

# Bleeding Complications in Relation to the International Normalized Ratio for Dental Extractions in Patients under Chronic Anticoagulant Therapy - An Evaluative Study

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## Abstract

**Introduction:** Recent simple dental extraction protocols suggest that therapeutic levels of the anticoagulant drug should be maintained because bleeding complications could be managed with local haemostasis manoeuvres. The aim of the present study was to evaluate the association between bleeding complications and the international normalized ratio (INR) values in patients after dental extractions completed with a plug of bismuth subgallate, without interrupting anticoagulant administration. **Materials and Methods:** Patients undergoing oral Vitamin K antagonist chronic anticoagulant therapy requiring simple dental extractions were included in the study. INRs were recorded on the day of the surgery, and dental extractions were performed applying bismuth subgallate as a haemostatic agent. Patients took their anticoagulation drug normally. Bleeding complications were recorded. **Results:** The study included 694 patients, of whom 11 (1.58%) presented mediate post-operative bleeding that was effectively controlled through local manoeuvres. No episode of thromboembolism or infectious endocarditis was observed. The incidence of bleeding complications was not related to the INR values ( $P > 0.05$ ). **Discussion:** INR values were not related to bleeding complications when simple dental extractions were performed applying bismuth subgallate as a haemostatic agent.

**Keywords:** Bismuth subgallate, chronic anticoagulant therapy, dental extraction, haemorrhage, international normalized ratio

## INTRODUCTION

Patients undergoing chronic oral anticoagulant therapy are prone to bleeding complications after surgeries, including dental extractions.<sup>[1]</sup> There has been a considerable increase in the number of patients requiring dental extraction,<sup>[2]</sup> which is an acute intervention that may produce immediate or mediate bleeding complications.<sup>[3]</sup> Conventionally, treatment protocol included discontinuation of the oral anticoagulant drug some days before surgery, bridging it with heparin,<sup>[4,5]</sup> but the current recommendation is to maintain the anticoagulation therapy and improve the haemostatic process using local haemostatic agents.<sup>[4,6,7]</sup>

Bismuth subgallate is a haemostatic agent that does not interfere with the wound-healing process<sup>[8,9]</sup> or post-extraction bone healing,<sup>[10]</sup> whose effectiveness is similar to fibrin tissue adhesive.<sup>[11]</sup> However, the importance of the international normalized ratio (INR) in the prediction of bleeding episodes after dental extraction with bismuth subgallate is unknown.

The aim of the present study was to evaluate bleeding events in relation to the INR values in patients under chronic anticoagulant therapy after dental extractions in which a bismuth subgallate haemostatic agent was used.

## PATIENTS AND METHODS

This study included dental extractions in patients under chronic oral Vitamin K antagonist anticoagulant therapy who visited the Oral and Maxillofacial Department at the School of Dentistry of the University of Buenos Aires from July 2014 to December 2019. The study design was approved by the

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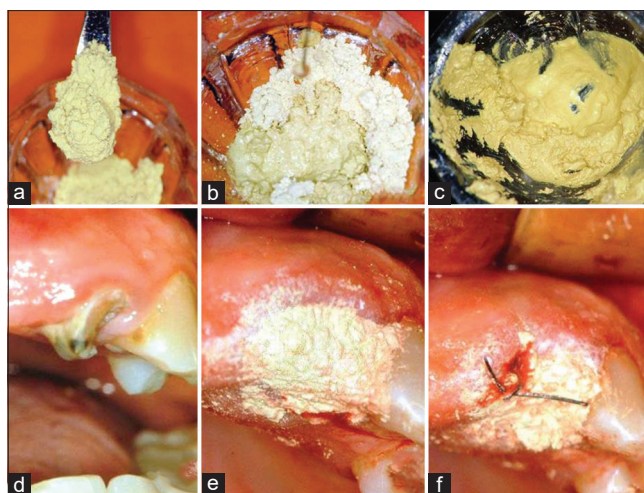
Ethics Committee of the University of Buenos Aires (Research Ethics Committee No. 006 CD48607), following the ethical guidelines of the Declaration of Helsinki. Written informed consent was obtained before surgeries.

The inclusion criteria for this study were age >18 years, patients under chronic oral Vitamin K antagonist treatment, simple dental extractions and signature in an informed consent form. The exclusion criteria were medical conditions contraindicating surgery (such as uncontrolled systemic diseases), patients under chronic new oral anticoagulant drugs (such as rivaroxaban, apixaban or edoxaban), patients unable to receive any standard medications, third molar surgeries and patients with hepatic disease or taking drugs able to affect hepatic functions.

Each patient's clinical, radiographic and systemic coagulant situation was evaluated. Tooth decay or periodontal disease were the main aetiologies for extractions. None of the patients interrupted their systemic anticoagulant therapy. INR values at the time of surgery were recorded. Prophylactic antibiotic treatment was only applied to patients at risk of bacterial endocarditis according to the standardised guidelines of the American Heart Association.<sup>[12]</sup> Patients were allocated to one of four groups according to INR values: G1 = INR <2.0, G2 = INR  $\geq$ 2.0-2.99, G3 = INR  $\geq$ 3.0-3.5 and G4 = INR >3.5.

Teeth were extracted by a single professional, specialised in treating patients with bleeding disorders. Surgeries consisted of applying local anaesthesia (4% articaine chlorhydrate and 1:100,000 adrenaline, Laboratorio Bernabo, Argentina), intracrevicular incision, minimal dissection of the gingiva, no ostectomy or flap raising, using elevator and forceps. After extraction and wound toilette, the local haemostatic plug was placed in the socket, and the wound was sutured. Bismuth subgallate powder was mixed with saline in a ratio of 0.5 g powder for every 0.3 ml of liquid, preparing enough paste to fill the socket completely [Figure 1]. All patients received the same post-operative indications, which included a cold soft diet for 48 h, intermittent application of cold on facial skin and non-steroid anti-inflammatory drugs (paracetamol). Patients were instructed to contact the service immediately if a haemorrhagic episode occurred. Patients were initially checked at 30 min after surgery to evaluate bleeding episodes, and a compressive pack was applied for four hours. A different professional evaluated patients on the second and seventh days after the extraction. If a bleeding episode occurred, it was controlled by the wound curettage, replacement of bismuth subgallate, suture of the wound and a compressive gauze pack for four hours.

A previously established standard protocol was used to compile the following data: age, gender, reason for anticoagulant therapy, INR, immediate bleeding and mediate bleeding. None of the patients dropped out. Statistical analysis included descriptive statistics of numerical variables, including arithmetic mean, standard deviation, minimum and maximum (range). INR values were compared between groups with Kruskal–Wallis test. The association between categorical



**Figure 1:** Bismuth subgallate haemostatic agent. (a) powder, (b) powder mixed with saline, (c) bismuth subgallate paste ready to use, (d) lateral upper incisor before extraction, (e) haemostatic agent inside extraction socket and (f) sutured wound

variables was examined using Pearson's Chi-square. Statistical analysis was performed with the SPSS software. The level of significance was set at 0.05. The sample size was estimated with the data analysis of the first 60 patients.

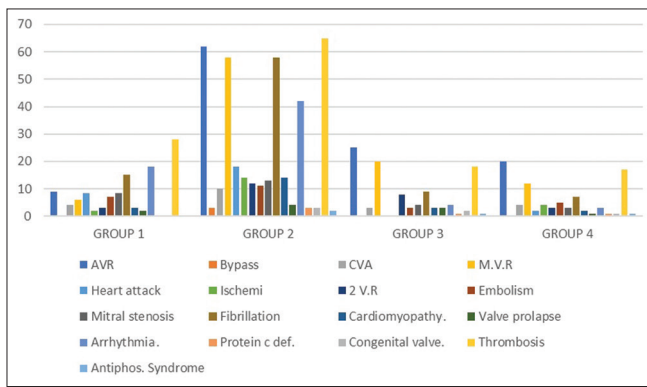
## RESULTS

A total of 854 dental extractions were performed on 694 anticoagulated patients (310 males and 384 females) aged 25–89 years (mean 60 years). The most frequent reasons for patients being under anticoagulant therapy were valve replacement and thrombosis [Table 1]. None of the patients presented a bleeding event during the immediate post-operative time, but 11 patients (1.58%) presented mediate bleeding (first to third day post-operative) [Table 2].

Among patients in G1 with INR <2.0 (mean value 1.82), 156 dental extractions were performed on 116 patients. Two patients (1.72%) presented mediate bleeding. A 42-year-old female with INR = 1.64, on anticoagulation for venous thrombosis, who underwent one dental extraction, had a bleeding episode 24 h after surgery. A 64-year-old male with INR = 1.87, on anticoagulation following an aortic valve replacement, who underwent two dental extractions, had bleeding episodes 48 h after surgery.

Among patients in G2 with INR  $\geq$ 2.0-2.99 (mean value 2.63), 480 dental extractions were performed on 395 patients. Six of them (1.52%) (mean value 2.74) had bleeding events during the post-operative period. Two of them were on anticoagulation for mitral stenosis and thrombophlebitis (females aged 67 and 70 years), underwent multiple dental extractions and had bleeding events 24 h after surgery. Three patients (males aged 53, 64 and 68 years) suffering from dilated cardiomyopathy, venous thrombosis and auricular fibrillation, underwent a single dental extraction and had a bleeding event 48 h after surgery. One patient (63-year-old female) was on anticoagulation for

**Table 1: Anticoagulant therapy indications**



**Table 2: Mediate post-operative bleeding complications in patients in all four groups. P > 0.05**

GROUP	n	Bleeding Events (patients)	Bleeding Events (percentage)
I	116	2	1.72%
II	395	6	1.52%
III	104	2	1.92%
IV	79	1	1.27%
Total	694	11	1.58%

venous thrombosis, underwent two dental extractions and had a bleeding event 72 h after surgery.

Among patients in G3 with INR ≥3.0-3.5 (mean value 3.17), 132 dental extractions were performed on 104 patients. Two patients (1.92%) (INR 3.04 and 3.2) suffered post-operative bleeding. One was on anticoagulation for auricular fibrillation (61-year-old female) and the other was for aortic and mitral valve replacement (65-year-old female). Dental extractions were performed and bleeding events occurred 24 h after surgery.

Among patients in G4 with INR >3.5 (mean value 3.79), 86 dental extractions were performed on 79 patients. Only one of them (1.27%) (INR = 4.2) suffered post-operative bleeding 72 h after surgery. This patient (59-year-old female) was on anticoagulant therapy for venous thrombosis.

The incidence of post-operative bleeding did not differ significantly among the study groups (P > 0.05). The INR values of 11 patients that presented post-operative bleeding did not differ significantly from those of the 683 patients without post-operative bleeding (P > 0.05).

None of the 11 patients with post-operative bleeding required Vitamin K treatment, transfusions or hospitalisation. No thromboembolic episode or infectious endocarditis was recorded in the four study groups.

## DISCUSSION

The traditional practice of replacing oral anticoagulant drugs with heparin considerably increases the costs of oral surgery

due to its high price and the need for hospitalisation.<sup>[5]</sup> Recent studies recommend not interrupting oral anticoagulant therapy, but applying haemostatic agents when simple dental extractions are performed.<sup>[4,6,7,11,13,14]</sup> One study found that the frequency of embolism was three times higher than post-surgical haemorrhages in patients whose anticoagulant therapy was interrupted.<sup>[15]</sup> Moreover, a dental bleeding complication is treated by means of a simple and effective procedure and is preferable to a cardiovascular episode.<sup>[16]</sup>

The role of local haemostatic agents has recently received increased attention. Several highly effective local haemostatics have been reported. The best-known are fibrin tissue glue,<sup>[17]</sup> microfibrillar collagen,<sup>[11]</sup> tranexamic acid,<sup>[18]</sup> oxidised cellulose,<sup>[19]</sup> fibrin gelatine sponge<sup>[20]</sup> and bismuth subgallate.<sup>[11]</sup> In the present study, bismuth subgallate was used as a local haemostatic placed within the socket. This drug has haemostatic properties, acting on coagulation factor XII (Hageman factor), thus leading to the activation of the coagulation cascade and improving the early formation of the fibrin clot. It is a light astringent, precipitating vascular proteins that may obliterate the small capillary vessels.<sup>[21]</sup> Previous studies in rats showed that bismuth subgallate does not interfere with the wound-healing process<sup>[8,9]</sup> or post-extraction bone healing.<sup>[10]</sup> Optimal results were obtained when bismuth subgallate was applied as a haemostatic agent for simple dental extractions in patients.<sup>[11]</sup> Its low cost is an additional advantage, which helps to reduce the cost of the surgical procedure.

INR values before a surgical intervention are important for predicting a patient’s haemostasis, and useful to check whether the values are in the patient’s therapeutic range.<sup>[22]</sup> A study on 122 patients undergoing oral surgeries found that 69 were within this range, but 13 were over and 40 patients were below their range.<sup>[23]</sup> Some studies reported a correlation between a higher INR level and increased post-operative haemorrhage when dental extractions were performed without haemostatic agents.<sup>[24,25]</sup> Al-Mubarak *et al.* found that bleeding frequency at day 1 postoperatively was significantly less in patients with INR 1-2 (13.6%) or >2-3 (19.8%) than in patients with INR >3 (54.21%); although not applying haemostatic agents may be the reason for high percentages of post-operative bleeding.<sup>[24]</sup> Hasegawa *et al.* performed 732 extractions without haemostatic agents and observed a high percentage (25.7%) of bleeding events. They reported INR value to be a significant predictor of post-operative haemorrhage, as the average INR value in patients with and without post-operative haemorrhage was 2.1 ± 0.7 and 1.9 ± 0.5, respectively.<sup>[25]</sup> Other studies reported that no significant association existed between the INR value and post-operative bleeding. Blinder *et al.* observed that 12% of patients had bleeding complications after 543 dental extractions with the application of gelatine sponges and sutures, but did not observe any statistically significant correlation between the frequency of post-operative bleeding and the INR value.<sup>[20]</sup> Bodner *et al.* observed only three cases of bleeding after dental extractions with the application of fibrin sealant in 69 patients, also with no correlation with INR values.<sup>[26]</sup> In a clinical study

of dental extractions applying oxidised cellulose and sutures comprising 270 patients, Morimoto *et al.* found that the incidence of post-operative haemorrhage was 3.6% and was unrelated to INR values.<sup>[19]</sup> Our research is the first in the literature to study the association between bleeding events and the degree of anticoagulation when bismuth subgallate is applied as a haemostatic agent. Only 1.58% of patients in this study presented bleeding complications after dental extractions applying bismuth subgallate and sutures, with no association with INR values. This finding supports the idea that the degree of anticoagulation (INR value) is not a key factor for predictions of bleeding complications after simple dental extractions when haemostatic agents are applied. Factors such as the previous infection at the site of extraction,<sup>[27]</sup> excessive surgical trauma, drug interactions,<sup>[28]</sup> periodontal disease<sup>[14]</sup> and multiple extractions,<sup>[29,30]</sup> account for most cases of post-operative bleeding. Possibly, an adequate control of the above factors should be considered to decrease in the incidence of post-operative bleeding in patients under chronic anticoagulation therapy. Although the use of bismuth subgallate as a topical haemostatic agent was extensively reported in adenotonsillectomy, few trials were performed in dentistry. Optimal results were observed for dental extractions,<sup>[11]</sup> and soft-tissue grafts surgeries.<sup>[31]</sup> This local haemostatic agent was found to decrease bleeding time, when compared to moistened gauze pressure, for palatal wounds when performing free soft-tissue grafts.<sup>[31]</sup> Other dental procedures may benefit from the features of this haemostatic agent.

## CONCLUSION

No association between bleeding complication and INR values was observed when simple dental extractions were performed applying bismuth subgallate as a haemostatic agent.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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## Conflicts of interest

There are no conflicts of interest.

## REFERENCES

- Inokoshi M, Kubota K, Yamaga E, Ueda K, Minakuchi S. Postoperative bleeding after dental extraction among elderly patients under anticoagulant therapy. *Clin Oral Investig* 2021;25:2363-71.
- Matarese M, Cervino G, Fiorillo L, Stelitano C, Imbesi Bellantoni M, Meto A, *et al.* A cohort study on anticoagulant therapy risks in dental patients after multiple extractions. *Minerva Dent Oral Sci* 2021;70:196-205.
- Yagyuu T, Kawakami M, Ueyama Y, Imada M, Kurihara M, Matsusue Y, *et al.* Risks of postextraction bleeding after receiving direct oral anticoagulants or warfarin: A retrospective cohort study. *BMJ Open* 2017;7:e015952.
- Lu SY, Lin LH, Hsue SS. Management of dental extractions in patients on warfarin and antiplatelet therapy. *J Formos Med Assoc* 2018;117:979-86.
- Ehrhard S, Burkhard JP, Exadaktylos AK, Sauter TC. Severe enoral bleeding with a direct oral anticoagulant after tooth extraction and heparin bridging treatment. *Case Rep Emerg Med* 2019;2019:6208604.
- Lee JS, Kim MK, Kang SH. Effect of warfarin discontinuation on the incidence of postoperative bleeding in tooth extraction. *J Korean Assoc Oral Maxillofac Surg* 2020;46:228-34.
- Ahmed I, Younis M, Shah AA. Extraction in patients on oral anticoagulant therapy with and without stopping the drug: A comparative study. *J Maxillofac Oral Surg* 2019;18:555-8.
- Tramontina VA, Machado MA, Nogueira Filho Gda R, Kim SH, Vizzioli MR, Toledo Sd. Effect of bismuth subgallate (local hemostatic agent) on wound healing in rats. *Histological and histometric findings. Braz Dent J* 2002;13:11-6.
- Santos RM, Sampaio CP, Moraes DP, Lima RL. Evaluation of the effects of bismuth subgallate on wound healing in rats. *Histological findings. Int Arch Otorhinolaryngol* 2016;20:377-81.
- Puia SA, Renou SJ, Rey EA, Guglielmotti MB, Bozzini CE. Effect of bismuth subgallate (a hemostatic agent) on bone repair; a histologic, radiographic and histomorphometric study in rats. *Int J Oral Maxillofac Surg* 2009;38:785-9.
- Puia SA, Hilber EM, Garcia-Blanco M. Randomized clinical trial comparing three local hemostatic agents for dental extractions in patients under chronic anticoagulant therapy – A comparative study. *Ann Maxillofac Surg* 2020;10:292-6.
- Suda KJ, Henschel H, Patel U, Fitzpatrick MA, Evans CT. Use of antibiotic prophylaxis for tooth extractions, dental implants, and periodontal surgical procedures. *Open Forum Infect Dis* 2018;5:ofx250.
- Engelen ET, Schutgens RE, Mauser-Bunschoten EP, van Es RJ, van Galen KP. Antifibrinolytic therapy for preventing oral bleeding in people on anticoagulants undergoing minor oral surgery or dental extractions. *Cochrane Database Syst Rev* 2018;7:CD012293.
- Rodríguez-Cabrera MA, Barona-Dorado C, Leco-Berrocal I, Gómez-Moreno G, Martínez-González JM. Extractions without eliminating anticoagulant treatment: A literature review. *Med Oral Patol Oral Cir Bucal* 2011;16:e800-4.
- Wahl MJ. Myths of dental surgery in patients receiving anticoagulant therapy. *J Am Dent Assoc* 2000;131:77-81.
- Aldous JA, Olson CJ. Managing patients on warfarin therapy: A case report. *Spec Care Dentist* 2001;21:109-12.
- Halfpenny W, Fraser JS, Adlam DM. Comparison of 2 hemostatic agents for the prevention of postextraction hemorrhage in patients on anticoagulants. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2001;92:257-9.
- Jaiswal P, Agrawal R, Gandhi A, Jain A, Kumar A, Relu R. Managing anticoagulant patients undergoing dental extraction by using hemostatic agent: Tranexamic acid mouthrinse. *J Pharm Bioallied Sci* 2021;13:S469-72.
- Morimoto Y, Niwa H, Minematsu K. Hemostatic management of tooth extractions in patients on oral antithrombotic therapy. *J Oral Maxillofac Surg* 2008;66:51-7.
- 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;30:518-21.
- Celsi F, Staffa P, Lamba M, Castro V, Chermetz M, Orzan E, *et al.* Photobiomodulation for lowering pain after tonsillectomy: Low efficacy and a possible unexpected adverse effect. *Life (Basel)* 2022;12:202.
- Kassab MM, Radmer TW, Glore JW, Visotcky A, Robertson J, Degroot B. A retrospective review of clinical international normalized ratio results and their implications. *J Am Dent Assoc* 2011;142:1252-7.
- Lombardi N, Varoni EM, Sorrentino D, Lodi G. International

- normalized ratio (INR) values in patients receiving oral vitamin K antagonists and undergoing oral surgery: A clinical audit. *Spec Care Dentist* 2020;40:374-81.
24. Al-Mubarak S, Al-Ali N, Abou-Rass M, Al-Sohail A, Robert A, Al-Zoman K, *et al.* Evaluation of dental extractions, suturing and INR on postoperative bleeding of patients maintained on oral anticoagulant therapy. *Br Dent J* 2007;203:E15.
  25. Hasegawa T, Yanamoto S, Tachibana A, Kojima Y, Koyama Y, Maeda M, *et al.* The risk factors associated with postoperative hemorrhage after tooth extraction: A multi-center retrospective study of patients receiving oral antithrombotic therapy. *Oral Maxillofac Surg* 2017;21:397-404.
  26. Bodner L, Weinstein JM, Baumgarten AK. Efficacy of fibrin sealant in patients on various levels of oral anticoagulant undergoing oral surgery. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1998;86:421-4.
  27. 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;88:137-40.
  28. Scully C, Wolff A. Oral surgery in patients on anticoagulant therapy. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2002;94:57-64.
  29. Dudek D, Marchionni S, Gabriele M, Iurlaro A, Helewski K, Toti P, *et al.* Bleeding. *J Craniofac Surg* 2016;27:1228-33.
  30. Rocha AL, Oliveira SR, Souza AF, Travassos DV, Abreu LG, Ribeiro DD, *et al.* Bleeding assessment in oral surgery: A cohort study comparing individuals on anticoagulant therapy and a non-anticoagulated group. *J Craniomaxillofac Surg* 2019;47:798-804.
  31. Kim SH, Tramontina VA, Papalexiou V, Luczyszyn SM. Bismuth subgallate as a topical hemostatic agent at palatal donor sites. *Quintessence Int* 2010;41:645-9.