attack, and cerebrovascular incidents; with only a mild (0.12%) increase of spontaneous hemorrhage risk.<sup>30</sup>

All the doctors surveyed who had been asked for consent before dental therapy on their patients with antiplatelet regimens recommended bleeding time, clotting time, ECG, routine investigations, blood sugar level, and blood pressure tests. Only 10% of the doctors advised chest X-rays, and only 10% advised an International Normalized Ratio (INR) in order to know the status of coagulation. An INR is advised for all patients on warfarin or heparin therapy.<sup>31</sup>

Although there is no suitable test to assess the increased risk of bleeding in patients taking antiplatelet therapy, platelet function is normally assessed using the cutaneous bleeding time test. In a normal healthy patient, bleeding time ranges from 2 to 10 minutes.<sup>32</sup> Prothrombin time (PT) and partial thromboplastin time have been used to evaluate anticoagulant levels. The INR was introduced in 1983 by the World Health Organization Committee on Biological Standards, who defined the INR as the ratio of the patient's PT to a control PT, raised to the power of the International Sensitivity Index (ISI).<sup>33</sup>

The INR is a more reliable and sensitive test for determining the level of anticoagulation as it depends on both the patient's blood and the sensitivity of the assigned ISI value. The PT alone would not be an accurate gauge in the evaluation of a patient's anticoagulant status. A patient

with a normal coagulation profile would have an INR of 1. It is recommended that a patient undergoing invasive treatment should have a PT 1.5-2.0 times the normal value (INR = 1.5-2.5 when the ISI is 1).<sup>33</sup> In patients on antiplatelet therapy, the recommended INR is 2.0-3.0 for most procedures. This range of INR (2.0-3.0, average 2.5) minimizes the risk of both hemorrhage and thromboembolic events.<sup>34</sup> Nevertheless, minor surgical dental procedures can safely be performed with an INR between 2 and 4, while being aware that local measures may be needed to control bleeding.<sup>6</sup> In patients on warfarin and heparin, the INR should be checked within 24 hours prior to the procedure.<sup>31</sup>

A correlation between bleeding time test results and the rate of surgical bleeding complications has not been established.<sup>35</sup> Shalom & Wong concluded that cutaneous bleeding tests should not be used to estimate the hemorrhagic risk in patients on anticoagulant therapy.<sup>36</sup> Of the doctors surveyed, all reported 1 or 2 cases of thromboembolic events after discontinuation of antiplatelet therapy.

Thromboembolic events following the cessation of antiplatelet medications have also been reported in the literature. One retrospective analysis study reported that out of 475 patients admitted with myocardial infarction, 11 (2.3%) had discontinued aspirin within 15 days prior to the attack.<sup>37</sup> Nine patients discontinued aspirin due to a planned procedure, 1 of which was a dental procedure.<sup>37</sup> Another study by the same author reported that 5% of the patients who were admitted for acute coronary syndrome had admitted they had stopped using oral anticoagulant agents, and the authors concluded that a rebound effect occurs after an interruption of oral antiplatelet medication.<sup>38</sup> In a study by Ferrari et al, the mean delay time between aspirin withdrawal and an acute coronary event was  $10 \pm 1.9$  days (range 4-17 days); and 13 of the patients (25.5%) who discontinued their aspirin medication did so prior to dental treatment.<sup>22</sup> Maulaz et al reported the mean interval between treatment disruption and cerebral infarction was  $9.5 \pm 7$  days.<sup>39</sup> Kovich & Otley estimated that the risk of thromboembolic events associated with the withdrawal of aspirin 3-14 days prior to cutaneous surgery was approximately 0.005%.<sup>40</sup>

## Management of patients on antiplatelet therapy in a dental office

According to Scully & Wolff, oral surgical procedures must be done at the beginning of the day, as it allows more time to deal with any bleeding episode.<sup>41</sup> Procedures should also be performed early in the week so that prompt management of any delayed bleeding can be done.

Local anaesthetic containing a vasoconstrictor should be administered. Field blocks are contraindicated. If no alternative exists, local anaesthetic should be administered cautiously with repeated aspiration.<sup>42,43</sup>

Atraumatic and careful manipulation of tissues is recommended. Bleeding should be stopped by local measures, such as use of pressure packs for 15-30 minutes, packing of sockets with absorbable hemostatic dressings (oxidised cellulose, haemocollagen, or resorbable gelatin sponge), and suturing.<sup>42,43</sup>

The use of aspirin leads to increased bleeding time. If it increases to >20 minutes and surgery has to be performed as an emergency procedure, 1-desamino-8-D-arginine vasopressin can be used to shorten the bleeding time.<sup>44</sup> This involves the enhancement of Von Willebrand's factor which in turn acts as a platelet aggregant. It can be used at a dose of 0.3 µg/kg of body weight—not exceeding 20-24 µg—or as a nasal spray. This should be administered under a physician's guidance as this can cause drug-induced thrombosis in older subjects.<sup>8</sup>

Paracetamol is the painkiller drug of choice for patients on antiplatelet therapy. Nonsteroidal anti-inflammatory drugs (NSAIDs) are avoided, as they carry the potential risk of increasing bleeding time by having a reversible effect on platelet aggregation and function.<sup>4</sup> To ensure the absence of any antiplatelet effect, NSAIDs should be discontinued 5 half-lives before the procedure.<sup>45</sup>

Scully & Cawson developed the following list of instructions to be given to patients for the management of a clot in the postoperative period.<sup>46</sup>

- Rest until the local anesthetic wears off and the clot forms (2-3 hours).
- Avoid rinsing the mouth for 24 hours.
- Do not suck forcefully or disturb the socket with the tongue or any foreign objects.
- Avoid hot liquids and hard foods for the first day.

- Avoid chewing on the affected side until it is clear that a stable clot has formed.
- Apply pressure over the socket using a folded clean handkerchief or gauze pad for 20 minutes if bleeding continues or restarts. If bleeding does not stop, consultation with the dentist is advised.<sup>46</sup>

Patients with the following medical problems taking antiplatelet medications should not be treated in primary care without medical advice or should be referred to a hospital-based dental clinic: liver impairment and/or alcoholism; renal failure; hemostasis disorders; and patients currently receiving cytotoxic medication or dual antiplatelet therapy.<sup>42,43,47</sup>

A consensus opinion from *American Heart Association, American College of Cardiology, Society for Cardiovascular Angiography and Interventions, American College of Surgeons, and American Dental Association* recommended continuing aspirin and clopidogrel therapy for minor dental surgical procedures in patients who have coronary artery stents, or delaying the treatment until the prescribed regimen is completed.<sup>48</sup> When >3 teeth need to be extracted, multiple visits are required. Scaling and gingival surgery should initially be restricted to a limited area.<sup>49</sup>

When a definite increase in intraoperative bleeding is anticipated, or when surgical hemostasis could possibly be difficult, aspirin can be replaced for a 10-day period by a shorter-acting NSAID regimen, interrupted the day before surgery. Postoperative antiplatelet therapy should be resumed immediately after surgery (first 6 hours).<sup>49</sup>

Medical consent is mandatory in cardiac patients taking antiplatelet therapy in order to know the exact medical condition of the patient and to prevent any unwanted sequelae. Properly structured consent forms should be mandatory. Eighty percent of the cardiologists surveyed did not have printed consent forms.

## Conclusion

The Hippocratic oath states, "First do no harm." This must be considered immediately when deciding whether or not to temporarily discontinue antiplatelet therapy before dental treatment. Careful appraisal of the type of procedure, vascular status of the patient, and chances of

complications—along with a risk-benefit analysis—should be undertaken in consultation with a cardiologist to ensure the complete well-being of the patient. The dental surgeon and physician should exercise judgment based on their skill, experience, and the facilities at their disposal so as to provide the best postoperative care to the patient. Fifty percent of the doctors surveyed in this study based their decisions on whether to temporarily discontinue antiplatelet therapy before a dental procedure on both clinical experience and evidence-based research; 25% percent based their decisions solely on evidence-based research; and the remaining 25% based their decisions predominantly on their clinical experience.

Clinical experience is a critical tool in the successful management of patients, but in today's world of ethical and lawful guidelines, clinical decisions need also to be based on evidence-based research.

## Author information

Dr. R. Banthia is a professor, Department of Periodontics, Modern Dental College & Research Centre, Indore, India, where P. Singh, Gupta, and Rajee are postgraduate students. Dr. P. Banthia is a professor and head, Department of Periodontics, Inderprastha Dental College, Ghaziabad, India. Dr. R. Singh is a medical officer, Employees' State Insurance Corporation (ESIC) Hospital, Indore, India.

## References

1. Bristol Laboratories Ltd. *Dispersible Aspirin Tablets BP 75mg* [product description]. Available at: <http://www.mhra.gov.uk/home/groups/l-unit1/documents/websites-resources/con2023488.pdf>. Accessed August 20, 2014.
2. Owens CD, Belkin M. Thrombosis and coagulation: operative management of the anticoagulated patient. *Surg Clin North Am.* 2005;85(6):1179-1189.
3. University of Dundee. *Surgical Management of the Primary Care Dental Patient on Antiplatelet Medication*. Available at: <http://www.app.dundee.ac.uk/tuith/Static/info/antiplatelet.pdf>. Accessed August 20, 2014.
4. Dogne JM, de Leval X, Benoit P, Delarge J, Masereel B, David JL. Recent advances in antiplatelet agents. *Curr Med Chem.* 2002;9(5):577-589.
5. Pototski M, Amenabar JM. Dental management of patients receiving anticoagulation or antiplatelet treatment. *J Oral Sci.* 2007;49(4):253-258.
6. Pharmacist's Letter. *Managing Anticoagulant and Antiplatelet Drugs Before Dental Procedures*. Available at: [http://drkney.com/pdfs/dentist\\_anticoag\\_0511.pdf](http://drkney.com/pdfs/dentist_anticoag_0511.pdf). Accessed August 20, 2014.
7. Jaya Kumar A, Kumari MM, Arora N, Haritha A. Is antiplatelet therapy interruption a real clinical issue? Its

- implications in dentistry and particularly in periodontics. *J Ind Soc Periodontol.* 2009;13(3):121-125.
8. Merritt JC, Bhatt DL. The efficacy and safety of perioperative antiplatelet therapy. *J Thromb Thrombolysis.* 2002;13(2):97-103.
  9. Sweetman SC, ed. *Martindale: The Complete Drug Reference.* 34th ed. London: Pharmaceutical Press; 2013.
  10. Harder S, Klinkhardt U, Alvarez JM. Avoidance of bleeding during surgery in patients receiving anticoagulant and/or antiplatelet therapy. Pharmacokinetic and pharmacodynamic considerations. *Clin Pharmacokinet.* 2004;43(14):963-981.
  11. Alam M, Goldberg LH. Serious adverse vascular events associated with perioperative interruption of antiplatelet and anticoagulant therapy. *Dermatol Surg.* 2002;28(11):992-998; discussion 998.
  12. Collet JP, Montalescot G. Premature withdrawal and alternative therapies to dual oral antiplatelet therapy. *Eur Heart J.* 2006;8:G46-G52.
  13. Mielke CH Jr. Aspirin prolongation of the template bleeding time: influence of venostasis and direction of incision. *Blood.* 1982;60(5):1139-1142.
  14. Lecompte T, Hardy JF. Antiplatelet agents and perioperative bleeding. *Can J Anaesth.* 2006;53(6 Suppl): S103-S112.
  15. Burger W, Chemnitus JM, Kneissl GD, Rucker G. Low-dose aspirin for secondary cardiovascular prevention - cardiovascular risks after its perioperative withdrawal versus bleeding risks with its continuation - review and meta-analysis. *J Intern Med.* 2005;257(5):399-414.
  16. Lenz TL, Hilleman DE. Aggrenox: a fixed-dose combination of aspirin and dipyridamole. *Ann Pharmacother.* 2000;34(11):1283-1290.
  17. Wahl MJ. Myths of dental surgery in patients receiving anticoagulant therapy. *J Am Dent Assoc.* 2000;131(1): 77-81.
  18. Ardekian L, Gasper R, Peled M, Brenner B, Laufer D. Does low-dose aspirin therapy complicate oral surgical procedures? *J Am Dent Assoc.* 2000;131(3):331-335.
  19. Little JW, Miller CS, Henry RG, McIntosh BA. Anti-thrombotic agents: implications in dentistry. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2002;93(5): 544-551.
  20. Schafer AI. Effects of nonsteroidal antiinflammatory drugs on platelet function and systemic hemostasis. *J Clin Pharmacol.* 1995;35(3):209-219.
  21. Cahill RA, McGreat GT, Crowe BH, et al. Duration of increased bleeding tendency after cessation of aspirin therapy. *J Am Coll Surg.* 2005;200(4): 564-573, quiz A59-A61.
  22. Ferrari E, Benhamou M, Cerboni P, Marcel B. Coronary syndromes following aspirin withdrawal: a special risk for late stent thrombosis. *J Am Coll Cardiol.* 2005; 45(3):456-459.
  23. Lockhart PB, Gibson J, Pond SH, Leitch J. Dental management considerations for the patient with an acquired coagulopathy. Part 1: coagulopathies from systemic disease. *Br Dent J.* 2003;195(8):439-445.
  24. Jeske AH, Suchko GD, ADA Council on Scientific Affairs and Division of Science. Lack of a scientific basis for routine discontinuation of oral anticoagulation therapy before dental treatment. *J Am Dental Assoc.* 2003; 134(11):1492-1497.
  25. Matocha DL. Postsurgical complications. *Emerg Med Clin North Am.* 2000;18(3):549-564.
  26. McGaul T. Postoperative bleeding caused by aspirin. *J Dent.* 1978;6(3):207-209.
  27. Thomason JM, Seymour RA, Murphy P, Brigham KM, Jones P. Aspirin-induced post-gingivectomy haemorrhage: a timely reminder. *J Clin Periodontol.* 1999; 24(2):136-138.
  28. Napenas JJ, Hong CH, Brennan MT, Furney SL, Fox PC, Lockhart PB. The frequency of bleeding complications after invasive dental treatment in patients receiving single and dual anti-platelet therapy. *J Am Dent Assoc.* 2009;140(6):690-695.
  29. Partridge CG, Campbell JH, Alvarado F. The effect of platelet-altering medications on bleeding from minor oral surgery procedures. *J Oral Maxillofac Surg.* 2008; 66(1):93-97.
  30. Antiplatelet Trialists' Collaboration. Collaborative overview of randomized trials of antiplatelet therapy—I: prevention of death, myocardial infarction and stroke by prolonged antiplatelet therapy in various categories of patients. *Br Med J.* 1994;308(6921):81-106.
  31. University of Dundee. *Surgical Management of the Primary Care Dental Patient on Warfarin.* Available at: <http://www.app.dundee.ac.uk/tuith/Static/info/warfarin.pdf>. Accessed August 20, 2014.
  32. Guyton AC, Hall JE. Hemostasis and blood coagulation. In: *Guyton and Hall Textbook of Medical Physiology.* 11th ed. New York: Saunders Elsevier; 2006: 457-468.
  33. Hirsh J, Poller L. The international normalised ratio. A guide to understanding and correcting its problems. *Arch Intern Med.* 1994;154(3):282-288.
  34. Hirsh J, Dalen J, Anderson DR, et al. Oral anticoagulants: mechanism of action, clinical effectiveness, and optimal therapeutic range. *Chest.* 2001;119(1 Suppl): 8S-21S.
  35. Samama CM et al. Antiplatelet agents in the perioperative period: expert recommendations of the French Society of Anesthesiology and Intensive Care (SFAR) 2001—summary statement. *Can J Anaesth.* 2002; 49(6):S26-S35.
  36. Shalom A, Wong L. Outcome of aspirin use during excision of cutaneous lesions. *Ann Plast Surg.* 2003; 50(3):296-298.
  37. Collet JP, Himbert D, Steg PG. Myocardial infarction after aspirin cessation in stable coronary artery disease patients. *Int J Cardiol.* 2000;76(2-3):257-258.
  38. Collet JP, Montalescot G, Blanchet B, et al. Impact of prior use or recent withdrawal of oral antiplatelet agents on acute coronary syndromes. *Circulation.* 2004;110(16):2361-2367.
  39. Maulaz AB, Bezerra DC, Michel P, Bogousslavsky J. Effect of discontinuing aspirin therapy on the risk of brain ischemic stroke. *Arch Neurol.* 2005;62(8):1217-1220.
  40. Kovich O, Otley CC. Thrombotic complications related to discontinuation of warfarin and aspirin therapy perioperatively for cutaneous operation. *J Am Acad Dermatol.* 2003;48(2):233-237.
  41. Scully C, Wolff A. Oral surgery in patients on anticoagulant therapy. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2002;94(1):57-64.
  42. Lockhart PB, Gibson J, Pond SH, Leitch J. Dental management considerations for the patient with an acquired coagulopathy. Part 1: coagulopathies from systemic disease. *Br Dent J.* 2003;195:439-445.
  43. Pototski M, Amenabar JM. Dental management of patients receiving anticoagulation or antiplatelet treatment. *J Oral Sci.* 2007;49(4):253-258.
  44. Little JW, Miller CS, Henry RG, McIntosh BA. Anti-thrombotic agents: implications in dentistry. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2002;93(5): 544-551.
  45. Douketis JD, Berger PB, Dunn AS, et al. The perioperative management of antithrombotic therapy: *American College of Chest Physicians Evidence-Based Clinical Practice Guidelines* (8th Edition). *Chest.* 2008;133(6 Suppl):299S-339S.
  46. Scully C, Cawson RA. *Medical Problems in Dentistry.* 4th ed. Oxford: Wright Butterworth-Heinemann; 1998: 49-100.
  47. Daniel NG, Goulet J, Bergeron M, Paquin R and Landry PE. Antiplatelet drugs: is there a surgical risk? *J Can Dent Assoc.* 2002;68(11):683-687.
  48. Grines CL, Bonow RO, Casey DE, Jr, et al. 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. *J Am Dent Assoc.* 2007;138(5):652-655.
  49. Brennan MT, Wynn RL, Miller CS. Aspirin and bleeding in dentistry: an update and recommendations. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2007;104(3):316-323.