Antiplatelet Therapy and Lumbar Transforaminal Epidural Steroid Injections

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Myth: Antiplatelet therapy must be discontinued prior to all lumbar transforaminal epidural steroid injections.

Fact: The decision to withhold antiplatelet therapy prior to lumbar transforaminal epidural steroid injections should be made on a case-by-case basis, weighing the relative risk of hemorrhage versus the risk of thrombosis for each patient.

Cardiovascular disease (CVD), heart attack, stroke, and deep vein thrombosis/pulmonary embolus are the leading cause of death globally [1]. The underlying pathophysiology in 90% of those deaths is vascular thrombosis [2]. Antithrombotic therapy (anticoagulant [AC] and antiplatelet therapy [APT]) is a mainstay pharmacological strategy for the prevention and treatment of CVD. The benefits and risks of withholding ACs for spine interventions have been reviewed in a separate publication [3]. This FactFinder examines the evidence regarding the risk of continuing or withholding APT prior to lumbar transforaminal epidural steroid injection (LTFESI).

Common oral antiplatelet agents include aspirin (ASA), platelet P2Y12 receptor blockers (clopidogrel [Plavix], prasugrel, ticagrelor, and ticlodine), dipyridamole, and cilostazol. Multiple randomized controlled trials and meta-analyses have demonstrated the efficacy of aspirin in reducing the risk of thrombotic events and all-cause mortality in patients with prior myocardial infarction, stroke, and peripheral vascular disease [4,5,6]. Dual antiplatelet therapy (ASA plus Plavix) is an established treatment for the prevention of coronary thrombosis following revascularization and stent [7]. Both American and European cardiology guidelines recommend dual antiplatelet therapy for secondary prevention [8,9]. In patients with established coronary artery disease (CAD) who have undergone revascularization or stent placement, the annual risk of coronary artery thrombosis ranges from 1-15%, depending upon stent characteristics and patient comorbidities [9]. APT is also the principal agent for secondary prevention following a non-cardioembolic ischemic stroke or transient ischemic attack (TIA) [10,11]. The decision of whether or not to discontinue APT prior to a LTFESI, therefore, must take into account the consequences of increased risk of coronary, cerebral, and peripheral vascular thrombosis.

The flip side to thrombotic risk is hemorrhagic risk. Spinal epidural hematoma (SEH) is a rare potential complication of lumbar epidural steroid injections (ESI) and may result in significant morbidity. SEH complications have not been found in large case series (n=65,000) of mixed transforaminal and interlaminar ESI presumably performed on participants who were not on antithrombotics [12-15]. Single case reports of SEH have occurred in association with pain interventions involving spinal cord stimulator lead placement or removal, and interlaminar injections. In most cases there was no history of antithrombotic therapy, no history of coagulopathy, or antithrombotic therapy was appropriately withheld pre-procedure [16]. There are three case reports of hemorrhagic complications following LTFESI; however, in all three cases, technical uncertainties exist. None of the three reports were associated with APT (or any other antithrombotic therapy). In one case, the needle was not near the foramen and therefore should not be considered a transforaminal injection [17]. In the other two cases [18, 19], pre-procedure MRIs demonstrated severe central stenosis and severe foraminal stenosis, respectively. Both injections were performed at the level of the pathology.

Observational studies have supported the safety of performing LTFESI in patients on antiplatelet medication. No bleeding complications were reported in one study that included one patient on dabigatran, 19 patients on clopidogrel, and 98 patients on aspirin [21]. In a large cohort of patients who continued antiplatelet medication for LTFESI, no bleeding complications were found in 1,168 patients who continued on clopidogrel, 20 on aspirin/dipyridamole, 25 on dabigatran, 23 on cilostazol, 18 on ticagrelor, and one on prasugrel [22].

An in-depth and nuanced analysis of the known thrombotic and hemorrhagic risks of continuing versus discontinuing antithrombotic medication prior to spinal interventions has recently been published [23]. Smith *et al*. presented three lines of evidence that suggest increased safety of LTFESI over the interlaminar approach. The first argument is anatomical. According to SIS Guidelines [20], the final needle tip position for a LTFESI lies outside of the central spinal canal, whereas for lumbar interlaminar ESI (LILESI) the needle tip is located within the confines of the central canal in close proximity to the dorsal epidural venous plexus. Based on contrast flow patterns commonly seen for LTFESI, any potential bleeding would be expected to result in a low resistance effusion into the extraspinal tissues. A paraspinous hematoma would likely be clinically insignificant. The second argument was that, in spite of widespread adoption of the transforaminal approach, they were unable to identify any reports of SEH or paraspinal hematomas as a consequence of LTFESI whether patients were on antithrombotics or not. The third, and most compelling argument, involved the estimated risks of thrombotic complications arising from withholding antithrombotic therapy. Endres *et al*. [22,24] reported that serious complications (i.e. myocardial infarction, stroke, pulmonary embolism) arose from withholding antithrombotic therapy prior to spinal interventions. Those complications occurred in 0.4% (0.2 – 0.7%) of their study population.

The observed harm of stopping APT prior to spinal interventions and/or surgery is disputed. In the Endres study population, all of the thrombotic complications followed discontinuation of ACs and no patient experienced a complication as the result of stopping APT. A systematic review of the hazards of discontinuing or non-adherence to aspirin therapy resulted in a three-fold increase in adverse cardiac events [25]. In their review, Luni *et al* [26] concluded that planned discontinuation of ASA prior to surgery did not result in a significant risk of major adverse cardiac events (OR= 1.17, CI= 0.76- 1.81, P= 0.05) but the trend is toward worse outcomes. A recent Cochrane Review concluded that continuation or discontinuation of APT prior to surgery had little or no effect on outcomes; however, they report an absolute effect of 17 fewer participants per 1,000 with an ischemic event in the continuation group [26]. Although the interventional and surgical literature predict minimal risk in withholding APT, the cardiovascular literature predicts substantial risk associated with withholding APT in patients with established CVD [27] as well as increased stroke risk in qualified patients taking APT [28].

The commonly referenced American Society of Regional Anesthesia and Pain Medicine (ASRA) guidelines aimed at reducing the incidence of thrombotic and hemorrhagic complications have been recently updated and now recommend that LTFESI and LILESI both be classified as "moderate risk" [16]. These guidelines recommend a "shared assessment and risk stratification, and stopping ASA is not essential." While these guidelines do not recommend a universal policy to withhold ASA prior to intermediate risk spinal interventions, they do recommend discontinuing the antiplatelet agent clopidogrel prior to all intermediate risk procedures regardless of thrombotic risk. This recommendation may not be consistent with the facts derived from available published evidence.

All spinal interventions performed for pain involve risk, and all reasonable measures should be considered to minimize those risks for each individual patient. The utility of any intervention should be weighed against non-interventional treatment. In the case of LTFESI, the available evidence indicates that for the majority of patients, the thrombotic risk of withholding APT exceeds the hemorrhagic risk of continuing it. However, the risk should be assessed for each individual situation. Decisions concerning discontinuation of APT should be coordinated with the prescribing physician.

Conclusions

1. The decision to proceed with LTFESI for a patient who is on APT or to cancel the procedure should be based on current evidence, and the decision should be left to the individual physician.
2. For the majority of patients, the current evidence suggests that the risk of thrombotic complications from withholding APT may be greater than the risk of hemorrhagic complications when APT is continued.

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