

Management of patients undergoing anticoagulant treatment

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

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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

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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: ■■■■

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 be-

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	
	Percentage	Number
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

tween 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 considered 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

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

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 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 a 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 com-

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%.		

prehensive 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.

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.

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).

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.

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