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Assessment of the risk of haemorrhage and its control following minor oral surgical procedures in patients on anti-platelet therapy: a prospective study

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Abstract. Controversy exists concerning the suspension or maintenance of anti-platelet drugs before elective surgical procedures. We assessed the association of the risk of prolonged postoperative bleeding with anti-platelet therapy by type of minor surgical procedure and the association between anti-platelet therapy and the level of hemostatic measures required. Five hundred and forty-six patients were included in the study group: those on aspirin ($n = 310$), clopidogrel ($n = 97$), and aspirin + clopidogrel dual therapy ($n = 139$); the control group comprised 575 healthy individuals. Cramer's V test was significant ($P < 0.05$) but showed a weak association between anti-platelet therapy and prolonged immediate postoperative bleeding. Compared to controls, the odds ratio revealed that the risk of prolonged bleeding in the immediate postoperative period was significantly higher with dual therapy, followed by clopidogrel and aspirin. Prolonged bleeding occurred in 22 patients in the study group and 20 in the control group, and was successfully controlled with local hemostatic measures. Fisher's exact test showed a significant association between dual therapy and higher levels of hemostatic measures ($P = 0.004$; $P = 0.035$). Prolonged bleeding in patients on anti-platelet therapy was independent of the type of minor surgical procedure. The greatest risk of prolonged bleeding was found in patients on dual therapy; this required higher levels of hemostatic measures.

Key words: anti-platelet therapy; minor oral surgery; risk of prolonged postoperative bleeding; local hemostatic measures.

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Advances in medical science have ensured an increased lifespan for humans. Unfortunately, this has come at the price of a greater incidence of medically compromising conditions such as angina, ischaemic heart disease, post-myocardial infarction, post-bypass surgery, post angioplasty/angiography, stroke, and transient ischaemic attacks. Such conditions are of concern to the oral surgeon, as these patients are maintained on anti-thrombotic agents. These agents include anti-platelet therapies and anti-coagulants, which are used to prevent thrombosis in both high-risk patients with known occlusive vascular disease and in low-risk healthy individuals with no known history of vascular disease. A considerable number of patients presenting to an oral surgeon are on anti-platelet therapy for primary or secondary prevention of cardiovascular events. The most commonly prescribed anti-platelet drugs are aspirin and clopidogrel, used as single therapy or in combination (aspirin + clopidogrel, dual therapy). The optimal dental management of such patients on long-term anti-platelet treatment is not clearly defined. The fear of uncontrolled or excessive bleeding has prompted medical practitioners to cease or alter the use of these drugs before surgical procedures. Hence, the current study was undertaken in order to assess: (1) the association between anti-platelet therapy and prolonged postoperative bleeding; (2) the association between prolonged postoperative bleeding and the type of minor surgical procedure performed; and (3) the association between anti-platelet therapy and the level of hemostatic measures required.

Aspirin is a non-steroidal anti-inflammatory drug that exhibits analgesic, antipyretic, anti-inflammatory, and anti-platelet properties. It has been shown to be a powerful secondary prevention agent, reducing the risk of myocardial infarction and ischaemic stroke by up to 20% in patients diagnosed with cardiovascular disease.[1] Its mechanism of action involves an irreversible inhibition of cyclooxygenase, which is responsible for the conversion of arachidonic acid into prostaglandins, prostacyclin, and thromboxane. The Antiplatelet Trialists' Collaboration, in a collaborative overview of randomized trials of anti-platelet therapy, confirmed the prophylactic effects of aspirin and other oral anti-platelet drugs after a previous myocardial infarction, angina, stroke, and bypass surgery, and established its efficacy in women as well as men.[2] Vascular events are reduced by 20–25% in the first few years after the index event, and all-cause mortality is reduced by 12%. Evidence suggests that a 75–100 mg daily dose of aspirin is optimal for the long-term prevention of serious vascular events in high-risk patients.[3]

Clopidogrel is an anti-platelet drug causing irreversible inhibition of an adenosine diphosphate receptor (P2Y12) important in promoting platelet aggregation and cross-linking of platelets by fibrin. The dosage used is 75–100 mg/day, with a half-life of 8 h.

Many patients receive a combination of anti-platelet drugs, e.g. aspirin and clopidogrel[4–6]; this has been shown to have a synergistic anti-platelet action, with the risk of bleeding complications much greater for combined therapy than for single-drug therapy.[5] The combination of aspirin (150 mg) and clopidogrel (75 mg) therapy has been shown to help prevent thrombotic complications following percutaneous coronary stent interventions.[7]

Materials and methods

A prospective randomized study was performed involving 1121 patients undergoing minor oral surgical procedures over an 18-month period (January 2011–June 2012) in a department of oral and maxillofacial surgery. The study group comprised 546 patients who were on uninterrupted anti-platelet therapy (aspirin/clopidogrel/dual therapy); the control group consisted of 575 healthy individuals who had never been on anti-platelet therapy. The study group was further categorized into three subgroups: group A, who were on aspirin therapy ($n = 310$), group B on clopidogrel therapy ($n = 97$), and group C who were on dual therapy ($n = 139$). The control group was designated group D. The dose of aspirin used by patients in the study group ranged from 75 to 150 mg, and clopidogrel was used at 75 mg. For dual therapy, doses ranged from aspirin 75 + clopidogrel 75 to aspirin 150 + clopidogrel 75.

Surgical procedures performed in all groups included multiple extractions, surgical extractions, flap surgery, biopsies, and alveoloplasties (Table 1).

The various indications for which patients were on anti-platelet therapy are shown in Table 2.

The following patients were excluded from the study: those with uncontrolled diabetes/hypertension or other endocrine disorders and pregnant women. Patients on concurrent therapies such as the birth control pill, hormone replacement therapy, and anticoagulants were also excluded, as were alcoholics. The following patients were included: those on single and dual anti-platelet therapy, with a normal blood count and coagulation profile. The institutional ethics committee approved the study protocol, and all the study participants provided informed consent.

Preoperative haematological investigations comprising a complete blood count and coagulation profile were performed for all patients. These are the first-line basic laboratory tests of platelet function used to investigate bleeding diathesis.[8]

The patient's cardiologist/physician, who had advised discontinuation of anti-platelet therapy, received a written explanation of the nature of the procedure to be carried out and assurance of hemostasis being achieved in the chair. Written consent to carry out the surgery without stopping the anti-platelet therapy was received. All vital signs such as blood pressure, pulse rate, respiratory rate, and temperature were recorded prior to the commencement of the procedure.

All of the minor surgical procedures were performed on an outpatient basis under local anaesthesia with lignocaine hydrochloride 2%–1:80,000 adrenaline. Following surgery, a pressure pack was applied for 30 min. Suturing using a simple interrupted technique with 3-0 mersilk was done as part of the procedure protocol in certain cases of multiple extractions involving full quadrant, surgical extractions, alveoloplasties, and biopsies. However, all cases of flap surgery required suturing. Patients were kept under observation for a further 30 min with the pressure pack in place after completion of the procedure. Prolonged bleeding was defined as uncontrolled bleeding that continued in spite of the pressure pack given for 30 min post-surgery. For the purpose of this study, the postoperative period was classified into immediate, within 24 h, and after 24 h.

If bleeding persisted, it was controlled with various local hemostatic measures, such as a pressure pack, suturing (simple interrupted technique), use of local hemostatic agents like gel foam, and surgical diathermy. The local hemostatic agents most commonly used by oral and maxillofacial surgeons are absorbable gelatin, oxidized regenerated cellulose, and collagen with suture. Initially these agents raised concerns regarding the potential for infection in a heme-rich environment, but recent *in vitro* studies have shown their protective effect against a variety of bacterial pathogens.[9] Other agents include topical thrombin, tranexamic acid,[10] and 1% feracrylum solution.[8] Gel foam is used