Aspirin Therapy and Exodontia: Review of Literature

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Article history
Received: 01 November 2013
Accepted: 10 January 2014
Available Online: 31 January 2014

Abstract
Aspirin is one of the commonly used anti-platelet drugs in medical practice. The fear of excessive and uncontrolled intra-operative and post-operative bleeding prompts the medical practitioners to stop the aspirin before surgical procedures. However, the majority of recommendations to stop aspirin therapy were not from dental literature. The amount of blood loss depends on the invasiveness of the surgical procedure. No surgical interventions are alike and therefore strict guidelines to alter or stop these medications without considering the invasiveness of the surgical procedure is a gross mistake. The current recommendations and consensus are in favor of continuing aspirin therapy prior to dental extractions. The purpose of this article is to present the review of literature regarding safety of dental extraction procedure in patients on aspirin therapy.

Keywords
Aspirin;
Clopidogrel;
Antiplatelet Drugs;
Extractions;
Hemostatic Agents

Introduction
Life span of human beings has increased due to advancements in medical sciences. Unfortunately, large populations of such individuals suffer from medically compromising conditions. Oral & maxillofacial surgeons may have to treat cardiac patients maintained on oral anti-platelet drugs. Nowadays, a number of newer anti-platelet drugs are available, but aspirin is commonly used because of its reliable efficacy and lower cost. Medical practitioners advise
these patients to either stop or alter these medications prior to invasive surgical procedure because of fear of excessive and uncontrolled bleeding. However, this alteration may predispose the patient to thromboembolic events such as cerebrovascular accidents and myocardial infarction. Although, there is increased risk of intra-operative and post-operative bleeding if aspirin is continued, but there is increased risk of thromboembolic events if medication is altered or discontinued.\(^1\)

The amount of blood loss depends on the invasiveness of the surgical procedure. No surgical interventions are alike and therefore strict guidelines to alter or stop these medications without considering the invasiveness of the surgical procedure is a gross mistake. The aim of this article is to evaluate the safety of dental extractions in patients on aspirin therapy.

**Review of Literature**

Platelets provide a lipoprotein surface for various reactions during formation of thrombin clot. Platelets have a contractile protein named thromosthenin which is responsible for clot retraction. The platelets play an important role in the process of atherosclerosis, thrombosis, myocardial angina, myocardial infarction and cerebrovascular accidents.\(^2\)

The anti-thrombotic effect of aspirin is mediated by irreversible inhibition of cyclooxygenase activity in platelets. On activation phospholipase-A\(_2\) acts on the cell membrane to release arachidonic acid. Cyclooxygenase acts on arachidonic acid to produce thromboxane A\(_2\). Thromboxane A\(_2\) is a potent platelet stimulant leading to degranulation of platelet and platelet aggregation. Aspirin inhibit cyclooxygenase enzyme and thus decreases the level of platelet stimulant thromboxane A\(_2\).\(^3\)

Aspirin have anti-platelet, analgesic and anti-inflammatory effects based on the dose. The anti-platelet effect of aspirin is elicited at a low dose of 0.5 to 1.5 mg/ kg body weight/ day. The analgesic and anti-inflammatory effects are present at the doses of 5 to 10 mg/ kg body weight/ day and > 30 mg/ kg body weight/ day respectively.\(^4\) Therefore, aspirin is effective as anti-platelet drug at much lower doses than that required for analgesic and anti-inflammatory functions.\(^5\) Anti-platelet activity of aspirin has been seen even at dose as low as 40 mg/day.\(^6\) The anti-platelet properties are effective up to 320 mg daily dose.\(^5\)

In fact doses of aspirin > 320 mg/ day may even decrease the effectiveness as anti-platelet agent due to inhibition of prostacyclin production.\(^7\)

When platelets activity is altered, a longer time period is required to stop bleeding from a cut surface because of alteration in primary hemostasis mediated by platelet plug formation.\(^8\) It was recommended traditionally to stop the aspirin 7-10 days prior to invasive surgical procedure. However, there is scientific evidence which showed that stopping anti-platelet therapy is associated with a progressive recovery of platelet function and with a potential risk of rebound of thromboembolic vascular events. On stopping aspirin there is excessive
thromboxane A$_2$ activity and decreased fibrinolytic activity.$^9$

The fear of excessive and uncontrolled intra-operative and post-operative bleeding prompts the medical practitioners to stop the aspirin before surgical procedures.$^{10}$ However, there is abundant dental literature which documented safety of dental extractions in patients on continued aspirin therapy.

Napenas et al conducted a retrospective study to assess the bleeding complications in patients on single or dual anti-platelet therapy. Forty three patients on single or dual anti-platelet therapy underwent invasive surgical procedures consisting of dental extractions, periodontal surgery, sub-gingival scaling and root planning. They concluded that there is negligible risk of bleeding complications after invasive dental surgical procedures in patients taking single or dual anti-platelet therapy.$^{11}$

Medeiros FB et al performed simple single tooth extraction (molar tooth) in patient on aspirin therapy. Sixty three patients involved in the study were randomly divided into two groups. Group S- patients (n=31) have suspended their aspirin therapy 7 days prior to extraction. Group NS- patients (n=32) have not suspended their aspirin therapy (100 mg/day) and undergone extraction. Suturing was used as a hemostatic measure in all the patients. Additional use of biological adhesive was restricted to those patients who showed increased intra-operative bleeding as compared to other. None of the patient exhibited any bleeding complication postoperatively. Although the mean blood loss per tooth extraction was greater in group NS, this was not statistically significant. Based on these results, they concluded that there is no need to suspend aspirin therapy (100 mg/day) prior to single molar extraction.$^{12}$

Ardekian et al conducted a prospective study to evaluate the risk of bleeding after tooth extraction with the use of aspirin 100 mg/day. Thirty nine patients were divided into two groups. Nineteen patients in group-1 continued their aspirin therapy, while 20 patients in group-2 stopped their aspirin regimen 7 days prior to therapy. A total of 6 patients showed increased intra-operative bleeding (4 in group-1 who continued aspirin and 2 in group-2 who stopped aspirin). Suturing and gauze pressure pack was used in all the cases to achieve hemostasis. The additional measure for hemostasis in 6 patients who have increased intra-operative bleeding was tranexamic acid pressure pack. No postoperative bleeding and other complications were reported at 1 week. They suggested that, there is no need to stop aspirin therapy prior to dental extractions which predispose the patient to thromboembolic events.$^{13}$

Canigral A et al performed simple and complex (surgical and multiple teeth extractions) dental procedures in patients on aspirin or clopidogrel or aspirin + clopidogrel or non-steroidal anti-inflammatory drugs (NSAIDs) or low molecular weight heparin (LMWH) therapy. In majority of cases (92%), bleeding was mild which subside within 10 minutes with the help of gauze pressure. In 8% cases of bleeding, it was described as moderate, which was easily controlled by local hemostatic measures. The results showed
safety of dental extractions in patients on continued anti-thrombotic therapy.\textsuperscript{14}

Hemelik M et al performed 151 tooth extractions in 65 patients on 100 mg/day aspirin therapy. The frequency of postoperative bleeding was 1.54\% in patients on aspirin therapy. All bleeding episodes were handled easily. They concluded that there is no need to stop 100 mg/day aspirin prior to dental extractions.\textsuperscript{15}

Partridge et al performed prospective observational study to evaluate the effect of platelet altering medications on bleeding from minor oral surgical procedures. The two groups involved in the study were, experimental group taking platelet altering medications and control group in which platelet altering medications were stopped at least 10 days prior to surgery. The minor oral surgical procedures performed were simple and surgical extractions of the teeth, alveoplasty, biopsy and frenectomy. Each surgical procedure was assigned units based on surface area of surgical field and anticipated manipulation. Mean blood loss per surgical unit was compared in both groups. In patients who continue aspirin therapy the mean blood loss per surgical unit ± standard deviation was 1.97 ± 1.48 gm and is comparable to that in control group (1.96 ± 1.66 gm). There is no statistically significant difference in relation to amount of blood loss per unit surgical area in both groups. Based on these results they concluded that, patients on platelet altering medications can undergo minor oral surgical procedures without alteration of their medication schedule.\textsuperscript{16}

Bajkin BV et al conducted a prospective study to evaluate the postoperative bleeding in patients on combined oral anticoagulant and aspirin therapy. A total of 213 patients were divided into three groups with 71 participants in each group. Group-A patients received combined oral anticoagulant + aspirin therapy. Patients in group-B received oral anticoagulant therapy. Patients in group-C received aspirin only. Three (4.2\%) patients in group A, two (2.8\%) in group B and none (0.0\%) in group C presented with postoperative bleeding. The difference was not statistically significant. All the cases of postoperative bleeding were easily controlled by local hemostatic measures.\textsuperscript{17}

Krishnan B et al in a prospective clinical study, performed extraction procedures on patients taking aspirin, stopped aspirin preoperatively and in normal patients [25 patients in each group]. Simple intra-alveolar extractions were performed and hemostasis achieved with wet gauze pressure pack for 30 minutes. Krishnan et al. concluded that patient continuing aspirin therapy can undergo routine dental extractions without increased risk of excessive or prolonged bleeding.\textsuperscript{18}

Shah A et al performed a prospective study to compare the incidence of bleeding complications among patients taking aspirin and those not taking aspirin at all. A total of 254 patients were enrolled in the study. Group-I patients (n=127) were taking 75-150 mg/day aspirin and continued it prior to extraction. Group-II (n=127) patients constitute the control group who were not taking any aspirin dose prior to extraction. One tooth was extracted by simple method in each patient of
both groups. The results showed that 5 patients (3.93%) in aspirin group and 3 patients (2.36%) in control group presented with prolonged immediate bleeding which was managed by additional hemostatic measures. The difference was not statistically significant. Also 2 patients (1.57%) in aspirin group and 1 patient (0.78%) in control group presented with late bleeding at 12 hour postoperatively. This difference was again not statistically significant. Hemostasis was achieved easily by patient themselves with the help of pressure pack at home. None of the patient exhibited very late bleeding. They concluded that it is a safe practice to perform simple extraction of 1 tooth in patients taking 75-150 mg aspirin daily.19

Lillis T et al performed a prospective study to compare the incidence of bleeding complications among patients taking aspirin monotherapy, clopidogrel monotherapy, dual therapy with both aspirin and clopidogrel and patients not taking aspirin at all. Out of 643 patients enrolled in the study, 111 patients were on anti-platelet therapy: aspirin monotherapy (n=42), clopidogrel monotherapy (n=36), dual therapy with both aspirin and clopidogrel (n=33). Patient not taking any antiplatelet drugs serve as control (n=532). After extraction of tooth hemostasis was achieved by sterile gauze pressure pack for 30 minutes. No patient exhibited late bleeding. Although there is greater incidence of prolonged immediate bleeding in dual anti-platelet therapy group, hemostasis was achieved easily by local hemostatic measures.20

Nooh performed simple and surgical extractions in patients taking aspirin. He compared the bleeding complication in experimental group patients on continued aspirin therapy with control group not taking aspirin. The method to achieve hemostasis includes wet gauze pressure pack for 30 minutes in cases of simple extractions and figure of 8 suturing in case of surgical extractions. Patients on continued aspirin therapy undergone surgical extractions showed mild oozing easily controlled by pressure packs. Based on these findings Nooh concluded that, patients taking 81 mg of aspirin can undergo dental extractions and there is no increased bleeding risk.21

Madan GA et al performed minor oral surgical procedures in patients on low-dose aspirin therapy (75-100 mg/day). The surgical procedures performed were simple & surgical extractions and implant placement. Suturing and pressure pack for 30 minute was used as hemostatic measure in all the cases. The results showed that only 1 patient after 3rd molar extraction show excessive bleeding intra-operatively which was easily managed by pressure pack soaked in 1% ferracrylum solution. There was no postoperative bleeding in any case. These authors concluded that most minor oral surgical procedures can be carried out safely without interrupting long term low-dose aspirin therapy.22

A prospective trial conducted by Cardona-Tortajada F et al involving 155 patients on anti-platelet therapy, confirmed that local measures to achieve hemostasis are sufficient.
to control postoperative hemorrhage after tooth extraction.\textsuperscript{23}

Park MW et al performed a case controlled study to evaluate the safety of dental extractions in patients with coronary drug eluting stents without stopping multiple anti-platelet agents. A total of 100 patients on multiple anti-platelet agents constituted the experimental group. Out of 100 patients 59 patients were taking dual anti-platelet therapy (aspirin 100 or 200 mg/day plus clopidogrel 75 mg/day) and 41 patients were on triple anti-platelet therapy (aspirin 100 or 200 mg/day plus clopidogrel 75 mg/day plus cilostazol 100 mg/day). A total of 100 matched pairs of patients were used as control group. Hemostasis was achieved by suturing and pressure pack in all the cases. The authors concluded that dental extractions can be performed safely in patients on multiple anti-platelet agents.\textsuperscript{24}

Morimoto et al conducted a prospective clinical study involving patients on anti-thrombotic therapy. Three groups involved in the study were patients on warfarin mono-therapy (n= 134), patients taking antiplatelet monotherapy (87) and patients taking combination therapy with warfarin and aspirin (n=49). Intra-alveolar extractions of teeth were performed followed by placement of oxidized cellulose in extraction sockets and suturing in all cases to achieve hemostasis. A total of 513 teeth were extracted on 306 occasions. The reported incidence of postoperative bleeding was 3.6%. It includes 7 patients on warfarin mono-therapy and 2 on combination therapy. No patient on aspirin mono-therapy showed postoperative bleeding. The authors concluded that hemostasis can be achieved easily after tooth extraction in patients on warfarin (INR <3.0) and antiplatelet therapy.\textsuperscript{25}

Duygu et al performed a clinical study to assess the effect of anti-platelet drugs on risk of bleeding complications after teeth extractions. Simple dental extractions were performed in experimental group patients on continued aspirin therapy (n= 25) and control group patients who stopped aspirin 7 days prior to extractions (n= 19). The experimental group patients were on aspirin dose in the range of 75-300 mg. Local hemostatic measures were able to maintain primary hemostasis in all cases. There were no intra-operative and post-operative bleeding complications in any case. No statistically significant difference was there between two groups with respect to postoperative bleeding complications. They concluded that, there is no need for interruption of long term aspirin therapy prior to dental extractions.\textsuperscript{26}

Brennan MT et al performed a double blind randomized controlled study in healthy patients. A total of 36 healthy patients were randomly divided into two groups. Group-1 patients (n=17) were given aspirin 325 mg/day two days preoperatively and continued for further 2 days after extraction (total 4 days). Group-2 patients (n=19) received placebo with similar time schedule as followed in group-1. Single tooth extractions were performed in both groups. There was no statistically significant difference between two groups with respect to postoperative bleeding. They concluded that there is no indication to stop
aspirin in patients requiring single tooth extraction. Garnier J et al., in a retrospective analysis of 52 patients reported that tooth extraction can be performed without stopping aspirin therapy. A total of 218 teeth were extracted without stopping aspirin therapy. Suturing and pressure pack was used as hemostasis measure in all cases. Only one patient (1.9%) [three extraction sockets (1.3%)] presented with continuous bleeding which require additional local hemostatic measure. No systemic hemostatic measure was required. They concluded that the haemorrhagic risk in patients on aspirin therapy can be managed by local hemostasis protocol.

**Conclusion**

Based on the review of literature, it can be concluded that current recommendations and consensus are in favor of continuing antiplatelet dose of aspirin prior to tooth extraction. The safety of dental extractions in such patients is supported by studies reported in literature. It must be emphasized that appropriate use of local hemostatic measures should always be considered whenever indicated. There is no justification to predispose the patient to the risk of thromboembolism at the expense of minor bleeding which can be easily controlled.

**References**


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