Review article

Evaluation of the effects of anticoagulant drugs on the rate of bleeding of oral surgeries and warfarin alternatives

Amirhosein Pakravan1, Tahmine Bamdadian2, Pouya Akbari3, Arash Alimirzaei3, Ali Samiei3, Mahdi Babaei Hatkehloui3, Mahdi Taghian1

1. Assistant Professor, Department of oral and maxillofacial surgery, Faculty of Dentistry, Mazandaran University of Medical Sciences, Sari, Iran

2. Assistant Professor, Department of prosthodontics, Faculty of Dentistry, Mazandaran University of Medical Sciences, Sari, Iran

3. Dentistry Student, Faculty of Dentistry, Student Research Committee, Mazandaran University of Medical Sciences, Sari, Iran.

*correspondence: **Mahdi Taghian** Assistant professor, department of oral and maxillofacial surgery, faculty of dentistry, Mazandaran University of medical sciences, Sari, Iran. Email: drmehdi_taghian@yahoo.com

Abstract:

Introduction: Today, with advances in the treatment of cardiovascular patients such as intravascular stents, cardiac valves and intracavitary pacemakers and cardiac transplantation, many cardiovascular patients should use anticoagulants such as warfarin, aspirin, Plavix and Sosix, Ticlopidine and other drugs. The aim of this study was to investigate the effects of coagulation drugs on the rate of bleeding of oral surgeries and warfarin alternative.

Methods: For access to studies on anticoagulant drugs and their effect on the bleeding of oral surgery in heart patients, the PUBMED, MEDLINE, MAGIRAN, SID, ELMNET and GOOGLE databases have been used since 1998 to 2015. Keywords include oral surgery, anticoagulants, warfarin, dentistry and bleeding.

Findings: In the investigations done on the studied articles, it seems that patients with anticoagulant drugs that are supposed to undergo minor dental surgeries do not require discontinuation, dose reduction, or even control of coagulation factors and bleeding can only be controlled by local dental procedures such as suturing, mouthwash, gel sponge. And the risk of severe complications in case of warfarin interruption and thrombosis is more than uncontrolled bleeding from the teeth. There is also no need for alternative warfarin medicines.

Conclusion: The hazard of severe complications in case of warfarin interruption and thrombosis is more than uncontrolled hemorrhage from the teeth. There is also no need for alternative warfarin treatments.

Keywords: Oral Surgery, Anticoagulants, Warfarin, Dentistry, Bleeding

Introduction:

Today, with advances in the treatment of cardiovascular patients such as intravascular stents, cardiac valves and intracavitary pacemakers and cardiac transplantation, many cardiovascular patients should use anticoagulants such as warfarin, aspirin, Plavix and Sosix, Ticlopidine and other drugs (1). These patients sometimes need simple oral surgical procedures, such as removing one or two teeth , in the past, it was strongly recommended that the anticoagulants used in these patients were cut or reduced several days before the teeth were extracted, and then the actions were carried out (2). In patients with coagulation disorders, the coagulation status is evaluated based on specific laboratory tests, including those that can be used to evaluate prothrombin time (PT), INR is a unit of measurement that includes the patient's PT and PT of control, and its normal value is 2-3 for medical and dental treatments (3). The mechanism of anticoagulant activity of warfarin is through control of factors II, VII, IX and factor X. The final anticoagulant effect of warfarin is delayed until normal blood clotting factors, especially prothrombin, are removed from circulation. The warfarin threshold dose is not observed for 36 to 72 hours after drug administration, which is due to plasma half-life of factor II, which is approximately 3 days (4). Temporary interruption of anticoagulant drugs will reduce the risk of valve thrombosis, closure of coronary arteries, and the risk of death and various types of embolic events. In these patients, in some cases, dental procedures such as tooth extraction, dental extraction and other interventions are required, with the advancement and development of dental treatments and use of local anesthetics for patients, even for patients with an INR level of 2-4, Dental procedures can be done. Most general dentists refer patients taking anticoagulants, especially warfarin, to jaw surgeons for tooth extraction (5). To reduce the dangers of dental procedures for patients with bleeding problems, we need to get acquainted with the blood and disorders and the cases that affect it, and some considerations must be observed for these patients (6). The aim of this study was to investigate the effects of coagulation drugs on the rate of bleeding of oral surgeries and warfarin alternative.

Methods:

For access to studies on anticoagulant drugs and their effect on the bleeding of oral surgery in heart patients, the PUBMED, MEDLINE, MAGIRAN, SID, ELMNET and GOOGLE databases have been used since 1998 to 2015. Keywords include oral surgery, anticoagulants, warfarin, dentistry and bleeding. 24 articles including review articles, descriptive studies, cross-sectional research, prospective articles, and case reports that contain the latest information on dental procedures and the use of anticoagulant drugs (warfarin, aspirin, Plavix, etc.) were analyzed. Among the searched articles, 24 of them had all the data required for the study and also, the latest anti-coagulant therapies were reviewed before and after dental procedures in cardiac patients. In the past, for these patients it was strongly recommended to discontinue or reduce anticoagulants several days before

the dental procedure, even for simple oral surgery such as removing one or two teeth and then the desired actions were taken (2). All heart patients treated with synthetic materials (Metal valves, patients with arrhythmias such as AF) should be treated with anticoagulants for prolonged periods to prevent events such as DVT and ambulatory events (7-11). Dentists are required to ask for an INR test and prothrombin time (PT) test and consult their cardiologist before dental practitioners. And then decide on the use of the patient's medications (12-14). We will explain the types of anticoagulants.

Warfarin

Warfarin is an anticoagulant which is used to reduce blood coagulation. This substance inhibits the coagulation factors associated with vitamin K. Despite the risk of bleeding, warfarin is the most common oral medication used today as anticoagulant. Warfarin can be used alone or in combination with other selective drugs. In a study conducted by Zhang et al., The incidence of bleeding following warfarin administration alone or in combination with some other drugs was investigated (15).

Rivaroxaban (XARELTO)

Rivaroxaban is used as oral pills to treat and prevent deep vein thrombosis (DVT) and pulmonary embolism, as well as to reduce the risk of stroke in patients with non-valvular AF in order to prevent venous thromboembolism (VTE) in patients undergoing knee replacement or pelvic surgery. For patients undergoing pelvic surgery, the duration of treatment is 5 weeks. For patients undergoing major knee surgery, the duration of treatment is 2 weeks. It is also used to prevent stroke in people with atrial fibrillation (AF). In patients with AF, the dose is 20 mg once a day. Rivaroxaban is also used in the treatment of deep vein thromboembolism (DVT) and pulmonary embolism and is approved by the FDA. In this case, Rivaroxaban is given at a dose of 15 mg twice daily for the first 3 weeks, followed by 20 mg once a day (16).

Aspirin and Plavix

The most commonly used drug for heart disease is aspirin and Plavix. The use of low dose aspirin in addition to warfarin is recommended in patients at risk for thromboembolism because the use of this amount of aspirin reduces the risk of clotting without increasing the risk of bleeding. Plavix inhibits platelet aggregation by reducing or stopping platelets from joining blood vessels or injured tissues. The side effects of these drugs are due to their anticoagulant effect and may be needed to discontinue them in extensive surgical procedures. However, studies have shown that dental procedures that do not have a high risk of bleeding can be applied to all dental procedures with local control measures (9-10).

Discussion:

Due to the severe and dangerous side effects of discontinuing anticoagulant drugs for several days (such as types of embolisms, DVT and vascular thrombosis, and increased risk of stroke and MI) the use of alternative methods instead of interrupting or reducing the dose of anticoagulant drugs and saving

time is recommended for patients and dentists who have had to control INR, PT and blood tests in the past. For example, in a study by Leeilles et al., in 2011 which was conducted on 111 patients treated with anticoagulant drugs, aspirin and colopridogrel (Plavix) all complications of bleeding were ultimately controlled only by local hemostatic therapies and there was no need for treatment discontinuation and being under the risks associated with discontinuation of treatment (17). Also, in a study by Dr. Peymani Mojaver et al. in 2011, which was conducted as a clinical trial, on 22 patients with warfarin consuming who had tooth extraction, bleeding control was done using gelatinous sponge and sterile gas (without localized homeostasis) and it was concluded that warfarin users do not need to stop or reduce their dose of warfarin. The use of 4% / 8 Tranexamic acid is effective as local homeostasis without suturing (18). In the study of Morimoto et al in 2009, on 270 patients with heart problems treated with warfarin or other anticoagulant drugs, it was concluded that in most cases of teeth extraction treated with anticoagulant drugs, warfarin (INR <3.0) and antithrombotic drugs, homeostasis can be adequate. Additionally, suitable localized homeostasis techniques can occur when bleeding occurs after an operation (19). Sacco et al. (2007), in a randomized, prospective, retrospective study of 131 patients undergoing anticoagulant therapy that performed simple dental surgery indicated that using simple measures for localized homeostasis, reducing oral anticoagulant therapy in patients undergoing simple dental surgery is unnecessary (1). In a 2007 study by Salam et al., 150 patients treated with anticoagulant, who had an INR of 4, and those who performed tooth extraction in the hospital, had no significant clinical bleeding after surgery (20). In a 2005 cross-sectional study by Dr. Haraji et al. and an observational study conducted on 362 patients treated with anticoagulants, The percentage of bleeding after simple extraction of the tooth in these patients without discontinuing these drugs during dental treatment and analyzing the percentage of bleeding was assessed based on the use of INR size, finally, the percentage of bleeding in the studied groups did not show significant difference and thus no changes were needed in regard with discontinuation or reduction of the dosage of consumed medications. The simple removal of teeth in these patients is possible, and topical bleeding can be controlled with the use of topical hemostatic materials and stitching the edges of the cavity (5) or in the study of Elblasi et al. in 2003, the use of histoacryl adhesive in reducing the local bleeding of oral surgeries in patients treated with anticoagulants was studied. Multiple teeth extraction can be performed in patients who use anticoagulant drugs without changing their anticoagulants, so that effective local hemostasis can be achieved. In this regard, the histoacryl adhesive, used as a topical adhesive from the porous edges of the wound, provides a temporary and effective stasis for oral surgery in these patients (21). Another study by Evans et al. in 2002, on 109 patients as a randomized controlled trial was performed. It was concluded that the continuation of warfarin when INR <4.1 could lead to increased

bleeding after extraction of the tooth, but there was no evidence of an increase in significant clinical bleeding (22). In addition, in several other studies conducted in Japan, the United States and Iran, even without using some homeostasis methods, there was no significant difference between users of anticoagulants and those with a few days interval who had discontinuation or reduction of medication. Like a study done by Campbell and his colleagues on two groups of patients treated with anti-coagulant drugs, a group discontinued the drug for 72 to 96 hours prior to oral surgery and The second group went under tooth extraction without discontinuing medication, there was no significant difference in bleeding during and after surgery (23-24). In a study by Blinder et al., in 1999, performed on 150 patients undergoing tooth extraction, instead of interrupting warfarin, three methods of topical homeostasis including: 1-gelatin sponge + suture 2-gelatin sponge + suture + mouthwash 3- Tranexamic acid + Gelatin Sponge + Suture + Fibrin Glue were used. Only 13 cases of hemorrhage have been reported suggesting that these methods are very effective and do not require medication discontinuation (25).

Conclusion:

In the investigations done on the studied articles, it seems that patients with anticoagulant drugs that are supposed to undergo minor dental surgeries do not require discontinuation, dose reduction, or even control of coagulation factors and bleeding can only be controlled by local dental procedures such as suturing, mouthwash, gel sponge. And the risk of severe complications in case of warfarin interruption and thrombosis is more than uncontrolled bleeding from the teeth. There is also no need for alternative warfarin medicines.

References:

1. 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 Jul;104(1):e18-21.
2. Roser SM, Rosenbloom B. Continued anticoagulation in oral surgery procedures. Oral Surg Oral Med Oral Pathol. 1975 Oct;40(4):448-57.
3. Fonseca RJ. Oral and maxillofacial surgery. 1st ed. Philadelphia: W.B. Saunders Co; 2000.
4. O'Reilly RA, Aggeler PM. Studies on coumarin anticoagulant drugs: Initiation of warfarin therapy without a loading dose. Circulation 1968; 38(1): 169-77.
5. Haraji A, Zare Mahmood Abadi, Khadem Hosseini A. Dental extractions in patients maintained on oral anticoagulant therapy: comparison of International Normalized Ratio (INR) value with occurrence of postoperative bleeding. Dent J Mashhad Univ Medi Scie 2005; 29: 45-50.
6. Bonow RO, Carabello B, de Leon AC, Edmunds LH Jr, Fedderly BJ, Freed MD,et al.ACC/AHA guidelines for the management of patients with valvular heart disease. Executive summary. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Management of Patients With Valvular Heart Disease). J Heart Valve Dis. 1998 Nov;7(6):672-707.
7. Hirsh J, Fuster V, Ansell J, Halperin JL .American Heart Association/American College of Cardiology foundation guide to warfarin therapy. Circulation. 2003 Apr 1;107(12):1692-711.
8. Al-Harkan AM, Al-Ayoub GA .Should antiplatelet and anticoagulant medications be

discontinued before minor oral surgery procedures?. J Can Dent Assoc. 2012;78:c24.
9. Girotra C, Padhye M, Mandlik G, Dabir M, Gite M, Dhonnar R, Pandhi V ,et al.Assessment of the risk of haemorrhage and its control following minor oral surgical procedures in patients on anti-platelet therapy: a prospective study. Int J Oral Maxillofac Surg. 2014 Jan;43(1):99-106.
10. Napeñas JJ, Hong CH, Brennan MT, Furney SL, Fox PC, Lockhart PB. The frequency of bleeding complications after invasive dental treatment in patients receiving single and dual antiplatelet therapy. J Am Dent Assoc. 2009 Jun;140(6):690-5.
11. Ciske D, Robinson E, Ford M. Periprocedural and Regional Anesthesia Management with Antithrombotic Therapy – Adult – Inpatient and Ambulatory– Clinical Practice Guideline. Wisconsin univ
12. Pototski M1, Amenábar JM. Dental management of patients receiving anticoagulation or antiplatelet treatment. J Oral Sci. 2007 Dec;49(4):253-8.
13. Wahl MJ, Pinto A, Kilham J, Lalla RV. Dental surgery in anticoagulated patients. Oral Surg Oral Med Oral Pathol Oral Radiol. 2015 Feb;119(2):136-57.
14. Alexander R, Ferretti AC, Sorensen JR. Stop the nonsense not the anticoagulants: a matter of life and death. N Y State Dent J. 2002 Nov;68(9):24-6.
15. Zhang K, Yong C, Berger J. Administrative claims analysis of the relationship between warfarin use and risk of hemorrhage including drug-drug and drug-disease interactions. J Manag Care Pharm 2006; 12: 640-8.
16. Abdulsattar Y, Bhambri R, Nogid A. Rivaroxaban (xarelto) for the prevention of thromboembolic disease: an inside look at the oral direct factor xa inhibitor. P T. 2009 May;34(5):238-44.
17. Lillis T, Ziakas A, Koskinas K, Tsirlis A, Giannoglou G. Safety of dental extractions during uninterrupted single or dual antiplatelet treatment. Am J Cardiol. 2011 Oct 1;108(7):964-7.
18. Peymani Mojaver A, Soltani M, Bakhshi H. Effect of Gelatin Sponge and Tranexamic Acid M.rinses on Prevention of Bleeding after Dental Extraction in Patients Taking Warfarin. J Mash Dent Sch 2011; 35(1): 17-22.
19. Morimoto Y, Niwa H, Minematsu K. Hemostatic management of toothextractions in patients on oral antithrombotic therapy. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2009 Dec;108(6):889-96.
20. Salam S, Yusuf H, Milosevic A. Bleeding after dental extractions in patients taking warfarin. Br J Oral Maxillofac Surg. 2007 Sep;45(6):463-6.
21. Al-Belasy FA, Amer MZ.Hemostatic effect of n-butyl-2-cyanoacrylate (histoacryl) glue in warfarin-treated patients undergoing oral surgery. Journal of oral and maxillofacial surgery. J Oral Maxillofac Surg. 2003 Dec;61(12):1405-9.
22. 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 Jun;40(3):248-52.
23. Campbell JH, Alvarado F, Murray RA.Anticoagulation and minor oral surgery: should the anticoagulation regimen be altered?. J Oral Maxillofac Surg. 2000 Feb;58(2):131-5.
24. Pooria A, Teimouri H, Cheraghi M, Ahmadi BB, Namdari M, Alipoor R. Comparison of postoperative bleeding in patients undergoing coronary artery bypass surgery in two groups taking aspirin and aspirin plus CLS clopidogrel. Middle East Journal of Family Medicine. 2017 Oct 1;7(10):17.
25. 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 Aug;88(2):137-40.