# SURGICAL MANAGEMENT OF THE PRIMARY CARE DENTAL PATIENT ON WARFARIN


## *Summary*

## Warfarin does not need to be stopped before primary care dental surgical procedures

- The consensus from reviews on the management of dental patients taking warfarin is that patients requiring dental surgical procedures in primary care and who have an International Normalised Ratio (INR) below 4.0 should continue warfarin therapy without dose adjustment.
- Continuing warfarin during dental surgical procedures may increase the risk of postoperative bleeding requiring intervention.
- Most cases of postoperative bleeding are easily treated with local measures such as packing with a haemostatic dressing, suturing and pressure.
- Stopping warfarin increases the risk of thromboembolic events; the risk of thromboembolism after withdrawal of warfarin therapy outweighs the risk of oral bleeding as bleeding complications, while inconvenient, do not carry the same risks as thromboembolic complications.
- Stopping warfarin is no guarantee that the risk of postoperative bleeding requiring intervention will be eliminated as serious bleeding can occur in non-anticoagulated patients.

## Tranexamic acid mouthwash should not be used routinely in primary dental care

- Tranexamic acid mouthwash in primary dental practice is expensive, difficult to obtain and of no more benefit than other local haemostatic measures.
- When used alone with no local haemostatic dressing, tranexamic acid mouthwash reduces postoperative bleeding compared to placebo mouthwash.
- When used in combination with local haemostatic measures and suturing, tranexamic acid mouthwash provides little additional reduction in postoperative bleeding.



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# SURGICAL MANAGEMENT OF THE PRIMARY CARE DENTAL PATIENT ON WARFARIN

## Warfarin does not need to be stopped before primary care dental surgical procedures

Page

### Contents



## Tranexamic acid mouthwash

### Contents

## Are patients at risk of thromboembolic events if warfarin is stopped? Top

**SUMMARY OF EVIDENCE**

- Stopping warfarin for two days increases the risk of thromboembolic events.
- This risk is difficult to estimate but is probably between 0.02% and 1%.

It has been common in primary care dental practice to discontinue warfarin treatment for a few days prior to dental surgery in order to limit bleeding problems. It has been assumed that stopping warfarin for a short period presents a negligible risk to the patient. However, data from trials and published case reports do not support this assumption.

Wahl[1] reviewed 542 documented cases involving 493 patients in whom anticoagulation was withdrawn prior to a variety of dental procedures. He reported that:

- 4 patients experienced fatal thromboembolic events (2 cerebral thromboses, 1 myocardial infarction (MI), 1 embolus - type not specified).
- 1 patient experienced two non-fatal thromboembolic complications (1 cerebral embolus, 1 brachial artery embolus).
- the majority of patients had no adverse effects.

This gives an incidence of serious thromboembolic complications of 1%. There has been criticism of this finding as the length of time that the anticoagulant was stopped was either longer than normal practice (range 5-19 days) or unknown.[2] In addition, although the data suggest that stopping anticoagulant therapy caused the thromboembolic events, this cannot be assumed.

The risk of thromboembolic events associated with the perioperative withdrawal of oral anticoagulants is also relevant to non-dental procedures. One survey among American dermatologists estimated that following withdrawal of warfarin for between two and seven days, one thromboembolic event occurred for every 6,219 cutaneous excisions (0.02%) conducted.[3]

A small prospective non-randomised study involving 40 patients undergoing 50 vascular or general surgical operations was undertaken to determine the risk of operating on patients anticoagulated with warfarin compared to the risk in patients initially anticoagulated with heparin or converted to heparin for the perioperative period.[4] There were no thromboembolic events in the 20 patients (30 operations) maintained on warfarin. However, five thromboembolic events (three clotted grafts, one stroke and one brachial artery embolism) occurred in the 15 patients in whom warfarin had been stopped, an incidence of 33%. Four of these events were in patients who were not started on heparin because their risk of thromboembolism was considered to be low, i.e. the same assumption as is often made in primary dental practice.[4]

A study looking at the risk of stroke in anticoagulated patients with atrial fibrillation undergoing endoscopy found that of 987 patients (1,137 procedures) in whom the anticoagulant was adjusted, 12 patients suffered a stroke within 30 days of the procedure, 9 of which were within 7 days of the procedure. In 438 patients (457 procedures) in whom the anticoagulant was not adjusted none suffered a stroke. The authors calculated the risk of stroke as 0.79% at 7 days after the procedure and 1.06% at 30 days after the procedure if the anticoagulant was adjusted. Patients with more complex procedures and those with co-morbid illnesses were at an increased risk. [5]

In a prospective study, 412 patients admitted with stroke or transient ischemic attack (TIA) within the previous seven days, were interviewed to determine their previous use of warfarin and whether or not it had been stopped in the 14 days prior to the event.[6] 23 patients had previously been taking warfarin, of whom eight had stopped it briefly, four due to a dental extraction. The median period of warfarin cessation was 4.5 days (range 2 to 8), and the median duration from cessation to onset of stroke/TIA was 7.5 days (range 5 to 17). Strokes were cardioembolic in all patients who stopped warfarin and the median NIH Stroke Scale score was higher than that in the non-cessation group (19 vs. 3.5 respectively, p=0.033), indicating greater disability.

None of the above studies give an estimate of the excess risk of thromboembolism associated with withdrawal of oral anticoagulant therapy. This risk can be estimated from a systematic review of perioperative management of patients on long-term anticoagulant therapy that analysed data from 31 studies involving 1,868 patients. Thromboembolic events occurred in 1 of 237 (0.4%) patients who continued their oral anticoagulant, 6 of 996 (0.6%) patients who stopped their oral anticoagulant and 1 of 372 (0.3%) patients who stopped their oral anticoagulant and were given

perioperative heparin/low molecular weight heparin. The management strategy was unspecified or unclear for 263 patients.[7] This suggests that the incidence of thromboembolic events is increased by 0.2% in patients in whom oral anticoagulation is stopped before a surgical procedure.

Dodson also attempted to estimate excess risk associated with withdrawal of oral anticoagulants for a short period. He calculated the difference in the incidence of stroke over one year between patients with atrial fibrillation on warfarin (1.4%) and those who discontinued warfarin (5.0%), and multiplied this difference by 2/365 (for 2 days). On this basis, he calculated that the excess risk of stroke in patients with atrial fibrillation who discontinue warfarin for 2 days to be 1 in 5,069 (0.02%). A similar calculation suggests that in patients taking warfarin for prosthetic valve replacement, the figure is 1 in 6,083 cases (0.02%).[8]

Beirne reviews the risk of thromboembolism after stopping warfarin and concludes that not all patients on anticoagulant therapy have an equal risk of developing thromboembolism.[9] He says that anticoagulated patients can be stratified into the following groups for thromboembolic risk:
**High risk** - mechanical mitral valve, ball-cage valve, venous thrombosis <3 months ago, hypercoagulable state, atrial fibrillation (AF) with a history of stroke, acute MI <3 months ago or recent stroke or TIA(<1 month ago).
**Intermediate risk** - bileaflet tilting disc aortic valve with ≥2 stroke risk factors, chronic AF with >2 stroke risk factors, venous thromboembolism <6 months ago.
**Low risk** - AF without stroke, cardiomyopathy without AF, venous thrombosis >6 months ago, bileaflet aortic valve and <2 stroke risk factors.

Patients with prosthetic heart valves classed as high risk have a 9% to 22% per year risk of developing thromboembolism if they are not anticoagulated; the risk of interrupting warfarin for 6 to 8 days can be extrapolated to be 0.17% to 0.42%. Most patients with AF have a risk of 3% to 7% per year of developing thromboembolism when not anticoagulated. The risk of thromboembolism when warfarin is stopped for 6 to 8 days ranges from 0.02% to 0.38%.

The estimated risk of thromboembolic events if warfarin is discontinued prior to surgical procedures therefore varies considerably between studies. The risk appears to vary from 0.02% to 1%.

**Hypercoagulable state**
It has been suggested that stopping warfarin therapy can lead to a rebound hypercoagulable state.[1,7,10,11,12,13] Biochemical evidence indicates that an increase in clotting factors and thrombin activity occurs after withdrawal of warfarin. However, the clinical significance of this is unclear as a hypercoagulable state has yet to be demonstrated by clinical studies.[14]

## Are patients at increased risk of bleeding if warfarin continues? Top

**Yes.** Treatment with warfarin impairs clotting and consequently patients have an increased risk of bleeding during surgical procedures and postoperatively. Bleeding in the mouth can be excessive, even in non-anticoagulated patients. This is because the tooth support structures are highly vascular and, in addition, saliva contains constituents with a fibrinolytic action.

## If warfarin is continued what is the incidence of postoperative bleeding and is it clinically significant? Top

**SUMMARY OF EVIDENCE**
- Continuing warfarin during dental surgical procedures will increase the risk of postoperative bleeding requiring intervention.
- Stopping warfarin is no guarantee that the risk of postoperative bleeding requiring intervention will be eliminated as serious bleeding can occur in non-anticoagulated patients.
- Most cases of postoperative bleeding can be managed by pressure or repacking and resuturing the socket.
- The incidence of postoperative bleeding not controlled by local measures varies from 0% to 3.8%.

Clinically significant postoperative bleeding following dental procedures has been defined[15] as that which:

1. Continues beyond 12 hours, or
2. Causes the patient to call or return to the dental practice or accident and emergency department, or
3. Results in the development of a large haematoma or ecchymosis within the oral soft tissues, or
4. Requires a blood transfusion.

**Volume of blood**

Few studies have investigated the volume of blood lost during dental surgical procedures, but those that have report losses varying from 9.7ml per tooth in anticoagulated patients to an average of 223ml per session in patients not taking anticoagulants. A small study found no difference in the blood loss between patients who continued warfarin and those who stopped it 72 to 96 hours before the procedure. [12]

**Postoperative bleeding risk**

Wahl estimated the incidence of serious bleeding problems in 950 patients receiving anticoagulation undergoing 2,400 individual dental procedures.[16] Only 12 patients (1.3%) experienced bleeding uncontrolled by local measures and none of the patients were reported to have experienced serious harm. Of these 12 patients:

- 7 had higher than recommended anticoagulation levels
  - 3 of these were given a course of postoperative antibiotics, which may have interacted with the warfarin.
- 2 were started on a placebo mouthwash several times a day immediately after the procedure, which is contrary to standard advice to avoid rinsing for the first 24 hours.

Beirne reviewed the evidence for continuing oral anticoagulant therapy for ambulatory oral surgery and concluded that the risk of developing life-threatening bleeding or bleeding that could not be controlled using local measures following dental extractions, alveoloplasties, or dental implants is so low that there is no need to stop warfarin.

Recent publications have focussed less on whether or not anticoagulation should be continued or stopped and more on effective ways to manage patients who continue their anticoagulant therapy. Table 1 details the initial haemostatic management and the incidence and control of postoperative bleeding from studies involving almost 1,500 dental patients who continued anticoagulation during dental surgical procedures.

Of the patients detailed in Table 1, 138 (9.4%) had delayed postoperative bleeding and in 56 cases (3.8%) this was classed as serious (not controlled by local measures). One patient required a transfusion to reverse the effects of the warfarin, one patient who had received no haemostatic dressing or postoperative compression required vitamin K and one patient who had received no haemostatic dressing or postoperative compression required fresh frozen plasma. Among 260 patients from these studies (data not in table) who had never taken an oral anticoagulant there were 3 serious bleeds (1.2%).[12,17]

Interpretation of bleeding rates is difficult as rates for different procedures are not analysed separately and different definitions for serious bleeding are used. This may explain some of the divergence between the figures cited above and those from a systematic review that found an incidence of serious bleeding of between 0 and 2% in anticoagulated patients undergoing minor procedures including dental surgery. [7]

**Table 1 Haemostatic management and postoperative bleeding incidence in dental surgical patients when oral anticoagulation was continued**

| Trial | No. pts* | Anticoagulant | INR range** (protocol INR range) | Mean INR | Haemostatic dressing used (number of patients) | Suture | Delayed post op bleeds (serious***) | Control of bleeding |
|---|---|---|---|---|---|---|---|---|
| Sindet-Pederson et al.[18‡] (RCT) | 39 | Warfarin dicoumarol | -[#] (estimate 2.5 – 4.8) | -[#] | None (20) | Yes – type not specified (15 pts) | 10 (5) | 1 = Compression<br>4 = Compression with gauze soaked in tranexamic acid<br>5 = local anaesthetic, haemostatic dressing and resuturing<br>1 = Fresh-frozen plasma |
| | | | | | None + tranexamic acid mouthwash (19) | Yes – type not specified (13 pts) | 1 (1) | |
| Ramstrom G et al. [19‡] (RCT) | 89 | Phenprocoumon warfarin dicoumarol | 2.1 – 4.0 estimate[#] (therapeutic range) | -[#] | None (45) | Yes – type not specified | 10 (7) | 3 = Compression with gauze soaked in tranexamic acid +mouthwash<br>6 = local anaesthetic, haemostatic dressing and resuturing<br>1 = Vitamin K + local anaesthetic, haemostatic dressing and resuturing |
| | | | | | None + tranexamic acid mouthwash (44) | Yes – type not specified | 0 | |
| Souto et al.[20 ‡] (RCT) | 53 | Acenocoumarol | 1.5 – 5.2 (2 – 4) | 3.1 | None, antifibrinolytic mouthwash | None | 7 (0) | Epinephrine**** instillation and compression with gauze soaked in antifibrinolytic |
| Devani et al.[13‡] (RCT) | 33 | Warfarin | 2.2 – 3.9 (2 – 4) | 2.7 | Oxidised cellulose Surgicel (all) | Catgut | 1 (1) | Saline irrigation, repack and suture |
| Campbell et al.[12] (CT) | 12 | Warfarin | 1.2 - 2.9 | 2.0 | None | None | 1 (0) | Not specified |
| Blinder et al. [21‡] (CT) | 150 | 'Coumarin' | 1.5 – 4.0 (1.5 – 4) | 2.2 | Gelatin sponge + tranexamic acid mouthwash (50) | Silk | 4 (2) | 2 = pressure with tranexamic acid soaked gauze<br>2 = curettage, gelatin sponge, fibrin glue and suture |
| | | | | 2.7 | Gelatin sponge + fibrin glue (50) | Silk | 6 (2) | 4 = pressure with tranexamic acid soaked gauze<br>2 = curettage, gelatin sponge, fibrin glue and suture |
| | | | | 2.4 | Gelatin sponge (50) | Silk | 3 (3) | 3 = curettage, gelatin sponge, fibrin glue and suture |
| Blinder et al. [22] (case series) | 249 | 'Coumarin' | 1.5 - >3.5 (1.5 - >3.5) | 2.5 | Gelatin sponge (all) | Silk | 30 (17) | 13 = pressure and tranexamic acid soaked gauze<br>17 = curettage, repack and suture |
| Halfpenny et al.[23] (RCT) | 46 | Warfarin | 2 – 4.1 (2 – 4.5) | 2.8 | Oxidised cellulose (26) | Softgut | 1(1) | 1 = repack and suture |
| | | | | | Fibrin glue (20) | Softgut | 2 (2) | 1 = repack and suture<br>1 = hospital admission |
| Evans et al.[24] (RCT) | 57 | Warfarin | 1.2 – 4.7 (<4) | 2.5 | Oxidised cellulose (all) | Synthetic absorbable | 12 (2) | 10 = pressure<br>2 = repack and suture, 1 requiring hospital admission |
| Barrero et al. [25] (case series) | 125 pts = 229 sessions | Acenocoumarol | 2 – 3 (2 – 3) | Not stated | Oxidised cellulose (167 sessions) Tranexamic acid soaked gauze compression and mouthwash (all sessions) | 50 sessions only | 19 patients bled for >5 mins (1) | 1 required transfusion |
| Alexander et al. [26] (personal experience) | 15 | Warfarin | 1.9 – 3.6 (2 – 4) | 2.6 | Surgicel (7)<br>Gelfoam (3)<br>None (5) | Yes – type not specified | 0 (0) | |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Zanon et al.[17] (case control series) | 250 | Warfarin | 1.8 – 4 (1.8 – 4) | Not stated | Oxidised cellulose, tranexamic acid soaked gauze (all) | Silk | 4 (4) | Gelatin sponge pack and suturing, tranexamic soaked gauze |
| Cannon et al. [27] (CT) | 35 | Warfarin | 2.1- 4 (2 - 4) | 3.4 | Surgicel (all) | Catgut | 2(0) | Local pressure |
| Ramli R et al.[28] (case series) | 30 | Warfarin | 1.9 – 3.5 (1.5 – 4) | Not stated | Surgicel (all) (tranexamic acid mouthwash if fulfilled specific criteria) | Synthetic absorbable | 4 (0) | Local pressure, 1 with lidocaine 2% + adrenaline 1:80, 000 impregnated gauze |
| Sacco R et al.[29] (RCT) | 65 (assumed) | Not specified | 2.5 – 3.3 (Not specified) | 2.9 | Oxidised cellulose or collagen sponge, tranexamic acid mouthwash (all) | Yes – type not specified | 6 (6) | Insertion of oxidised cellulose |
| Al-Mubarak S et al.[30] (RCT) | 81 (assumed) | Warfarin | 1.7 – 3.4 (Not specified) | 2.5 | None | Yes (41, assumed-) type not specified | 11(0) | Not specified |
| Carter G et al.[31] (RCT) | 85 | Warfarin | (2 – 4) | 2.75 | Surgicel soaked in tranexamic acid + irrigation with tranexamic acid + tranexamic acid mouthwash (2 days = 43 vs. 5 days = 42) | Synthetic absorbable | 3 (0)<br>2 = 2 days' mouthwash, 1 = 5 days' mouthwash | Irrigation with tranexamic acid and compression |
| Carter G et al.[32] (RCT) | 49 | Warfarin | 2.3 - 4.0 (2 – 4) | 3.0 | Surgicel soaked in tranexamic acid + irrigation with tranexamic acid + tranexamic acid mouthwash (26) | Synthetic absorbable | 0 | |
| | | | 2.1 – 4.0 (2 – 4) | 3.1 | Surgicel and fibrin glue (23) | Synthetic absorbable | 2 (2) | Compression and fibrin glue |
| **Total no. patients =** | **1463** | | | | | | **139 (9.5%) delayed postoperative bleeds (56 (3.8%) serious***)** | |

* This column indicates the number of patients for whom oral anticoagulation was continued; some trials also included a group of patients for whom oral anticoagulation was stopped or a group of patients not taking an oral anticoagulant.
** Measured range for study participants
*** Serious = requiring intervention e.g. repacking and resuturing
**** epinephrine = adrenaline
[#] = Thrombotest and prothrombin-proconvertin tests used to measure anticoagulation
[‡] = Studies included in Wahl's review
RCT = randomised controlled trial
CT = controlled trial

## How do the risks of thromboembolic events and postoperative bleeding balance? Top

**SUMMARY OF EVIDENCE**

- Bleeding complications, while inconvenient, do not carry the same risks as thromboembolic complications.
- Patients whose INR results are within the acceptable therapeutic range are more at risk of permanent disability or death if they have their warfarin stopped prior to a surgical procedure than if they continue it.
- Patients with a target INR between 3.0 and 4.0 are at a high risk of thromboembolism and stopping or reducing their INR exposes them to an increased risk of life threatening thrombosis.
- Published reviews of the available literature advise that oral anticoagulants should not be stopped prior to dental surgical procedures.

Increased postoperative bleeding must be balanced against the consequences of thromboembolism.

Management of anticoagulation in the perioperative period should be dictated by the thromboembolic risk associated with stopping anticoagulant therapy and the risk of haemorrhage associated with the procedure. Seamless anticoagulation is preferred and is considered safe for most minor procedures.[33]

Thromboembolic events are associated with considerable morbidity and mortality. Permanent disability or death occur in:

- 70% to 75% of patients who experience an arterial thromboembolism (e.g. stroke, myocardial infarction, pulmonary embolism)'
- 4% to 10% of patients who have a venous thromboembolism (e.g. deep vein thrombosis).

Patients with heart valve replacements or recurrent thromboembolism (INR target between 3.0 and 4.0) are at the highest risk for serious thromboembolic events if their anticoagulant therapy is temporarily stopped or decreased.[9,31]

In compiling this review no cases of permanent disability or death, reported as a consequence of postoperative bleeding associated with a dental surgical procedure in which the patient continued oral anticoagulation, were found.

The majority of publications that have considered the risks of stopping versus continuing oral anticoagulation for dental procedures have concluded that most dental patients can undergo procedures without alteration to their oral anticoagulant provided that local haemostatic measures are used to control bleeding.[1,7-10,12,13,15-17,34]

In January 2006 the National Patient Safety Agency (NPSA) published a risk assessment of oral and injectable anticoagulant therapy and identified a series of actions to reduce the risk of harm to patients.[35] One of the risks identified was the way in which patients receiving dental treatment were being managed. The NPSA concluded that dental practitioners should manage patients on anticoagulants according to evidence based therapeutic guidelines. In most cases dental treatment should proceed as normal and oral anticoagulant treatment should not stopped or the dosage decreased inappropriately.[36] A chart has been produced by the NPSA, the British Dental Association (BDA) and the British Society for Haematology (BSH) for dental practitioners summarising the management strategy for patients receiving anticoagulants; *Managing patients who are taking warfarin and undergoing dental treatment*.[37] The chart advises that if a patient on warfarin has an INR of below 4.0 they can usually receive their dental treatment in primary care without needing to stop their warfarin or reduce their dose.

## Which patients taking warfarin should not undergo surgical procedures in primary care? Top

Patients who have an INR greater than 4.0 should not undergo any form of surgical procedure without consultation with the clinician who is responsible for maintaining their anticoagulation (this may be a physician or pharmacist in primary care or the hospital anticoagulant clinic). The warfarin dose will need to be adjusted prior to the procedure. Patients who are maintained with an INR >4.0 or who have very erratic control may need to be referred to a dental hospital or hospital based oral/maxillofacial surgeon.

The following medical problems may affect coagulation and clotting:[13,34,37,38,39]

- liver impairment and/or alcoholism
- renal failure
- thrombocytopenia, haemophilia or other disorder of haemostasis
- those currently receiving a course of cytotoxic medication.

Patients with any of these conditions who also take warfarin should not be treated in primary care but referred to a dental hospital or hospital-based dental clinic.

Patients requiring major surgery are unlikely to be treated in the primary care setting.

## What is the normal INR range? Top

The activity of warfarin is expressed using the international normalised ratio (INR). For an individual not taking warfarin a normal coagulation profile is an INR of 1.0.

UK guidelines recommend the following target INRs:

| Indication | UK INR target | Acceptable range |
|---|---|---|
| Pulmonary embolus (PE) | 2.5 | 2.0-3.0 |
| Deep vein thrombosis (DVT) | 2.5 | 2.0-3.0 |
| Atrial fibrillation (AF) | 2.5 | 2.0-3.0 |
| Antiphospholipid syndrome | 2.5 | 2.0-3.0 |
| Recurrence of embolism when warfarin stopped | 2.5 | 2.0-3.0 |
| Bileaflet aortic valve | 2.5 | 2.0-3.0 |
| Tilting disk aortic valve | 3.0 | 2.5-3.5 |
| Bileaflet mitral valve | 3.0 | 2.5-3.5 |
| Tilting disk mitral valve | 3.0 | 2.5-3.5 |
| Caged ball or caged disk aortic or mitral valve | 3.5 | 3.0-4.0 |
| Recurrence of embolism while taking warfarin | 3.5 | 3.0-4.0 |

In theory all patients will have an INR below 4.0.

## Up to what INR value can dental procedures be carried out in primary care? Top

**SUMMARY OF EVIDENCE**

- Published trial data suggests that minor dental surgical procedures can be safely carried out on patients with an INR ≤4.0.
- The consensus from reviews on the management of dental patients taking warfarin is that minor dental surgical procedures should be carried out without alteration to the patient's warfarin therapy if the INR is within the therapeutic range (INR 2.0 – 4.0).
- Dentists from general and community dental practice have reported no problems in carrying out minor dental surgical procedures on patients with an INR within the therapeutic range.

Of the 18 trials/case series listed in Table 1, one stated that minor dental surgical procedures could be carried out with the INR ≤4.5, 12 limited the INR to 'within the therapeutic range' or ≤4.0,[13,17,18-21,24,26-28,31,32] one stated the INR could be ≥3.5, one limited the INR to ≤3.0[25] and three trials stated no limits but included patients with INRs up to 2.9, 3.3, and 3.4. Results suggest that limiting the INR to ≤4.0 enables procedures to be carried out safely without excessive postoperative bleeding.

Reviews discussing the continuation of oral anticoagulation during minor dental surgical procedures have advocated that procedures can safely be carried out when the INR is within the therapeutic range (2.0 – 4.0) and local haemostatic measures are used to control bleeding.[1,7-10,16,40,41,42,43,44,45] Others have advocated upper limits of 3.5[34,46,47,48] or 3.0.[49]

A series of letters in the *British Dental Journal* in 2002/2003[50,51,52,53,54,55,56,57,58,59] highlight the lack of consensus, but a gradual change in practice, in the management of dental patients who take warfarin. The series includes letters from practitioners in general dental practice and community dental practice[53,55] reporting that they routinely carry out dental procedures without any problems in patients whose INR is within the therapeutic range.

The NPSA/BDA/BSH advise that if a patient on warfarin has an INR of below 4.0 they can usually receive their dental treatment in primary care without needing to stop their warfarin or reduce their dose.

## When should the INR be measured before a dental procedure? Top

The INR must be measured prior to dental procedures, ideally within 24 hours before the procedure.[17,21,22,23,24,25,26,34,38,46,47] However, this is sometimes difficult to achieve in primary care dental practice. For patients who have a stable INR, an INR measured within 72 hours before the

procedure is acceptable.[37,38] Patients will need either to co-ordinate their dental treatment with their next planned INR measurement or have an extra INR measurement within 72 hours of their planned dental treatment.

N.B. The INR is valid only for patients who have stable anticoagulant therapy. Patients presenting with an INR much higher than their normal value, even if it is less than 4.0, should have their procedure postponed and should be referred back to the clinician maintaining their anticoagulant therapy.

## Should the primary care dentist ever advise an alteration to the warfarin regimen? Top

**No.** The GP, anticoagulant clinic or haematologist must do this.

## For what procedures can warfarin be continued safely? Top

**Minor surgical procedures**
Minor surgical procedures can be safely carried out without altering the warfarin dose. Those likely to be carried out in primary care will be classified as minor e.g. simple extraction of up to 3 teeth, gingival surgery, crown and bridge procedures, dental scaling and the surgical removal of teeth.[10,15,26,39,47]

When more than 3 teeth need to be extracted then multiple visits will be required. The extractions may be planned to remove 2-3 teeth at a time, by quadrants, or singly at separate vists.[8,26,38]

**Periodontal procedures**
Periodontal examinations and supragingival scaling are considered to be low risk for bleeding. However, subgingival debridement may cause significant bleeding especially if the gums are inflamed.[60] Good plaque control is important before performing periodontal procedures in anticoagulated patients. Scaling and root planing should initially be restricted to a limited area e.g. one quadrant, to assess if the bleeding is problematic.

## How should the risk of bleeding be managed? Top

**Timing**
Think about the timing of the surgery. Planned surgery should ideally be:

- At the beginning of the day - this allows more time to deal with immediate re-bleeding problems.
- Early in the week- this allows for delayed re-bleeding episodes occurring after 24–48 hours to be dealt with during the working week. For example a Tuesday morning procedure allows the patient to have their INR measured on Monday.[37,47]

**Local anaesthetic**
A local anaesthetic containing a vasoconstrictor should be administered by infiltration or by intraligamentary injection wherever practical.[15,37] The use of a short 27-gauge needle will minimise tissue damage. Regional nerve blocks should be avoided when possible. However, if there is no alternative, local anaesthetic should be administered cautiously using an aspirating syringe.[22,38] Local vasoconstriction may be encouraged by infiltrating a small amount of local anaesthetic containing adrenaline (epinephrine) close to the site of surgery.[37,49]

**Local haemostasis**
Sockets should be gently packed with an absorbable haemostatic dressing[9,10,15,28,37,38,39,42,45,47] e.g. oxidised cellulose (Surgicel®), collagen sponge (Haemocollagen®) or resorbable gelatin sponge (Spongostan®), then carefully sutured. Haemostatic dressings promote and stabilise clot formation by providing a mechanical matrix. Trials in patients who have continued anticoagulant therapy throughout the perioperative period have used resorbable (catgut or synthetic (polyglactin, Vicryl®)) or non-resorbable (silk, polyamide, polypropylene) sutures. Resorbable sutures are preferable as they attract less plaque.[47] If non-resorbable sutures are used they should be removed after 4-7 days. Following closure, pressure should be applied to the socket(s) by using a gauze pad that the patient bites down on for 20 minutes.

Efforts should be made to make the procedure as atraumatic as possible and any bleeding should be managed using local measures.

The use of tranexamic acid mouthwash, which acts as a local antifibrinolytic agent, has been investigated but is not recommended routinely in primary care (see page 13).

**Postoperative management**
Patients should be given clear instructions (preferably in writing) on the management of the clot in the postoperative period and advised:[61,62]

- to look after the initial clot by resting while the local anaesthetic wears off and the clot fully forms (2-3 hours),
- to avoid rinsing the mouth for 24 hours,
- not to suck hard or disturb the socket with the tongue or any foreign object,
- to avoid hot liquids and hard foods for the rest of the day,
- to avoid chewing on the affected side until it is clear that a stable clot has formed. Care should then be taken to avoid dislodging the clot,
- if bleeding continues or restarts to apply pressure over the socket using a folded clean handkerchief or gauze pad. Place the pad over the socket and bite down firmly for 20 minutes. If bleeding does not stop, the dentist should be contacted; repacking and resuturing of the socket may be required.
- Who to contact if they have excessive or prolonged postoperative bleeding. The surgery and out of hours/on call dentist's name/number should be provided. There should be a facility for the patient to be reviewed and treated immediately by a dentist if a bleeding problem occurs. If it is not possible for the patient to be seen immediately by a dentist then the patient should be referred to their local accident and emergency department.
- On pain control – see below.

The National Patient Safety Agency, with the support of the British Dental Association (BDA), has produced a leaflet for patients taking warfarin and requiring dental treatment called *Oral anticoagulant therapy Important information for dental patients.*

## How should postoperative pain control be managed? Top

Patients should follow the advice of their anticoagulant clinic with regard to the choice of analgesia for short-term mild to moderate pain.[63] Generally paracetamol is considered the safest simple analgesic for patients taking warfarin and it may be taken in normal doses if pain control is needed and no contraindication exists. Patients should be advised **not** to take aspirin, aspirin containing compound analgesic preparations or non-steroidal anti-inflammatory drugs (NSAIDs) e.g. ibuprofen, which are considered less safe than paracetamol in patients taking warfarin.

If analgesia is to be prescribed additional options include;

- **Dihydrocodeine** – an opioid analgesic with similar analgesic efficacy to codeine that can be prescribed on an NHS prescription. Its use should be considered second line and only when other drugs are unsuitable. It is effective for mild to moderate pain but has no anti-inflammatory activity and is of limited value in pain of dental origin.[64]

## Are there any drug interactions that are relevant to this patient group undergoing dental surgical procedures? Top

**Amoxicillin** - There are anecdotal reports that amoxicillin interacts with warfarin causing increased INR and/or bleeding but documented cases of an interaction are relatively rare considering how frequently the drug is used; the broad picture is that no clinically relevant interaction normally occurs with amoxicillin and most penicillins.[65,66] A single 3 gram dose given for endocarditis prophylaxis has not been shown to produce a clinically relevant interaction. Prophylactic antibiotics do not appear to affect the bleeding risk postoperatively.

Patients taking warfarin requiring a course of amoxicillin should be advised to be vigilant for any signs of increased bleeding and concurrent use should be monitored so that the very occasional and unpredictable cases INR increase or decrease can be identified.

**Clindamycin** - Clindamycin does not interact with warfarin when given as a single dose for endocarditis prophylaxis. Prophylactic antibiotics do not appear to affect the bleeding risk

postoperatively.[24] There is a single case report of an interaction between warfarin and a course of clindamycin.[66,67]

**Metronidazole** – *CAUTION:* metronidazole interacts with warfarin and should be avoided wherever possible. If it cannot be avoided the warfarin dose may need to be reduced by a third to a half by the GP or anticoagulant clinic.[66,68] The patient must seek advice from the person managing their anticoagulation before taking metronidazole.

**Erythromycin** - Erythromycin interacts with warfarin unpredictably and only affects certain individuals. Most are unlikely to develop a clinically important interaction. Patients should be advised to be vigilant for any signs of increased bleeding, concurrent use should be monitored especially in the elderly.[66,69]

**Paracetamol -** The anticoagulant effect of warfarin is normally not affected, or only increased by a small amount, by occasional doses of paracetamol (no more than about 2.5 to 3 g weekly).[70] Paracetamol is considered to be safer than aspirin as an analgesic in patients taking warfarin and is the analgesic advised by anticoagulant clinics and the patient held 'Oral Anticoagulant Therapy' booklet. The anticoagulant effect of warfarin may be enhanced by prolonged regular use of paracetamol.

**Aspirin -** *AVOID* use as an analgesic and anti-inflammatory agent. Concurrent aspirin increases the likelihood of bleeding by 3-5 times, increases the bleeding time and may damage the stomach lining.[71] The interaction is well documented and clinically important.

**Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)** e.g. ibuprofen, diclofenac. – *AVOID:* Care should be taken when using NSAIDs because, to a greater or lesser extent, they irritate the stomach lining, which can result in gastrointestinal bleeding, which will be more severe in anticoagulated patients.[72] Although no interaction usually occurs with normal doses of ibuprofen and probably diclofenac, isolated cases of raised INRs have been described. Some NSAIDs have effects on platelet activity, which can affect bleeding times.[72]

# TRANEXAMIC ACID MOUTHWASH

## What is tranexamic acid? Top

Tranexamic acid is an antifibrinolytic agent that inhibits the breakdown of fibrin clots. Its primary action is to block the binding of plasminogen and plasmin to fibrin therefore preventing fibrinolysis.[73] It has been used in anticoagulated dental patients as a local haemostatic agent in the form of a mouthwash.

## What is the evidence of benefit for tranexamic acid mouthwash? Top

**SUMMARY OF EVIDENCE**

- When used alone with no local haemostatic dressing, tranexamic acid mouthwash reduces postoperative bleeding compared to placebo mouthwash.
- When used in combination with local haemostatic measures and suturing, tranexamic acid mouthwash provides little additional reduction in postoperative bleeding.

Two of the first studies[18,19] to compare a 4.8% tranexamic acid mouthwash with placebo mouthwash in dental patients recruited a total of 128 anticoagulated patients undergoing oral surgery. Patients were instructed to rinse 10ml of the solution around the mouth for two minutes then expectorate four times a day for seven days. Both studies used the same protocol. No other local haemostatic agents or procedures were used, although all extraction sites were sutured. Patients using tranexamic acid mouthwash experienced fewer bleeding episodes requiring treatment postoperatively than those using placebo mouthwash (1.6% vs. 30.8% respectively, $p \leq 0.01$).

Following these initial studies other studies[17,20,21,25] have employed tranexamic acid with or without local haemostatic measures in anticoagulated patients.

In one study comparing three local haemostatic measures following tooth extraction in 150 anticoagulated patients (INR range 1.5-4.0), all patients had resorbable gelatin sponges inserted into the socket(s), followed by suturing and, in addition, either:

- nothing, or
- tranexamic acid 500mg in a mouthwash used for two minutes four times a day for four days, or
- fibrin glue prior to suturing.

Patients receiving only gelatin sponges and suturing had fewer episodes of postoperative bleeding (6%) than those using additional tranexamic acid (8%) or fibrin glue (12%). However, the differences among the three groups were small and not significant (p=0.54).

In a study of 250 anticoagulated patients who had compression applied with a tranexamic acid soaked gauze pad in addition to local haemostatic dressing and suturing, 1.6% had serious postoperative bleeding.

In a case controlled series, 125 patients (229 sessions) used tranexamic acid as a mouthwash for two days postoperatively, but in less than half the sessions a haemostatic dressing and suturing were used; bleeding lasting longer than 5 minutes occurred after 8.3% of sessions; one patient required a transfusion.

In a randomised controlled trial, 40 fully anticoagulated patients received tranexamic acid mouthwash for two days postoperatively with no haemostatic dressing or suturing. Three patients (7.5%) experienced bleeding requiring local intervention.[20]

Most recently, two Australian studies have investigated the use of tranexamic acid following dental extractions.[31,32] In the first study 85 anticoagulated patients (INR range 2.0 – 4.0) requiring dental extractions were randomly divided into two groups. Both groups received 4.8% tranexamic acid mouthwash to be used for two minutes four times a day; the first group used the mouthwash for two days; the second group for five days. All sockets were irrigated with tranexamic acid solution

before being packed with Surgicel® soaked in tranexamic acid solution. Sockets were sutured with resorbable sutures. There was no significant difference in postoperative bleeding between the two groups (p=0.57). The incidence of postoperative bleeding was 4%. In total there were three cases of delayed postoperative bleeding all occurring within 48 hours of surgery whilst the patients were still using the mouthwash; none required resuturing.

In the second Australian study, 49 anticoagulated patients (INR range 2.0 – 4.0) were randomly allocated to one of two groups. In the first group all sockets were irrigated with tranexamic acid 4.8% solution then packed with Surgicel® soaked in tranexamic acid solution before being sutured with resorbable sutures. Postoperatively patients were given 4.8% tranexamic acid mouthwash to be used for two minutes four times a day for seven days. The second group received autologous fibrin glue (prepared from blood taken one to two weeks before surgery) intraoperatively. Immediately after extraction the socket was curetted and Surgicel® was placed in the apical third of the socket; fibrin glue was applied to the socket walls before suturing and over each sutured socket. There were no cases of postoperative bleeding in the tranexamic mouthwash group. Two patients had light bleeding in the fibrin glue group, neither required resuturing. There was no significant difference in the rate of postoperative bleeding between the two groups (p=0.12).

Pooling the results from the five studies above where tranexamic acid mouthwash was used, delayed postoperative bleeding requiring treatment occurred in 3.6% of patients.[18,19,21,31,32] These rates compare to a serious postoperative bleeding rate of 5.4% when results were pooled from studies where local haemostatic measures and suturing were used without tranexamic acid.[13,21,22,23,24,27]

## What are the practical issues associated with the use of tranexamic acid in primary care?

Top

Tranexamic acid mouthwash is not available commercially. An unlicensed preparation can be obtained by special order from a limited number of commercial or NHS 'special-order' manufacturers.

Tranexamic acid mouthwash cannot be prescribed on an NHS prescription but can be prescribed privately. Dentists may write private prescriptions for patients receiving NHS treatment. Community pharmacists can obtain the unlicensed mouthwash from the 'special-order' manufacturer to fill a prescription. N.B. When a private prescription is issued the patient will pay the full price of the mouthwash plus a dispensing fee.

For treatment of private patients (but not NHS patients) the dental practice can order supplies directly from the manufacturer and supply them to the patient. However, 'special order' supplies have a limited shelf life (1-3 months) and can be very expensive (from around £65 to over £200 for a 7 day course[74,75]).

If tranexamic acid mouthwash is supplied by the dentist directly to the patient it must comply fully with the 'labelling of dispensed medicinal products' requirements (Medicines Act 1968).[76,77] This requires that the container must be labelled with:

1. the name of the product
2. directions for use
3. any precautions relating to the use of the medicinal product
4. the name of the person to whom the medicine is to be administered
5. the date of dispensing
6. the name and address of the dentist supplying the medicinal product
7. the words "Keep out of reach of children" or words with a similar meaning

A container need not be labelled if it is enclosed in a package which is labelled with the required particulars.

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# Management of dental patients on warfarin undergoing surgical procedures in primary care

Does the patient have one of the following medical problems:
- liver impairment and/or alcoholism
- renal failure
- thrombocytopenia, haemophilia or other disorder of haemostasis

OR
- is currently receiving a course of cytotoxic medication?

YES → REFER to a dental hospital or hospital-based oral/maxillofacial surgeon.

NO ↓

Obtain an INR measured ideally within 24 hours but not more than 72 hours before the procedure.

↓

Does the patient have a stable INR of 4.0 or below?

NO → Reschedule the procedure for when the INR is <4.0. Consider referral to a dental hospital or hospital-based oral or maxillofacial surgeon if the INR is maintained >4.0 or control is erratic.

YES ↓

Does the patient need prophylactic antibiotics (i.e. are they at risk of endocarditis)?

YES → Follow current guidelines for endocarditis prophylaxis (interactions see page 11).

NO ↓

**Consider the timing of the procedure**
In the morning – immediate re-bleeding problems can be managed during the working day.
At the beginning of the week – delayed re-bleeding problems can be managed during the working week.

↓

Use a local anaesthetic containing a vasoconstrictor.

↓

Give local anaesthetics by infiltration or intraligamentary injection wherever practical. Avoid regional nerve blocks where possible. However, if there is no alternative administer cautiously using an aspirating syringe.

↓

Gently pack the socket with an absorbable haemostatic dressing (e.g. Surgicel®, Haemacollagen®, Spongostan®).

↓

Carefully suture the socket.

↓

There is no indication for routinely prescribing antibiotics following minor dental surgical procedures in this group of patients (interactions see page 11).

↓

Does the patient require postoperative analgesia?

YES → Paracetamol is the analgesic of choice.
AVOID non-steroidal anti-inflammatory drugs (NSAIDs) e.g. ibuprofen, aspirin, diclofenac (interactions see page 11). Dihydrocodeine is available on NHS prescription.

NO ↓

Patients should be given clear instructions on the management of the clot in the postoperative period (see page 10).

## Appendix 1

### Will I be paid if I use a haemostatic dressing and sutures? Top

Extraction of teeth including minor oral surgery to remove e.g. buried roots, unerupted or impacted teeth, is classed as 'Band 2' within the 2006 General Dental Services Contract and attracts 3.0 units of dental activity. Additional units of dental activity can be claimed for removal of sutures (1.0) and arrest of bleeding (1.2).[78] There is no additional payment for local haemostatic management of patients taking warfarin.

## Appendix 2

### Will I be at risk of litigation if the patient bleeds? Top

We live in an increasingly litigious society and there will always be the possibility that a patient may pursue a legal claim. Adherence to clinical practice guidelines is one way to limit potential liability.

Dental defence societies assess each case individually but take the following general view:[79,80]

- Practitioners should be aware of and abide by best evidence-based medicine, current teaching and guidance from a responsible body of opinion.
- If contrary advice is received from another medical practitioner a discussion around the differing opinions is advised with this practitioner. It is important that the patient is not compromised in any way.

When defence societies assess cases involving patients who take warfarin they consider that:[79,80]

- Practitioners should be aware of guidance which assesses the risk versus benefit of stopping or continuing warfarin and concludes that the potential risk of stopping therapy is greater than the risk from bleeding following simple dental extraction.
- If practitioners adhere to guidance advising that warfarin is not stopped prior to minor surgical procedures in primary dental care, especially with respect to local haemostasis and suturing, then the practitioner could be defended should problems arise.

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Top


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