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Safety of Perioperative Anticoagulant Discontinuation in Cardiovascular Patients Undergoing Periodontal Therapy

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Periodontists are encountering increasing number of cases in their practices where patients present with cardiovascular diseases. Patients with a history of myocardial infarction, ischaemic stroke, acute coronary syndrome or peripheral vascular disease are prescribed anticoagulant medications by cardiologists, such as aspirin, warfarin, clopidogrel, ticlopidine, prasugrel, dipyridamole, cilostazol or dabigatran- either as monotherapy or dual therapy, for prevention of further thromboembolic events during lifetime. As because these agents act by inhibiting platelet aggregation, they tend to prolong bleeding time. Concerns regarding excessive periprocedural bleeding in patients receiving such drugs have led to some clinicians recommending periprocedural discontinuation of anticoagulant therapy. However, several studies, including systematic reviews and meta-analyses, have proved that there is no significantly increased risk of bleeding associated with continuing anticoagulant therapy when compared with discontinuation or modification of the anticoagulant regimen. In fact, without the anticoagulant medication, these patients have been found to be at increased risk of thromboembolic events with potentially serious consequences. The accepted recommendation, therefore, is that the anticoagulant drug regimens should not be altered or discontinued prior to periodontal treatment procedures, as the risks associated with such discontinuation far outweigh the consequences of prolonged bleeding, which can be well controlled with local measures.

KEYWORDS: Cardiovascular disease, Anticoagulants, Aspirin, Clopidogrel, Bleeding time

INTRODUCTION

Anticoagulant medications such as aspirin, warfarin, clopidogrel, ticlopidine, prasugrel, dipyridamole, cilostazol and dabigatran are used for the prevention of atherothrombotic events in patients with a history of myocardial infarction, ischaemic stroke, acute coronary syndrome or peripheral arterial diseases, particularly in those who have undergone stent placement following percutaneous coronary intervention, coronary artery bypass surgery, or prosthetic valve replantation.¹ All anticoagulant medications affect clotting by irreversibly inhibiting platelet aggregation within one (e.g., aspirin, prasugrel) to two (e.g., clopidogrel) hours of administration, with the inhibition lasting for the entire lifespan of the platelets (i.e., 7-10 days).² This anticoagulant effect can only be overcome by the production of new platelets.³ Complete recovery of platelet function occurs by day four in 80% of the cases.⁴ In contrast, non-steroidal anti-inflammatory drugs (NSAIDs) other than aspirin (e.g., ibuprofen, diclofenac, piroxicam etc.) have a reversible effect on platelet aggregation, and normal platelet function is restored once the drug is cleared from the circulatory system.³ Thus, NSAIDs other than aspirin are not used clinically for anticoagulant therapy.

All patients receiving anticoagulant therapy are likely to possess drug-induced altered platelet function.⁵ Low-dose aspirin can double the baseline bleeding time while clopidogrel may prolong it by 1.5

to 3 times; however, the resulting bleeding time may still be within the normal limits.^{3,6} In a placebo-controlled study, designed to assess the effect of cessation of low-dose aspirin on bleeding time in healthy volunteers after 14 days of treatment, the mean prolongation of bleeding time after 24 hours of cessation of treatment was 22 secs, 105 secs, and 211 secs, respectively, for patients on placebo, 75 mg aspirin, and 300 mg aspirin (normal range of bleeding time specified in the study: 120-600 secs).⁷ Bleeding times in all the subjects returned to baseline values by the sixth day. Although the effect on primary hemostasis is marginal when anticoagulants are used as monotherapy,⁸ there is likely to be an increased bleeding tendency if they are used as a combination therapy.⁶

Risk Associated with Perioperative Anticoagulant Discontinuation

Because of concerns about excessive periprocedural and postprocedural bleeding, many clinicians recommend reducing the dosage or completely stopping anticoagulant medications prior to carrying out periodontal surgical therapy and even subgingival scaling and root surface debridement. However, evidence from the extant literature and current consensus indicate that anticoagulant drug regimens should not be altered prior to dental surgical procedures.⁹⁻¹³ Stroke and myocardial infarction have been increasingly associated with

perioperative interruption or cessation of anticoagulant drug regimen. In a prospective cohort study of 1358 hospitalized patients with acute coronary syndrome, 6% (n=73) had recently (within 12 days prior to admission) discontinued oral anticoagulants for planned surgery.¹⁴ Many of these patients had suffered catastrophic outcomes during the 30-day follow-up period with a two-fold increase in mortality rate and major bleeding episodes when compared with those who did not discontinue. In a similar study of 1236 patients admitted to the hospital for acute coronary syndrome, it was found that 4% of the patients (n=51) had stopped aspirin in the month prior to admission.⁴ However, 13.3% of all recurrences were from this group, with the mean (\pm SD) delay between aspirin withdrawal and the acute coronary event being 10 (\pm 1.9) days (range: 4-17 days). Of these, 13 patients (25.5%) discontinued aspirin prior to receiving periodontal treatment and dental extractions. In a retrospective study involving 475 hospitalized patients with myocardial infarction, one patient, who had been stable and symptom free on aspirin for 10 years, discontinued aspirin therapy prior to a planned periodontal surgical procedure and suffered a myocardial infarction 10 days after discontinuing aspirin therapy.¹⁵

A meta-analysis of studies reporting on the cardiovascular risks associated with the continued use of low-dose aspirin versus its perioperative discontinuation, found that out of 93 patients presenting with acute vascular events after cessation of low-dose aspirin, 14 (15.1%) had discontinued due to planned dental surgery.¹⁶ The time interval between aspirin discontinuation and acute vascular event was 8.5 (\pm 3.6) days for acute coronary syndrome, 14.3 (\pm 11.3) days for acute cerebral events, and 25.8 (\pm 18.1) days for acute peripheral vascular events. These observations reinforce the belief that rebound hypercoagulability may occur following abrupt cessation of anticoagulant medication resulting in an increased cardiovascular risk of about 11 events per 1000 patients per week (the background cardiovascular event rate being about 1.4/1000 patients/week).¹⁶ Patients with coronary stents are at high risk of thromboembolic events and are usually prescribed dual anticoagulant therapy for the prevention of such events in future.

In these patients, it has been observed that the greatest risk for stent thrombosis after implantation is premature discontinuation of clopidogrel. A systematic review examining the effects of short-

term discontinuation of anticoagulant therapy in patients with drug-eluting stents found that out of the 161 cases of late stent thrombosis (occurring \geq 30 days after insertion), 142 (88%) had stopped one or both of their anticoagulant medications perioperatively.¹⁷ In 33 patients who discontinued both anticoagulants simultaneously, the median time to event was 7 days (39% occurred within 5 days of cessation). In 15 patients who stopped aspirin after having previously discontinued clopidogrel, the median time to event was also 7 days (27% occurred within 5 days). Moreover, in 94 patients who stopped clopidogrel but remained on aspirin, the median time to event was 122 days (2% within 5 days). There were no events in patients who stopped aspirin but continued with clopidogrel.

Risk of Bleeding Associated with Continuation of Anticoagulant Medications

Patients taking oral anticoagulants have a prolonged bleeding time; however, this may not be clinically relevant. Clinically significant post-operative bleeding following dental procedures has been defined as bleeding that continues beyond 12 hours, causes the patient to return to the dental clinic or to an emergency department, results in the development of a large haematoma or ecchymosis within the oral soft tissues, or requires a blood transfusion.¹⁸ When compared with some other types of systemic surgical procedures, routine periodontal therapeutic procedures and minor dental surgeries carried out in the clinic setting, are less likely to be affected by prolonged bleeding time.^{19,20} Blood loss is usually minimal and has minor consequences for the patient even if prolonged. Furthermore, local hemostatic measures can be easily applied in the oral cavity. Thus, for most dental procedures, any increased risk of bleeding does not necessarily increase clinically significant adverse outcomes for the patient or affect the result of the procedure.¹ In a randomized placebo-controlled study involving 36 healthy patients receiving either aspirin 325 mg or placebo for two days prior to periodontal therapy like flap curettage and two days post treatment, no significant difference between aspirin and placebo was found with respect to intra-oral bleeding time (7.2 [\pm 5.9] and 5.9 [\pm 6.2] min, respectively; P=0.51) or the duration of bleeding following flap curettage (3.5 [\pm 2.9] and 5.2 [\pm 6.3] hrs, respectively; P=0.31).²¹

In another prospective study comprising 82 patients undergoing open flap debridement, the mean

bleeding time for those who stopped their regular low-dose aspirin before surgery (n=25) was not clinically or statistically significantly increased when compared with those who continued aspirin therapy without any interruption or alteration (n=32) and those who had never taken anticoagulant medication (3 min [\pm 2 min 45 sec] vs. 2 min 45 sec [\pm 1 min 38 sec] and 1 min 49 sec [\pm 39 sec], respectively).²² No patient experienced any episode of prolonged or significant bleeding post-surgery. In another study conducted on 39 patients undergoing dental extractions, none of the patients who continued with aspirin as prescribed (n=19) had a bleeding time outside normal range.²³ Intraoperative bleeding was controlled in 85% of the patients (n=33) with gauze packing and proper suturing. The remaining 6 patients had tranexamic acid added to the gauze pack. No patient experienced uncontrolled bleeding in the immediate postoperative period or in the week following the procedure. In contrast to anticoagulant monotherapy, fewer studies are available on the bleeding risks of dual anticoagulant therapy. Reports suggest that the use of aspirin in combination with dipyridamole does not increase bleeding risk.²⁴ In a retrospective cohort study involving 43 patients on single (n=14) or dual (n=29) anticoagulant therapy (aspirin+ clopidogrel, n=26; aspirin+dipyridamole, n=2; aspirin+ticlopidine, n=1) who had received at least one invasive dental procedure, no episodes of postoperative bleeding complications were observed in the 213 dental extractions (including 19 surgical extractions) performed.²⁵ Although published studies on the relative risks of perioperative bleeding with clopidogrel or dipyridamole monotherapy are limited, the pharmacological mechanisms underlying their anticoagulant action suggest that patients taking these medications as monotherapy will be at no greater risk of bleeding than those taking aspirin. Therefore, patients on either clopidogrel or dipyridamole monotherapy should not have their therapy discontinued or altered prior to undertaking periodontal surgical procedures.²⁶ NSAIDs other than aspirin may also increase bleeding time; however, this seldom exceeds normal limits. Even major surgery is usually not complicated by these drugs, and therefore, they should not be discontinued prior to undertaking periodontal therapeutic procedures.²⁷

Weighing the Risk of Thromboembolic Events with that of Perioperative Bleeding

Risk of thromboembolic complications, including fatalities, associated with perioperative cessation of anticoagulant monotherapy is well documented. Although the risk is relatively low, the adverse outcome is potentially serious. On the contrary, not a single report exists of uncontrollable bleeding following dental or periodontal treatment undertaken without anticoagulant discontinuation. The meta analysis carried out by Burger and colleagues¹⁶ examining the cardiovascular risks associated with perioperative discontinuation of low-dose aspirin therapy prior to surgical procedures versus the bleeding risks associated with the continuation of therapy found that surgeons who were blinded to treatment failed to distinguish between patients taking aspirin and those discontinues it. In most cases, bleeding complications were handled in the same way as they would be without the effect of aspirin. The study also showed that discontinuation of aspirin resulted in serious adverse consequences such as stroke, myocardial infarction, and cardiovascular death. In the light of available evidence, guidance documents have been published advising that anticoagulant therapy should only be discontinued in the perioperative period when the haemorrhagic risk of continuing them is categorically higher than the cardiovascular risk associated with their discontinuation.⁵ Furthermore, since the premature interruption of clopidogrel or aspirin plus clopidogrel carries the risk of major adverse cardiovascular events that have devastating consequences, patients taking dual anticoagulant therapy should never have their anticoagulant regimen altered without the advice of an interventional cardiologist.¹

The American Dental Association, American Heart Association, American College of Cardiology, American College of Surgeons, and Society for Cardiovascular Angiography and Interventions have issued a joint advisory statement specifying the importance of preventing premature discontinuation of dual anticoagulant therapy in patients with coronary artery stents.[28] It states that there is little or no indication to interrupt anticoagulant drug regimen for dental procedures.

Managing the Risk of Bleeding in Patients Receiving Anticoagulant Therapy

Dental procedures that can be undertaken in the clinic, including nonsurgical extraction of upto three teeth, surgical removal of teeth, gingivectomy, periodontal flap surgery, apicoectomy, scaling and root planing, etc., can be safely carried out without altering or interrupting anticoagulant medication.¹⁸ Such patients should ideally be scheduled at the beginning of the day, preferably at the beginning of the week. Local anaesthetic containing a vasoconstrictor should ideally be used in these patients.^{18,29} Regional nerve blocks should be avoided wherever possible. In case of tooth extraction, the extraction sockets should be cleaned and gently packed with a resorbable hemostatic dressing, such as oxidised cellulose, collagen sponge, or resorbable gelatin sponge and carefully sutured.³⁰ Resorbable sutures are preferred as they attract less plaque accumulation.³⁰ For the management of postoperative pain, paracetamol is a safe over-the-counter analgesic in these patients and can be taken in normal doses for pain control. Additional options include dihydrocodeine. Other NSAIDs are considered less safe and should be avoided if possible. They may damage the gut lining leading to bleeding and ulceration, which may be further worsened by aspirin or clopidogrel administration. Some patients under anticoagulant medications may have additional medical problems, such as liver or renal impairment, thrombocytopenia, haemophilia, or other coagulation disorders, which might compound or increase the risk of prolonged bleeding after dental extractions and/or periodontal surgeries.¹ Before treating these patients, the dentist must consult with the patient's physician or haematologist to determine whether or not care can be safely delivered in the dental clinic.

CONCLUSION

Bleeding complications, while troublesome, do not carry the same risks as thromboembolic complications. Bleeding time in patients receiving anticoagulant medications is likely to be prolonged; however, perioperative or postoperative blood loss in these patients is usually minimal and should be manageable using local haemostatic measures only. These patients are placed at an increased risk of severe thromboembolic events with potentially serious consequences if their regular anticoagulant medications are discontinued. The recommendation therefore is that the anticoagulant drug regimen

should never be stopped or altered prior to any dental surgical procedure, which includes periodontal surgical therapy as well as exodontia.

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