Comparison of different warfarin reversal protocols on surgical delay and complication rate in hip fracture patients

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ABSTRACT

Purpose. To compare the effects of different warfarin reversal protocols on surgical delay and complication rate in hip fracture patients.

Methods. Records of 7 men and 17 women aged 68 to 93 (mean, 82) years who were on warfarin and underwent surgery for femoral neck fractures were reviewed. The time to surgery, complication rate, and mortality were recorded, as were the International Normalised Ratio (INR) on admission and the day of operation, as well as the dose, route, and time of administration of vitamin K for reversing the anticoagulation effect of warfarin. Patients were divided into 4 groups based on the warfarin reversal treatment. Group 1 (n=4) included patients who did not receive reversal treatment, as their admission INR was ≤1.5. Group 2 (n=6) included patients who did not receive reversal treatment even though their INR was >1.6. Group 3 (n=5) included patients who received inappropriate reversal treatment (late or low-dose oral administration). Group 4 (n=9) included patients who received appropriate reversal treatment in terms of dose, route, and time of administration.

Results. Among the 4 groups, the mean INR was 2.2 (range, 1.3–4.6) on admission and 1.4 (range, 1.0–1.6) on the day of surgery. Group 1 was excluded from further analysis. Respectively in groups 2, 3, and 4, the mean times to surgery were 2.3, 2.6, and 1.2 days, and the complication rates were 67%, 20%, and 11%.

Conclusion. Early administration of intravenous vitamin K for hip fracture patients on warfarin is recommended to ensure early operative management and avoid postoperative complications.

Key words: blood platelets; hip fractures; International Normalized ratio; vitamin K; warfarin

INTRODUCTION

In the United Kingdom, femoral neck fractures account for 60 000 new cases per year. The 30-day mortality after surgical treatment is 10%. The Royal College of Physicians recommends that surgery be performed within 24 hours of admission to increase...
the chance of survival.³ Operative delay beyond 48 hours increases the 30-day mortality by 41% and the one-year mortality by 32%.⁴ The British Orthopaedic Association recommends that the maximum acceptable delay in surgery for hip fractures is 48 hours.⁵ Over 75% of surgical delays are due to medical problems (57%) and delayed investigations (20%).⁶,⁷ Coagulation problems are a cause of surgical delay. In 6 to 11% of patients, surgery is delayed by >48 hours because their International Normalised Ratio (INR) is >1.6.⁸

Warfarin is a long-term oral anticoagulant for use in treating patients at risk of thromboembolic events. Common indications for warfarin include atrial fibrillation, prosthetic heart valves, acute venous thromboembolism, pulmonary embolism, and cerebrovascular events.⁹ Its mechanism of action involves antagonising the effects of vitamin K to decrease production of modified clotting factors II, VII, IX, and X.¹⁰ Owing to its long half life, it can take up to 5 days for INR levels to return to normal after ceasing treatment.¹⁰ Vitamin K (phytomenadione) is administered to replenish the liver’s reserves and thus reverse the effect of warfarin.¹⁰ The decision to ‘watch and wait’ or ‘actively reverse’ warfarin anticoagulation is controversial. Active reversal of warfarin’s effect with Vitamin K reduces surgical delay by 44 hours, with no additional complications.¹¹ The mean time to surgery was 2 days longer in patients whose warfarin’s effect was not actively reversed with Vitamin K.¹²

According to the Scottish Intercollegiate Guidelines Network, reversing the anticoagulant effects of warfarin with oral or intravenous vitamin K is necessary to ensure early operative management of hip fractures in elderly people.¹³ A dose of 1 to 2.5 mg of vitamin K can be given orally or intravenously; the decrease in INR levels is greater in the first 4 hours after intravenous administration.¹⁴

The National Institute for Health and Clinical Excellence emphasises that surgical management of hip fractures should be performed on the day of or after admission, and that surgery should not be delayed by any correctible co-morbidity, such as anticoagulation.¹⁴

This study compared the effects of different warfarin reversal protocols on surgical delay, morbidity, and mortality in hip fracture patients.

MATERIALS AND METHODS

Records of 7 men and 17 women aged 68 to 93 (mean, 82) years who were on warfarin and underwent surgery for femoral neck fractures between January 2010 and August 2011 were reviewed. The American Society of Anesthesiologists grading of the patients was either 3 or 4. All patients had 3 to 5 co-morbidities that could contribute to increased 30-day mortality and surgical delay.¹⁵ The time to surgery, complication rate, and mortality were recorded, as were the INR on admission and the day of operation, as well as the dose, route, and time of vitamin K administration. The current practice of our hospital was to operate on patients with hip fractures when their INR was ≤1.5.

Patients were divided into 4 groups based on the warfarin reversal treatment. Group 1 (n=4) included patients who did not receive reversal treatment, as their admission INR was ≤1.5. Group 2 (n=6) included patients who did not receive reversal treatment even though their INR was >1.6. Group 3 (n=5) included patients who received inappropriate reversal treatment (late or low-dose oral administration); 3 of whom received a further dose. Group 4 (n=9) included patients who received appropriate reversal treatment in terms of dose, route, and time of administration.

The time to surgery and postoperative complications of the groups were analysed using the Fisher’s exact test. A p value of <0.05 was considered statistically significant.

RESULTS

Among the 4 groups, the mean INR was 2.2 (range, 1.3–4.6) on admission and 1.4 (range, 1.0–1.6) on the day of surgery. The mean time to surgery was 1.9 (range, 0–3) days. Six of the patients developed complications, including gastrointestinal bleeding, ileus, chest infection, respiratory failure, and perioperative cardiac arrest; one patient died.

Group 1 was excluded from further analysis. Respectively in groups 2, 3, and 4, the mean times to surgery were 2.3, 2.6, and 1.2 days, and the complication rates were 67%, 20%, and 11% (Table).

DISCUSSION

Patients on warfarin who did not receive reversal pharmacotherapy (5 to 10 mg of intravenous Vitamin K) waited longer for surgery, compared to those who received it (4.4 vs. 2.4 days).¹² 64% of the hip fracture patients on warfarin waited over 72 hours for surgery as a result of non-administration of reversal treatment.¹⁶ Even a small dose (1 mg) of intravenous vitamin K can reduce the mean time to surgery by a mean of 4 days.¹⁶

The National Institute for Health and Clinical
Excellence recommends that surgery be performed on the day of or after admission to achieve better outcome in terms of mortality, return to independent living, complications, and duration of hospital stay.\textsuperscript{14}

Initiatives to prevent surgical delays should be a high priority, as surgery is the best form of analgesia. On humanitarian grounds, hip fracture patients should not spend more than one night in hospital without an operation.\textsuperscript{14}

Warfarin itself confers its own complication for surgery, as anticoagulated patients are at increased risk of bleeding. Patients on warfarin undergoing a surgery had a rate of 9.5\% for haemorrhagic complications.\textsuperscript{17}

Major orthopaedic surgery per se confers a high risk of bleeding complications, and thus anticoagulation should be reversed rapidly before surgery and re-started as soon as possible thereafter.\textsuperscript{17}

No conflicts of interest were declared by the authors.

### REFERENCES


### Table

Comparison of different warfarin reversal protocols in terms of the time to surgery and complication rate

<table>
<thead>
<tr>
<th>Warfarin reversal protocols</th>
<th>Mean time to surgery (days)</th>
<th>p Value (Fisher’s exact test)</th>
<th>Complication rate (%)</th>
<th>p Value (Fisher’s exact test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not reversed (n=6) vs. appropriately reversed (n=9)</td>
<td>2.3 vs. 1.2</td>
<td>0.04</td>
<td>67 vs. 11</td>
<td>0.08</td>
</tr>
<tr>
<td>Inappropriately reversed (n=5) vs. appropriately reversed (n=9)</td>
<td>2.6 vs. 1.2</td>
<td>0.02</td>
<td>20 vs. 11</td>
<td>1</td>
</tr>
<tr>
<td>Not reversed + inappropriately reversed vs. appropriately reversed</td>
<td>2.4 vs. 1.2</td>
<td>0.01</td>
<td>45 vs. 11</td>
<td>0.15</td>
</tr>
</tbody>
</table>

Allergic reactions and resistance to warfarin are common adverse effects after administration of high doses (10–40 mg) of vitamin K.\textsuperscript{18,19} Nonetheless, administration of smaller doses orally or intravenously were not associated with resistance or allergic reactions.\textsuperscript{18,19}

Limitations of this study were its retrospective nature and the small number of patients. Early administration of intravenous vitamin K for hip fracture patients on warfarin is recommended to ensure early operative management and avoid postoperative complications.

