● Case Report

Uneventful Removal of an Epidural Catheter Guided by Impedance Aggregometry in a Patient With Recent Coronary Stenting and Treated With Clopidogrel and Acetylsalicylic Acid

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Objective: This report suggests that impedance aggregometry can be helpful to assess optimum time for and minimize the risk of catheter removal during double antiplatelet therapy.

Case Report: A 52-year-old patient undergoing cystectomy during combined general and epidural anesthesia suffered an acute myocardial infarction, and required coronary artery stenting and dual antiplatelet function therapy.

Conclusions: Balancing the risks of stent occlusion and epidural bleeding, bedside impedance aggregometry helped to identify the optimum time window for epidural catheter removal with the lowest bleeding risk in this patient. *Reg Anesth Pain Med 2007;32:354-357.*

Key Words: Regional anesthesia, Antiplatelet therapy, Epidural catheter removal, Point-of-care testing, Platelet aggregometry, Multiplate.

Perioperative acute myocardial infarction occurs in 0.3 to 2.7% of patients[1,2] and is frequently evaluated by coronary angiography. In the majority of patients with critical coronary stenoses simultaneous coronary angioplasty and stent implantation are performed. Aggressive inhibition of platelet aggregation is recommended for at least 4 weeks to prevent coronary thrombosis and reocclusion even following bare metal stent implantation.[3,4] Accordingly, if removal of an epidural catheter during this period is required, the risk of discontinuation of platelet function inhibitors, coronary thrombosis, and stent occlusion has to be balanced against that of formation of an epidural hematoma with neurological deficit.

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We report a case with acute major perioperative myocardial infarction in a patient undergoing cystectomy under combined general and epidural anesthesia, where impedance aggregometry helped to identify the optimal point of time for epidural catheter removal with the lowest bleeding risk.

Case Report

A 52-year-old man (height, 176 cm; body weight, 75 kg) underwent cystectomy for treatment of a bladder tumor. His medical history was unremarkable except for nicotine abuse. Preoperative coagulation studies and platelet count were normal. After application of a 6-electrode-derived 12-lead electrocardiogram, and pulse oximetry, an epidural catheter (20 gauge) was inserted uneventfully at the T10-T11 interspace via an 18-gauge Tuohy needle. Loss of resistance had been encountered at 6 cm, and the catheter had been inserted for 10 cm below skin level. Bupivacaine 0.5% (10 mL) was administered via the catheter after an uneventful injection of a 3 mL bupivacaine 0.5% test dose. A catheter was inserted into the left radial artery for measurement of arterial pressure and blood sampling. General anesthesia was induced by intravenous administra-

tion of etomidate (20 mg), fentanyl (0.3 mg), and rocuronium, and was maintained with isoflurane and epidural bupivacaine 0.25% (5 mL/h).

The intraoperative course was uneventful except for a 2-minute period of tachycardia and a decrease in arterial blood pressure to 90/60 mm Hg associated with ST segment depression in leads V_3 through V_5. Intravenous metoprolol (5 mg) decreased heart rate from 105 to 75 beats per minute and normalized cardiac repolarization and blood pressure. After intensive care unit admission a 12-lead electrocardiogram revealed no signs of myocardial ischemia and plasma troponin I was normal. However, 3 hours later, troponin I had increased to 100 μg/L. In parallel, ST segment depression in leads V_3 through V_6 indicated acute myocardial ischemia. Transesophageal echocardiography showed impaired left ventricular function (estimated ejection fraction of 0.20) with inferior and anteroseptal akinesia. Immediately, heparin (5,000 U) and acetylsalicylic acid (ASA) (500 mg) were administered intravenously. Urgent coronary angiography revealed three vessel coronary artery disease, with chronic occlusion of the left anterior descending and critical stenosis of the right coronary artery. Immediate angioplasty and stenting of the right coronary artery stenosis was performed using a drug eluting stent; the left anterior descending occlusion could not be recanalized. Clopidogrel (600 mg) was administered to inhibit platelet function. Daily administration of clopidogrel (75 mg) and ASA (100 mg) was prescribed by the cardiologist. The patient also received unfractionated heparin intravenously. Due to progressive hemodynamic instability and worsening left ventricular function, an intra-aortic balloon pump and a pulmonary artery catheter were inserted, and cardiac index (L/min/m^2) was increased from 1.9 to 3.5 by administration of epinephrine, norepinephrine, and milrinone, and later levosimendan, as required.

During hemodynamic instability the patient was kept sedated and was mechanically ventilated for 2 weeks due to nosocomial pneumonia and agitation, but was weaned successfully from intra-aortic balloon pump. After 4 weeks a high fever and suspected infection required removal of the epidural catheter. At this time the patient was responsive and able to move arms and legs on request. To minimize the risk of stent occlusion we decided to discontinue clopidogrel and ASA for 24 hours, but to assess coagulation with a more sophisticated methodology.

Rotational thrombelastometry (ROTEM™, Pentapharm, Munich, Germany) demonstrated normal coagulation, but does not measure platelet function. Because it is uncertain whether platelet function is continuously inhibited by clopidogrel or partially recovers prior to the next dose we also performed impedance aggregometry using a Multiple Platelet Function Analyzer™ (Dynabyte Medical; Munich, Germany). Platelet aggregation evoked by adenosine phosphate (ADP) improved markedly when tested 24 hours after administration of clopidogrel, as demonstrated by an increased area under the aggregation time curve (AUC) from 292 to 832 (reference range, 607-963 area units [AU] · min) (Figs 1A and 1B). In contrast, platelet aggregation evoked by arachidonic acid barely improved showing an ongoing ASA effect on platelet function (104 to 214 AU · min; reference range 505-1086) (Figs 1C and 1D). Partial recovery of platelet function encouraged us to remove the epidural catheter 24 hours after the latest administration of clopidogrel and ASA, and after heparin infusion was stopped for 4 hours. Prior to catheter removal the activated partial thromboplastin time had decreased from 48.6 to 30.2 seconds, and the platelet count was 196 × 109/L.

After catheter removal (the catheter being in place at the initial insertion depth) no signs of epidural hematoma occurred. Six hours after catheter removal the patient again received clopidogrel, unfractioned heparin, and ASA. After 2 more weeks, the patient was discharged from the intensive care unit.

Discussion

This case suggests that point-of-care testing with platelet impedance aggregometry and rotational thrombelastometry may be helpful in increasing the margin of safety for epidural catheter removal during combined antiplatelet and heparin therapy.

The American Society of Regional Anesthesia and the German Society of Anaesthesia and Intensive Care Medicine in their latest consensus conferences both recommend an interval of 7 days between discontinuation of clopidogrel therapy and neuraxial blockade.[5,6] The risk of epidural hematoma formation after epidural catheterization or catheter removal is increased in patients with coagulation disorders and those treated with anticoagulants.[7-9] Furthermore, combination of antiplatelet drugs, like ASA and clopidogrel, significantly increases bleeding time and evokes more bleeding complications than either drug alone.[10] The occurrence of stent occlusion after platelet transfusion in a patient with a normal platelet count is unknown, and considering this, we did not transfuse the patient.

If systemic infection is present, epidural catheters should be removed immediately to exclude a potential bacterial focus and to minimize the risk of epidural abscess formation.[11] On the other hand,

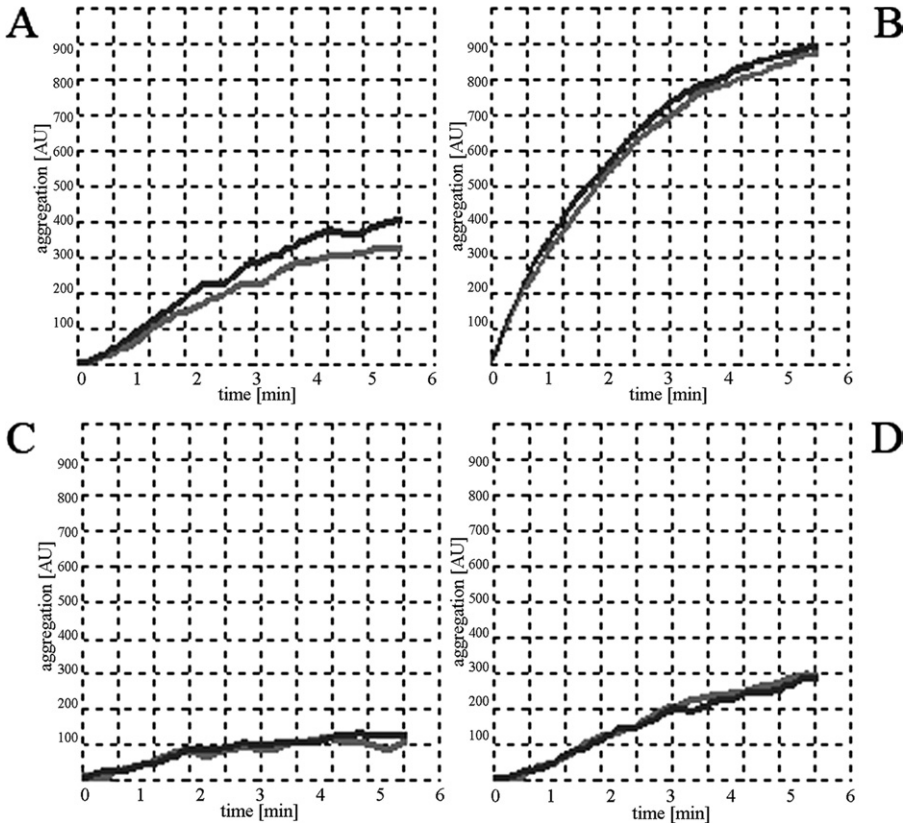

Fig 1. Duplicate measurement for each assay. (A) Time course of platelet aggregation (impedance time curve) evoked by adenosine phosphate (ADP) showed a diminished area under the curve (AUC) of 292 area units (AU) · min (reference range, 607-963) 2 hours after clopidogrel intake. (B) Platelet aggregation evoked by ADP increased up to 912 AU · min (reference range, 607-963) 24 hours after the last dose of clopidogrel. (C) Time course of platelet aggregation evoked by arachidonic acid showed an AUC of 104 AU · min (reference range, 505-1086) 2 hours after acetylsalicylic acid (ASA) intake. (D) Time course of platelet aggregation evoked by arachidonic acid. AUC increased up to 214 AU · min (reference range, 505-1086) 24 hours after the last dose of ASA, but did not reach the normal range.

clopidogrel should not be paused because of potential for stent occlusion. If an epidural hematoma forms, surgical evacuation by laminectomy may be required and may be associated with further cardiac events or death in patients at risk.

There are no prior reports addressing this particular situation and we had to balance the risk of spinal hematoma formation against that of stent occlusion. Although a few articles about clopidogrel resistance have been published recently,[12,13] it is still unknown whether platelet function is continuously inhibited or partially recovers before the next dose. We therefore used point-of-care platelet impedance aggregometry to evaluate platelet function and its time course following medication.

The Multiple Platelet Function Analyzer™ technology is an improvement of impedance aggregometry and allows point-of-care assessment of platelet aggregation in whole blood. During analysis, an electrode pair is placed into the blood sample. Adding reagents such as ADP and arachidonic acid evokes platelet aggregation and results in increased impedance proportional to platelet aggregation. The magnitude of platelet aggregation is assessed by the integral of the impedance time relationship (AUC). Blood samples from patients taking ASA demonstrate diminished platelet activation after addition of arachidonic acid, due to irreversible inhibition of the platelets' cyclooxygenase.[14] This test is not impaired in patients receiving inhibitors of ADP-induced platelet aggregation. Clopidogrel is a potent noncompetitive inhibitor of ADP-induced platelet aggregation, inhibiting the binding of ADP to platelet membrane receptors.[15] ADP binding is necessary for activation of the glycoprotein IIb/IIIa receptor, which is the binding site for fibrinogen. Accordingly, platelet activation by ADP is diminished in patients receiving effective doses of clopidogrel. This test is not impaired in patients taking ASA.

Twenty-four hours after the last administration of clopidogrel and aspirin, analysis revealed improved platelet function for ADP-induced aggregation and impaired platelet function in response to arachidonic acid. Decreased responsiveness to the antiplatelet effects of clopidogrel has been reported recently.[12,13] Possible causes include genetic polymorphism, defects in signaling pathways downstream from the receptor, heightened platelet reactivity before drug administration, and inadequate dosing in patients with increased body mass index or comorbidities. Accordingly, we assumed that the risk for spinal hematoma formation in this particular situation was acceptable before administration of the next clopidogrel dose due to normal AUC with ADP-induced platelet aggregation. Considering the risk of bleeding vs. stent occlusion we

thought that the safest time for epidural catheter removal would be 24 hours after the last clopidogrel intake.

Obviously, our report cannot establish any guidelines as to the safety of epidural catheter removal during combination antiplatelet therapy. However, it suggests that a window of opportunity can be sought by point-of-care platelet function testing in selected patients. In summary, the Multiple Platelet Function Analyzer™ is a new and interesting point-of-care tool that assesses the effects of antiplatelet drugs on platelet aggregation by evaluation of time-related effects of antiplatelet drugs and may assist in decision-making.

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