

Is stopping of anticoagulant therapy really required in a minor dental surgery?

- How about in an endodontic microsurgery?

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Nowadays, oral anticoagulants are commonly prescribed to numerous patients for preventing cardiovascular accident such as thromboembolism. An important side effect of anticoagulant is anti-hemostasis. In a major surgery, the oral anticoagulant therapy (OAT) regimen must be changed before the surgery for proper post-operative bleeding control. However, in a minor dental surgery and endodontic surgery, the necessity for changing or discontinuing the OAT is open to debate. In this study, risks of the consequences were weighed and analyzed. In patients who stop the OAT, the occurrence of thromboembolic complication is rare but the result is fatal. In patients who continuing the OAT, post-operative bleeding can be controlled well with the local hemostatic measures. In the endodontic surgery, there are almost no studies about this issue. The intra-operative bleeding control is particularly important in the endodontic surgery because of its delicate and sensitive procedures such as inspection of resected root surface using dental microscope and retrograde filling. Further studies are necessary about this issue in the viewpoint of endodontic surgery. (*Restor Dent Endod* 2013;38(3):113-118)

Key words: Anticoagulants; Bleeding control; Endodontic microsurgery; Hemorrhage; Post-operative bleeding; Thromboembolism

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Introduction

The oral anticoagulant is commonly prescribed for preventing complications such as thromboembolism in patients with prosthetic heart valves, congestive heart failures and valvular defects.^{1,2} One side effect of this beneficial drug is that it makes prolonged bleeding time after surgical procedures because its anticoagulative action is antagonistic to vitamin K which is essential to achieve hemostasis.¹⁻³

In order to monitor the anticoagulation level, the use of the international normalized ratio (INR) has been recommended.⁴⁻⁸ The recommended therapeutic range of INR is 2 to 3 for general indications, but more strict level of anticoagulation is required for patients with prosthetic valves: INR range 3 to 4.^{1,5,7,8} In the medical field, if the INR range is between 2 to 4, a major general surgery is not performed because it has potential to induce much hemorrhage which cannot be controlled without changing or discontinuing the oral anticoagulant therapy (OAT).^{1,2,7} If a major surgery is proceeded without any consideration of changing or stopping anticoagulants, severe post-operative bleeding can occur and it may lead patients to life-threatening situations. But, in a minor dental surgery such as extraction, periodontal surgery and endodontic surgery, the necessity of changing or discontinuing the OAT is still questionable.

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In a normal patient, most of minor dental surgery can be performed under local anesthesia with vasoconstrictor, and post-operative hemorrhage can be controlled in most circumstances with local hemostatic methods such as local hemostatic material (bonewax, surgical, etc.), local hemostatic agent (epinephrine solution, ferric sulfate, calcium sulfate, etc.), suture, pressure dressing, and periodontal pack application.^{5,9-16} However, the effectiveness of the local hemostatic methods in patients who take the anticoagulants is not well known. Especially in endodontic surgery, it is important to control the intra-operative hemorrhage as well as post-operative hemorrhage. Inadequate bleeding control during endodontic surgery leads to the failure of apical seal, and it may result in the failure of endodontic surgery itself.¹⁷ Thus, it is also important to investigate the necessity of changing or discontinuing the OAT in endodontic surgery.

The purpose of this paper is to review the literatures about evidence that supports either changing/discontinuing or continuing the OAT for minor dental surgery and endodontic surgery, and to suggest the strategies for patients taking the OAT.

Review

Risk assessment

1. Risk of thromboembolism - Discontinue the OAT

When the patients stop the OAT, many studies reported that the risk of thromboembolism increases. In Michael's study, after discontinuing the OAT in 169 patients, the thromboembolic event occurred in 22% patients. Furthermore, 7 patients died due to thromboembolism.¹⁸ In this study, the author said that if anyone stops the OAT, he or she will soon encounter the risk of thromboembolic event regardless of the period of discontinuation. Furthermore, there is no method to select the low-risk patient, so OAT should be continued for the patient's whole life. Tulloch and Wright reported a case of a patient who discontinued the OAT for 8 days before the oral surgery, and re-took the OAT just after the surgery. Two days after the surgery, cerebral embolus occurred to that patient, and 4 days after the surgery, branchial artery embolus occurred.¹⁹ Akbarian *et al.* also reported a similar case that after temporary discontinuation of the OAT for dental procedures, the thromboembolism occurred, which later led the patient to death.²⁰ In 1998, Wahl reviewed the papers about fatal complications after withdrawal of the OAT from 1950 to 1997. There were 4 deaths and 2 nonfatal embolisms in 493 patients, and incidence of thromboembolic complication was about 1%. This is a small number of incidences, but the outcomes were very serious.¹⁶

2. Risk of hemorrhage - Continue the OAT

In 1957 Ziffer *et al.* reported two cases that the profound bleeding occurred after dental extraction in the patients who continued the OAT during the extraction²¹. After this case report, few case reports about post-operative bleeding as a consequence of continuing the OAT were followed by other authors.²²

However, Wahl reviewed more than 2,400 cases of dental surgical procedure performed on more than 950 patients receiving the continuous OAT. Only 12 patients (13 cases) experienced post-operative bleeding which later was controlled by local measures.¹⁶ The author suspected that in three of those 12 patients, the post-operative bleeding might have been caused by the concomitant administration of antibiotics. Antibiotics such as erythromycin and penicillin may enhance warfarin's anticoagulant effect, especially when administered in multiple doses.^{23,24} Campbell *et al.* reported that there is no significant difference in total blood loss during surgical procedure between continued OAT group and withdrawn OAT group at randomized controlled trial.²⁵ In a systematic review of Madrid and Sanz, the authors studied five randomized controlled trials and 11 controlled trials. They concluded that the results from these studies were very homogenous and showed minor bleedings in very few OAT-stopped patients without significant differences.²⁶ In other words, there was no significant difference in post-operative hemorrhage between the patients who continued the OAT with the recommended INR range of 2 to 4 and the patients who discontinued the OAT. Also, post-operative bleeding did not correlate with the INR status.

In most studies, post-operative bleeding was controlled well only with local hemostatic measures, such as tranexamic acid mouthwashes, gelatin sponges and cellulose gauze application.^{8,10-12,14,15,27} The incidence of postoperative bleeding which could not be controlled by the common local measures varied from 0% to 3.5%.^{13,28} It is also reported that when the post-operative hemorrhage occurred, the cause was not necessarily the prolonged INR or hemostatic modalities; instead, it was severe local infection such as a severe periodontitis at extraction site.^{28,29}

Meaning of INR value

In general, most of anticoagulation therapy aims at INR range 2.5 to 3.5. In a few cases, which need more powerful anti-thrombogenic efficacy, the INR value is kept around 4.^{5,7,8} If a patient has the INR value above 5, the risk of spontaneous bleeding increases. Spontaneous intestinal bleeding may be very dangerous, therefore it is recommended to uppermost level of INR value around 4. Almost every patient who takes the OAT has INR range 2 to

4 and a healthy adult has INR range 0.9 to 1.3.

There were several reports about the relationship between INR value and bleeding. In 2001, Blinder *et al.* reported that INR value did not significantly influence the incidence of post-operative bleeding, and concluded that there was no significant correlation between INR value and post-operative bleeding if the proper hemostatic measures were used.^{4,27} The INR value must be regarded as one of the reference index, and not an absolute predictive index for post-operative bleeding tendency.^{4,10,25,30-33}

In conclusion, even if the INR value is in therapeutic range (2 - 4), post-operative hemorrhage can not be so serious and can be well controlled in a dental minor surgery, especially when the local hemostatic methods are used appropriately.

Weighing the risks

Bleeding complications can cause troublesome and worrisome situations for patients, but in fact, they are less dangerous and less risky than thromboembolic complications. Although the risk of thromboembolism is relatively low, the consequence is serious and can be fatal.³⁴ In addition, the possibility of thromboembolic complications is not predictable because these complications often have sudden onset. Because of its sudden onset, the anticoagulation therapy must be continued in order to lower the possibility of thromboembolism.

In the literature's view, a few case reports supported the discontinuing the anticoagulant therapy, while, a number of randomized and/or controlled clinical trial supported the continuing the OAT.^{3-7,14-16,18,19,22,25,27,31-33,35-37} According to the recommendation recently published in Evidence-Based Clinical Practice Guidelines from American college of Chest Physicians, in patients who require a minor dental procedure, it is suggested to continue the Vitamin K antagonist (VKAs) such as warfarin (which is used for antithrombogenesis) with co-administration of an oral prohemostatic agent or to stop the VKAs only for 2 to 3 days before the dental procedure when the patient has low risk of complications.²

Clinical strategies

There are several strategies about the peri-operative OAT control in clinical situation¹. First strategy is to discontinue the OAT. Routinely, the anticoagulants such as warfarin have been recommended to be stopped for 5 - 7 days before a surgery in dental practice. According to the articles which were reviewed, this routine strategy of stopping the anticoagulants 5 - 7 days before minor dental surgery and re-taking after surgery is not recommended any more.^{1,2,4,5,31} Potential mortality risks associated with

the intravascular thromboembolism obviously outweigh the post-operative bleeding complication after dental surgery such as post-operative bleeding, regardless of how severe dental condition can be.

Second strategy is decreasing the level of anticoagulation. This strategy has been recommended for patients with high INR values because of the risk of severe post-operative bleeding. However, the correlation between the INR value and the incidence of post-operative bleeding is significantly low. Pre-operative INR value is not an absolute indicator of the post-operative bleeding risk.^{6,10,25,30-33}

Third strategy is 'bridging therapy' which means replacing oral anticoagulants with heparin injections.^{29,36} The main advantage of this approach is that it reduces the unprotected time down to 12 - 24 hours. But there are many disadvantages; it requires hospitalization and additional procedure before surgery; it is complex and expensive. The bridging therapy is recommended for the patient who has very high risk of thromboembolism, requires post-operative INR monitoring and has risk of major post-operative bleeding. To optimally implement this strategy, the high level of interdisciplinary cooperation is necessary.

The last strategy is continuing the anticoagulant therapy. According to our literature review, the current scientific evidence did not support the modification of the OAT regimen in patients with INR < 3.5.^{30,35} As mentioned earlier, the risks of thromboembolism resulting from the discontinuing the anticoagulation or the decreased anticoagulation level is greater than the risk of local post-operative bleeding. The evidence weighs heavily in favor of not changing the OAT regimen before minor surgery. In some rare cases, bleeding after surgery can occur, but it can be well controlled by the oral prohemostatic agent such as tranexamic acid mouthwash and/or local hemostatic measures such as material (bonewax, surgical), agent (epinephrine solution, ferric sulfate, calcium sulfate), suture, pressure dressing, and periodontal pack application.

However, this strategy does not mean that a dentist can do any kind of minor surgery without consultation with a patient's physician. The dentist must consult with the physician and verify that the patient's systemic status is acceptable for the minor surgical procedure. The purpose of the consultation is first, the confirmation of INR value within therapeutic range for dental surgical procedures. Second, it is to let the physician know that the patient will be taken some kind of dental minor surgery. Third, it is to schedule the dental surgery appointment 2 - 3 days after the patient's routine INR check appointment if possible.

Viewpoint of endodontic microsurgery

Bleeding control after a tooth extraction in the patients with anticoagulants was well studied and reviewed in

numerous articles.^{8,10-12,14,15,27} In these studies, post-extraction bleeding cases were generally well-controlled using local hemostatic measures. Pre-operative tranexamic acid mouthwash was proven effective in several articles, and post-operative procedures such as sutures, local pressure, and gauze biting were also effective in the post-extraction bleeding control.^{3,11,12,28,30}

However, there is a difference between endodontic microsurgery and tooth extraction. The endodontic surgeries include an apicoectomy, a retrograde preparation of root canal, a retrograde filling procedure, and an endodontic microsurgery, which is performed under an operating microscope.^{17,38-40} These endodontic procedures are very delicate and technique sensitive in nature. Especially when a dentist tries to identify the cause of failures of prior non-surgical or surgical endodontic treatment by inspecting and examining the resected root surface, intra-operative bleeding control is essential to achieve a successful result.^{17,41-43}

In the retrograde filling procedure, bleeding control is also one of the most critical steps to accomplish a tight seal with retrograde filling materials. Mineral Trioxide Aggregate (MTA), which is widely used for retrograde filling material nowadays, is interrupted to set if a direct contact with the serum and/or blood is present.⁴⁴⁻⁴⁶ Another retrograde filling material, super-ethoxybenzoic acid (superEBA), was not significantly affected by storage in serum for 24 hours, but further long-term studies are necessary.⁴⁶

In spite of the importance of bleeding control in endodontic microsurgery, there were almost no studies about the difficulty of intra-operative bleeding control in the patients who continue the anticoagulant therapy for the endodontic procedures. It is just assumed that if a patient has been prescribed the anticoagulant, then the patient's bleeding tendency will be increased and it will be harder to achieve a clean view and a perfect hemostasis during the inspection of the resected root surface and the retrograde filling procedure.

Now, it is important to study and investigate about effectiveness of the local hemostatic measures in endodontic surgery in the patients with anticoagulants. There were many old articles which emphasized that the bleeding can be controlled well using the local hemostatic measures in the numerous cases but none of them was an endodontic surgery case. Further study is required about intra-operative bleeding control in endodontic surgery patient who is taking the oral anticoagulant therapy.

Conclusions

In a minor dental surgery, the anticoagulation therapy should not be discontinued in the majority of patients. The risk of significant bleeding in patients on the oral anticoagulants is low; the risk of thromboembolism may

increase in patients on the oral anticoagulants if the OAT is temporarily discontinued, which can be fatal.

In patients who are continuing the anticoagulation therapy, post-operative bleeding can be well controlled with the local hemostatic measures. In the endodontic surgery, further research is necessary to find out whether intra-operative bleeding control can be achieved well only with local hemostatic measures in patients who continue the anticoagulation therapy.

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References

1. Spyropoulos AC, Douketis JD. How I treat anticoagulated patients undergoing an elective procedure or surgery. *Blood* 2012;120:2954-2962.
2. Douketis JD, Spyropoulos AC, Spencer FA, Mayr M, Jaffer AK, Eckman MH, Dunn AS, Kunz R; American College of Chest Physicians. Perioperative management of antithrombotic therapy: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest* 2012;141:e326S-350S.
3. Wahl MJ. Myths of dental surgery in patients receiving anticoagulant therapy. *J Am Dent Assoc* 2000;131:77-81.
4. Perry DJ, Noakes TJ, Helliwell PS; British Dental Society. Guidelines for the management of patients on oral anticoagulants requiring dental surgery. *Br Dent J* 2007;203:389-393.
5. Sacco R, Sacco M, Carpenedo M, Mannucci PM. Oral surgery in patients on oral anticoagulant therapy: a randomized comparison of different intensity targets. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2007;104:e18-21.
6. Salam S, Yusuf H, Milosevic A. Bleeding after dental extractions in patients taking warfarin. *Br J Oral Maxillofac Surg* 2007;45:463-466.
7. Devani P, Lavery KM, Howell CJ. Dental extractions in patients on warfarin: is alteration of anticoagulant regime necessary? *Br J Oral Maxillofac Surg* 1998;36:107-111.
8. Aframian DJ, Lalla RV, Peterson DE. Management of dental patients taking common hemostasis-altering medications. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2007;103 Suppl:S45.e1-11.
9. Al-Mubarak S, Al-Ali N, Abou-Rass M, Al-Sohail A, Robert A, Al-Zoman K, Al-Suwayed A, Ciancio S. Evaluation of dental extractions, suturing and INR on postoperative bleeding of patients maintained on oral anticoagulant therapy. *Br Dent J* 2007;203:E15;discussion 410-411.
10. Blinder D, Manor Y, Martinowitz U, Taicher S, Hashomer

- T. Dental extractions in patients maintained on continued oral anticoagulant: comparison of local hemostatic modalities. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1999;88:137-140.
11. Carter G, Goss A. Tranexamic acid mouthwash—a prospective randomized study of a 2-day regimen vs 5-day regimen to prevent postoperative bleeding in anticoagulated patients requiring dental extractions. *Int J Oral Maxillofac Surg* 2003;32:504-507.
 12. Carter G, Goss A, Lloyd J, Tocchetti R. Tranexamic acid mouthwash versus autologous fibrin glue in patients taking warfarin undergoing dental extractions: a randomized prospective clinical study. *J Oral Maxillofac Surg* 2003;61:1432-1435.
 13. Pototski M, Amenábar JM. Dental management of patients receiving anticoagulation or antiplatelet treatment. *J Oral Sci* 2007;49:253-258.
 14. Ramström G, Sindet-Pedersen S, Hall G, Blombäck M, Alander U. Prevention of postsurgical bleeding in oral surgery using tranexamic acid without dose modification of oral anticoagulants. *J Oral Maxillofac Surg* 1993;51:1211-1216.
 15. Souto JC, Oliver A, Zuazu-Jausoro I, Vives A, Fontcuberta J. Oral surgery in anticoagulated patients without reducing the dose of oral anticoagulant: a prospective randomized study. *J Oral Maxillofac Surg* 1996;54:27-32;discussion 323.
 16. Wahl MJ. Dental surgery in anticoagulated patients. *Arch Intern Med* 1998;158:1610-1616.
 17. Kim S, Kratchman S. Modern endodontic surgery concepts and practice: a review. *J Endod* 2006;32:601-623.
 18. Michaels L. Recurrence of thromboembolic disease after discontinuing anticoagulant therapy. A study of factors affecting incidence. *Br Heart J* 1970;32:359-364.
 19. Tulloch J, Wright IS. Long-term anticoagulant therapy; further experiences. *Circulation* 1954;9:823-834.
 20. Akbarian M, Austen G, Yurchak PM, Scannell JG. Thromboembolic complications of prosthetic cardiac valves. *Circulation* 1968;37:826-831.
 21. Ziffer AM, Scopp IW, Beck J, Baum J, Berger AR. Profound bleeding after dental extractions during dicumarol therapy. *N Engl J Med* 1957;256:351-353.
 22. Schmitt J, Ingram RC, Harpole HJ. Hematoma following dental extractions in a patient receiving unreported anticoagulant therapy. *Oral Surg Oral Med Oral Pathol* 1960;13:791-794.
 23. Bandrowsky T, Vorono AA, Borris TJ, Marcantoni HW. Amoxicillin-related postextraction bleeding in an anticoagulated patient with tranexamic acid rinses. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1996;82:610-612.
 24. Wood GD, Deeble T. Warfarin: dangers with antibiotics. *Dent Update* 1993;20:350,352-353.
 25. Campbell JH, Alvarado F, Murray RA. Anticoagulation and minor oral surgery: should the anticoagulation regimen be altered? *J Oral Maxillofac Surg* 2000;58:131-135;discussion 135-136.
 26. Madrid C, Sanz M. What influence do anticoagulants have on oral implant therapy? A systematic review. *Clin Oral Implants Res* 2009;20 Suppl 4:96-106.
 27. Blinder D, Manor Y, Martinowitz U, Taicher S. Dental extractions in patients maintained on oral anticoagulant therapy: comparison of INR value with occurrence of postoperative bleeding. *Int J Oral Maxillofac Surg* 2001;30:518-521.
 28. Morimoto Y, Niwa H, Minematsu K. Hemostatic management of tooth extractions in patients on oral antithrombotic therapy. *J Oral Maxillofac Surg* 2008;66:51-57.
 29. Bajkin BV, Popovic SL, Selakovic SD. Randomized, prospective trial comparing bridging therapy using low-molecular-weight heparin with maintenance of oral anticoagulation during extraction of teeth. *J Oral Maxillofac Surg* 2009;67:990-995.
 30. Al-Mubarak S, Rass MA, Alsuwyed A, Alabdulaaly A, Ciancio S. Thromboembolic risk and bleeding in patients maintaining or stopping oral anticoagulant therapy during dental extraction. *J Thromb Haemost* 2006;4:689-691.
 31. Balevi B. Should warfarin be discontinued before a dental extraction? A decision-tree analysis. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2010;110:691-697.
 32. Beirne OR. Evidence to continue oral anticoagulant therapy for ambulatory oral surgery. *J Oral Maxillofac Surg* 2005;63:540-545.
 33. Martinowitz U, Mazar AL, Taicher S, Varon D, Gitel SN, Ramot B, Rakocz M. Dental extraction for patients on oral anticoagulant therapy. *Oral Surg Oral Med Oral Pathol* 1990;70:274-277.
 34. Dunn AS, Turpie AG. Perioperative management of patients receiving oral anticoagulants: a systematic review. *Arch Intern Med* 2003;163:901-908.
 35. Evans IL, Sayers MS, Gibbons AJ, Price G, Snooks H, Sugar AW. Can warfarin be continued during dental extraction? Results of a randomized controlled trial. *Br J Oral Maxillofac Surg* 2002;40:248-252.
 36. Herman WW, Konzelman JL Jr, Sutley SH. Current perspectives on dental patients receiving coumarin anticoagulant therapy. *J Am Dent Assoc* 1997;128:327-335.
 37. Sacco R, Sacco M, Carpenedo M, Moia M. Oral surgery in patients on oral anticoagulant therapy: a randomized comparison of different INR targets. *J Thromb Haemost* 2006;4:688-689.
 38. Song M, Shin SJ, Kim E. Outcomes of endodontic microsurgery: a prospective clinical study. *J Endod* 2011;

- 37:316-320.
39. Song M, Chung W, Lee SJ, Kim E. Long-term outcome of the cases classified as successes based on short-term follow-up in endodontic microsurgery. *J Endod* 2012; 38:1192-1196.
40. Song M, Kim E. Success and failure of endodontic microsurgery. *J Korean Acad Conserv Dent* 2011;36:465-476.
41. Scarano A, Artese L, Piattelli A, Carinci F, Mancino C, Iezzi G. Hemostasis control in endodontic surgery: a comparative study of calcium sulfate versus gauzes and versus ferric sulfate. *J Endod* 2012;38:20-23.
42. Setzer FC, Kohli MR, Shah SB, Karabucak B, Kim S. Outcome of endodontic surgery: a meta-analysis of the literature-Part 2: Comparison of endodontic microsurgical techniques with and without the use of higher magnification. *J Endod* 2012;38:1-10.
43. Song M, Kim HC, Lee W, Kim E. Analysis of the cause of failure in nonsurgical endodontic treatment by microscopic inspection during endodontic microsurgery. *J Endod* 2011;37:1516-1519.
44. Kim Y, Kim S, Shin YS, Jung IY, Lee SJ. Failure of setting of mineral trioxide aggregate in the presence of fetal bovine serum and its prevention. *J Endod* 2012; 38:536-540.
45. Chang SW. Chemical characteristics of mineral trioxide aggregate and its hydration reaction. *Restor Dent Endod* 2012;37:188-193.
46. Kang JS, Rhim EM, Huh SY, Ahn SJ, Kim DS, Kim SY, Park SH. The effects of humidity and serum on the surface microhardness and morphology of five retrograde filling materials. *Scanning* 2012;34:207-214.