Use of Prothrombin Complex Concentrate (PCC) for warfarin reversal - Audit of North Thames Practice

S. Allard, D. Mold, D. Harvey, M. Laffan

1. Northwick Park Hospital, 2. QEII Hospital, 3. Hammersmith Hospital

Introduction

Oral anticoagulant therapy is associated with a significant incidence of life threatening bleeding as follows:

Fatal haemorrhage on warfarin: 0.25% pa
Intracranial haemorrhage on warfarin: 0.7% pa for >70 yrs

The BCSH guidelines on anticoagulation recommend the use of Prothrombin Complex Concentrate (PCC) for reversal of warfarin therapy if severe haemorrhage (British Journal of Haematology 2005; 132, 277-285).

The BCSH guidelines on the Use of Fresh Frozen Plasma (FFP) recommend that FFP should not be used for warfarin reversal (British Journal of Haematology 2004; 126, 1-12).

PCC results in a rapid and more complete reversal of warfarin (Makris et al Thrombosis and Haemostasis 1997; 77, 477-480). The relative merits and disadvantages of PCC vs FFP in warfarin reversal are summarized below:

- PCC
  - 15ml/kg: large volume
  - Minimal volume
  - Time to thaw
  - Rapid reconstitution
  - Time to administer
  - Immediate effect
  - Effect on levels is small
  - Single donor, untreated
  - Blood Group required
  - Prothrombotic
  - Generally available
  - Limited availability/Cost

- FFP
  - Standard Dose given: 40 u/kg
  - Vitamin K also given
  - INR = >6 50 u/kg
  - INR = 4-6 35 u/kg
  - (Variable Dose given by all 4 centres: INR = 2-3.9 25 u/kg)

There are several PCC products available but none of these are currently licensed for reversal of warfarin. The relative properties of 4 PCC products available are summarized in the table below:

<table>
<thead>
<tr>
<th>Product</th>
<th>Manufacturer</th>
<th>Viral inactivation</th>
<th>II</th>
<th>VII</th>
<th>IX</th>
<th>X</th>
<th>PC</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIMA-STOP</td>
<td>SNBTS</td>
<td></td>
<td>100</td>
<td>90</td>
<td>80</td>
<td>70</td>
<td>60</td>
</tr>
<tr>
<td>Prothromplex T</td>
<td>HITACHI</td>
<td></td>
<td>600</td>
<td>500</td>
<td>400</td>
<td>300</td>
<td>200</td>
</tr>
<tr>
<td>Relytrol</td>
<td>ZLB</td>
<td></td>
<td>300</td>
<td>200</td>
<td>100</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Octaphorix</td>
<td>Octapharma</td>
<td></td>
<td>220</td>
<td>150</td>
<td>100</td>
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</tr>
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This audit was undertaken on behalf of the North Thames Regional Transfusion Committee to determine if there were differences in practice in relation to warfarin reversal.

Methodology

- A postal questionnaire was designed and sent to both the Consultants in charge of Transfusion and the Blood Bank Managers at all hospitals in the North Thames Region.
- Respondents were also asked to send a copy of their Trust’s protocol with the completed questionnaire.

Questionnaire Response

- Questionnaires were sent to the Consultant in charge of Transfusion and the Blood Bank Manager at twenty five (25) Trusts.
- Seventeen questionnaires were returned which represented 20 (80%) hospitals and seventeen (85%) trusts.

Reversal of warfarin in non bleeding patients needing emergency surgery:

- Of 5 respondents, none experienced adverse events for the use of PCCs and all reported that their Trusts kept a stock of PCCs on site.
- Stocks were kept in the blood transfusion laboratory (4 sites) and a Haemophilia centre (1 site).

Which PCC Product

<table>
<thead>
<tr>
<th>Trusts not using PCCs</th>
<th>Trusts using PCCs</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Northwick Park Hospital</td>
<td>1. Northwick Park Hospital</td>
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<tr>
<td>2. QEII Hospital</td>
<td>2. QEII Hospital</td>
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<tr>
<td>3. Hammersmith Hospital</td>
<td>3. Hammersmith Hospital</td>
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<tr>
<td>4. Watford General Hospital</td>
<td>4. Watford General Hospital</td>
</tr>
</tbody>
</table>

Adverse events and availability of PCCs

Of 5 respondents, none experienced adverse events for the use of PCCs and all reported that their Trusts kept a stock of PCCs on site. Stocks were kept in the blood transfusion laboratory (4 sites) and a Haemophilia centre (1 site).

Conclusions

In conclusion, only 30% of Trusts in North Thames are using PCC for warfarin reversal in major bleeding.

Only 11% of Trusts are using PCC to prevent bleeding in anticoagulated patients undergoing emergency surgery.

There is widespread inappropriate use of FFP out of keeping with current best practice.

We recommend that all Trusts treating patients with warfarin should have a stock of PCC with guidelines for use for urgent reversal of oral anticoagulation and this should be facilitated via local networks.

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