Research Article

AHB Advances in Human Biology

Adv Hum Biol 2013; 3(3):28-33.

Relationship between Use of Aspirin and Post-Extraction Bleeding Time: A Single Blind Study

Kruti A Shah[1*] Milind A Patel[2] Rohit Tatu[3] Vandana Patel[4]

[1] Professor, Department of Oral and Maxillofacial Surgery, KM Shah Dental College, Vadodara, Gujarat, India.
[2] Post Graduate Student, Department of Oral and Maxillofacial Surgery, KM Shah Dental College, Vadodara, Gujarat, India.
[3] Lecturer, Department of Oral and Maxillofacial Surgery, KM Shah Dental College, Vadodara, Gujarat, India.
[4] Lecturer, Department of Oral and Maxillofacial Surgery, KM Shah Dental College, Vadodara, Gujarat, India.

ABSTRACT

Background: The purpose of the study was to evaluate the effect of low dose aspirin before tooth extraction.

Materials and Method: The study group consisted of 50 patients who were scheduled to undergo dental extractions. All patients were receiving 75 - 150 milligrams of aspirin daily on a regular basis. The authors randomly divided the patients into two groups: those who stopped the aspirin therapy before the procedure and those who continued the aspirin therapy. One hour before the procedures, all patients underwent a bleeding time test.

Results: The mean (±Standard Deviation) bleeding time was 1.8±0.47 minutes for patients who stopped aspirin therapy one week before the procedure. For patients who continued aspirin therapy, the bleeding time was 3.1±0.65 minutes. 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 intra operative or postoperative bleeding were noted.

Conclusion: Low-dose aspirin therapy should not be stopped before oral surgery. Local haemostasis is sufficient to control bleeding.

Keywords: Aspirin, Bleeding time, International Normalized Ratio.

INTRODUCTION

Antiplatelet and anticoagulant agents have been extensively researched and developed as potential therapies in the prevention and management of arterial and venous thrombosis. On the other hand, antiplatelet and anticoagulant drugs have also been associated with an increase in the bleeding time and risk of post-operative hemorrhage. Because of this, some dentists still recommend the patient to stop the aspirin for at least 3 days before any oral surgical procedure. However, stopping the use of this drug exposes the patient to vascular problems, with the potential for significant morbidity.

Thrombotic and thromboembolic occlusions of blood vessels are the main cause of ischaemic events in heart, lungs and brain[1]. Since the observation that thrombi occluding arteries were rich in platelets, antiplatelet agents and anticoagulants have been extensively researched and developed as potential therapies for the

Received: Aug. 28, 2013: **Accepted**: Oct. 2, 2013
***Correspondence**: **Dr. Kruti A Shah**
Department of Oral and Maxillofacial Surgery, KM Shah Dental College, Vadodara, Gujarat, India.
E-mail: krutiashah@rediffmail.com

pISSN 2321-8568
eISSN 2348-4691

prevention and management of arterial thrombosis[1]. Platelet activation and aggregation is considered to be central to arterial thrombus production[2]. Platelets are the 'major players' in arterial thrombosis and therefore are attractive targets in the prevention and treatment of cardiovascular diseases such as myocardial infarction, cerebral ischemia and peripheral arterial insufficiency[1]. Even though several antiplatelet and anticoagulant agents have been developed in recent years, acetylsalicylic acid (aspirin) and warfarin are the standard drugs for preventing vascular diseases[3].

Aspirin works by irreversibly inhibiting platelet function and cyclo-oxygenase type 1 (COX-1) through a selective acetylation of human COX-1, lasting for the life of the platelet (approximately 10 days). Aspirin irreversibly inactivates COX-1 activity by binding to the active site of the enzyme at the arginine 120 residue and acetylating the serine 529 residue. Acetylation prevents arachidonic acid from gaining contact with Tyr 385, which is the normal first step in its cyclo-oxygenation. Aspirin is a 150- to 200-fold more potent inhibitor of COX-1 than COX-2, and COX-1 is sensitive to low doses of aspirin (40-80 mg daily).

Blood clotting mechanism is initiated by one of two pathways: intrinsic and extrinsic. The intrinsic pathway is initiated by damage, or alteration, to blood independent of contact with damaged tissue, whereas the extrinsic pathway is initiated by exposure to damages tissue[4].

The purpose of this study is to determine whether there is evidence to demonstrate that adverse outcomes are associated with the use of aspirin & post-operative bleeding in patients during dental procedure.

MATERIAL AND METHOD

This study was conducted at the dental outpatient department of Oral and Maxillofacial surgery. Patients' included in the study were: aged between 40 to 65 years, who were indicated for extraction and were prescribed aspirin drug only. Patients' who were on warfarin, heparin, steroids, or non-steroidal anti-inflammatory drugs & patients with systemic diseases like diabetes were excluded from the study.

Hospital's ethical committee provided the ethical approval for this study. Informed consent was obtained from all study subjects by ensuring confidentiality and explaining the risks benefits involved.

50 patients, both male and female, attending Department of Oral & Maxillofacial Surgery for removal of teeth were enrolled in this study. Patients were randomly divided into two groups: those in the group I continued to receive aspirin therapy, while patients in the group II stopped aspirin therapy seven days before their extraction and did not resume treatment until the day after the surgical procedure.

Pre-operative dental examination, vital signs (blood pressure & pulse), bleeding time (White & Lee technique), clotting time (Ivy's technique), INR were measured. If INR was in range of 1 to 1.30 only then extraction was carried out. Local anesthetic injection containing 2% lignocaine with 1:200,000 adrenaline was administered to patient. Aspiration was done prior to injecting the anesthetic both for infiltration and regional block to avoid direct entry of needle into a vessel. The tooth was extracted and presence or absence of bleeding was observed. Bleeding time was recorded after extraction. Analgesic was prescribed as needed for pain, and the patient was instructed not to take any other medications for pain.

Chi square test was done to evaluate the relative frequencies of patients in different groups. Differences of parametric variables were tested with analysis of variance.

RESULTS

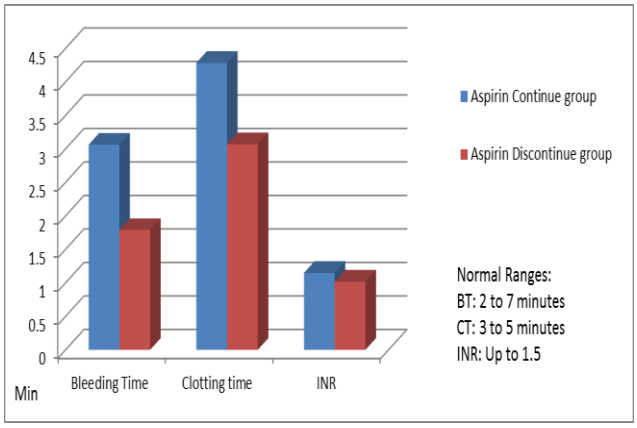
The mean (± Standard Deviation) bleeding time was 1.8 ± 0.47 minutes in patients who discontinued low-dose aspirin therapy one week before oral surgery; in comparison, patients who continued aspirin therapy throughout the study period had a bleeding time of 3.1 ± 0.65 minutes. This difference was statistically significant (p =.002) [Table 1] but both groups of patients were still within the normal bleeding time range: 2 to 7 minutes (according to White and Lee). The mean (± SD) clotting time was 3.1 ± 0.69 minutes in group 1 and of 4.3 ± 0.66 minutes in group 2. Normal clotting time range is 3 to 5 minutes (according to

Table 1: Test statistics

	MIN 5	MIN 10
Chi-Square(a)	9.680	38.720
Df	1	1
p VALUE	0.002	<0.0001

0 cells (.0%) have expected frequencies less than 5. The minimum expected cell frequency is 25.0.

Graph 1: Comparision of bleeding time, clotting time and INR among both the groups.



Ivy's Method). [Graph 1] The normal range of INR patients who continued with the anticoagulant therapy was up to 1.5.

DISCUSSION

Until the early 1980s, aspirin was used as an anti-inflammatory, analgesic and antipyretic drug for short periods only. The major side effects of aspirin— namely, gastrointestinal irritation and ulcers; tendency to develop gingival, nasal and intestinal hemorrhage; and asthma like attacks in asthmatic patients—limited administration of the drug to short periods (from two to five days)[5].

Studies conducted since the early 1980s have shown that the antiplatelet effect is elicited at low doses—of about 0.5 to 1.0 mg per kilogram per day— while the analgesic and antipyretic effects occur only at a daily dosage of 5 to 10 mg/kg, and the anti-inflammatory effect is achieved at a dosage of more than 30 mg/kg/day[9]. Thus, low doses of aspirin are sufficient for achieving anticoagulation with reduced side effects. Therefore, within the last decade there has been a rapid increase in the use of low-dose aspirin as a secondary preventive drug by patients who have cardio-vascular and peripheral vascular diseases[6]. The increasing popularity of aspirin, either alone or in combination with other drugs, has presented physicians and dentists with the dilemma of whether to advise patients to discontinue aspirin therapy before surgical procedures are performed.

Controversy exists in the literature regarding this issue. Many studies[7,8] have advocated stopping aspirin therapy seven to 10 days before elective surgery[9]. Conversely, other researchers have suggested that aspirin therapy should be continued regardless of the surgical procedure[10,11].

Lawrence and colleagues[11] recommended the continuation of aspirin therapy before elective dermatologic surgery if the patient's bleeding time was within normal limits. They found that bleeding time was prolonged in six (37.5 percent) of 16 patients receiving aspirin therapy; however, all of these patients had been receiving high doses of aspirin. The results of our study showed that when patients received a low dose of aspirin (100 mg), their bleeding time remained, without exception, within normal limits. On the other hand, Scher[12] advocated stopping aspirin therapy before any surgical procedure performed on a non- emergency basis. He found that diffuse postoperative bleeding was associated with preoperative use of aspirin. However, the patients in his study were also receiving a high dose of aspirin. Thomason and colleagues[13] described a patient receiving low-dose aspirin therapy whose platelet function was completely impaired and required infusion of platelets to control hemorrhage after gingivectomy. These authors suggested that the rarity of such cases points to a considerable variability in the individual platelet response to the drug.

Our study demonstrated that dental extractions, even the more complex procedures, did not result in uncontrolled intra operative or postoperative hemorrhage in patients receiving low-dose aspirin therapy on a long-term basis. No radical steps were needed to stop the bleeding in these patients and in most cases suturing was the only haemostatic tool used. Furthermore, the results of all of the patients' bleeding time tests— the only reliable test for the activity of platelets[14,15] — were within the normal range, regardless of

whether patients continued or discontinued aspirin therapy. Thus, it seems that there is no need to stop low-dose aspirin therapy in most patients, perhaps even in patients with anemia. Although no complication were observed in patients in whom aspirin therapy was temporarily stopped.

Valerin et al[16] enrolled thirty-six patients (mean age 40.3 +/10. 4:19 male) with 17 patients randomized to aspirin and 19 to placebo. No differences were noted between groups in baseline information, extraction time, difficulty of extraction, location of extraction sites, and compliance between the groups. They found no differences in bleeding outcomes for patients on aspirin versus placebo. Their findings suggest that there is no indication to discontinue the use of aspirin in patients requiring single tooth extraction.

Adchariyapetch compared the postoperative stoppage of bleeding in subjects who stopped or continued taking aspirin seven days before simple dental extraction. The mean bleeding time in both groups was normal before and after procedure and bleeding stopped in both groups within 30 minutes by biting the gauze, except for 1 patient who required a gauze biting time of between 31 to 60 minutes. They therefore concluded that simple tooth extraction of 1-3 teeth in patients taking low dose aspirin (< 100 mg) could be done without the necessity of stopping aspirin[17].

Two studies have evaluated bleeding on probing (BOP) for people taking aspirin. The first study randomized 46 persons to placebo, 81 mg aspirin, or 325 mg aspirin[14] (Schrodi et al., 2002)[18]. The people with baseline gingivitis (> 20% BOP sites) randomized to 325 mg aspirin had an increase in BOP compared with the placebo group. In a similar study, significant differences in BOP between placebo and both 81 mg aspirin and 325 mg aspirin were identified (Royzman et al., 2004)[19].

Despite the absence of a clear link between aspirin use and significant bleeding following invasive dental procedures, there are still recommendations to delay invasive procedures for a minimum of 3 days following cessation of aspirin, until a time when the numbers of new, functional platelets have returned to a sufficient level (Little et al., 2002)[20]. The problems associated with this practice include a delay in treatment for emergent odontogenic problems, the loss of the anti-thrombotic benefit of aspirin when it is prescribed for cardiovascular disease, and unnecessary time and expense for unwarranted bleeding time testing (De Rossi and Glick, 1996)[21].

The weight of evidence in the dental clinical literature does not support the long-held belief that an oral anticoagulant regimen must be altered or discontinued before most dental procedures, including oral surgery. Currently, the INR does not require alteration of the therapy regimen unless the INR value is greater than 4.0, provided that local hemostatic measures are used. INR values greater than 5.0, however, contraindicate a patient's undergoing a surgical procedure[22,23].

In 2003, Zanon and colleagues[24] reported the results of a single-blind, prospective study of 250 patients who were receiving anticoagulation therapy and had INR values between 1.8 and 5.0, as well as 265 patients who were not receiving anticoagulation therapy and who underwent both simple and surgical extractions. In all of the procedures in patients receiving anticoagulation therapy, oxidized cellulose was placed in the surgical site and stabilized with silk sutures, tranexamic acid-saturated gauze square was placed for 30 to 60 minutes, and an ice pack was placed on the cheek for one hour postoperatively. The total number of bleeding complications in the group of patients receiving anticoagulation therapy (four out of 250) did not differ significantly from the rate of occurrence in the control group (three out of 250).

Wahl[25] reviewed the literature on this subject in 2000, reporting that in an aggregate of 950 patients receiving continuous anticoagulation therapy, only 12 (< 1.3 percent) required more than local measures to control hemorrhage. The author went on to note that while discontinuation of anticoagulation therapy has been a common practice, bleeding after dental surgery rarely is life-threatening, and, more importantly, there have been four case reports of fatal thromboembolisms resulting from this practice. Loeliger and colleagues[26], however, have shown that INR values greater than 5.0 are accompanied by an unacceptable risk of serious hemorrhage and patients with INRs greater than 5.0 are not candidates for surgery.

CONCLUSSION

Low-dose aspirin (75 - 150 mg) therapy should not be stopped before oral surgery. Local haemostasis is sufficient to control bleeding. Patients receiving aspirin therapy to prevent blood clot formation may be subject to emboli formation if the treatment is stopped. The results of this study show that aspirin therapy should be continued throughout oral surgical procedures.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

REFRENCES

1. Owens CD, Belkin M. Thrombosis and coagulation: operative management of the anti-coagulated patient. Surg Clin North Am 2005; 85:1179-89.
2. Monroe DM, Hoffman M, Roberts HR. Platelets and thrombosis generation. Arterioscler Thromb Vasc Biol 2002; 22:1381-89.
3. Dogne J-M, de Leval X, Benoit P, delarge J, Masereel B, David JL. Recent advances in antiplatelet agents, Curr Med Chem 2002; 9: 577-89.
4. Conley CL, Mountcastle VB ed, Mosby, St Louis. Hemostasis; In Medical Physiology 2004; 1137-46.
5. Patrono C. Aspirin and human platelets: from clinical trials to acetylation of cyclooxygenase and back. Trends Pharmacol Sci 1989; 10 (11):453-8.
6. Ferraris VA, Ferraris SP, Lough FC, Berry WR. Preoperative aspirin ingestion increases operative blood loss after coronary artery bypass grafting. Ann Thorac Surg 1988; 45:71-4.
7. Watson CJ, Deane AM, Doyle PT, Bullock KN. Identifiable factors in post-prostatectomy haemorrhage: the role of aspirin. Br J Urol 1990; 66(1):85-7.
8. Kitchen L, Erichson RB, Sideropoulos H. Effect of drug-induced platelet dysfunction on surgical bleeding. Am J Surg 1982; 143(2):215-7.
9. Conti CR. Aspirin and elective surgical procedures (editorial). Clin Cardiol 1992; 15(10):709-10.
10. Ferraris VA, Swanson E. Aspirin usage and intraoperative blood loss in patients undergoing unexpected operations. Surg Gynecol Obstet 1983; 156 (4):439-42.
11. Lawrence C, Sakuntabhai A, Tiling Grosse S. Effect of aspirin and nonsteroidal antiinflammatory drug therapy on bleeding complications in dermatologic surgical patients. J Am Acad Dermatol 1994; 31(6):988-92.
12. Scher KS. Unplanned reoperation for bleeding. Am Surg 1996; 62(1):52-5.
13. Thomason JM, Seymour RA, Murphy P, Brigham KM, Jones P. Aspirin-induced post-gingivectomy haemorrhage: a timely reminder. J Clin Periodontol 1997; 24(2):136-8.
14. Mielke CH Jr. Aspirin prolongation of the template bleeding time: influence of veno-stasis and direction of incision. Blood 1982; 60(5):1139-42.
15. Harker LA, Slichter SJ. The bleeding time as a screening test for evaluation of platelet function. N Engl J Med 1972; 287(4):155-9.
16. Brennan MT, Valerin MA, Noll JL, Napeñas JJ, Kent ML, Fox PC, et al. Relationship between aspirin use and post operative bleeding from dental extractions in a healthy population. J Dent Res 2008; 87(8):740-4.
17. Adchariyapetch R. Dental extraction in patients on aspirin. Vajira Med J 2009; 53:283-89.
18. Schrodi J, Recio L, Fiorellini J, Howell H, Goodson M, Karimbux N. The effect of aspirin on the periodontal parameter bleeding on probing. J Periodontol 2002; 73:871-76.

19. Royzman D, Recio L, Badovinac RL, Fiorellini J, Goodson M, Howell H, et al. The effect of aspirin intake on bleeding on probing in patients with gingivitis. J Periodontol 2004; 75:679-84.

20. 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.

21. De Rossi SS, Glick M. Bleeding time: an unreliable predictor of clinical hemostasis. J Oral Maxillofac Surg 1996; 54:1119-20.

22. Loeliger EA, van den Besselaar AM, Lewis SM. Reliability and clinical impact of normalization of the prothrombin times in oral anticoagulant control. Thromb Haemost 1985; 53:148-54.

23. Beirne OR, Koehler JR. Surgical management of patients on warfarin sodium. J Oral Maxillofac Surg 1996; 54:1115-8.

24. Zanon E, Martinelli F, Bacci C, Cordioli G, Girolami A. Safety of dental extraction among consecutive patients on oral anticoagulant treatment managed using a specific dental management protocol. Blood Coag Fibrinolyis; 14:27-30.

25. Wahl MJ. Myths of dental surgery in patients receiving anticoagulant therapy. JADA 2000; 131:77-81.

26. Sindet-Pedersen S, Ramstrom G, Bernvil S, Blomback M. Hemostatic effect of tranexamic acid mouthwash in anticoagulant-treated patients undergoing oral surgery. N Engl J Med 1989; 320:840-3.