An audit of the role of vitamin K in the reversal of International Normalised Ratio (INR) in patients undergoing surgery for hip fracture

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ABSTRACT

INTRODUCTION The objective of this prospective audit was to compare two methods of anticoagulation reversal in the pre-operative period for hip fracture patients.

PATIENTS AND METHODS In the first part of the audit, our current practice was analysed. Data relating to the number of days from admission to surgery and the reasons for delay to surgery were collected. Also, data concerning common reasons for which the patients were started on warfarin and the time required for INR to drop to 1.5 or below were collected. In the second part of the audit, 45 patients with INR above 1.5 were given a single dose of vitamin K (1 mg i.v.) in addition to stopping warfarin.

RESULTS The mean difference in the time for INR < 1.5 in the two groups was 2 days (52 h; $P < 0.05$). The mean difference in wait for surgery since admission between the two groups was 4 days (91 h; $P < 0.05$). There was no significant difference between the two groups as regards the average number of co-morbidities in the patient groups.

CONCLUSIONS A single 1 mg intravenous dose of vitamin K significantly reduces the time for the reversal of INR and the pre-operative delay to surgery, in patients on long-term warfarin. We conclude that 1 mg of intravenous vitamin K on admission is a safe and effective treatment to avoid delay in the treatment in this group of patients.

KEYWORDS

Hip fracture – Vitamin K – INR

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A delay in surgery for patients with fractured neck of femur is associated with poorer outcome due to complications of prolonged recumbence and is associated with increased health costs.¹ Most of these patients are elderly, with associated co-morbidities such as atrial fibrillation. The prevalence of atrial fibrillation in the UK is high, requiring long-term anticoagulation for these patients.² Warfarin is the most commonly prescribed anticoagulant in the UK;³ about 1–1.5% of the population in the UK is on warfarin prophylaxis.^{4,5} As orthopaedic surgeons, we are faced with an increasing number of elderly anticoagulated patients who require urgent surgery for osteoporotic fractures.

An International Normalised Ratio (INR) of > 1.5 is considered high risk for intra- or postoperative bleeding.⁶ Warfarin reversal, in the past, was passively achieved by omitting it on admission alone, resulting in delay of surgery.⁷ The objective of this prospective audit was to compare two methods of anticoagulation reversal in the pre-operative

period for hip fracture patients. In the initial arm of the audit, the anticoagulation was reversed passively by omitting the patient's medication. A review of the literature suggested that warfarin reversal could be achieved safely and rapidly with vitamin K. A single dose given intravenously (i.v.) was sufficient in three-quarters of the patients.⁵ This was set as the gold standard and changes in practice were implemented. A trust-wide protocol was developed between the haematology department and the orthopaedic surgeons where every patient with proximal femoral fracture with INR above 1.5 was given 1 mg of vitamin K i.v. (Fig. 1). This was given as soon as the INR results were available. This new protocol was subsequently re-audited.

Patients and Methods

This was a prospective audit carried out simultaneously at two hospital sites in the trust. There was no statistically

significant difference in age and sex distribution, INR on admission and medical co-morbidities between patients considered in the two arms of the audit. Inclusion criteria were all patients on warfarin with an INR of more than 1.5 on admission, with a neck of femur fracture requiring operative management. Patients on other types of anticoagulant therapy, those with INR level 1.5 or below on admission were excluded. Initial INR was checked in the accident and emergency department on presentation and was repeated on a daily basis until surgery.

In the first part of the audit, our current practice was analysed. All the proximal hip fracture patients on warfarin, admitted from October 2005 to April 2006 were included. Thirteen patients had a dynamic hip screw fixation and 32 had a hemi-arthroplasty of the hip. These patients had their warfarin omitted and their INR allowed to normalise passively. Data relating to the number of days from admission to surgery and the reasons for delay to surgery were collected. Also, data concerning common reasons for which the patients were started on warfarin and the time required for INR to drop to 1.5 or below were collected.

In the second part of the audit, 45 patients with INR above 1.5, admitted during May 2006 to December 2006, were given a single stat dose of vitamin K (1 mg i.v.) in addition to stopping warfarin. This was given as soon as the INR results were available after admission. Twenty patients had dynamic hip screw fixation and 25 had hemi-arthroplasty of the hip.

All patients in both groups were started on a prophylactic dose of 40 mg of subcutaneous Enoxaparin. One patient

in the non-vitamin K group and two patients in the vitamin K administered group received additional intravenous heparin for thrombosis prophylaxis for prosthetic cardiac valves. None of the patients was operated unless the INR dropped below the target level of 1.5 and there were no exclusions to this criterion. Previous case histories and anti-coagulation clinic cards of all the patients were consulted.

Postoperative re-warfarinisation commenced on the evening after the day of surgery, in both groups, with a loading dose of 10 mg of warfarin followed by 5 mg on the 2nd and 3rd days. The INR was recorded and further doses adjusted accordingly.

The two study groups were compared with the Student's *t*-test using the SPSS statistical package (SPSS Inc, Chicago, IL, USA).

Results

The medical indications for the study patients being on warfarin included atrial fibrillation (AF; 50), past history of deep vein thrombosis (DVT; 29), pulmonary embolism (PE; 8) and heart valve (3) as shown in Figure 2. There was no significant difference in the indications in the two groups. The average INR on admission in the initial arm was 2.9 (1.5–6.5) and in the re-audit was 2.5 (1.9–7.1).

Over the first 7 months, 45 consecutive patients fulfilled the entry criteria and were treated with traditionally accepted method of omission of warfarin on admission for INR > 1.5. INR levels decreased to 1.5 or less in a mean time of 3

Figure 2 Indications for the total 90 patients in the study for being on long-term warfarin anticoagulation. Most of the patients (50) were on warfarin for atrial fibrillation.

days (mean, 91 h; range, 44–130 h; Table 1). Only seven out of 45 (15.5%) had the INR ≤ 1.5 after the first 12 h. The remaining 38 patients took an average of 106 h for the INR to drop below 1.5. The average delay to surgery in non-treated group was 6 days (mean, 158 h; range, 80–245 h).

The 45 patients included in the re-audit over the next 8 months were treated actively with injectable vitamin K on admission (1 mg) in addition to omission of warfarin. INR levels decreased to 1.5 or less in 2 days (mean, 38 h; range, 15–64 h; Table 1). In 27 of 45 patients (60%), the INR decreased to below 1.5 in 12 h. The remaining 18 patients took an average of 78 h for the INR to drop below 1.5. These patients were not administered an additional dose of vitamin K during this period. The average delay in surgery in this group was 3 days (mean, 67 h; range, 16–110 h; Table 1). In none of the 45 patients did the INR rise again after the vitamin K had been administered intravenously.

Two patients in the vitamin K administered group developed congestive cardiac failure secondary to myocardial infarction proven by fresh ECG changes and raised troponin levels. These

complications, however, occurred on the 18th and 29th postoperative days, respectively. Both these patients had a past medical history of atrial fibrillation and myocardial infarction. Hence, we did not relate it directly to administration of vitamin K.

The mean difference in the time for INR < 1.5 in the two groups was 2 days (52 h; $P < 0.05$). The mean difference in wait for surgery since admission between the two groups was 4 days (91 h; $P < 0.05$). There was no significant difference between the two groups as regards the average number of co-morbidities in the patient groups (Table 2).

Discussion

The British Committee for Standards in Haematology⁸ recommends vitamin K mediated reversal of warfarin for patients on long-term warfarin who require surgery. However, the guidelines published in 2003, as well as the update in 2006, fail to mention a protocol for reversal of warfarin in patients requiring urgent orthopaedic surgery. As there are no specific guidelines currently available, practice ranges from simple omission of warfarin to active reversal using vitamin K.

For INR to reduce from between 2 and 3 to below 1.5, takes 4–5 days.⁹ This period is even greater if initial INR is more than 3.¹⁰ There is also individual variation in the rate of reversal of action of warfarin. These findings suggest that a wait-and-watch policy for INR to drop to below 1.5 is impractical for urgent surgery, including surgery for neck femur fractures, which ideally should be undertaken within 24 h after admission.¹¹ Studies reveal median time span of 24–27 h for the reversal of INR to below 1.5 after a 1 mg intravenous dose of vitamin K.¹² This time period in our re-audit was 38 h. Vitamin K can also be given orally; however, the intravenous route achieves the quickest correction of anticoagulation, with significant effect on prothrombin time in 4–6 h.¹²

Review of literature suggests an increased risk of intra- and postoperative bleeding when surgery is performed in patients who are receiving an anticoagulant.^{15–17} INR > 4 raises the risk of major haemorrhage.¹⁶ With an INR > 1.5 , patients undergoing surgery have an increased risk of postoperative bleeding complications.^{9,15,17} In our audit, the target INR for

Table 1 Time duration for INR to reach target level after admission and time duration to surgery

Group	Mean time for INR to drop to target level (< 1.5)	Mean time to surgery
No vitamin K	6 days (158 h)	4 days (91 h)
Vitamin K administered	3 days (63 h)	2 days (38 h)

Table 2 Comparison of age, sex and average number of co-morbidities in the two audit groups

Audit	Age (average yrs)	Sex	Co-morbidities (median)
Initial	71.3	M 16 F 29	3
Repeat	74.1	M 12 F 33	3

patients undergoing surgery was 1.5 and there were no exclusions from this criterion.

The relative safety of discontinuing warfarin largely depends on the clinical indication for taking warfarin, the total duration for which the patient omits the warfarin and the type of surgery.^{9,17} Patients with mechanical heart valves have high risk of thrombosis; therefore, we covered these patients with intravenous heparin during the time they were off warfarin. Patients on warfarin for atrial fibrillation and deep vein thrombosis treated for more than 6 months have lower risk of thrombosis.^{9,17} In our study, none of the patients in either group developed complications related to thrombosis, including DVT or PE, during the time they were off warfarin. Our patients were covered during this period with 40 mg subcutaneous Enoxaparin.

Vitamin K intravenously has been found to be both safe and effective, although adverse reactions are known. Only two out of 105 patients in a study by Shields¹² developed unexpected adverse reactions to intravenous phytonadione in the form of dyspnoea and chest tightness during infusion. None of the 45 patients in our study developed complications directly related to vitamin K administration. Two patients in the vitamin K administered group in our study who developed congestive cardiac failure secondary to myocardial infarction; these complications were not thought to be related directly to administration of vitamin K. They occurred on the 18th and 29th postoperative days, respectively, and both these patients had a medical history of atrial fibrillation and myocardial infarction.

Post trauma surgery re-warfarinisation of patients is a major issue which lacks set guidelines. According to the British Committee for Standards in Haematology guidelines, patients requiring rapid initiation of oral anticoagulation start with single 10 mg dose followed by 5 mg doses.^{2,18} In our study, the regimen of loading the patient with 10 mg of warfarin on the first postoperative day followed by two doses of 5 mg each on day 2 and 3 was based on local guidelines. Warfarin re-institution and post-surgery stabilisation of INR, however, were out of remit of our study.

Two other papers have also looked at this subject. Tharmarajah et al.³ studied 48 consecutive patients on warfarin who underwent various trauma surgeries after active reversal of anticoagulation. Unlike our study, they included emergency surgeries like fasciotomy for compartment syndrome. Also, the patients were given vitamin K intravenously as well as orally and, in some cases, repeated doses of vitamin K were administered. They included a retrospective arm followed by a prospective one in their study. We included only prospective femur fracture patients who were given a single dose of intravenous vitamin K in the re-audit study.

Al-Rashid et al.⁷ studied 33 hip fracture patients. They included patients who were given fresh frozen plasma and only 12% of patients in their study were administered vitamin K. Unlike in our study, the acceptable INR was not defined and the average INR at surgery in their study was 2.2. Eight patients in their study had intracapsular neck femur fractures and were treated with

percutaneous screw fixation regardless of the INR. In our study, the target INR for patients undergoing surgery was 1.5 and there were no exclusions from this criterion.

Study limitations

The conclusions derived from this study are limited by the fact that it is a non-randomised study. However, this is a prospective audit study with good sample size with similar patient population in both groups.

Conclusions

A single 1 mg intravenous dose of vitamin K significantly reduces the time for the reversal of INR and the pre-operative delay to surgery, in patients on long-term warfarin. We conclude that 1 mg of intravenous vitamin K on admission is a safe and effective treatment to avoid delay in the treatment in this group of patients.

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