Bleeding after dental extractions in patients taking warfarin

Short title: Warfarin and post-extraction bleeding

**Abstract**

Objectives: To assess the incidence of bleeding after dental extractions in subjects taking warfarin continuously before and after operations whose International Normalised Ratio (INR) was below 4.0 at the time of extraction.

Methods: This was a case series study of 150 patients without controls who required extraction of at least one tooth under local anaesthetic. All sockets were subsequently packed with absorbable oxycellulose and sutured.

Results: A total of 58 women and 92 men were included (mean age 66 years); their ages were similar. The mean INR (SD) was 2.5 (0.56), although most patients had an INR less than 2.5 (n = 101). Ten patients (7%) bled after extraction, enough to require a return to hospital. Five patients of 101 with an INR $\leq 2.5$, and five with an INR $>2.5$ out of 49 bled after extraction ($p = 0.29$). Bleeding after extraction was not associated with operative antibiotics. All patients who bled were managed conservatively and none was admitted to hospital.

Conclusion: Patients taking warfarin whose INR is up to 4.0 and who have dental extractions in hospital do not bleed seriously after the operation.

Keywords: warfarin, INR, dental extractions, post-operative bleeding

## Introduction

Warfarin is one of the coumarin group of drugs and is prescribed for various conditions (Table 1). It blocks the formation of prothrombin and factors II, VII, IX, and X, which are involved in both the extrinsic and common coagulation pathways, and prevents the metabolism of vitamin K to its active form that is needed for the synthesis of these factors. Other vitamin-K-dependent proteins inhibited by warfarin include proteins C and S, which are involved in the fibrinolytic system. Because coumarins bind strongly to plasma proteins, warfarin has a half-life of 36 hours and acts slowly. Conversely, its discontinuation results in a prolonged latent effect, which explains advice to discontinue its use 2-3 days before dental extractions.[1]

The activity of warfarin is expressed as the International Normalised Ratio (INR), [2] which is the standard introduced by the World Health Organization 20 years ago. It is a prothrombin ratio obtained by dividing the prothrombin time by the laboratory control prothrombin time. The therapeutic range is the value of INR or degree of anticoagulation that is required to prevent the development of serious thromboembolism and it is normally maintained between 2.0 and 4.0.[3] The desirable range for the INR depends on the condition being treated (Table 1), and the risk of bleeding increases as the INR rises.[2]

The management of patients who take warfarin has varied, and included stopping two days before an operation, reduction in the dose, no change in the dose provided the INR was <4.0,

and changing from the normal regular dose of warfarin to one of low molecular weight heparin preoperatively.[1] The risk of operative or postoperative bleeding must be balanced against the risk of thromboembolism in patients in whom warfarin is interrupted. A random control trial (RCT) on 57 anticoagulated patients found no increase in clinically important bleeding, and only one patient needed admission for observation after closure of an oroantral communication. Nine patients who had delayed bleeds were treated at home.[4] Past practice (to discontinue treatment with anticoagulants before operation) increases the risk of a rebound thromboembolus.[1, 4-7]

The Dental Practitioners' Formulary 2002-2004 stated that "patients requiring minor dental surgery and who have an INR below 3.0 may continue warfarin without dose adjustment".[8] Uncomplicated extraction of 1-3 teeth with forceps was acceptable for patients with an INR of < 3.5 in the absence of other risk factors.[9] Recent guidance from the North West Medicines Information Centre and British Association of Oral and Maxillofacial Surgeons gives a higher limit of 4.0, which should theoretically cover all patients on oral anticoagulants, as this is the upper therapeutic limit, usually in patients with prosthetic heart valves.[10] However, patients with impaired liver function (with or without alcoholic liver disease), renal failure, additional coagulopathy, taking cytotoxic medication, or who had an unstable INR, were thought to require treatment in hospital.[10] Periodontal flaps, placement of implants, and apicectomy were inadvisable in patients with an INR of 3.0 to 4.0.[11]
In this study we aimed to investigate the incidence of post extraction bleeds in patients who take warfarin regularly and whose INR was no more than 4.0.

## Method

We under took a retrospective uncontrolled cohort study to assess the incidence of bleeding after extraction in patients taking warfarin who attended the oral surgery department at the Royal Oldham Hospital, the accident and emergency department, and Clinic V at Liverpool University Dental Hospital between 2001 and 2004. All patients taking warfarin were referred by either a general dental or medical practitioner, and were included if they needed extractions. Patients with an INR >4.0, and those who required a biopsy were excluded. Patients did not change their regular dose before the extractions and they were all given review appointments within two weeks.

A series of 150 consecutive patients who took warfarin were included in the study. An anticoagulation history was taken that included the reason for taking the warfarin, dose, and duration of use. The medical history was assessed with particular attention paid to the presence of liver disease, whether they took any vitamin K supplements, and whether results of liver function tests indicated any further coagulopathy. Other drugs were recorded with emphasis on those that could potentially interact with warfarin, including antihypertensives, antifungals, carbemazepine, steroids, phenytoin, aspirin, and antibiotics. Any antibiotics that were taken during the four weeks before the extractions were also noted. The INR was measured within 24 hours of the extraction. The number of teeth extracted was recorded, and whether it was a surgical or non-surgical extraction. A surgical extraction was defined as raising a mucoperiosteal flap, and removal of bone with a bur. The standard haemostatic method used in all cases was an oxycellulose

dressing (Surgicell™) that was placed into each socket and closed with 3/0 polyglactin (Vicryl™) sutures, and pressure by biting on a gauze swab for 10 minutes, followed by a 10-minute period of observation before being discharged. No patient had electrocautery at the time of extraction, or tranexamic acid mouthrinse afterwards.

Antibiotic prophylaxis, steroids, and other drugs given postoperatively were recorded. Attendance for postoperative bleeding and other complications such as dry socket were noted, as was the grade of operator (senior house officer/specialist registrar, staff grade surgeon, or consultant). None of the operators were aware that we were assessing possible postoperative complications and so the teeth were extracted under normal conditions. Review appointments were not compulsory and for the purposes of this study, any bleeds after extraction that were managed at home were not included.

All data were entered into the Statistical Package for the Social Sciences version 12 (SPSS v12.0) on an "intention to treat basis". Categorical data were analysed using the Chi square test. We also used the Mann-Whitney U test, and Fisher's exact test, as appropriate. Data are expressed as mean (SD) except where otherwise stated.

**Results**

A total of 150 patients were included (58 women and 92 men, mean age 66.1 years, range 33-92). The reasons for taking warfarin are shown in Table 1.The age and gender distribution is shown in Table 2. Ages did not differ significantly between men and women or between the two centres studied. The INR ranged from 0.9 to 4.2, the mean

(SD) being 2.5 (0.6) (median 2.3). One hundred and one patients (67%) had an INR of ≤2.5 and 49 (33%) had an INR >2.5.

A total of 249 teeth (of a total of 279) required non-surgical forceps extractions. Only 30 teeth needed an operation for their removal. In this group 25 patients had one tooth removed. The distribution of INRs is shown in Table 3.

Table 4 presents the incidence of postoperative bleeds depending on whether the INR was above or below the mean of 2.5. Only ten subjects had postoperative bleeds, five in each INR category either side of the mean ($p = 0.29$). Postoperative haemorrhage was not associated with the dose of warfarin or duration of its use. The 10 patients who bled postoperatively and returned to hospital for attention were older (71 years) than the rest (66 years) but this was not significant although the trend among the whole group was for older subjects to have higher INRs. The use of antibiotics during operation did not correlate with postoperative bleeding.

**Discussion**

Ten patients had postoperative bleeds, which were managed by repacking and resuturing under local anaesthetic followed by application of pressure. Bleeding was defined as that which continued for more than 12 hours and required the patient to return to hospital. Patients who managed to control bleeding at home were not included. Comparison between studies is somewhat difficult given the different definitions of bleeding. The previously reported incidence of bleeds after extraction was no greater in patients with a mean INR of 2.7 who continued to take warfarin compared with a control group who had stopped taking it 2 days before the extraction.[1] Thirty-two patients stopped taking warfarin two days preoperatively, and 33 continued to take it with only two reported

cases of postoperative bleeding, one from each group. The authors concluded that the risk of thromboembolism outweighed the risk of postoperative bleeding.[1]

In a controlled case series of 109 patients, 52 were allocated to a control group (warfarin stopped 2 days before extraction) and 57 were allocated to the intervention group (warfarin continued).[4] The incidence of bleeding in the intervention group was higher (15/57, 26%) than in the control group (7/52, 14%) as recorded in logbook entries or by telephone, but this difference was not significant and all patients were managed at home by application of pressure. The authors concluded that continuation of warfarin with an INR up to 4.0 may lead to an increase in bleeding after extraction but that it was manageable and not clinically important. Regimens where warfarin was not modified pre-operatively compared to warfarin reduction and heparin addition or to non-warfarinised patients were not associated with a greater incidence of bleeding [12,13] Blinder et al. studied three management regimens in 150 patients undergoing 359 extractions with INR values ranging from 1.5-4.0. Thirteen patients (9%) bled postoperatively but local haemostasis with gelatin sponge and sutures alone were as effective as adjunctive treatment including tranexamic acid mouth-rinse and fibrin glue.[14]

Of 950 patients who underwent 2400 operations and remained on continuous anticoagulants, only 12 required more than local measures to control haemorrhage.[5] Wahl[6] also reported that of 526 patients who experienced 575 interruptions in continuous anticoagulion, only five had serious embolic complications; four of them died. Serious embolic complications, including death, were three times more likely to occur in patients whose anticoagulation was interrupted than were bleeding complications in patients

whose treatment was continued (and whose INRs were within or below therapeutic levels). Dentists were advised to maintain therapeutic levels of anticoagulation before dental surgery and to liaise with the patient's physician.

Bleeding has been shown to be more common among older patients.[15-17] Although age should not be considered an indication for a smaller dose of warfarin, our results suggest a trend in that older patients are at greater risk of bleeding if warfarin is continued. Clinicians may, therefore, wish to follow-up older patients more often. One subject however, a 72-year-old female, with an INR of 4.2 was included on an intention to treat basis because she was in pain and had an “emergency” extraction which did not result any problem.

Drugs such as metronidazole, erythromycin, aspirin, anti-epileptic and antifungal substances may also interact with warfarin and affect its action.[18] Haemorrhage has also been associated with the use of herbal remedies. Herbs and dietary supplements such as garlic, ginko, and ginseng, inhibit platelet adhesion and aggregation, or may contain coumarins.[19] St John’s wort is a popular herbal remedy used for treating mild depression, but it can induce drug-metabolising enzymes and reduce the anticoagulant effect of warfarin. To control this potential interaction with herbal remedies, all patients were advised to stop taking them at least two weeks before the extraction. Dentists should ask patients if they use herbal remedies.

This study provides further evidence that patients who are taking warfarin and have an INR $\leq 4.0$ can be managed in primary care practice. General dental practitioners should follow published guidance, particularly for single, straight-forward extractions.[10, 11] Many GDPs, however, refer patients taking warfarin to their local hospital, so increasing waiting times for consultation before extraction. We support dental extraction in general practice, which saves valuable time and resources in secondary care, which in turn could lead to the reduction of waiting lists.[20, 21]

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Table 1: Medical conditions and therapeutic ranges of International Normalised Ratio (INR)

| **Indication** | **Therapeutic INR range** | **No (%) of patients affected** |
|---|---|---|
| Atrial fibrillation | 2.0 – 3.0 | 40 (27) |
| Deep vein thrombosis/Pulmonary embolus | 2.0 – 3.0 | 39 (26) |
| Transient ischaemic attack/Cerebrovascular accident | 2.0 – 3.0 | 13 (9) |
| Recurrent embolism taking warfarin | 3.0 – 4.0 | - |
| Mechanical heart valves | 3.0 – 4.0 | 32 (21) |
| Myocardial infarction | 3.0 – 4.0 | 12 (8) |
| Valvular disorders | 3.0 – 4.0 | 9 (6) |
| Other | | 5 (3) |

Table 2. Age (years) and gender

| | Male (n = 92) | Female (n = 58) |
|---|---|---|
| Mean (SD) age (years) | 66 (13) | 67 (12) |

Table 3. Subjects grouped according to INR values

| INR value | No (%) |
|---|---|
| <2.5 | 101 (67) |
| 2.5 – 3.0 | 22 (15) |
| >3.1 – 3.4 | 18 (12) |
| 3.5 – 4.0 | 8 (5) |
| >4.0 | 1 (1) |
| Total | 150 |

Table 4. Incidence of postoperative bleeding according to an INR threshold above or below the mean of 2.5

| Postoperative bleeding | | | |
|---|---|---|---|
| INR | No | Yes | Total |
| ≤ 2.5 | 96 | 5 | 101 |
| > 2.5 | 44 | 5 | 49 |
| | 140 | 10 | 150 |