

See discussions, stats, and author profiles for this publication at: <https://www.researchgate.net/publication/46096062>

Management of dental extraction in patients undergoing anticoagulant treatment. Results from a large, multicentre, prospective, case-control study

ARTICLE *in* THROMBOSIS AND HAEMOSTASIS · NOVEMBER 2010

Impact Factor: 4.98 · Source: PubMed

CITATIONS

21

READS

229

7 AUTHORS, INCLUDING:



Michele Maglione

Università degli Studi di Trieste

36 PUBLICATIONS 204 CITATIONS

SEE PROFILE



Favero Lorenzo

University of Padova

24 PUBLICATIONS 372 CITATIONS

SEE PROFILE



Roberto Di Lenarda

Università degli Studi di Trieste

218 PUBLICATIONS 2,927 CITATIONS

SEE PROFILE



Ezio Zanon

University of Padova

97 PUBLICATIONS 1,312 CITATIONS

SEE PROFILE

Management of dental extraction in patients undergoing anticoagulant treatment

Results from a large, multicentre, prospective, case-control study

Christian Bacci^{1,2}; Michele Maglione³; Lorenzo Favero¹; Alessandro Perini³; Roberto Di Lenarda³; Mario Berengo¹; Ezio Zanon⁴

¹Department of Medical and Surgical Science, Section of Clinical Dentistry, University of Padova, Padova, Italy; ²Department of Dentistry, Unit of Dentistry and Stomatology, Provincial Health Service of Trento, Trento, Italy; ³Department of Biomedicine, Unit of Dental Sciences and Biomaterials, University of Trieste, Trieste, Italy; ⁴Department of Cardiac, Thoracic and Vascular Science, Second Chair of Internal Medicine, University of Padova, Padova, Italy

Summary

Following favourable results from a previous study, a large, multicentre, prospective, case-control study was performed to further assess the incidence of bleeding complications after dental extraction in patients taking oral anticoagulant therapy (OAT). Four hundred fifty-one patients being treated with warfarin who required dental extraction were compared with a control group of 449 non-anticoagulated subjects undergoing the same procedure. In the warfarin-treated group, the oral anticoagulant regimen was maintained unchanged, such that the patients had an International Normalised Ratio ranging between 1.8 and 4, and local haemostatic measures (i.e. fibrin sponges, silk sutures and gauzes saturated with tranexamic acid) were adopted. All the procedures were performed in an outpatient setting. Seven bleeding complications occurred in the OAT group and four in the control group; the dif-

ference in the number of bleeding events between the two groups was not statistically significant (OR=1.754; 95% CI 0.510 – 6.034; $p=0.3727$). No post-operative late bleeds requiring hospitalisation and/or blood transfusions were recorded, and the adjunctive local haemostatic measures were adequate to stop the bleeding. The results of our protocol applied in this large, multicenter study show that dental extractions can be performed easily and safely in anticoagulated outpatients without any modification of the ongoing anticoagulant therapy, thus minimising costs and reducing discomfort for patients.

Keywords

Dental extraction, anticoagulated patients, warfarin therapy, multicenter study

Correspondence to:

Dr. Christian Bacci
Department of Medical and Surgical Science
Section of Clinical Dentistry
University of Padova, Padova, Italy
Via Giustiniani, 2, 35100 Padova, Italy
E-mail: bax-1@libero.it, christian.bacci@unipd.it

Received: February 24, 2010

Accepted after major revision: July 2, 2010

Prepublished online: August 30, 2010

doi:10.1160/TH10-02-0139

Thromb Haemost 2010; 104: 972–975

Introduction

The proper approach to dental extractions in patients on oral anticoagulant therapy (OAT) remains a matter of debate focused on the balance between the risk of thromboembolic events and bleeding complications (1). In fact, three decades of research on this issue have produced conflicting results. Some authors recommend the withdrawal of OAT for several days or prescribe heparin before the dental procedure (2, 3). Other authors recommend a reduction of OAT until an International Normalised Ratio (INR) value of 1.5 is reached (4, 5). More recently, it has been proposed that the OAT regimen could be left unchanged and the patient be treated with several post-procedural local haemostatic measures (e.g. gelatine sponges, oxidized cellulose, fibrin glue, sutures and tranexamic acid) to control the bleeding risk (6–10). In fact, no fatal bleeding complications have been reported in the literature in association with this approach, while some deaths related to OAT withdrawal

for dental extractions have occurred (11). Interestingly, already in 1966, McIntyre had suggested maintaining anticoagulant treatment when performing dental extractions (12).

Following recent consistent evidence in favour of the maintenance of OAT when a dental extraction must be performed and suggestions that this might be the gold standard for the management of patients on OAT (13, 14), a specific protocol for the management of such patients was published by our group, drawing on the results of a prospective case-control study conducted in 2003 (20). That study, which compared the incidence of bleeding complications after dental extraction between a group of healthy patients and a group of anticoagulated patients treated without withdrawal of OAT, did not show any statistical difference between groups in the bleeding outcome. The results of the study have already been taken into account by guidelines (15–18), but, in order to further validate our protocol, we performed a large, prospective, multicentre, case-control study.

Materials and methods

A total of 480 patients undergoing OAT (warfarin), who required dental extractions, were referred to our Units of Oral Surgery between January 1, 2006 and December 2008. At enrolment into the study all patients had been receiving warfarin for at least three months, and were on stable OAT. Before commencing the study, the 480 patients were asked to give informed consent to the protocol: it was explained that they would be treated without withdrawal of their therapy, and they were made aware of the possibility of a higher risk of bleeding but a lower risk of thromboembolism. Of the 480 patients initially identified, 473 gave informed consent to their participation in the study. Thereafter, four patients with an INR value out of range (> 4) (19) were referred to their physicians for new therapy titration; 15 patients with an INR value lower than 1.8 and three more patients lost during the follow-up were subsequently excluded from the study. It was decided to exclude the patients with an INR < 1.8 because these subjects were not adequately anticoagulated and were at a low risk of haemorrhagic complications. The case-group, therefore, consisted of 451 patients on OAT. The indications for OAT are reported in ► Table 1.

Four hundred eighty patients not receiving any drug affecting coagulation, but requiring dental extraction and meeting the inclusion criteria, were enrolled in the control group. Of these 480 non-anticoagulated patients of the control group, 478 gave informed consent to the surgical procedure. The patients in both the OAT group and the control group had similar indications for dental extraction. Before surgery, all control group patients were asked about their recent clinical history, and their INR values were determined. Careful questioning of the patients about any bleeding episodes they or relatives had had, liver diseases, and recent intake of drugs with anticoagulant effects, led to the exclusion of 29 control subjects. The final control group, therefore, consisted of 449 subjects.

Dental extractions were performed by the same five qualified oral surgeons, both in the OAT and in the control group. Surgery was carried out in three medical centres: the Dental Clinic, Clinical-University Department of Biomedicine, University of Trieste, the Unit of Dentistry and Stomatology, Department of Dentistry, Provincial Health Service of Trento and the Oral Surgery Unit, Department of Medical-Surgical Specialties, Section of Dentistry, University of Padua, Italy.

The same protocol, based on previous findings, was applied (20). The prothrombin time (PT) and INR values were measured 1 hour (h) before dental surgery; the surgeons were blinded to which group the patients belonged, making this a single-blind study. All patients were instructed to communicate any bleeding complications after surgery. The haemostatic procedures used were not different for molar, wisdom or incisor teeth. Control group patients with bleeding events were investigated for the presence of congenital coagulation defects.

Local analgesia was obtained by plexus, intraligamentous or truncal infiltration using mepivacaine hydrochloride 3% without adrenaline to avoid bleeding after the end of the adrenaline's effect (21). Single or multiple extractions were performed. We consider-

Table 1: Indications for anticoagulant therapy in the 451 patients enrolled in the study. Two indications for anticoagulant therapy were recorded in 42 patients. Mean INR in the cases 2.14 (SD 0.66), mean INR in the controls 1.01 (SD 0.06).

| Indication | Patients | |
|------------------------|----------|-----|
| Atrial fibrillation | 23.3% | 105 |
| Prosthetic valve | 19.1% | 86 |
| Myocardial infarction | 17.5% | 79 |
| Stroke | 17.1% | 77 |
| Venous thromboembolism | 15.1% | 68 |
| Valvulopathy | 7.1% | 32 |
| Unknown | 0.9% | 4 |

ed a surgical extraction any procedure that included a surgical incision of the gum. After the extraction, a piece of oxidised cellulose (Tabotamp, Johnson & Johnson, New Brunswick, NJ, USA) was applied to the wound and a resorbable suture (Vycril, Ployglactin, Johnson & Johnson) was used in all patients (22). Gauze saturated with tranexamic acid was then kept in place for 30–40 minutes (12, 13–21). An ice bag was placed on the cheek, and kept in place for at least 1 h. Antibiotic prophylaxis (amoxicillin 2 g, 1 h before surgery or clindamycin 600 mg in two patients with a history of penicillin allergy) was given to patients with prosthetic valves; surgeons were blinded to which patients received antibiotic prophylaxis (23). Cephalosporines, macrolides, and quinolones were not administered because these drugs may interfere with the coagulation cascade. For the same reason, we avoided the administration of acetylsalicylic acid (ASA) and used analgesic drugs such as paracetamol, ibuprofen and noramidopirin. In the follow-up, patients from both groups were re-evaluated on days 3 and 8 after surgery by the same oral surgeons, to detect the presence of swelling, pain, local infection, oozing or major bleeding. Sutures were not removed at this time. All the procedures were performed in an outpatient setting, and general anaesthesia or endotracheal intubation was never used.

Differences in the prevalence of bleeding events between the case group and control group were evaluated for significance using the Chi-square test. Two-tailed *p*-values < 0.05 were considered statistically significant.

Results

The main characteristics of the enrolled patients and the number of dental extractions in the OAT patients and in the control group are reported in ► Table 2. In OAT group, seven late bleeding complications were reported after the extraction of four molars, two wisdom teeth, and one incisor. In six out of seven events, the late bleeding occurred two days after the extraction; in one patient the late bleeding was observed six days after the procedure together with an infection of the surgical site. A surgical exploration of the

Table 2: Patients, number and type of dental extractions.

| | N | Age (mean) | Age (range) | Gender | | Dental extractions | | | |
|---------------|-----|------------|-------------|--------|--------|------------------------------------|----------------------|--------------------|----------------------|
| | | | | Male | Female | Total number of dental extractions | Surgical extractions | Single extractions | Multiple extractions |
| Case group | 451 | 63.5 | 38/89 | 246 | 205 | 926 | 379 | 477 | 449 |
| Control group | 449 | 66.4 | 35/92 | 202 | 247 | 894 | 339 | 452 | 442 |

wound was performed, and a new suture was applied with a gelatine sponge and gauze saturated with tranexamic acid. These local haemostatic measures were sufficient to control the post-operative bleeding complications, with no patients requiring either hospitalisation or transfusion. In the control group, four late bleeding complications (two molars, two wisdom teeth) were observed two days after extraction and were managed with surgical treatment and sutures. The number of bleeding complications in the anticoagulated patients and in the control group were not statistically different (odds ratio [OR] 1.754; 95% confidence interval [CI] 0.510 – 6.034; $p=0.3727$).

Even hypothesising that all three patients lost to follow-up had bleeding complications, from an statistical point of view, the association was not statistically significant (OR 2.506; 95% CI 0.780 – 8.048; $p=0.1229$).

Data on bleeding complications are summarised in ► Table 3. The local measures were effective at contrasting bleeding in all patients, and further systemic drug administration, changes of anticoagulant therapy, hospital admissions and blood transfusions were never necessary. No defects of components of the coagulation cascade were detected in the control patients who showed excessive bleeding.

No thromboembolic complications were detected in any patient.

Discussion

A definitive, standardised protocol for the management of dental extractions in anticoagulated patients is still lacking. Recently published literature consistently suggests that there is no need to change ongoing OAT and that the application of local haemostatic measures is sufficient to prevent bleeding complications (24). In spite of this recent view on OAT maintenance, many oral surgeons are still not adopting this approach (4).

In fact, the best local haemostatic measures to adopt in OAT patients (e.g. which type of gelatine sponge, sutures or no sutures, mouthwash with tranexamic acid) and the range of INR values for safe dental extraction are still matters of debate (25). In his comprehensive review, Wahl established the following: (a) the risk of haemorrhage after dental extraction is minimal in patients maintained at a therapeutic level of anticoagulation and managed with local measures; (b) no well-documented case-reports of serious bleeding complications following dental surgery in anticoagulated

patients are currently available; and (c) several documented cases of serious embolic complications in patients whose warfarin therapy was withdrawn for dental treatment have been reported (17).

The large majority of the studies evaluated a low number of patients. To our knowledge, the sample size of this multicentre, prospective, case-control study is the largest reported literature evaluating the incidence of bleeding complications after dental extraction in a group of anticoagulated patients compared with normal subjects. According to our protocol, which was designed on the basis of the results of many, in our opinion, well-designed studies, the local haemostatic measures were the gelatine sponge, suture and gauze saturated with tranexamic acid (12–21).

This protocol differs in several aspects from that of our previous study. In this second trial, the surgeons were blinded regarding the patients' use or not of OAT (single-blind study) in order to avoid differences in the surgical procedure between groups. In both groups, the INR was always assessed 1 h before surgery. All the sockets were sutured and a gelatine sponge was placed; furthermore gauze saturated with tranexamic acid was kept in place. In contrast with the previous protocol, an absorbable suture was used because we think that leaving an absorbable suture in place is less traumatic than removing a non-absorbable one (26).

The number of bleeding complications was not statistically different between surgical extractions and non-surgical ones or according to the type of tooth extracted (molar, wisdom, incisor).

We did not perform dental extractions in patients with an INR higher than 4. Although we believe that it could be possible, in our opinion this value should be considered as the upper cut-off of the range for the procedure, and in patients not needing surgery for an emergency medical condition, we preferred to refer the patient to the physician for an adjustment of the OAT (27).

Table 3: Number of bleeding complications in the anticoagulated patients and in the control group.

| Number of patients | Number of bleeding complications | Onset of bleeding |
|--------------------|----------------------------------|--|
| Case group | 7 | Two days after extraction (n=6) Six days after extraction (n=1) |
| Control group | 4 | Two days after extraction |

OR=1.754; 95% CI 0.510 – 6.034; $p=0.3727$. Incidence of bleeding in the cases: 1.55%. Incidence of bleeding in the controls: 0.89%.

What is known about this topic?

- Dental surgery in patients undergoing oral anticoagulants is a topic widely debated in the literature. Many different protocols for the management are purposed.
- A great risk related to alterations of anticoagulant regimen is known. Even mortal complications are reported in the literature.

What does this paper add?

- This paper proposes to evaluate with a prospective large sample a protocol of not-suspension of anticoagulants for dental surgery. The protocol purposed show no statistical differences in the incidence of bleeding complications between healthy and anticoagulated patients.
- This multicentric study underlines the possibility to perform dental extractions without suspending anticoagulants, avoiding risks concerning thromboembolic complications.

All the procedures were performed in an outpatient setting, and none of the post-operative late bleeds required hospitalisation, transfusions or further drug prescription as local measure were sufficient to stop the bleeding. The management procedures are more extensive and time-consuming than those routinely performed, but are nevertheless completely feasible and easily used in an ordinary dental office. Indeed, the significance of this study is that it demonstrates that patients under OAT are safely and easily managed in a dental office, with the adoption of only a few, precise strategies.

The present study confirms that, in OAT patients treated with local measures, no serious bleeding complications are expected after dental surgery. The incidence of bleeding complications was not statistically different between patients maintained on their OAT and those in the control group. In conclusion, dental extractions can be safely performed in anticoagulated patients on an outpatient basis, with a cost reduction for the community and less discomfort for the patients.

References

1. Wahl MJ. Myths of dental surgery in patients receiving anticoagulant therapy. *J Am Dent Assoc* 2000; 131: 77–81.
2. Pavlek V, Bigl P. Stomatological treatment of patients with artificial heart valves: coagulation control and antibiotic cover. *Int Dent J* 1993; 43: 59–61.
3. Mulligan R, Weitzel KG. Pretreatment management of the patients receiving anticoagulation drugs. *J Am Dent Assoc* 1988; 117: 479–483.
4. Troulis MJ, Head TW, Lecter JR. Dental extraction in patients on oral anticoagulant: a survey of practices in north America. *J Oral Maxillofac Surg* 1998; 56: 914–917.
5. DeClerck D, Vinkier F, Vermeylen J. The influence of anticoagulation on blood loss following dental extraction. *J Dent Res* 1992; 71: 387–390.
6. Gaspar R, Brenner B, Ardekian L, et al. Use of tranexamic acid mouthwash to prevent postoperative bleeding in oral surgery patients on oral anticoagulant medication. *Quintessence Int* 1997; 28: 375–379.
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. Bailey BMW, Fordyce AM. Complications of dental extraction in patients receiving warfarin anticoagulant therapy: a controlled clinical trial. *Br Dent J* 1983; 155: 308–310.
9. Ramstrom G, Sindet-Pedersen S, Hall G, et al. Prevention of postsurgical bleeding in oral surgery using tranexamic acid without dose modification of oral anti-coagulants. *J Oral Maxillofac Surg* 1993; 51: 1211–1216.
10. Sindet-Pedersen S, Ramstrom G, Bernvil S, et al. Hemostatic effect of tranexamic acid mouthwash in anticoagulant-treated patients undergoing oral surgery. *N Engl J Med* 1989; 320: 840–843.
11. Wahl MJ. Dental surgery in anticoagulated patients. *Arch Int Med* 1998; 158: 1610–1616.
12. McIntyre H. Management, during dental surgery, of patients on anticoagulants. *Lancet* 1966; 2: 99–100.
13. Nematullah A, Alabousi A, Blanas N, et al. Dental surgery for patients on anti-coagulant therapy with warfarin: a systematic review and meta-analysis. *J Can Dent Assoc* 2009; 75: 41.
14. Brewer AK. Continuing warfarin therapy does not increased risk of bleeding for patients undergoing minor dental procedures. *Evid Based Dent* 2009; 10: 52.
15. Prisco D, Baudo F, Moia M, et al. Terapia anticoagulante orale, chirurgia e manovre invasive. Raccomandazioni della fcsa per la task force della fcsa su Anticoagulazione, Chirurgia e manovre invasive. November 2005. Available at: <http://www.fcsa.it/sito2008/raccomandazioni/FCSAchirurgiaDefinitiva.pdf>. Available at: Accessed June 30, 2010.
16. Perry DJ, Nokes TJC, Helliwell PS. Guidelines for the management of patients on oral anticoagulants requiring dental surgery. British Committee for Standards in Haematology. September 2007. <http://www.bcsghguidelines.com/pdf/WarfarinandOralSurgery26407.pdf>. Accessed June 30, 2010.
17. Linnebur SA, Ellis SL, Astroth JD. Educational practices regarding anticoagulation and dental procedures in U.S. dental schools. *J Dent Educ* 2007; 71: 296–303.
18. 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.
19. Salam S, Yusuf H, Milosevic A. Bleeding after dental extractions in patients taking warfarin. *Br J Oral Maxillofac Surg* 2007; 45: 463–466.
20. Zanon E, Martinelli F, Bacci C, et al. Safety of dental extraction among consecutive patients on oral anticoagulant treatment managed using a specific dental management protocol. *Blood Coagul Fibrinolysis* 2003; 14: 27–30.
21. Borea G, Montebugnoli L, Capuzzi P, et al. Tranexamic acid as a mouthwash in anticoagulant-treated patients undergoing oral surgery. *Oral Surg Oral Pathol Oral Med* 1993; 75: 29–31.
22. Halfpenny W, Fraser JS, Adlam DM. Comparison of 2 hemostatic agents for the prevention of postextraction haemorrhage in patients on anticoagulants. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2001; 92: 257–259.
23. Wilson W, Taubert KA, Gewitz M, Lockhart PB, Baddour LM, Levison M, et al. Prevention of bacterial endocarditis: Recommendations by the American Heart Association Circulation 2007; 116: 1736–1754. Erratum in: *Circulation* 2007; 116: e376–377.
24. Ferrieri GB, Castiglioni S, Carmagnola D, et al. Oral surgery in patients on anti-coagulant treatment without therapy interruption. *J Oral Maxillofac Surg* 2007; 65: 1149–1154.
25. Benoliel R, Leviner E, Katz J, Tzuket A. Dental treatment for patients on anti-coagulant therapy: prothrombin time value. *Oral Surg Oral Med Oral Pathol* 1986; 62: 149–152.
26. 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; discussion 410–411.
27. Scully C, Wolff A. Oral surgery in patients on anticoagulant therapy. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2002; 94: 57–64.