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Dental Surgery and Antiplatelet Agents: Bleed or Die

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ABSTRACT

In patients taking antiplatelet medications who are undergoing dental surgery, physicians and dentists must weigh the bleeding risks in continuing antiplatelet medications versus the thrombotic risks in interrupting antiplatelet medications. Bleeding complications requiring more than local measures for hemostasis are rare after dental surgery in patients taking antiplatelet medications. Conversely, the risk for thrombotic complications after interruption of antiplatelet therapy for dental procedures apparently is significant, although small. When a clinician is faced with a decision to continue or interrupt antiplatelet therapy for a dental surgical patient, the decision comes down to "bleed or die." That is, there is a remote chance that continuing antiplatelet therapy will result in a (nonfatal) bleeding problem requiring more than local measures for hemostasis versus a small but significant chance that interrupting antiplatelet therapy will result in a (possibly fatal) thromboembolic complication. The decision is simple: It is time to stop interrupting antiplatelet therapy for dental surgery.
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KEYWORDS: Antiplatelet agents; Aspirin; Dental; Dental surgery; Stroke

The history of aspirin (acetylsalicylic acid) dates back more than 2000 years ago, when Hippocrates recommended chewing on willow leaves (which contain salicylic acid) during childbirth for analgesia. In 1899, the chemist Felix Hoffman of Bayer AG (Leverkusen, Germany) was the first to isolate pure acetylsalicylic acid, later calling it "Aspirin" for commercial manufacture and sale. Since then, Bayer AG lost or sold its rights to the trademark, and the "wonder drug" aspirin is widely used for its analgesic, antipyretic, anti-inflammatory, and anti-thrombotic effects.

Aspirin's antithrombotic indications include atrial fibrillation, history of angina or myocardial infarction, coronary artery disease prevention, history of coronary bypass surgery, and percutaneous coronary intervention and stent implantation. Newer antiplatelet medications include clopidogrel (Plavix; Bristol-Myers Squibb, New York, NY), ticlopidine (Ticlid; Roche Laboratories, Basel, Switzerland), cilostazol (Pletal; Otsuka America Pharmaceuticals Inc, Rockville, Md), dipyridamole (Persantine; Boehringer Ingelheim Pharmaceuticals, Inc, Ridgefield, Conn), ticagrelor (Brilinta; AstraZeneca, Paddington, London), and prasugrel (Effient; Ube Industries, Ube, Japan). Some of these newer agents are associated with greater antithrombotic efficacy but also higher bleeding risks than aspirin. When dental surgery is contemplated in patients taking 1 or more of these medications, dentists and physicians must weigh the potential bleeding risks in continuing the medications versus the thromboembolic risks in interrupting them before dental surgery.

Dentists frequently recommend aspirin withdrawal before dental surgery, even without consulting the patient's physician.[1] Both physicians and dentists frequently overestimate the bleeding risks of dental surgery in patients continuing antiplatelet medications and underestimate the thrombotic risks of interrupting antiplatelet therapy for dental procedures.[2-5] Dental surgery is unlike other types of surgery: Major vessels are unlikely to be encountered, and the perioperative and postoperative surgical sites are easily accessible to local measures for hemostasis, such as biting on gauze, absorbable gelatin sponges, and sutures. As early as 1987, Salzman[6] stated, "The hemostatic defect induced by aspirin in patients with otherwise normal hemostasis is usually minor…."

DENTAL SURGERY IN PATIENTS TAKING ANTIPLATELET MEDICATIONS

There have been many reports of patients continuing antiplatelet agents while undergoing dental surgery. Of at least

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1283 patients taking single or dual antiplatelet agents undergoing at least 2343 dental surgical procedures, including at least 2308 single and multiple, simple, and surgical dental extractions in at least 1334 visits, no more than 35 patients (2.7% of patients and 2.6% of visits) had bleeding complications requiring local measures for hemostasis and only 2 patients (0.2%) required more than local measures for hemostasis (**Table 1**).[7-35] It should be noted that the risks of bleeding may differ on the basis of the antiplatelet agent and the regimen used. Although some of the newer agents and regimens may be associated with higher bleeding risks, none of the patients taking nonaspirin or dual antiplatelet agents had bleeding complications that required more than local hemostatic measures.

CLINICAL SIGNIFICANCE

- In patients taking antiplatelet medications who are undergoing dental surgery, dentists and physicians must weigh the bleeding risks in continuing antiplatelet medications versus the thrombotic risks in interrupting antiplatelet medications.
- Bleeding complications requiring more than local measures for hemostasis are rare after dental surgery.
- The risk for thrombotic complications after interruption of antiplatelet therapy for dental procedures is apparently significant, although small.
- Therefore, antiplatelet medications should not be interrupted for dental surgery.

ANALYSIS OF THE TWO CASES OF POSTOPERATIVE HEMORRHAGE CONTROLLED BY MORE THAN LOCAL MEASURES FOR HEMOSTASIS

It is remarkable that there were only 2 patients (0.2%) taking continuous antiplatelet medications who required more than local measures for hemostasis after dental surgery, but even these 2 cases, 1 from 1974[18] and 1 from 1997,[35] do not support interruption of antiplatelet medications for dental surgery.

In 1974, Lemkin et al[18] reported on a patient taking 12 to 20 daily aspirin tablets (dosage unreported) who had uncontrolled bleeding after undergoing 18 extractions. The history included ethanol abuse, but the patient denied recent alcohol ingestion. Sutures and oxidized cellulose were unsuccessful for hemostasis, and the patient was admitted to the hospital the next day. Hemostasis was achieved after a platelet transfusion. Although the dose is unreported, 12 to 20 daily aspirin tablets were probably more than therapeutic and almost certainly more than the single daily tablet typically prescribed today for antithrombosis.

In 1997, Thomason et al[35] reported on a kidney transplant recipient who underwent a gingivectomy for gingival overgrowth and was taking aspirin 150 mg/day, in addition to cyclosporine, azathioprine, and amlodipine.[35] Hemostasis was achieved with pressure from gauze after the lower anterior gingivectomy, but after the upper anterior gingivectomy, there was excessive hemorrhage uncontrolled with local measures, and the patient was admitted to the hospital for a platelet transfusion, after which hemostasis was achieved. It is not clear that the relatively low dose of aspirin was the cause of the postoperative bleeding.

Although the evidence shows that dental surgery can be accomplished with minimal bleeding risk in patients receiving single or dual antiplatelet medications, some have recommended a 7- to 10-day interruption of antiplatelet therapy for dental extractions.[36]

ANTIPLATELET THERAPY INTERRUPTION FOR DENTAL PROCEDURES

There are various levels of thrombotic risk associated with continuous antiplatelet therapy interruption, depending on the reason for the antithrombotic therapy. For example, there is a relatively low risk of thrombotic complications when single antiplatelet therapy is withdrawn in primary prevention patients versus a relatively high risk when dual antiplatelet therapy is withdrawn in patients after recent percutaneous coronary intervention. Whenever antiplatelet therapy is interrupted, regardless of the reason, there is at least some increased risk of thrombotic complications. In a case-control study of 39,513 patients who had a first-ever prescription of low dose aspirin over a 7-year period, García Rodríguez et al[37] determined that patients who had recently interrupted aspirin were significantly more likely to have a myocardial infarction than patients whose aspirin therapy was continued. “For every 1000 patients, over a period of one year there were about four more cases of non-fatal myocardial infarction among patients who discontinued treatment with low dose aspirin (recent discontinuers) compared with patients who continued treatment.” Garcia Rodríguez et al[38] also showed a 40% increased risk of ischemic stroke or transient ischemic attack after withdrawal of aspirin within 1 to 3 months in patients with cardiovascular disease or cerebrovascular disease.

Biondi-Zoccai et al[39] conducted a meta-analysis of 50,279 patients in 6 studies and concluded that aspirin nonadherence or withdrawal was associated with a 3 times higher risk of a major adverse cardiac event versus continuing aspirin therapy. The authors concluded that the withdrawal of aspirin can have an “ominous prognostic implication” in patients at moderate or high risk for coronary artery disease. Sibon and Orgogozo[40] studied 289 patients with cerebral infarction and found that 13 of these patients had had antiplatelet drug interruption within 1 month before the ischemic stroke. Maulaz et al[41] conducted a case-control study of 309 patients admitted for stroke or transient ischemic attack who had been on

Table 1 Dental Surgery in Patients on Continuous Antiplatelet Drugs

Source	No. of Patients Treated	No. of Extractions (Surgical Procedures)	Antiplatelet Medications	Comment	Postoperative Bleeding Requiring Treatment with Local Measures (Other Than Immediately Postoperative)	Bleeding Complications Requiring More Than Local Measures
Ardekian et al[7] 2000	19	29 (29)	Aspirin 100 mg/d		0	0
Bajkin et al[8] 2012	71	119 (119)	Aspirin 100 mg/d		0	0
Brennan et al[9] 2008 Valerin et al[10] 2006	17	17 (17)	Aspirin 325 mg/d		0	0
Cañigral et al[11] 2010	51	51 (51)	ASA, clopidogrel, NSAIDS dosages not reported		5	0
Cardona-Tortajada et al[12] 2009	155	222 (222)	Aspirin 100-300 mg/d, clopidogrel 75 mg/d, ticlopidine 250 mg/d, or triflusal 300 mg/d		1	0
Duygu et al[13] 2010	25	50 (50)	Aspirin 75-300 mg/d		0	0
Garnier et al[14] 2007	52	218 (218)			1	0
Hepsö et al[15] 1976	23	46 (46)	Aspirin 1 g night before surgery and then 2 g daily for 3 d	Each patient underwent 2 extractions of impacted wisdom teeth.	5	0
Kale et al[16] 2012	40	80 (80)	Aspirin, clopidogrel, or ticlopidine dosage not reported		0	0
Krishnan et al[17] 2008	32	40 (40)	Aspirin 75-150 mg/d		0	0
Lemkin et al[18] 1974	1	18 (18)	12-20 daily aspirin tablets (dosage unreported)	Uncontrolled bleeding after 18 extractions. Hemostasis achieved after platelet transfusion.	1	1
Lillis et al[19] 2011	111	169 (169)	Aspirin, clopidogrel, aspirin-clopidogrel, dosage unreported		0	0
Madan et al[20] 2005	51	$\geq$46 ($\geq$57)	Aspirin 75-100 mg/d		0	0
McGaul[21] 1978	1	0 (2)	Postoperative aspirin 600 mg: 1 dose; 3 doses		2	0
Medeiros et al[22] 2011	32	32 (32)	Aspirin 100 mg/d		0	0
Morimoto et al[23,24] 2008 2011	87 (93 visits)	144 (144)	78 patients on aspirin 115.4 $\pm$ 48.2 mg/d, 8 patients on ticlopidine 218.2 $\pm$ 60.3 mg/d, 8 patients on cilostazol 135.7 $\pm$ 62.7 mg/d, 4 patients on dipyridamole 250.0 $\pm$ 100 mg/d		2	0
Morimoto et al[25] 2009	$\geq$7$\leq$15	0 (15)	Aspirin 81-243mg/d; ticlopidine 100-200mg/d, cilostazol 200mg/d 1 on patient on combined warfarin-aspirin therapy			0

Table 1 Continued

Source	No. of Patients Treated	No. of Extractions (Surgical Procedures)	Antiplatelet Medications	Comment	Postoperative Bleeding Requiring Treatment with Local Measures (Other Than Immediately Postoperative)	Bleeding Complications Requiring More Than Local Measures
Napeñas et al[26] 2009	≥25 (≥70 visits)	213 (≥213)	A total of 43 patients, but some were receiving deep subgingival scaling and root planing: 14 patients on single antiplatelet; 29 patients on dual antiplatelet: 88 invasive procedure visits; 70 extraction visits; various novel antiplatelet medication dosages not reported		0	0
Nooh[27] 2009	102	≥102 (≥102)	Aspirin 81 mg/d	≥49 surgical extractions	1	0
Park et al[28] 2012	100	176 (176)	Aspirin 100-200 mg/d with clopidogrel 75 mg/d and if needed cilostazol 100 mg 2 times per day		2	0
Partridge et al[29] 2008	27	38 (38)	Clopidogrel, aspirin, NSAIDs, at "therapeutic dosages"		0	0
Pawalk et al[30] 1978	20	20 (20)	Aspirin 2600 mg the day before and 2600 mg the day after surgery		0	0
Pereira et al[31] 2011	10	≥10 (≥10)	9 patients combined warfarin-aspirin, 1 aspirin only, aspirin dosages not reported		≤1	0
Sammartino et al[32] 2012	84	330 (330)	Clopidogrel, ticlopidine, aspirin dosages not reported Combined warfarin-antiplatelet therapy.	Some patients had warfarin withdrawn preoperatively; some did not	6	0
Shah et al[33] 2012	127	127 (127)	Aspirin 75-150 mg		1 at 12h	0
Svensson et al[34] 2013	11	≥11 (≥11)	ASA dosage not reported Warfarin continued		≤5	0
Thomason et al[35] 1997	1	0 (2)	Aspirin 150 mg/d	Hemostasis achieved with local measures after upper gingivectomy. Excessive hemorrhage uncontrolled with local measures after lower gingivectomy. Hemostasis achieved after platelet transfusion.	1	1
Totals	≥1282 patients (≥1334 visits)	≥2308 (≥2343)			≤35 (2.7% of patients and 2.6% of visits)	2 (0.16% of patients and 0.15% of visits)

NSAID = nonsteroidal anti-inflammatory drug.

Table 2 Antiplatelet Withdrawal for Dental Procedures

Source	No. of Patients Treated	No. of Cessations	No. of Extractions	Antiplatelet Medications	Comment	Days of Withdrawal	Thrombotic Complications
Ardekian et al[7] 2000	20	34	34	Aspirin		7	0
Candemir et al[45] 2010	1	1	1	Clopidogrel	Warfarin was continued	10	1 myocardial infarction due to very late stent thrombosis
Collet et al[46] 2000	1	1	Not reported	Aspirin		8	Myocardial infarction 10 d after aspirin withdrawal for dental surgery
Duygu et al[13] 2010	19	48	48	Aspirin		7	None reported
Ferrari et al[1] 2005	13	≥13	≥13	Aspirin		Not reported	13 cases of acute coronary syndrome
Ferreira-González et al[42] 2010	17	17	Not reported	Aspirin, clopidogrel, or both		Not reported	Not reported
Gagneja et al[43] 2007	1	1	6	ASA	Warfarin was continued	10	0
Kovacic et al[47] 2012	197	≥197	≥197	Aspirin, clopidogrel, aspirin and clopidogrel		Not reported	≥2 cases of stent thrombosis or acute myocardial infarction (J. Kovacic, personal communication, March 23, 2013)
Krishnan et al[17] 2008	25	28	28	Aspirin		1-10	0
Loomba et al[44] 2012	1	1	1	Aspirin		3	0
Medeiros et al[22] 2011	31	31	31	Aspirin		7	0
Napeñas et al[26] 2009	2	6	6	Clopidogrel	1 patient substituted aspirin for clopidogrel on day of 6 extractions; 1 patient stopped clopidogrel 3 d before an oral examination	1-3	0
Total	324	≥374					≥17 (5.0% of patients) thromboembolic complications

aspirin therapy versus 309 controls on aspirin with history of stroke but no stroke or transient ischemic attack within 6 months. There were 13 patients who had discontinued aspirin in the 4 weeks before the ischemic event, of whom 7 had been instructed to withdraw aspirin by a physician for a surgical procedure or because the physician thought aspirin was not necessary. The authors concluded that preoperative withdrawal of aspirin therapy "may not always be the best solution" before surgical procedures.

Although most studies of antiplatelet medication interruption for dental procedures have shown no thrombotic complications (**Table 2**),[7,13,17,22,26,42-44] there have been some cases of thrombotic complications when antiplatelet medications were interrupted for dental procedures (**Table 2**).

Candemir et al[45] reported a case of a 50-year-old man with chest pain, who had been on warfarin and clopidogrel but decided on his own to withdraw clopidogrel 10 days before a dental procedure. He was diagnosed with late stent thrombosis and myocardial infarction. Collet et al[46] retrospectively analyzed 475 consecutive patients with myocardial infarction, 11 of whom had interrupted aspirin therapy within 15 days before hospital admission. One of these patients discontinued aspirin 8 days before dental surgery and had a myocardial infarction 2 days later.

Ferrari et al[1] studied 1236 patients with acute coronary syndrome, 51 of whom were hospitalized within 1 month of aspirin withdrawal. In 13 cases, dental treatment was the reason for the aspirin withdrawal.

Kovacic et al[47] studied a group of 5681 patients receiving dual antiplatelet therapy with aspirin and clopidogrel after drug-eluting stent implantation. Of 1611 patients who had 1 or both antiplatelet agents interrupted over a 5-year period, 17 had stent thrombosis or acute myocardial infarction after the interruption. There were 197 patients whose antiplatelet therapy was interrupted for dental procedures, at least 2 of whom had stent thrombosis or acute myocardial infarction after the interruption (J. Kovacic, personal communication, March 23, 2013). The authors concluded that rates of stent thrombosis or acute myocardial infarction are low but not insignificant after drug-eluting stent implantation.

At least 17 of 324 patients (5%) whose antiplatelet medications were interrupted for dental surgery had thrombotic complications. The actual overall risk of antiplatelet cessation is probably significantly less than 5%, but more than zero. In the study by Kovacic et al,[47] the rate of thrombotic complications in patients whose antiplatelet medications were interrupted for any reason (not just dental procedures) was approximately 1% of all cessations, and even this number seems high. Patients receiving dual antiplatelet therapy after drug-eluting stent implantation are at higher risk than many other patients receiving antiplatelet therapy, so it is difficult to extrapolate these results to other patients receiving antiplatelet therapy, but because the risk of hemorrhage after dental surgery in patients receiving antiplatelet medications is extraordinarily low, antiplatelet medication interruption for dental procedures exposes patients to an unnecessarily increased risk (although still low) of serious thrombotic complications.

NATIONAL MEDICAL AND DENTAL GROUP RECOMMENDATIONS FOR DENTAL SURGERY IN PATIENTS TAKING ANTIPLATELET MEDICATIONS AND RECOMMENDATIONS OF OTHER REVIEWS

The American Heart Association, American College of Cardiology, Society for Cardiovascular Angiography and Interventions, American College of Surgeons, and American Dental Association have stated that single or dual antiplatelet therapy should not be interrupted for dental procedures, concluding, "Given the relative ease with which the incidence and severity of oral bleeding can be reduced with local measures during surgery (eg, absorbable gelatin sponge and sutures) and the unlikely occurrence of bleeding once an initial clot has formed, there is little or no indication to interrupt antiplatelet drugs for dental procedures."[48] The American College of Chest Physicians also recommends continuing aspirin for dental surgery.[49]

In reviewing the literature in 2007, Brennan et al[50] concluded that dental extractions can be performed with minimal bleeding risk in patients on continuous low-dose aspirin. In "extenuating" circumstances, when antiplatelet therapy should be interrupted, then the interruption should be for no more than 3 days to minimize the risk of thrombosis. Napeñas et al[51] conducted a literature review of bleeding complications in dental patients taking antiplatelet agents in 2013, focusing on 15 studies, which showed there is not a significantly increased risk of postoperative bleeding complications in patients receiving single or dual antiplatelet therapy, although there may be increased bleeding risk in patients receiving combination antiplatelet and anticoagulant therapy.[51] The authors concluded there is no need to stop single or dual antiplatelet therapy for invasive dental procedures, and local measures are adequate for hemostasis. van Diermen et al[52] searched the literature and expert recommendations from 2007 to 2012 and concluded that antithrombotic medications including dual antiplatelet therapy should not be interrupted for simple dental procedures, including extractions.

CONCLUSIONS

When a clinician is faced with a decision to continue or interrupt antiplatelet therapy for a dental surgical patient, the decision comes down to "bleed or die." That is, there is a remote (~0.2%) chance that continuing antiplatelet therapy will result in a (nonfatal) bleeding problem requiring more than local measures for hemostasis versus an unknown but significant chance that interrupting antiplatelet therapy will result in a (possibly fatal) thromboembolic complication. The decision is fairly simple: It is time to stop interrupting antiplatelet therapy for dental surgery.

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