

CAN ASPIRIN BE CONTINUED DURING DENTAL EXTRACTION?

DR. MADHULAXMI. M¹ AND DR. P.U. ABDUL WAHAB*¹*Department of Oral and Maxillofacial surgery, Saveetha Dental College, Chennai, India. Email: docwahab@hotmail.com

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ABSTRACT

Aspirin is the most commonly used preventive and therapeutic agent for vascular ischemic events [1]. Moreover, aspirin is indicated in other conditions such as inflammatory joint diseases [2]. Dental extraction is a very common procedure done under local anesthesia where the diseased, redundant or problematic tooth is removed. The prevalence of teeth mortality is more from 35 to 64 years [3]. This age range overlaps with those who are advised aspirin prophylaxis against thrombo embolic events. A general dental practitioner is always undecided or reluctant to do tooth extraction in these patients for the fear of postoperative uncontrolled bleeding. The aim of this article is to know whether it is justifiable to discontinue aspirin during extraction. We conclude that by stopping aspirin there is a risk of vascular problem which can cause high morbidity rate. So low dose Aspirin (75-300mg/day) monotherapy can be continued by taking local hemostatic measures during dental extraction.

Keywords: Aspirin, Dental Extraction, Bleeding, Thromboembolism.

INTRODUCTION

Aspirin is a common, chronically administered preventive treatment for cardiovascular disease [4]. It has been used traditionally as analgesic and anti-inflammatory for centuries and is one of the world's most widely used drug. Aspirin or acetyl salicylic acid is still the only non steroidal anti-inflammatory drug used in the treatment and prevention of thromboembolic diseases. This other most important function of aspirin as a blood thinner has made it a popular drug to reduce the risks of occlusive vascular events. Aspirin induces a long lasting functional defect in platelets, clinically detectable as a prolongation of the bleeding time [4]. This fear of uncontrolled bleeding often prompts medical practitioners to stop aspirin intake for seven to ten days before any surgical procedure. Dental extraction is a very common procedure done under local anesthesia where the diseased, redundant or problematic tooth is removed. The prevalence of teeth mortality is more from 35 to 64 years [3]. Patients taking aspirin have increased risk of bleeding

even during simple dental extraction. However, these patients receiving aspirin therapy to prevent blood clot formation may be subject to emboli formation if the treatment is stopped [5]. The debate as to stop or not to stop aspirin before minor surgical procedures like a simple dental extraction is a serious concern for patients and the dental practitioner. The aim of this article is to know whether it is justifiable to discontinue aspirin during tooth extraction.

Aspirin

Aspirin is a salicylate compound commercially available since 1899 and is used for its antipyretic, anti-inflammatory, and antiplatelet activities [6]. Of the different kind of effects, its antiplatelet action contributes most to its recent use. The antiplatelet activity of low-dose aspirin can prevent arterial thrombosis in both high-risk patients with known occlusive vascular disease and in low-risk healthy patients with no known history of vascular disease [7].

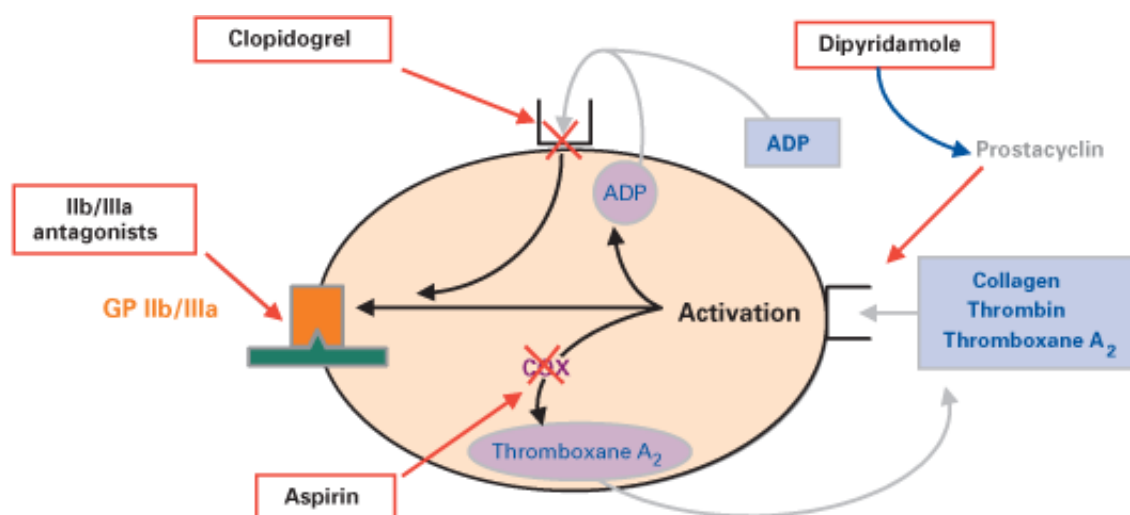


Fig. 1: Antiplatelet action of aspirin [8]

Aspirin is an approximately 150 to 200 fold more potent inhibitor of the constitutive enzyme COX-1 than the inducible isoform COX-2. Cyclo oxygenase-1 is highly sensitive to low doses of aspirin (40-80 mg daily) [9,10]. Complete inactivation of platelet COX-1 as well as maximum inhibition of collagen-induced platelet aggregation is achieved at 160 mg of aspirin taken daily [11]. The antithrombotic

properties of aspirin are effective upto 320mg daily [12]. Aspirin is maximally effective as an antithrombotic agent at doses much lower than those required for anti-inflammatory and analgesic functions [13]. Aspirin affects clotting by inhibiting platelet aggregation but they do so by a variety of different mechanisms. Aspirin irreversibly acetylates cyclooxygenase, inhibiting the production of

thromboxane A₂ [14]. This results in decreased platelet aggregation by adenosine diphosphate (ADP) and collagen. Patients on aspirin will have a prolonged bleeding postoperatively. Fearing this complication medical practitioners are prompted to stop aspirin intake for 7 to 10 days before any surgical procedure. The concept behind this is, platelets survive in vascular system for 7-10 days. Aspirin begins irreversibly inhibiting platelet aggregation within one hour of ingestion and this lasts for the life of the platelets (7-10 days) [14]. The effect is overcome by the manufacture of new platelets [15].

Hemostasis

Physiologically, hemostasis is the body's mechanism designed to prevent blood loss by forming a clot within injured blood vessels. Hemostasis in the healthy individual involves interaction between 4 biologic systems: the blood vessel wall, the blood platelets, the blood coagulation system, and the fibrinolytic system. Blood vessel constriction is an essential first stage (vascular phase); platelet adhesion (platelet phase) and aggregation (coagulation phase) follow. The haemostatic mechanism is initiated at the site of injury by local activation of surfaces and release of tissue thromboplastin, resulting ultimately in formation and deposition of fibrin. The coagulation process is regulated by physiologic anticoagulants. Activation of fibrinolysis is triggered by the presence of fibrin and tissue-type plasminogen activators at the site of fibrin formation, a process regulated by physiologic inhibitors such as antiplasmin, histidine-rich glycoprotein, and plasminogen activator inhibitor [16].

Fibrin clot formation after tooth extraction

Tooth extraction is a common procedure in dentistry. Soon after extraction the body attempts to form a fibrin clot [17]. The fibrin clot becomes granulation tissue which contains blood vessels, fibroblasts and chronic inflammatory cells programmed to prevent infection [18]. Antiplatelet drugs are drugs that interfere with the platelet phase by decreasing the platelet aggregation and interfere with the clot formation.

Aspirin resistance

Aspirin resistance is defined as persistent platelet activation occurring in individuals who take a therapeutic dose of aspirin [19]. The percentage of the population resistant to the cardio protective effects of aspirin has been reported to vary from 5% to 45% [13]. The mechanisms by which some patients are resistant to aspirin is unknown, [13] but may involve polymorphisms in the COX-1 gene affecting arginine 120, serine 529, or both. These gene polymorphisms are carried by 12% of the population [20,21]. Alternatively, enhanced platelet regeneration and an increased proportion of newly formed platelets expressing COX-2 in response to chronic aspirin administration could explain the development of resistance of platelets to inhibition by a low dose of aspirin. Aspirin resistance is partly reversible by increasing the dose of aspirin [22].

Platelet function test to monitor aspirin

Numerous lab tests (Cutaneous bleeding test, Platelet aggregation test, Serum thromboxane B₂, Urinary 11-dehydrothromboxane B₂) have been used to assess bleeding risk from antiplatelet therapy. Platelet function is commonly assessed using the cutaneous bleeding time test [13]. When platelet function is normal, bleeding time ranges from 2 to 10 minutes depending on the individual and the test used [5,23,24,25]. This range varies between institutions and depending on the method of measurement used. For years, the cutaneous bleeding time test has been commonly suggested as a reasonable measure of bleeding risk for patients who take aspirin, [26,27] and this test can often reveal increased bleeding time results in patients who take aspirin [27]. However, the vast majority of studies suggest that increased bleeding times do not predict increased blood loss from dental or even orthopedic surgery [5,28,23,29,30,31,32]. An additional limitation is that the bleeding test is very technique sensitive [33]. Therefore, there is sufficient evidence to not recommend the cutaneous bleeding time as a screening test to determine the bleeding risk from aspirin [34].

Impedance test (Platelet Aggregation) [13]

There are numerous laboratory tests currently available to measure platelet function from aspirin therapy. The impedance test is a more accurate screen than the cutaneous bleeding time test to determine the adequacy of platelet responsiveness to physiologic stimuli such as collagen, arachidonic acid, and adenosine diphosphate. 81 mg of aspirin is sufficient to impede aggregation by this test. Anyways, the platelet function tests are not very well studied and reported.

Risks of aspirin withdrawal

Aspirin cessation is associated with an increased risk of cardiac complications which peaks at 10 days. This risk is much higher after coronary stent placement [60]. In a retrospective analysis of 475 patients admitted to hospital with a myocardial infarction, 11 (2.3%) had discontinued aspirin therapy within 15 days prior to admission. Nine patients discontinued aspirin prior to planned surgical procedures, one of which was a dental procedure. The dental patient had been stable and symptom free on aspirin for 10 years but suffered a myocardial infarction 10 days after stopping aspirin therapy [61]. Ferrari et al [58] in his study have evaluated the role of aspirin withdrawal in a cohort of 1236 patients hospitalized for acute coronary syndrome. A total of 51 (4.1%) of these patients discontinued aspirin within 1 month of the acute coronary syndrome. 13 of these acute coronary syndrome cases were withdrawn from aspirin before a dental procedure. The mean delay between aspirin withdrawal and the acute coronary event was between 4-17 days [58]. The discontinuance of daily aspirin use increases the risk for adverse clinical cardiovascular outcomes during the first month after drug withdrawal [13].

Oral haemostatic measures to prevent bleeding complications

Oral haemostatic measures can be taken to control bleeding after tooth extraction by suturing the socket and by packing gauze bite firmly for 15 - 30 minutes [38]. Reabsorbable gelatin sponge, oxidized cellulose, microfibrillar collagen also can be used. If still bleeds, tranexamic acid can be applied topically [62]. Also advice the patient not to rinse the mouth for first 24 hours and not to disturb the extracted tooth socket with the tongue.

Literature supporting withdrawal of aspirin therapy for 7 days

Studies conducted in 1970s by Lemkin et al [35] and Mc Gaul et al [36] about postoperative bleeding after dental extraction due to aspirin have documented that there is increased postoperative bleeding after dental extraction and recommended to discontinue aspirin. According to Nach G. Daniel et al aspirin has been associated with increase in bleeding time and post operative haemorrhagic risk. For most surgical procedures it has been recommended that patient should stop taking aspirin before 7 - 10 days of the surgical procedure [37]. This was recommended on the basis of surgical studies which showed rise in both intraoperative and postoperative bleeding

[38,39,40,41]. Thomson et al [42] in his study have found that there is a risk of bleeding after gingival surgery due to continuation of aspirin use and advised to stop aspirin before the procedure.

Studies conducted in 1990s by Conti et al [43], Speechley et al [44] and Scher et al [45] have recommended to discontinue aspirin for 7 - 10 days since the platelet survives upto 10 days.

Literature supporting withdrawal of aspirin therapy for 3 days

Studies by Scully et al [26] and Little et al [27] in 2002 have advised to stop aspirin for 3 days until a time when the number of new platelets returned to a sufficient level before starting the dental procedures.

Literature supporting continuation of aspirin therapy

In contrast to the previous studies, Madan et al [46] and Valerin et al [47] in their study have stated that there is increased risk of thrombotic outcomes with the discontinuation of low dose aspirin therapy. Madan et al studied the effects of continuing aspirin therapy (75-100 mg/day) for 51 patients who were receiving oral surgical procedure. Only one case had increased bleeding during the

procedure and was controlled by local measures [46]. In an abstract presented at the American Academy of Oral Medicine in 2006 Valerian [47] reported the results regarding 36 patients taking 325 mg Aspirin 2 days before and 2 days after the tooth extraction. There was no difference in bleeding outcomes between the two groups who received the treatment.

Many studies have proved that patients on low dose aspirin can undergo dental extraction without discontinuing the drug [5,13,46,48,49]. Studies related to general and cardiovascular surgery did not show any significance increase in bleeding [50-54]. Ardekian et al [5] found that a daily dose of 100 mg of Aspirin did not increase the bleeding during tooth extraction. There was a statistical significance in bleeding time between the groups that continued and withdrew aspirin before tooth extraction. However, both groups were within the normal bleeding time range, and in both groups, a local hemostatic method was sufficient to control bleeding. No episodes of uncontrolled intraoperative or postoperative bleeding had been noted. Sonksen et al [55] showed that increase in bleeding time caused by daily aspirin dose of 300 mg did not exceed the normal limits in patients. Thus the patients need not stop taking Aspirin before dental surgery. Provided the hemorrhagic risk is not greater than thromboembolic risk associated by interrupting the dose of the drug.

According to Crispian Scully et al for uncomplicated forceps extraction of 1 to 3 teeth there is no need to interfere the aspirin dose. In patients taking 100 mg of aspirin daily bleeding can be controlled by suturing and local hemostatic measures. In patients taking higher dose of aspirin if the current value of bleeding is more than 20 minutes then surgical treatment should be postponed [56].

Current recommendations

Its advisable and safe to continue low - dose aspirin therapy when routine dental extractions are performed unless certain circumstances exist [57-59]. The current literature cautions dental practitioners not to discontinue aspirin therapy due to the risk of producing a thromboembolic event, increasing the morbidity and mortality risks for the patient

CONCLUSION

Aspirin is used for secondary prevention of thromboembolism which can cause bleeding complications. However in stopping aspirin there is risk of cardio vascular issues which can cause high morbidity rate. So low dose Aspirin (75-300mg/day) monotherapy can be continued during tooth extraction.

REFERENCES

- Hennekens CH, Dyken ML, Fuster V. Aspirin as a therapeutic agent in cardiovascular disease: a statement for healthcare professionals from the American Heart Association. *Circulation* 1997; 96(8):2751-3.
- Doron Jaframian, Rajesh VL, Doughlas EP. Management of dental patients taking common hemostasis- altering medications. *OOOOE* 2007; 103(3): Suppl 1.
- Andreia AFM, Elizangela PZ, Benedicto ECDT. Prevalence and reasons for tooth loss in a sample from a dental clinic in Brazil. *International journal of dentistry* 2012; 1-5.
- Carlo Patrono. Aspirin as an antiplatelet drug. *N Engl J Med* 1994; 330:1287-94.
- Ardekian L, Gaspar R, Peled M, Brener B and Laufer D. Does low-dose aspirin therapy complicate oral surgical procedures? *J Am Dent Assoc* 2000; 131: 331-5.
- Ajani UA, Ford ES, Greenland KJ, Giles WH, Mokdad AH. Aspirin use among U.S. adults: Behavioral Risk Factor Surveillance System. *Am J Prev Med* 2006; 30:74-7.
- Patrono C, Rocca B. Drug insight: aspirin resistance—fact or fashion? *Nat Clin Pract Cardiovasc Med* 2007; 4:42-50.
- Andrew McCann. Antiplatelet therapy after coronary occlusion. *Aust Prescr* 2007; 30:92-6.
- Patrignani P, Filabozzi P, Patrono C. Selective cumulative inhibition of platelet thromboxane production by low-dose aspirin in healthy subjects. *J Clin Invest* 1982; 69:1366-72.
- FitzGerald GA, Oates JA, Hawiger J, Maas RL, Roberts LJ 2nd, Lawson JA, et al. Endogenous biosynthesis of prostacyclin and thromboxane and platelet function during chronic administration of aspirin in man. *J Clin Invest* 1983; 71:676-88.
- Gan R, Teleg RA, Florento L, Bitanga ES. Effect of increasing doses of aspirin on platelet aggregation among stroke patients. *Cerebrovasc Dis* 2002; 14:252-5.
- Antithrombotic Trialists' Collaboration. Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. *BMJ* 2002; 324:71-86.
- Michael T. Brennan, DDS, MHS,a Richard L. Wynn, PhD,b and Craig S. Miller, DMD, MS,c Charlotte, NC, Baltimore, MD, and Lexington, KY. Aspirin and bleeding in dentistry: an update and recommendations. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2007; 104(3):316-23.
- Merritt JC and Bhatt DL. The efficacy and safety of perioperative antiplatelet therapy. *J Thromb Thrombolysis* 2002; 13: 97-103.
- Schafer AI. Effects of nonsteroidal antiinflammatory drugs on platelet function and systemic hemostasis. *J Clin Pharmacol* 1995; 35: 209-19.
- Deloughery TG. Hemostasis and thrombosis. Georgetown, Tex: Landes Publishing; 1999
- Amler MH et al, Histological and histochemical investigation of human alveolar socket healing in undisturbed extraction wounds. *J Am Dent Assoc* 1960; 61(7):32-44.
- Gregory GS et al. The Healing socket and socket regeneration. *Compendium* 2008; 29(2):1-11
- Sanderson S, Emery J, Baglin T, Kinmonth AL. Narrative review: aspirin resistance and its clinical implications. *Ann Intern Med* 2005; 142:370-80.
- Halushka MK, Walker LP, Halushka PV. Genetic variation in cyclooxygenase 1: effects on response to aspirin. *Clin Pharmacol Ther* 2003; 73:122-30.
- Maree AO, Curtin RJ, Chubb A, Dolan C, Cox D, O'Brien J, et al. Cyclooxygenase-1 haplotype modulates platelet response to aspirin. *J Thromb Haemost* 2005; 3:2340-5.
- Helgason CM, Bolin KM, Hoff JA, Winkler SR, Mangat A, Tortorice KL, et al. Development of aspirin resistance in persons with previous ischemic stroke. *Stroke* 1994; 25:2331-6.
- Brennan MT, Shariff G, Kent ML, Fox PC and Lockhart PB. Relationship between bleeding time test and postextraction bleeding in a healthy control population. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2002; 94: 439-43.
- Wallach J. 2000. Interpretation of diagnostic tests. 7th ed. Philadelphia: Lippincott Williams & Wilkins : 452-5.
- Cahill RA et al. Duration of increased bleeding tendency after cessation of aspirin therapy. *J Am Coll Surg* 2005; 200:564-73.
- Scully C, Wolff A. Oral surgery in patients on anticoagulant therapy. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2002; 94:57-64.
- Little JW, Miller CS, Henry RG, McIntosh BA. Antithrombotic agents: implications in dentistry. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2002; 93:544-51.
- Amrein PC, Ellman L, Harris WH. Aspirin-induced prolongation of bleeding time and perioperative blood loss. *JAMA* 1981; 245:1825-8.
- Lind SE. Prolonged bleeding time. *Am J Med* 1984; 77:305-12.
- Barber A, Green D, Galluzzo T, Ts'ao CH. The bleeding time as a preoperative screening test. *Am J Med* 1985; 78:761-4.
- De Caterina R, Lanza M, Manca G, Strata GB, Maffei S, Salvatore L. Bleeding time and bleeding: an analysis of the relationship of the bleeding time test with parameters of surgical bleeding. *Blood* 1994;84:3363-70.
- Pawlak DF, Itkin AB, Lapeyrolerie FM, Zweig B. Clinical effects of aspirin and acetaminophen on hemostasis after exodontics. *J Oral Surg* 1978; 36:944-7.
- Mielke CH Jr. Aspirin prolongation of the template bleeding time: influence of venostasis and direction of incision. *Blood* 1982; 60:1139-42.
- Peterson P, Hayes TE, Arkin CF, Bovill EG, Fairweather RB, Rock WA Jr, et al. The preoperative bleeding time test lacks clinical benefit: College of American Pathologists' and American

- Society of Clinical Pathologists' position article. Arch Surg 1998; 133:134-9.
35. Lemkin SR, Billesdon JE, Davee JS, Leake DL, Kattlove HE. Aspirin-induced oral bleeding: correction with platelet transfusion. A reminder. Oral Surg Oral Med Oral Pathol 1974; 37:498-501.
 36. McGaul T. Postoperative bleeding caused by aspirin. J Dent 1978; 6:207-9.
 37. NachG.Daniel, et al .Antiplatelet Drugs:Is There a Surgical Risk? Journal of Canadian dental association 2002; 68(11).
 38. Bick RL. Alterations of hemostasis associated with cardiopulmonary bypass: pathophysiology, prevention, diagnosis, and management. Semin Thromb Hemost 1976; 3(2):59-82.
 39. Torosian M, Michelson EL, Morganroth J, MacVaugh H 3rd. Aspirin- and coumadin-related bleeding after coronary-artery bypass graft surgery. Ann Intern Med 1978; 89(3):325-8.
 40. Michelson EL, Morganroth J, Tororsian M, MacVaugh H 3rd. Relation of preoperative use of aspirin to increased mediastinal blood loss after coronary artery bypass graft surgery. J Thorac Cardiovasc Surg 1978; 76(5):694-7.
 41. Ferraris VA, Ferraris SP, Lough FC, Berry WR. Preoperative aspirin ingestion increases operative blood loss after coronary artery bypass grafting. Ann Thorac Surg 1988; 45(1):71-4.
 42. Thomason JM, Seymour RA, Murphy P, Brigham KM, Jones P. Aspirin-induced post-gingivectomy haemorrhage: a timely reminder. J Clin Periodontol 1997; 24:136-8.
 43. Conti CR. Aspirin and elective surgical procedures. Clin Cardiol 1992; 15:709-10.
 44. Speechley JA, Rugman FP. Some problems with anticoagulants in dental surgery. Dent Update 1992; 19:204-6.
 45. Scher KS. Unplanned reoperation for bleeding. Am Surg 1996; 62:52-5.
 46. Madan GA, Madan SG, Madan G, Madan AD. Minor oral surgery without stopping daily low-dose aspirin therapy: a study of 51 patients. J Oral Maxillofac Surg. 2005; 63(9):1262-5.
 47. Valerin MA, Brennan MT, Noll JL, Napeñas JJ, Kent ML, Fox PC, et al. Relationship between aspirin use and postoperative bleeding from dental extractions in a healthy population. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2006; 102:326.
 48. Lillis T, Ziakas A, Koskinas K, Tsirlis A, Giannoglou G Safety of dental extractions during uninterrupted single or dual antiplatelet treatment. Am J Cardiol. 2011; 108(7):964-7.
 49. Medeiros FB et al. Bleeding evaluation during single tooth extraction in patients with coronary artery disease and acetylsalicylic acid therapy suspension: a prospective, double-blinded, and randomized study. J Oral Maxillofac Surg. 2011; 69(12):2949-55.
 50. Ferraris VA, Swanson E. Aspirin usage and perioperative blood loss in patients undergoing unexpected operations. Surg Gynecol Obstet 1983; 156:439-42.
 51. Weksler BB, Pett SB, Alonso D, Richter RC, Stelzer P, Subramanian V, and others. Differential inhibition by aspirin of vascular and platelet prostaglandin synthesis in atherosclerotic patients. N Eng J Med 1983; 308(14):800-5.
 52. Rajah SM, Salter MC, Donaldson DR, Subba Rao R, Boyle RM, Partridge JB, Watson DA. Acetylsalicylic acid and dipyridamole improve the early patency of aorta-coronary bypass grafts: a double blind, randomized trial. J Thorac Cardiovasc Surg 1985; 90(3):373-7.
 53. Karwande SV, Weksler BB, Gay WA Jr, Subramanian VA. Effect of preoperative antiplatelet drugs on vascular prostacyclin synthesis. Ann Thorac Surg 1987; 43(3):318-22.
 54. Bartlett GR. Does aspirin affect the outcome of minor cutaneous surgery? Br J Plast Surg 1999; 52(3):214-6.
 55. Sonksen JR, Kong KL, Holder R. Magnitude and time course of impaired haemostasis after stopping chronic low and medium dose aspirin in healthy volunteers. Br J Anesth 1999; 82(3):360-5.
 56. Crispian Scully. Oral surgery in patients on anticoagulant therapy. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2002; 94:57-64.
 57. Collet JP, Montalescot G, Blanchet B, Tanguy ML, Golmard JL, Choussat R, et al. Impact of prior use or recent withdrawal of oral antiplatelet agents on acute coronary syndromes Circulation 2004; 110:2361-7.
 58. 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; 45:456-9.
 59. Di Micco B, Di Micco G, Niglio A, Romano M, Di Micco P. Proximal deep venous thrombosis occurring after sudden clopi- dogrel suspension. Eur J Clin Pharmacol 2004; 60:63-4.
 60. Biondi-Zoccai GG, Lotrionte M, Agostoni P, et al. 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. Eur Heart J. 2006; 27(22):2667-2674.
 61. Collet JP, Himbert D and Steg PG. Myocardial infarction after aspirin cessation in stable coronary artery disease patients. Int J Cardiol 2000; 76: 257-58.
 62. Mariele Pototski and Jose M.Amenabar..Dental management of patients receiving anticoagulation or antiplatelet treatment. Journal of oral science 2007; 49(4):253-258.