Patients Erroneously administered Clopidogrel with an Epidural Catheter in situ: Case Series

Vidur Shyam, Alexander Corneman, Brian Simchison

ABSTRACT

Background: It is recommended that anticoagulation therapy with agents, such as clopidogrel (Plavix®) be discontinued 7 days prior to neuraxial blockade with an epidural catheter due to an increased risk of epidural haematoma. However, patients are occasionally erroneously restarted on clopidogrel prior to catheter removal. Little research exists regarding the prevalence of this clinical scenario or the clinical outcomes. This may be particularly important for clopidogrel, since, unlike other anticoagulants, there are no pharmacological reversal agents.

Objective: To examine the prevalence, management strategies and outcomes of patients given clopidogrel prior to epidural catheter removal at a medium-sized tertiary care teaching hospital.

Materials and methods: Following institutional Research Ethics Board approval, electronic medical records of all patients who received epidural analgesia over a 1 year period were retrospectively reviewed. The charts for those patients who were also given clopidogrel prior to catheter removal were examined to determine the management course and treatment outcomes.

Results: Of the 3959 patients who received epidural anaesthesia, three were given clopidogrel prior to catheter removal. No haematoma-related complications were reported. Patient management and treatment outcomes are described.

Conclusion: Although this error appears to be a rare occurrence at our center and no adverse events were reported, it has the potential for serious adverse outcomes. Clinicians at our center manage this scenario by increasing the time to catheter removal, withholding heparin, administering platelets, monitoring and educating patients with respect to potential complications. Given that no adverse events were observed, such management strategies may be effective and prudent.

Keywords: Clopidogrel, Plavix®, Epidural catheter, Epidural haematoma, Epidural anaesthesia.

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INTRODUCTION

Clopidogrel (Plavix® Bristol-Myers Squibb/Sanofi) is a common thienopyridine antiplatelet medication that irreversibly antagonizes platelet adenosine 52-diphosphate (ADP) receptors. It is primarily prescribed for patients with coronary artery disease, peripheral vascular disease or for thrombus prophylaxis after cerebrovascular accidents. Unlike other anticoagulants, there are no pharmacological compounds for the direct reversal of clopidogrel’s effects.

Epidural anaesthesia has long been used as an effective regional neuraxial block as it provides a means for intraoperative anaesthesia, while maintaining an indwelling catheter for postoperative analgesic administration. Given the frequency with which both clopidogrel and epidural anaesthesia are used, it is inevitable that the two are erroneously administered simultaneously, despite the known contraindication. The prevalence of simultaneous administration is not known.

The most likely adverse event to result from the combination of antiplatelet therapy in conjunction with an epidural catheter is the formation of an epidural haematoma, and those with certain conditions, such as preoperative coagulopathy, age greater than 60 years and preoperative haemoglobin less than 10 g/dl are considered at higher risk. Neurologic dysfunction occurs in approximately 1 in 150,000 epidural anaesthetic patients.1,2 Without early diagnosis, permanent neurologic effects ranging from sensory deficits to full motor loss can result from severe acute spinal cord compression.

The American Society of Regional Anesthesia (ASRA) recommends that clopidogrel therapy be discontinued 7 days prior to surgery in order for platelet function to normalize.3 These guidelines are based on anecdotal expert consensus opinion and pharmacokinetic data.

Depending upon the procedure, the epidural catheter often remains in place for several days postoperatively for continuous analgesia. Clopidogrel is not administered during this period due to risk of an epidural bleed while the catheter is in situ and upon removal of the catheter. Following removal, antiplatelet therapy can be appropriately reinstated.4

This paper aims to address the possibly under-reported error of clopidogrel administration prior to removal of the epidural. What should be done in such cases? Simply removing the catheter carries a significant risk of haematoma formation and could hinder patient recovery due to loss of this form of analgesia. The catheter can be removed early while platelets are administered to normalise the patient’s clotting ability,5 although exposure to blood products does carry a risk of infection and adverse reactions. Conversely, the catheter can be left in for a prolonged period while clopidogrel is again discontinued to allow for platelet
function restoration. Unfortunately, this greatly increases the risk of infection and in some cases, would prolong the hospital stay. This paper explores the prevalence of this clinical scenario at a medium-sized tertiary care centre with examination of subsequent management course and patient outcomes.

MATERIALS AND METHODS
Institutional research ethics board approval was obtained for presentation of the current case series. The Acute Pain management service (APMS) at our center uses a database developed by Cissec Corp., (Kingston, ON) to electronically document pain assessments. Patients receiving epidural catheters are also put into this database, which includes components, such as drug usage, side effect therapy, notable events, and consults, among others. Hospital Information technology personnel were asked to retrieve information on all patients in the APMS database who received epidural catheters and had been reportedly administered anti-platelet/anticoagulation therapy following surgery over the 1 year period between August 2011 and July 2012. Data was supplemented with information that from the patients’ medical record when post-operative clopidogrel was identified.

RESULTS
Over the 1 year period, 11,236 cases were entered into the APMS database. Of these, 3,959 had received epidural anesthesia, 3 of which were reportedly administered clopidogrel following their respective procedures prior to removal of the epidural catheter. A few others had been administered low molecular weight heparin or warfarin but are not detailed below since the focus of this report is upon nonreversible anticoagulant agents.

CASE REPORTS
Case 1
A 58-year-old male patient underwent laparotomy to resect an invasive pancreatic tail mass that was found to be metastatic to the liver during the procedure. His abdomen was closed and surgical therapy was abandoned. He was administered clopidogrel 75 mg on post-operative day 1. Standard heparin administration was withheld on post-operative day 3 and he was given 1 unit of platelets prior to catheter removal. The patient was observed for neurologic abnormalities for 24 hours in case of haematoma formation but no abnormalities were observed.

Case 2
A 67-year-old male was admitted for a cystectomy and subsequent construction of an ileal conduit secondary to bladder cancer. This patient was administered clopidogrel 75 mg once daily for 3 days post-operatively. Removal of his epidural catheter was delayed for 2 additional days. On the day of removal, standard heparin was withheld and the patient was given 2 units of platelets. The patient did well except for post-operative ileus that resolved with conservative management.

Case 3
A 65-year-old male underwent surgical repair of an abdominal aortic aneurysm. His past medical history was remarkable for left anterior descending and circumflex coronary artery stent placement in 2006. He was given clopidogrel 75 mg on post-operative day 2. Coagulation parameters were closely monitored and heparin was withheld. The epidural catheter was removed intact on post-operative day 5 and the patient was observed for neurological deficits for approximately 12 hours.

None of the three cases described above reported any occurrence of epidural haematoma or other significant complications.

DISCUSSION
The cases described here indicate that clinicians at our centre have opted to wait several days and in most cases, administer platelets prior to catheter removal when clopidogrel was erroneously administered with the epidural catheter in place.

Given that no serious adverse events occurred with the cases presented here, it would seem that a delay in epidural catheter removal and platelet administration are prudent, given that there are no pharmacological agents which can reverse the ADP inhibiting antiplatelet agents. Platelet infusion is currently the only effective agent in the setting of uncontrolled bleeding. However, the small sample size and lack of complications makes it difficult to discern whether the extended time to catheter removal and platelet administration actually altered the outcomes. Regardless, Table 1 lists risk factors associated with the development of epidural haematomas.

<table>
<thead>
<tr>
<th>Table 1: Risk factors for epidural haematoma8-10</th>
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<tbody>
<tr>
<td>Pre-operative coagulopathy</td>
</tr>
<tr>
<td>Undergoing multi level procedures</td>
</tr>
<tr>
<td>Pre-operative NSAIDs</td>
</tr>
<tr>
<td>Age &gt;60 years</td>
</tr>
<tr>
<td>Rh-positive blood type</td>
</tr>
<tr>
<td>Haemoglobin &lt;10 g/dl</td>
</tr>
<tr>
<td>Blood loss &gt;1l</td>
</tr>
<tr>
<td>INR &gt;2 within 48 hours post-operatively</td>
</tr>
</tbody>
</table>

NSAID = non-steroidal anti-inflammatory drug; INR = international normalised ratio
Good outcomes following the development of spinal epidural haematomas have been most importantly related to the severity of neurological deficit and the timing of treatment. Haematoma evacuation within 12 hours of symptom onset has shown full neurologic recovery in the majority of patients.9,11 Rate of symptom development is also a predictive factor but age and gender are not considered significant.11 Bladder dysfunction is noted as a common initial symptom of epidural haematoma, which should be recognised as it is not uncommon following normal epidural anaesthesia.8

It could be postulated that if the error is caught early enough, the epidural may be removed despite clopidogrel administration. The European society of anaesthesiology actually recommends clopidogrel be restarted immediately following catheter removal.9 Clopidogrel’s time to peak effect is 12 to 24 hours after a bolus of 300 to 600 mg or 3 to 7 days after 75 mg, so it is reasonable to expect a limited safe time frame for prompt catheter removal following administration. However, the safety profile following prompt removal of the catheter following erroneous clopidogrel administration has not been determined.

From the current report, it appears that the administration of clopidogrel in patients with a sited epidural catheter, at least at our institution, is a relatively rare event. Further investigations would be required to determine whether increased time to catheter removal and platelet administration actually altered the patient outcomes in this potentially hazardous clinical scenario. Likewise, other investigations would be required to determine the true impact of erroneous clopidogrel administration on extended length of stay and its associated financial impact.

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REFERENCES


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