Perioperative management of dabigatran: the Nelson experience to date

Dabigatran is a new anticoagulant that has been on the pharmaceutical schedule in New Zealand since 1 July 2011.\(^1\) Dabigatran presents many challenges as it has an inherent bleeding risk.\(^2\) To date an effective reversal method has not been developed and it is not possible to accurately measure the effect on coagulation with standard laboratory tests.

The pharmacologic properties of dabigatran have been studied and are used to guide the current clinical guidelines.\(^3\) The protocols for anticoagulant reversal and management of bleeding have been developed on a theoretical basis with limited clinical experience as guidance.

Dabigatran has some advantages over warfarin as shown in the RE-LY trial.\(^4\) However there is a large body of information regarding the management of haemorrhage on warfarin and reversal of anticoagulation if required. Comparatively dabigatran is unable to be reversed urgently - allowing time for renal clearance may necessitate deferring surgery to minimise residual anticoagulant effect.\(^5\) This becomes a problem in an emergency when surgery cannot be delayed and in patients who develop acute renal impairment.

Another issue that arises is that it is difficult to monitor the anticoagulant effect and therefore hard to judge when levels are low enough for surgery to take place. The activated partial thromboplastin time (APTT) is unlikely to reliably measure the anticoagulant effect,\(^5,6\) the INR is not sensitive enough and the thrombin time assay is too sensitive with no standardisation between laboratories.\(^6\)

The aim of this study is to look at how dabigatran has influenced the management of patients who have been admitted to Nelson or Wairau Hospitals requiring surgery while anticoagulated on dabigatran. By analysing the Nelson data we hope to paint a picture of the impact dabigatran has had on surgical practice in Nelson.

**Methods**—A search of the clinical records between 1 July 2011 and 12 December 2011 was carried out using the hospital pharmacy’s dispensing list. The records of patients on dabigatran were assessed in order to ascertain whether they required surgery and if so, how their dabigatran was managed.

The primary outcomes assessed for these patients were: delay in surgery, postoperative complications (primarily bleeding), time period preoperatively that dabigatran was stopped and time period postoperatively where it was restarted. The search returned 27 records of patients who had been admitted to Nelson or Wairau Hospitals.
Results—Four of the study participants required surgery resulting in five operations.

Table 1. Indications for dabigatran treatment

<table>
<thead>
<tr>
<th>Indication</th>
<th>Atrial Fibrillation</th>
<th>VTE Prophylaxis</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>25</td>
<td>2</td>
<td>27</td>
</tr>
</tbody>
</table>

Table 2. Demographics of patient population

<table>
<thead>
<tr>
<th>Age</th>
<th>Mean</th>
<th>Median</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>77.8 yrs</td>
<td>80 yrs</td>
<td>63–87 yrs</td>
</tr>
</tbody>
</table>

Table 3. Surgery required and perioperative management of dabigatran

<table>
<thead>
<tr>
<th>Patient</th>
<th>Specialty/Procedure</th>
<th>Preoperative Management</th>
<th>Postoperative Management</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>General Surgery - parathyroidectomy</td>
<td>Stopped 4 days prior</td>
<td>N/A</td>
<td>Acute Renal Failure &amp; Death</td>
</tr>
<tr>
<td>2</td>
<td>General Surgery - mastectomy</td>
<td>Stopped 14 days prior</td>
<td>Restarted 7 days post-op</td>
<td>Nil</td>
</tr>
<tr>
<td>3</td>
<td>Urology – bilateral orchidectomy</td>
<td>Stopped 24 hrs prior</td>
<td>Restarted 24 hrs post-op</td>
<td>Nil</td>
</tr>
<tr>
<td>4</td>
<td>Orthopaedic – L toe arthrodesis (local)</td>
<td>Stopped 24 hrs prior</td>
<td>Restarted 24 hrs post-op</td>
<td>Nil</td>
</tr>
<tr>
<td>5</td>
<td>Cardiothoracic - Coronary Artery Bypass Graft (performed in Wellington)</td>
<td>Stopped 10 days prior</td>
<td>Not restarted due to poor renal function</td>
<td>Nil</td>
</tr>
</tbody>
</table>

Records from the patient who passed away demonstrate that she presented for an urgent parathyroidectomy with hypercalcaemia. The dabigatran was stopped 4 days preoperatively, as per the clinical guidelines. In this case the patient developed acute renal impairment and her thrombin time was persistently prolonged requiring surgery to be postponed. Following this the patient became unstable and deteriorated clinically such that surgery was not an option.

She passed away 7 days after the original surgery was scheduled with the post mortem stating the likely cause of death as arrhythmia (consistent with hypercalcaemia) and cardiogenic shock.

Conclusions—Although this study is too small to draw any statistically significant conclusions it can provide information on how surgical patients on dabigatran are being managed in Nelson. The group who are being prescribed dabigatran are elderly and are therefore likely to have comorbidities potentially requiring surgery. They are also more likely to have renal impairment and thus may have problems clearing the drug.

It has been demonstrated in two cases that stopping dabigatran 24 hours preoperatively was adequate and in another two cases that a longer time period was also satisfactory. However it cannot be ignored that in the fifth case the dabigatran had been stopped with ample time but that the patient was unable to clear the drug.
Although these cases are rare and this study does not have a large enough sample to calculate a complication rate, it does demonstrate the potentially disastrous consequences in a specific clinical situation. Dabigatran may have a lower rate of bleeding complications than warfarin\(^9\) but when they do occur the medical profession has limited options for treating these complications.

Dabigatran is a promising anticoagulant for the future.\(^7\) In the right group of patients it provides an effective method of reducing thromboembolic risk without the use of warfarin. However it should be adopted with caution initially as there is limited experience with managing bleeding, surgery and trauma\(^8\) whilst on dabigatran.

Similarly, ongoing review of the perioperative management of patients on dabigatran is needed and the clinical guidelines should be continually developed as experience educates medical professionals. Until an assay to measure the anticoagulant effect of dabigatran and an effective reversal method is developed surgeons must continue to make decisions on a case by case basis, as to whether the benefit of surgery outweighs the risk of bleeding from dabigatran in an acute situation.

Elizabeth Travis
Trainee Intern, Christchurch School of Medicine
Nelson Hospital, Nelson Marlborough DHB
Lizzie.Travis@nmdhb.govt.nz

Dr Jane Strang
Consultant Surgeon, Department of General Surgery
Nelson Hospital, Nelson Marlborough DHB
Jane.Strang@nmdhb.govt.nz

References: