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Case Report

Neuraxial anesthesia in the presence of clinical anticoagulation: what are our options for pediatric patients?

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Abstract: The use of local anesthesia combined with general anesthesia to provide effective perioperative analgesia continues to increase in the pediatric population. Although neurological complications resulting from peridural hemorrhage following placement of neuraxial blockade is extremely rare in the absence of co-morbid conditions, the consequences can be devastating. Therefore, caution should be exercised, especially in patients receiving antithrombotic or thrombolytic therapy. We present two patients who received unplanned anticoagulation therapy perioperatively following placement of an epidural catheter for postoperative analgesia. Potential concerns with anticoagulation therapy in patients with epidural catheters are discussed and suggestions for the care of such patients are presented.

Keywords: Neuraxial anesthesia, anticoagulation, pediatric anesthesia

Introduction

Local anesthesia combined with general anesthesia is becoming a widely accepted method of advanced analgesia in pediatric population [1]. Although the incidence of neurological complications resulting from hemorrhage related to neuraxial blockade is low, the consequences can be devastating [2-4]. As such, caution should be exercised especially in patients receiving antithrombotic or thrombolytic therapy. The American Society of Regional Anesthesia and Pain Medicine (ASRA) has published evidence-based guidelines for the use of regional anesthesia in patients receiving antithrombotic or thrombolytic therapy [5]. We present two pediatric patients who intraoperatively required unplanned anticoagulation therapy following the placement of an epidural catheter for postoperative analgesia. Potential concerns with such therapy in the presence of epidural anesthesia are discussed and suggestions for care provided.

Case reports

Institutional Review Board approval is not required at Nationwide Children's Hospital for the presentation of case reports involving one or two patients.

Case #1

The patient was an 11-year-old, 41.5 kilogram girl with a history of Ewing's sarcoma of the lower extremity. She presented for reoperation of limb fixation and muscle flap with contralateral fibular bone harvesting and grafting. Following the induction of general anesthesia, an epidural catheter was placed on the first attempt via a median approach using a 20 gauge catheter inserted through an 18-gauge, 2" pediatric Tuohy needle with loss of resistance to saline at the L_{4-5} interspace. No complications, such as vascular puncture, were noted during the procedure and the catheter was threaded easily into the epidural space. A test dose of 2 mL (0.05 ml/kg) of 1.5% lidocaine with epinephrine (1:200,000) was administered

with no evidence of electrocardiographic, heart rate or blood pressure alterations. A bolus dose of 5 mL of 0.2% ropivacaine was subsequently administered followed by an infusion of 0.2% ropivacaine at 5 mL/hr. Seven hours into the surgery, an acute arterial thrombosis occurred during vascular anastomosis of the muscle flap requiring emergent anticoagulation with heparin. After discussing the risks and benefits with the surgeon, heparin (1,000 units) was administered intravenously over 10 minutes followed by a continuous infusion of 5 units/kg/hr until the completion of the surgical procedure (3 hours additional). At the completion of the case, the patient's trachea was extubated in the operating room. Following emergence from anesthesia, neurological examination including motor and sensation of the lower extremities was normal. Anticoagulation with enoxaparin (40 mg or 1 mg/kg, every 12 hours) was initiated postoperatively to prevent thrombosis of the muscle graft. The first dose of postoperative enoxaparin was administered approximately 3 hours after the procedure or 13.5 hours after the catheter placement and continued every 12 hours thereafter. On postoperative day (POD) 5, the enoxaparin dosing was held for 24 hours. Normal platelet count and coagulation testing (prothrombin time, partial thromboplastin time, and INR) results were confirmed. After a thorough discussions with the family and surgical team, the epidural catheter was removed uneventfully. Once-daily dosing of enoxaparin (30 mg every 24 hours) was subsequently reinitiated 5 hours after epidural catheter removal. The reminder of her postoperative course was unremarkable.

Case #2

The patient was a 16-year-old, 77.9 kilogram female diagnosed with visceral hyperalgesia, gastroparesis, and upper extremity deep vein thrombosis (DVT), who presented for placement of a gastric pacemaker. She was managed with enoxaparin 1 mg/kg every 12 hours for DVT, which was stopped 24 hours preoperatively. An epidural catheter was placed at the $T_{9\text{-}10}$ interspace prior to the induction of anesthesia. The aspiration test for both blood and cerebrospinal fluid was negative. A test dose of 3 mL of 1.5% lidocaine with epinephrine (1:200,000) was administered with no evidence of electrocardiographic, heart rate or blood pressure alterations. Intraoperatively, intermittent bolus doses of 0.25% bupivacaine with epinephrine (1:200,000) were administered incrementally as needed based on hemodynamic changes to surgical stimulation. Postoperatively, the epidural infusion was initiated with 0.2% ropivacaine at 8 mL/hr. On POD 1, enoxaparin was *inadvertently* restarted at the previous dose of 1 mg/kg every 12 hours. Despite appropriate communication between the pain and surgical teams, there was no fail safe mechanism in place in the electronic medical record ordering system to alert the caregivers involved. When a hand-off occurred between the surgical day team and night team, the order was inadvertently placed. This mistake was discovered on POD 2 during patient rounds by the pain team. At that time, the enoxaparin was discontinued. The patient remained neurologically intact and her examination revealed complete and strong motor function with intact sensation in her lower extremities. Her epidural site was clean and intact without evidence of bleeding. Her renal function was within normal range. Enoxaparin was held for 24 hours prior to removal of the epidural catheter on POD 3 without incident and restarted 24 hours after catheter removal. The remainder of her postoperative course was unremarkable.

Discussion

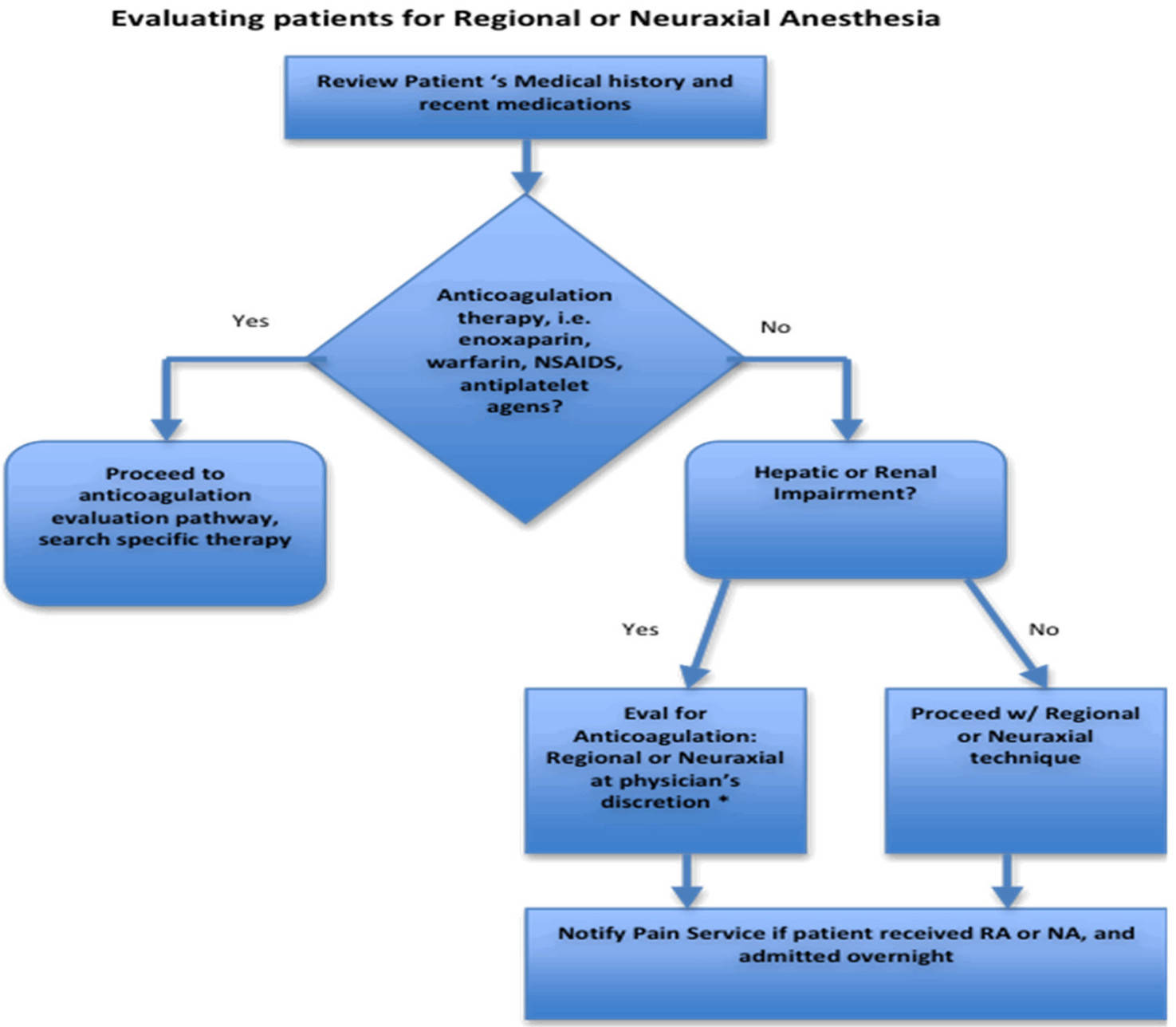
The complications stemming from neuraxial catheters in the presence of clinical anticoagulation can be severe, with spinal hematoma carrying potentially devastating consequences including requirement for surgical evacuation of the hematoma, residual lower extremity motor and sensory deficits, and permanent paraplegia. In the absence of anticoagulation therapy, Vandermuelen et al. reported the incidence of epidural hematoma formation to be approximately 1:220,000 after intrathecal anesthesia and 1:150,000 after epidural anesthesia [6]. However, Ruff and Dougherty reported 7 cases of spinal hematoma formation in 342 patients for an incidence of 2% when lumbar puncture was followed by anticoagulation with intravenous heparin [7]. In the 3rd National Audit Project (NAP3) of the Royal College of Anesthetists, approximately 21,500 central neuraxial blocks (CNB) were reviewed [2]. This included 18,050 caudal epidurals, 3,125 continuous lumbar or thoracic epidurals, and 325 intrathecal blocks that were performed during

the 1-year reporting phase in children in the United Kingdom. There were no permanent injuries due to CNB in the pediatric population. They estimated a 95% confidence interval for permanent harm following CNB in children as 0-14 in 100,000 [2].

In our first case, initial anticoagulation was started emergently in an effort to save the graft during the procedure with intravenous unfractionated heparin bolus followed by continuous infusion and then transitioned to low molecular weight heparin (LMWH), enoxaparin, in the immediate postoperative period. The risk factors associated with an increased incidence of spinal hematoma after lumbar puncture have been reported to be traumatic needle placement, starting anticoagulation within 60 minutes of the lumbar puncture, or concomitant aspirin treatment at the time of the lumbar puncture [7]. Multiple attempts are also assumed as one of the risk factors for spinal hematoma. Compared to atraumatic puncture followed by no heparin use, heparin anticoagulation less than 1 hour after neuraxial puncture has a relative risk (RR) of hematoma formation of 25.2. The estimated RR is 2.18 when heparin anticoagulation is initiated more than 1 hour after neuraxial puncture. The RR increases the most in the case of a traumatic tap followed by heparin anticoagulation (RR=112) [8]. In our case, anticoagulation with heparin administration was initiated approximately 7 hours after epidural catheter insertion which was placed on the first attempt without a traumatic tap. Additional information regarding the safety of such practice under controlled circumstances has been provided by reports of the use of neuraxial anesthesia in patients undergoing vascular surgery and the pediatric cardiac surgery population [9-11]. Peterson et al reported no adverse effects in a retrospective review of 220 pediatric cardiac procedures with regional anesthesia including epidural catheter placement as well as epidural and intrathecal single shot dosing when the catheter was placed at least 60 minutes prior to anticoagulation and without traumatic vascular puncture [10]. However, because the consequences may be too devastating for the perceived benefits, the ASRA has no established guidelines for such practices during cardiac surgery involving full heparinization [5]. Furthermore, the majority of adult and pediatric cardiac surgical centers due to rely on regional anesthesia for the provision of postoperative analgesia.

Given the time interval that had elapsed following epidural catheter placement (7 hours) and the absence of concerns regarding a traumatic tap during the insertion, we did not think that anticoagulation was contraindicated. However, in all cases, we would recommend communication with our surgical colleagues when such intervention is requested. Additionally, when feasible, we believe that the family should be included in such discussions regarding the risk: benefit ratio of anticoagulation.

In regards to the use of LMWH, the ASRA guidelines state that twice-daily dosing (treatment dose) of LMWH is associated with an increased risk of spinal hematoma formation and recommend the removal of an indwelling epidural catheter at least 2 hours prior to the initiation of LMWH therapy [5]. However, the ASRA guidelines have no recommendations regarding how long one should wait before removal of an epidural catheter once twice-daily dosing of LMWH has been initiated. On the other hand, they suggest that single-daily dosing of LMWH can be administered with the presence of indwelling epidural catheter. In those circumstances, the catheter should be removed a minimum of 10-12 hours after the last dose of LMWH. In the first case, twice-daily dosing of enoxaparin instead of a continuous heparin infusion was initiated postoperatively approximately 3 hours after completion of the procedure to protect the muscle graft from further thrombosis. The epidural catheter was removed uneventfully on POD 5 after the enoxaparin had been held for 24 hours. In our second patient, enoxaparin was restarted twice-daily on POD 1, approximately 20 hours after the completion of the case, due to miscommunication between the clinical teams, which was discovered on POD 2 and discontinued. The epidural catheter was removed after the enoxaparin dosing had been held for 24 hours on POD 3 without incident. This time-frame (24 hours) for catheter removal in both patients was based on the perceived half-life of enoxaparin with twice daily dosing. A longer period of time may be required in patients with renal insufficiency. Alternatively, when available, an anti-Xa level can be obtained when there are questions regarding the safety of catheter removal.


Evaluating patients for Regional or Neuraxial Anesthesia
Review Patient 's Medical history and recent medications
Anticoagulation therapy, i.e. enoxaparin, warfarin, NSAIDS, antiplatelet agens?
Yes
No
Proceed to anticoagulation evaluation pathway, search specific therapy
Hepatic or Renal Impairment?
Yes
No
Eval for Anticoagulation: Regional or Neuraxial at physician's discretion *
Proceed w/ Regional or Neuraxial technique
Notify Pain Service if patient received RA or NA, and admitted overnight

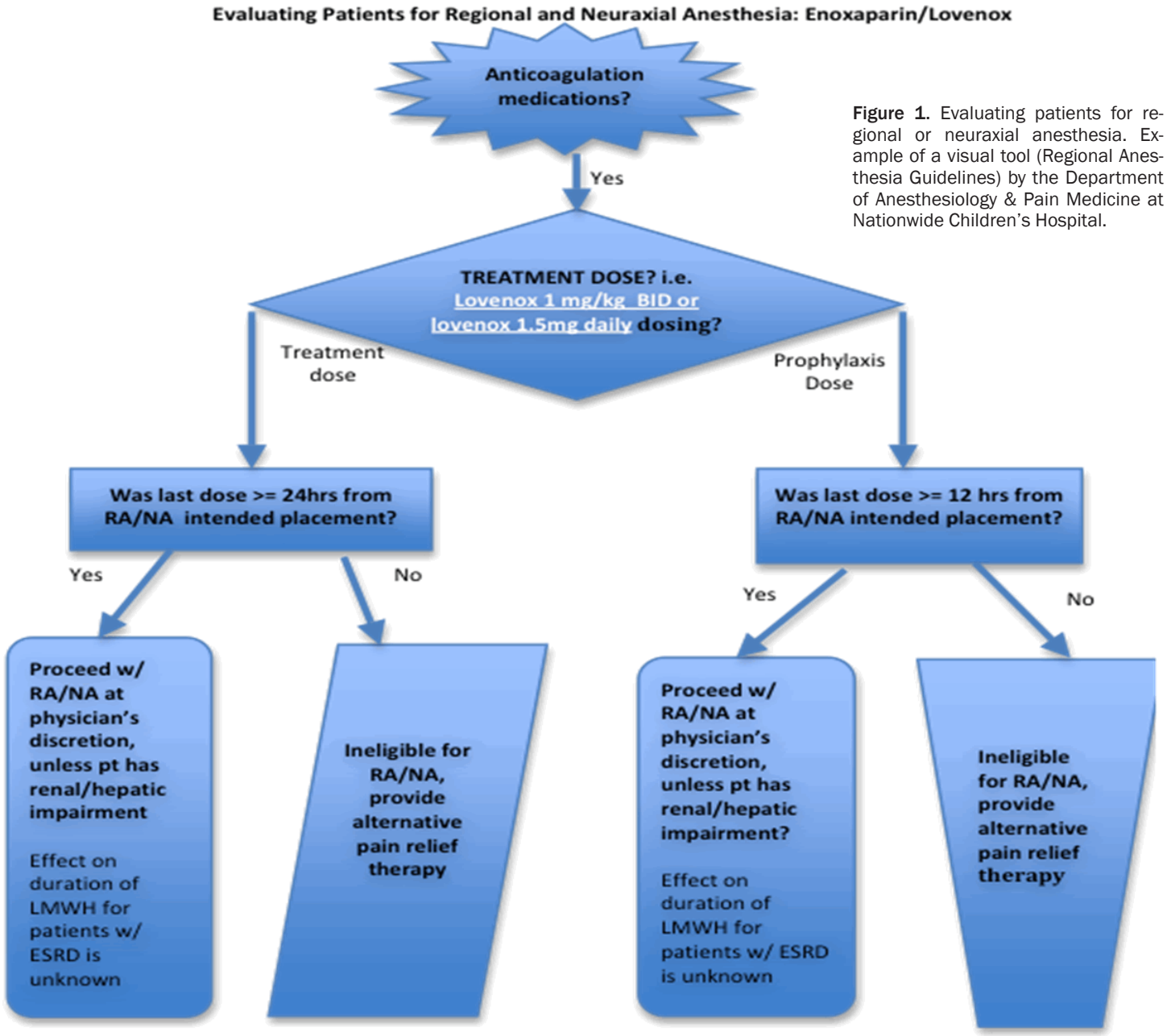


Figure 1. Evaluating patients for regional or neuraxial anesthesia. Example of a visual tool (Regional Anesthesia Guidelines) by the Department of Anesthesiology & Pain Medicine at Nationwide Children's Hospital.

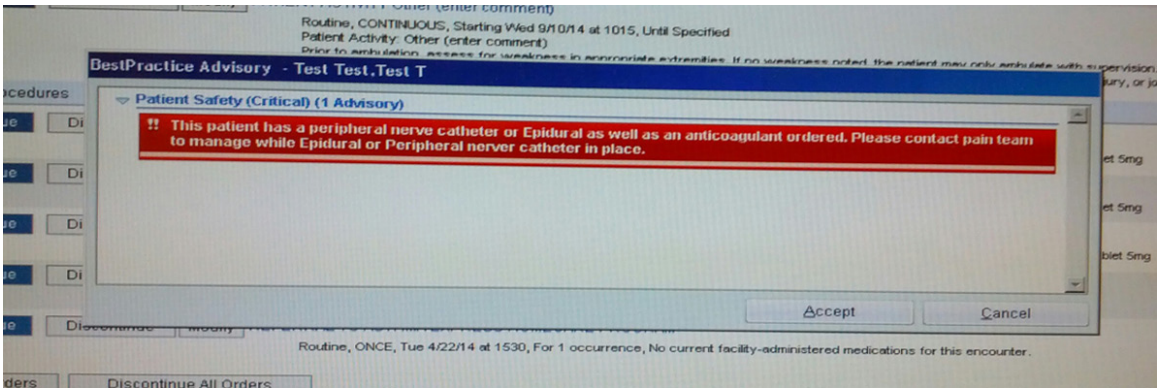


Figure 2. Fail safe alert in the electronic medical record ordering system. The alert shows up when anti-thrombotic agents or thrombolytic agents including aspirin, dipyridamole, clopidogrel, enoxaparin, warfarin, tissue-plasminogen activator, argatroban, dabigatran, and heparin are ordered.

These cases also served as the basis for quality improvement processes in our pediatric regional anesthesia program. Improved communication and clarification of ASRA guidelines with ongoing literature review by all health care providers can help decrease the possibility of mismanagement. Institutional process-flow mapping, summarizing regional anesthesia-related guidelines and current literature recommendations, would provide easy access to critical information to all health care professionals who are involved in the care of a patient with an indwelling epidural catheter (**Figure 1**). In the ASRA guidelines, "pharmacy fail-safe" is also mentioned as an important method to assist management of patients with indwelling catheters. Using a central computer system, pharmacists can be alerted to potential drug-drug interactions or medication errors [5]. After these cases, the fail safe alert in our hospital was established in the electronic medical record ordering system to alert the caregivers who order anticoagulants, antiplatelet agents or thrombolytic agents in patients with indwelling epidural catheter (**Figure 2**). This system works as a double-check system as this alert is also verified by the pharmacist who prepares the medications for the patient. In our case, inadvertent administration of enoxaparin was discovered by the pain team physician. Involvement of the pain service is strongly advocated for safety check alert, as well as early diagnosis of potential complications.

Despite its rarity, the potential for epidural hematoma formation should be considered in all patients with an indwelling epidural catheter given its potential morbidity. Horlocker reported that severe radicular back pain was a rare symptom of spinal hematoma [12, 13]. Variability in the presenting signs and symptoms of spinal hematoma may contribute to a delay in diagnosis. Serial neurologic examinations remain an important component in surveillance and early diagnosis. New onset of numbness, weakness, or bowel and bladder dysfunction should serve as concerning symptoms. Most importantly, communication between clinical teams is paramount to good clinical outcomes. Establishment of these multiple fail-safe systems can be greatly beneficial to avoid preventable and unintentional medical errors due to miscommunication, and also assist in early diagnosis of potential complications.

In these cases, the need for anticoagulation was not considered preoperatively as it was not part of the surgical plan. Given that a prolonged period of time had elapsed following epidural catheter placement and that placement was atraumatic, there was limited concern that anticoagulation would initiate bleeding. More important are the decision guidelines for catheter removal. Albeit rare, there is the potential for trauma of epidural veins with bleeding during removal. One retrospective analysis of case reports reported that almost half of hematoma formation developed after catheter removal, and one-third of them were under the influence of a therapeutic plasma level of heparinization at the time of catheter removal [14]. As such, catheter removal should not occur in the presence of anticoagulation. The ASRA guidelines

recommend to remove an indwelling neuraxial catheter 2-4 hours after the last unfractionated heparin dose and to assess the patient's coagulation status. Given the concern of heparin-induced thrombocytopenia, a platelet count is also recommended in patients who have received heparin for more than 2-4 days before catheter removal [1]. In the case of single-daily dosing of LMWH, the catheter should be removed a minimum of 10-12 hours after the last dose of LMWH [1]. The anti-Xa level has been reported not to predict the risk of bleeding. The presence of sensory and motor function in the lower extremities should be carefully assessed for at least 12 hours after the catheter removal.

In summary, we present two patients who received unintentional anticoagulation therapy in the presence of a continuous epidural catheter. In rare circumstances, such therapy may be emergently needed and therefore the question remains how best to manage such patients. Although the use of neuraxial anesthesia has been reported in both the adult and pediatric cardiac surgery population with full anticoagulation following epidural catheter placement, there are limited data to fully support the safety of this practice. As is true for all patient care, good communication between clinical teams remains essential, and constitutes the backbone to deliver the optimal care.

Disclosure of conflict of interest

None.

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