Bypassing agents prophylaxis in patients with haemophilia and inhibitors undergoing surgery: a decision analysis in Spain

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Introduction

- Haemophilia A is a genetic disease characterized by a deficiency of blood clotting factor VIII (FVIII) (in haemophilia A-1A) or factor IX (in haemophilia B-2B).
- Some patients can develop inhibitory antibodies which complicates the management of haemostasis since these antibodies neutralize the effects of replacement therapy. Approximately, 15-30% of patients with severe HA (FVIII<1%) develop FVIII inhibitory antibodies.
- Since surgery poses a risk condition for haemophilia patients with inhibitors, haemostatic prophylaxis therapy is always indicated in these situations to prevent bleeding complications. Prophylaxis should be given in most cases with bypassing agents, either activated prothrombin complex concentrate (aPCC) or recombinant activated factor VII (rFVIIa).

Objective

- To estimate the total cost of prophylaxis therapy with bypassing agents, aPCC or rFVIIa, in HA patients with inhibitors undergoing surgery, from the Spanish National Health System perspective.

Methods

- Although the available evidence suggests that both alternatives (aPCC and rFVIIa) have comparable efficacy as prophylactic strategy during surgical procedures, no direct comparison exists to justify the development of a cost-minimization analysis. Therefore, a conservative approach was chosen and a cost-analysis was designed.
- A decision tree model was developed to compare the treatment cost of aPCC (Fevity®, Shire) and rFVIIa (NovoSeven®, Novo Nordisk), for a typical HA inhibitor patient undergoing dental extraction, minor, or major surgery. A hypothetical cohort of 100 HA patients with inhibitors was used to feed the decision tree (Figure 1).
- Based on a national epidemiological study6, the proportion of adults (≥14 years) was around 77.70%, meanwhile children (<14 years) represent 22.30% of the haemophilia population. Average weights (27.9 kg in adults and 27.4 kg in children) of the haemophilia population were derived from literature6.
- The annual number of surgeries (0.33 surgeries/year/patient) as well as the distribution of type of surgery (dental extraction (19%), minor surgery (50%) and major surgery (31%)) were estimated from local data. An expert panel of 3 local haemostatologists validated these data as representative of the population of HA patients with inhibitors in Spain.
- For cost calculation, dental extraction and major surgery were assumed only to happen in adult population, while minor surgery occurrence was split into children and adult population, validated by the haemostatologists expert panel.
- The time horizon of the analysis comprised the duration of prophylactic regimen defined by each surgery (1 day for dental extraction, 4 days for minor surgery and 15 days for major surgery). In accordance with the information provided by the expert panel consulted.

Table 1. Bypassing agents dosage in clinical practice for each type of surgery

<table>
<thead>
<tr>
<th></th>
<th>aPCC (IU/kg)</th>
<th>rFVIIa (IU/kg)</th>
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</thead>
<tbody>
<tr>
<td>Children &lt;14 years</td>
<td>Adults ≥14 years</td>
<td>Adults ≥14 years</td>
</tr>
<tr>
<td>Daily dose (IU/kg)</td>
<td>(IU/kg)</td>
<td>(IU/kg)</td>
</tr>
<tr>
<td>Day 1</td>
<td>60</td>
<td>60</td>
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<tr>
<td>Day 2</td>
<td>60</td>
<td>60</td>
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<tr>
<td>Day 3–8</td>
<td>60</td>
<td>60</td>
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<tr>
<td>Day 8–15</td>
<td>60</td>
<td>60</td>
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</tbody>
</table>

Conclusion

Results suggest a 62.5% lower treatment drug cost with aPCC compared to rFVIIa in providing haemostatic coverage during surgery. Assumptions potentiably equivalent in efficacy, aPCC is a cost saving option, as prophylactic treatment preventing bleeds in HA inhibitors patients undergoing surgery.