

A Clinical Appraisal of Post-operative Bleeding in Routine Extractions in Patients on Uninterrupted Low-dose Aspirin Therapy- An in Vivo Study

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Abstract

Antiplatelet drugs are recommended globally for long term prevention of serious vascular events in high risk patients. Temporary withdrawal of these drugs seems to be an attractive option in dental office prior to minor surgical procedures to prevent a bleeding hazard. The benefit of averting anti-platelet drug induced hemorrhage needs to be balanced against the risk of potentially fatal thrombosis that may occur due to rebound phenomenon after withdrawal of the anti-platelet drug. This in-vivo prospective study was thus designed to assess post-operative bleeding in patients on aspirin therapy after extractions. The study sample comprised of 50 patients between 50 to 75 years of age on long term aspirin therapy requiring extractions were assessed for bleeding at 30 mins, 1, 2, 3, 24 and 48 hours post operatively. Results showed 4 patients had mild bleeding at 30 mins, 2 patients at 1hour, 1 patient at 2 hours and no patients with bleeding at 3 hours. In our study we had an 8% risk of bleeding after extractions in patients on long term low dose aspirin therapy. Given the low incidence and severity of bleeding which can be easily managed by local measures only, we conclude that patients need not discontinue taking aspirin prior to dental extractions.

Keywords: Acetylsalicylic acid, tooth extraction, exodontia, post-operative bleeding.

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INTRODUCTION

Advances in science and technology have contributed to ease the workload on mankind. Present day sedentary and physically inactive lifestyles, combined with poorly executed diets and habits like smoking precipitate lifestyle related diseases amongst which hypertension and cardiovascular diseases are most common.

Atherosclerotic plaques build up along the lining of blood vessels over many years in response to injury caused by high blood pressure, abnormal blood sugar levels, high blood cholesterol levels and toxins contained in tobacco [1-3]. Lipid-rich atherosclerotic plaques are vulnerable and their rupture can cause the formation of a platelet and fibrin-rich thrombus leading to myocardial infarction or a cerebrovascular accident [4].

In normal physiologic state a dynamic equilibrium exists between coagulation-anticoagulation

and fibrinolysis- antifibrinolysis. Disturbance in this equilibrium with shift favouring any of the mechanism will result in either bleeding or thrombosis [5].

Medical science has always been in a state of flux and with increasing research, newer medicines are being discovered to combat disease, thus increasing the lifespan of human beings. Antiplatelet agents like aspirin, clopidogrel, ticlopidine, cilostazol, dipyridamole, ticagrelor and prasugrel have been extensively researched and are used routinely for the prevention of arterial thrombosis in patients with conditions such as ischemic heart disease, prosthetic heart valves and coronary artery stents as well as those at risk of experiencing ischemic cerebrovascular accidents [6-8].

Although antiplatelet drugs are extensively used in cardiovascular diseases, it also increases the potential risk of bleeding particularly when performing minor surgical procedure like dental extraction [9]. The

fear of uncontrolled or excessive bleeding prompts clinicians to stop or alter these drugs before surgical procedures [10-12]. Stopping antiplatelet therapy may expose patients to the risk of thromboembolism, myocardial infarction or cerebrovascular accidents [13-26]. However, considerable debate has been generated with regard to balancing the risk of a post-surgical hemorrhage with that of precipitating a thromboembolic event [27].

Temporary withdrawal of anti-platelet therapy therefore seems an attractive option in dental office wherein minor surgical procedure may pose a bleeding hazard. However, the benefit of averting anti-platelet drug induced hemorrhage needs to be balanced against the risk of potentially fatal thrombosis that may occur due to rebound phenomenon after anti-platelet drug withdrawal [28-32]. Thus the following study was conducted to evaluate the bleeding following dental extraction in patients who are on long term low dose aspirin therapy.

MATERIALS AND METHODS

Our study was approved by the Institutional Ethics Committee of our Institute. We followed the World Declaration Guidelines of Helsinki. 50 patients referred to our Department of Oral and Maxillofacial Surgery indicated for extraction of teeth between the age group of 50 -75 years on long term aspirin therapy (75 mg – 150 mg per day) were selected for the study. A written informed consent was obtained from all the study participants.

Patients, with teeth in the area having local infection, systemic conditions like liver or kidney disease and acquired or congenital bleeding disorders with a potential for bleeding, history of gastrointestinal bleeding or intracranial hemorrhage, undergoing vascular surgery, on anticoagulant therapy like warfarin, heparin, enoxaparin, allergic to lignocaine or any local anesthetics, diabetes mellitus, bone marrow disorders and pregnancy were excluded from the study.

All the patients were evaluated at 30 minutes, 1 hour, 2 hours, 3 hours after extractions for bleeding in our Department of Oral and Maxillofacial Surgery. On discharge from the clinic these patients were followed up telephonically. They were also recalled back to the clinic 24 hours and 48 hours post-operatively for follow up.

To record the intra-oral bleeding, the extraction site was observed without gauze piece in situ. At the end of 30 minutes and onwards any bleeding that extended beyond the crest of the socket (i.e., onto surrounding gingival tissues) during an observation period of 1 min was considered as bleeding present. The bleeding record was maintained using the following bleeding score.

SCORING PATTERN FOR BLEEDING SCORE

Bleeding absent	Score 0
Bleeding present	Score 1

A detailed case history was obtained and details of the procedure were explained to the patient & the relatives. Pre-operative blood pressure was checked with manual sphygmomanometer by auscultatory method. Pre-operative investigations-blood sugar level, bleeding time, clotting time, platelet count, prothrombin time (PT), international normalized ratio (INR) were done. Bleeding time was checked using Duke's method and clotting time by Capillary Tube method. Physician's consent was obtained for every patient in lieu of blood pressure and cardiovascular status. An informed consent was obtained regarding the surgical procedure and follow up time for 3 hours and 24 hours and 48 hours post-operatively. Pre-operative intraoral periapical radiographs were obtained. Preoperative patient's oral cavity was prepared using 2% povidone-iodine germicidal gargle and routine barrier protection techniques were used by the operating surgeon. After following all the necessary surgical aseptic protocol, patients were prepared and draped for the surgical procedure. 15% lignocaine topical anesthetic spray was applied on the mucosa of area to be injected. Pterygomandibular nerve block was given using of 2% lignocaine hydrochloride without adrenaline for mandibular teeth. Local infiltration injection was used for maxillary teeth. The subjective and objective signs and symptoms of the anesthesia were confirmed. Extraction of teeth was performed as per routine.

After extraction the socket was curetted and was compressed for two minutes. The patients were then asked to bite hard on a piece of sterile gauze for 30 minutes and re-evaluated for bleeding upto 3 hours post operatively at regular intervals. Patients were discharged after 3 hours with a family member after giving routine post-operative instructions.

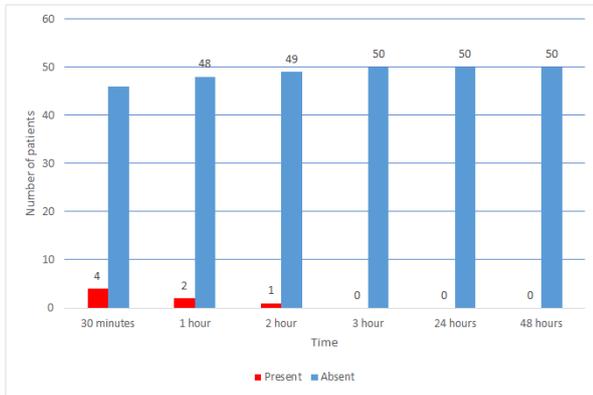
All patients were covered post-operatively with Amoxicillin-Trihydrate capsules 500mg 8 hourly and paracetamol tablets 500mg 8 hourly for five days.

RESULTS

Out of 50 patients, 29 were male and 21 were female. Age ranged from 50-75 years with a mean age of 59.90+7.11 years. The bleeding time of the patients ranged from 1.25 minutes to 2.85 minutes and clotting time ranged from 3.13 minutes to 5.53 minutes. Both the bleeding time and clotting time were within the normal range. Mean bleeding and clotting time were 1.89+0.43 minutes and 4.05 minutes respectively. In our study we observed bleeding beyond the crest of the socket in 4 patients at 30 minutes, out of which bleeding stopped in 2 patients after 30 minutes. 2 patients continued to bleed for 1 hour after extraction. In 1 of these patients, bleeding stopped after 1 hour, the

2nd patient experienced bleeding 2 hours post-operatively. Bleeding in all patients was controlled using a pressure pack.

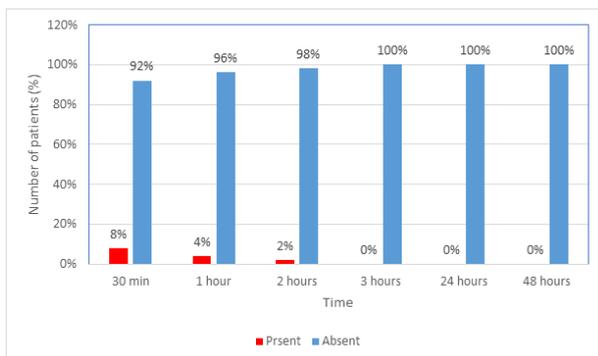
Graph 1 show that no patients had any bleeding after 3 hours, 24 and 48 hours. None required blood transfusion, hospitalization for bleeding or major cardiovascular event.



Graph-1: Showing distribution of bleeding status with respect to time post-operatively

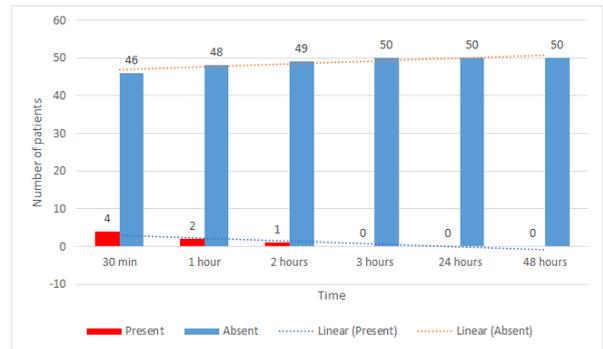
Chi square test was used to show an association between bleeding and time interval [P= 0.046]. Since P< 0.05, it indicates significant association between the status of bleeding and time point measurements. It implies that bleeding is absent as time progresses.

Graph 2 – Showing percentage distribution of bleeding with respect to time post-operatively



Graph-2: Shows that the overall risk of bleeding was 8% in our study

Graph-3: Shows that bleeding was present at 30 minutes in 4 patients which gradually decreased over time. In none of the patients, bleeding was observed beyond 2 hours.



Graph-3: Showing the trend line in the Bar Chart

DISCUSSION

Excessive post-extraction bleeding is defined as continuous bleeding from the extraction socket beyond the post-operative window of clot formation period [33]. Excessive bleeding in the patients is not only distressing for the patient, but also hinders the completion of the procedure and can compromise wound healing [34-38]. Lifestyle related diseases like hypertension and other cardiovascular diseases are invariably associated with increased blood levels of lipids, cholesterol and free radicals which facilitate the formation of atherosclerotic plaque causing lumpy thickening of the blood vessel, narrowing of the arterial lumen and slowing down the blood flow which leads to the formation of thrombus [39-41].

Since platelets have an important role in coagulation and, in particular, arterial thrombosis, anti-platelet drugs are in widespread use for the prevention of morbidity and mortality from vascular disease [42].

Complete or near-complete inhibition of platelet cyclo- oxygenase [COX-1] can be achieved with low doses of aspirin (75-150 mg) given once daily. In contrast, inhibition of COX-2-dependent patho-physiologic processes (eg, hyperalgesia, inflammation) requires larger doses of aspirin and a much shorter dosing interval because nucleated cells rapidly re-synthesize the enzyme. Thus, 10- to 100-fold higher daily doses of aspirin are required when the drug is used as an anti-inflammatory agent rather than as an anti-platelet agent. Lemkin *et al.* [43] and Mc Gaul *et al.* [9] have documented that there was an increased postoperative bleeding after dental extraction and recommended to discontinue aspirin. For most elective surgeries, few authors have recommended that the patient should stop taking aspirin 7 to 10 days before the procedure [44]. Some authors recommended discontinuing aspirin 3 days prior to the surgery since the platelet.

Inhibition achieved with aspirin, although irreversible for target platelets, lasts until a significant pool of new platelets is synthesized and complete recovery of platelet aggregation may occur in 50% of cases by day 3 and in 80% of cases by day 4 [45]. Some

investigators even suspect the existence of a biological platelet aggregation “rebound phenomenon”. Rapid withdrawal of aspirin may cause abnormally high levels of blood markers reflecting an increase of thromboxane -A₂ which may have possible hazardous effects in patients with cardiovascular disease [46]. The delicate balance between adequate antithrombotic effect and risk of bleeding remains a sensitive matter, which often influences a patient's or a physician's choice to discontinue daily anti-platelet therapy [47].

The best screening test for the effect of aspirin on coagulation is the platelet function analyzer (PFA-100) [13]. This test mimics the clotting process in vitro and allows for a more accurate determination of platelet function [44]. If this is not available, then the bleeding time can be used. Although aspirin affects platelets and the coagulation process through its effect on platelet release, it does not usually lead to a significant bleeding problem unless the bleeding time is greater than 20 minutes. If surgery is to be performed under emergency conditions and the bleeding time is in excess of 20 minutes, 1-desamino-8-D-arginine vasopressin (DDAVP) can be used to shorten the bleeding time [13].

In our study, patients were evaluated at 30 minutes, 1 hour, 2 hours, 3 hours, 24 hours and 48 hours from the time of extraction for bleeding. To record the intraoral bleeding, the extraction site was observed without gauze in place. Any bleeding that extended beyond the crest of the socket (i.e., onto surrounding gingival tissues) during an observation period of 1 minute was considered as bleeding present. In our study we observed bleeding beyond the crest of the socket in four patients at 30 minutes out of which bleeding stopped after 30 minutes in two patients. Two patients continued to bleed for 1 hour after extraction. None of the patients had bleeding after 2 hours, 3 hours, 24 hours and 48 hours. There were no cases of transfusion, hospitalization for bleeding or major cardiovascular events. The consequences of possible hemorrhage in non-compartment surgeries is greatly outweighed by the risk associated with cessation of anti-platelet therapy, which can result in acute coronary syndrome in serious cases [39].

Burger *et al.* [48] stated that, in patients on aspirin, the average risk of intra-operative bleeding increases by a factor of 1.5 [45]. In our study the overall risk of bleeding observed after extractions in patients on aspirin therapy was 8%. Probably the few cases of bleeding reported in our study could be contributed to the fact that in our study lignocaine was used without adrenaline and suturing was not included in our dental extraction protocol.

The American College of Chest Physicians Evidence-Based Clinical Practice Guidelines 2012 made the following recommendations like, in patients

who are receiving ASA for the secondary prevention of cardiovascular disease and are having minor dental or dermatologic procedures or cataract surgery, we suggest continuing ASA around the time of the procedure instead of stopping ASA 7 to 10 days before the procedure (Grade 2C-high risk patients), stopping anti-platelet agents is NOT recommended prior to most dental procedure. Dentists should obtain a medication history including any currently prescribed antiplatelet agents and when last taken. Given the low incidence and severity of bleeding following dental surgery, use of local measures (e.g. absorbable gelatin sponges and sutures) is adequate to control bleeding. Elective procedures with significant risk of bleeding should be postponed [13].

On the basis of our study and above recommendations we conclude that patients need not discontinue taking aspirin prior to dental extractions.

CONCLUSION

The main objective of our study was to evaluate the risk of bleeding in patients on long term aspirin therapy undergoing dental extractions.

In our study we had a 8% risk of bleeding after extractions in patients on long term low dose aspirin therapy. These patients were treated as any other normal patients and local measures were used to achieve hemostasis.

This study highlights that patients who are on long term low dose aspirin therapy need not discontinue their medications prior to dental extractions. Considering the small risk of post-operative bleeding it will be prudent to pack the extraction socket with absorbable gel foam and place single interrupted sutures to achieve hemostasis postoperatively.

REFERENCES

1. Pappachan, M. J. (2011). Increasing prevalence of lifestyle diseases: high time for action. *The Indian journal of medical research*, 134(2), 143.
2. Murray, C. J., & Lopez, A. D. (1997). Alternative projections of mortality and disability by cause 1990–2020: Global Burden of Disease Study. *The lancet*, 349(9064), 1498-1504.
3. Paikin, J.S., Eikelboom, J.W. (2012). Aspirin. *Circulation*, 125(10):e439-42.
4. Penz, S., Reininger, A. J., Brandl, R., Goyal, P., Rabie, T., Bernlochner, I., ... & Siess, W. (2005). Human atheromatous plaques stimulate thrombus formation by activating platelet glycoprotein VI. *The FASEB Journal*, 19(8), 898-909.
5. Cañigral, A., Silvestre Donat, F. J., Cañigral Ferrando, G., Alós Almiñana, M., García Herraiz, A., & Plaza Costa, A. (2010). Evaluation of bleeding risk and measurement methods in dental patients.

6. Madan, G. A., Madan, S. G., Madan, G., & Madan, A. D. (2005). Minor oral surgery without stopping daily low-dose aspirin therapy: a study of 51 patients. *Journal of oral and maxillofacial surgery*, 63(9), 1262-1265.
7. Brennan, M. T., Wynn, R. L., & Miller, C. S. (2007). Aspirin and bleeding in dentistry: an update and recommendations. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology*, 104(3), 316-323.
8. Pototski, M., & Amenábar, J. M. (2007). Dental management of patients receiving anticoagulation or antiplatelet treatment. *Journal of oral science*, 49(4), 253-258.
9. McGaul, T. (1978). Postoperative bleeding caused by aspirin. *Journal of dentistry*, 6(3), 207-209.
10. Taggart, D. P., Siddiqui, A., & Wheatley, D. J. (1990). Low-dose preoperative aspirin therapy, postoperative blood loss, and transfusion requirements. *The Annals of thoracic surgery*, 50(3), 425-428.
11. Ardekian, L., Gaspar, R., Peled, M., Brener, B., & Laufer, D. (2000). Does low-dose aspirin therapy complicate oral surgical procedures?. *The Journal of the American Dental Association*, 131(3), 331-335.
12. Collet, J. P., Himbert, D., & Steg, P. G. (2000). Myocardial infarction after aspirin cessation in stable coronary artery disease patients. *International journal of cardiology*, 76(2), 257-258.
13. Little, J. W., Miller, C. S., Henry, R. G., & McIntosh, B. A. (2002). Antithrombotic agents: implications in dentistry. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology*, 93(5), 544-551.
14. Scully, C., & Wolff, A. (2002). Oral surgery in patients on anticoagulant therapy. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology*, 94(1), 57-64.
15. Maulaz, A. B., Bezerra, D. C., Michel, P., & Bogousslavsky, J. (2005). Effect of discontinuing aspirin therapy on the risk of brain ischemic stroke. *Archives of Neurology*, 62(8), 1217-1220.
16. Aframian, D. J., Lalla, R. V., & Peterson, D. E. (2007). Management of dental patients taking common hemostasis-altering medications. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology*, 103, S45-e1.
17. Morimoto, Y., Niwa, H., & Minematsu, K. (2008). Hemostatic management of tooth extractions in patients on oral antithrombotic therapy. *Journal of oral and maxillofacial surgery*, 66(1), 51-57.
18. Partridge, C. G., Campbell, J. H., & Alvarado, F. (2008). The effect of platelet-altering medications on bleeding from minor oral surgery procedures. *Journal of oral and maxillofacial surgery*, 66(1), 93-97.
19. Brennan, M. T., Valerin, M. A., Noll, J. L., Napeñas, J. J., Kent, M. L., Fox, P. C., ... & Lockhart, P. B. (2008). Aspirin use and post-operative bleeding from dental extractions. *Journal of dental research*, 87(8), 740-744.
20. Krishnan, B., Shenoy, N. A., & Alexander, M. (2008). Exodontia and antiplatelet therapy. *Journal of Oral and Maxillofacial Surgery*, 66(10), 2063-2066.
21. Nooh, N. (2009). The effect of aspirin on bleeding after extraction of teeth. *The Saudi dental journal*, 21(2), 57-61.
22. Cardona Tortajada, F., Sainz Gómez, E., Figuerido Garmendia, J., Lirón de Robles Adsuar, A., Morte Casabó, A., Giner, F., ... & Vidán-Lizari, J. (2009). Dental extractions in patients on antiplatelet therapy. A study conducted by the Oral Health Department of the Navarre Health Service (Spain).
23. Head, J. N. S., Reader, S. M., & Student, S. K. P. (2017). Dental Extractions in Patients on Antiplatelet Therapy: A Clinical Study. *International Journal of Recent Surgical and Medical Sciences*, 3(01), 034-039.
24. Morimoto, Y., Niwa, H., & Minematsu, K. (2011). Risk factors affecting postoperative hemorrhage after tooth extraction in patients receiving oral antithrombotic therapy. *Journal of oral and maxillofacial surgery*, 69(6), 1550-1556.
25. Lillis, T., Ziakas, A., Koskinas, K., Tsirlis, A., & Giannoglou, G. (2011). Safety of dental extractions during uninterrupted single or dual antiplatelet treatment. *The American journal of cardiology*, 108(7), 964-967.
26. Hamad, T. Y. (2011). A prospective study to examine the bleeding tendency of patients receiving regular low-dose aspirin therapy.
27. Medeiros, F. B., de Andrade, A. C. P., Angelis, G. A., Conrado, V. C., Timerman, L., Farsky, P., & Dib, L. L. (2011). Bleeding evaluation during single tooth extraction in patients with coronary artery disease and acetylsalicylic acid therapy suspension: a prospective, double-blinded, and randomized study. *Journal of oral and maxillofacial surgery*, 69(12), 2949-2955.
28. van Diermen, D. E., Bruers, J. J., Hoogstraten, J., Bovenlander, M., van den Bosch, A., & van der Waal, I. (2011). Treating dental patients who use oral antithrombotic medication: a survey of dentists in the Netherlands. *The Journal of the American Dental Association*, 142(12), 1376-1382.
29. Park, M. W., Her, S. H., Kwon, J. B., Lee, J. B., Choi, M. S., Cho, J. S., ... & Kim, K. Y. (2012). Safety of Dental Extractions in Coronary Drug-Eluting Stenting Patients Without Stopping Multiple Antiplatelet Agents. *Clinical Cardiology*, 35(4), 225-230.
30. Bajkin, B. V., Bajkin, I. A., & Petrovic, B. B. (2012). The effects of combined oral anticoagulant-aspirin therapy in patients undergoing tooth extractions: a prospective study. *The Journal of the American Dental Association*, 143(7), 771-776.

31. Shah, A., Shah, S. T., & Shah, I. (2012). Post extraction bleeding associated with long term maintenance dose of aspirin 75-150mg. *Pakistan Oral & Dental Journal*, 32(2).
32. Dudek, D., Helewski, K., Wyrobiec, G., Harabin-Słowińska, M., Kowalczyk-Ziomek, G., Żaba, M., ... & Wojnicz, R. (2013). Therapy with acetylsalicylic acid does not interfere with oral surgery. *Open Medicine*, 8(4), 392-397.
33. Shah, K. A., Patel, M. A., Tatu, R., & Patel, V. (2013). Relationship between Use of Aspirin and Post-Extraction bleeding Time: A Single Blind Study. *Advances in Human Biology*, 3(3), 28.
34. Rai, R., Mohan, B., Singh, V. P., & Wander, G. S. (2013). The Risk Of Bleeding During Dental Extractions In Patients Receiving Antiplatelet Therapy. *Indian Journal of Dental Sciences*, 5(4).
35. Girotra, C., Padhye, M., Mandlik, G., Dabir, A., Gite, M., Dhonnar, R., ... & Vandekar, M. (2014). Assessment of the risk of haemorrhage and its control following minor oral surgical procedures in patients on anti-platelet therapy: a prospective study. *International journal of oral and maxillofacial surgery*, 43(1), 99-106.
36. Eichhorn, W., Kluwe, L., Heiland, M., & Gröbe, A. (2014). Lack of evidence for increased risk of postoperative bleeding after cutaneous surgery in the head and neck in patients taking aspirin. *British Journal of Oral and Maxillofacial Surgery*, 52(6), 527-529.
37. Darawade, D. A., Kumar, S., Desai, K., Hasan, B., & Mansata, A. V. (2014). Influence of aspirin on post-extraction bleeding—A clinical study. *Journal of International Society of Preventive & Community Dentistry*, 4(Suppl 1), S63.
38. Bajkin, B. V., Urosevic, I. M., Stankov, K. M., Petrovic, B. B., & Bajkin, I. A. (2015). Dental extractions and risk of bleeding in patients taking single and dual antiplatelet treatment. *British Journal of Oral and Maxillofacial Surgery*, 53(1), 39-43.
39. Hanken, H., Tieck, F., Kluwe, L., Smeets, R., Heiland, M., Precht, C., ... & Eichhorn, W. (2015). Lack of evidence for increased postoperative bleeding risk for dental osteotomy with continued aspirin therapy. *Oral surgery, oral medicine, oral pathology and oral radiology*, 119(1), 17-19.
40. Zhao, B., Wang, P., Dong, Y., Zhu, Y., & Zhao, H. (2015). Should aspirin be stopped before tooth extraction? A meta-analysis. *Oral surgery, oral medicine, oral pathology and oral radiology*, 119(5), 522-530.
41. Varghese, K. G., Manoharan, S., & Sadhanandan, M. (2015). Evaluation of bleeding following dental extraction in patients on long-term antiplatelet therapy: A clinical trial. *Indian Journal of Dental Research*, 26(3), 252.
42. Israels, S., Schwetz, N., Boyar, R., & McNicol, A. (2006). Bleeding disorders: characterization, dental considerations and management. *Journal of the Canadian Dental Association*, 72(9).
43. Jimenez, A. H., Stubbs, M. E., Tofler, G. H., Winther, K., Williams, G. H., & Muller, J. E. (1992). Rapidity and duration of platelet suppression by enteric-coated aspirin in healthy young men. *The American journal of cardiology*, 69(3), 258-262.
44. Ferrari, E., Benhamou, M., Cerboni, P., & Marcel, B. (2005). Coronary syndromes following aspirin withdrawal: a special risk for late stent thrombosis. *Journal of the American College of Cardiology*, 45(3), 456-459.
45. Chassot, P. G., Marcucci, C., Delabays, A., & Spahn, D. R. (2010). Perioperative antiplatelet therapy. *American family physician*, 82(12), 1484-1489.
46. Biondi-Zoccai, G. G., Lotrionte, M., Agostoni, P., Abbate, A., Fusaro, M., Burzotta, F., ... & Sangiorgi, G. (2006). A systematic review and meta-analysis on the hazards of discontinuing or not adhering to aspirin among 50 279 patients at risk for coronary artery disease. *European heart journal*, 27(22), 2667-2674.
47. Lordkipanidzé, M., Diodati, J. G., & Pharand, C. (2009). Possibility of a rebound phenomenon following antiplatelet therapy withdrawal: a look at the clinical and pharmacological evidence. *Pharmacology & therapeutics*, 123(2), 178-186.
48. Burger, W., Chemnitz, J. M., Kneissl, G. D., & Rucker, G. (2005). Low-dose aspirin for secondary cardiovascular prevention—cardiovascular risks after its perioperative withdrawal versus bleeding risks with its continuation—review and meta-analysis. *Journal of internal medicine*, 257(5), 399-414.