Interventional Pain Medicine 1 (2022) 100008

Contents lists available at ScienceDirect

Interventional Pain Medicine

journal homepage: www.journals.elsevier.com/interventional-pain-medicine

FactFinders

FactFinders for patient safety: Antithrombotics and interventional pain procedures -- lumbar transforaminal epidural steroid injections and lumbar medial branch radiofrequency neurotomy

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A B S T R A C T

This series of FactFinders presents a brief summary of the evidence and outlines recommendations regarding the safety of antithrombotics and two interventional pain procedures — lumbar transforaminal epidural steroid injections and lumbar medial branch radiofrequency neurotomy.

The evidence in support of the following facts is presented: (1) 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. (2) A clinically significant hemorrhagic complication has never been reported in the medical literature in association with a lumbar medial branch radiofrequency neurotomy procedure. (3) Discontinuing antithrombotics for lumbar radiofrequency neurotomy procedures, even for a short period of time, may lead to an increased incidence of cardiovascular and cerebrovascular events.

Antiplatelet Therapy and Lumbar Transforaminal Epidural Steroid Injections

David C. Miller, MD, MA; Clark Smith, MD, MPH; and Zachary L. McCormick, MD on behalf of the Spine Intervention Society's Patient Safety Committee.

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 $P2Y_{12}$ 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 [4–6]. 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 to 15%, depending upon stent characteristics and patient comorbidities [9]. APT is also the principal agent for secondary prevention following a non-cardioembolic

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https://doi.org/10.1016/j.inpm.2021.100008
Received 15 December 2021; Accepted 16 December 2021

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 [20]. In a large cohort of patients who continued antiplatelet medication for LTFESI, no bleeding complications were found in 1168 patients who continued on clopidogrel, 20 on aspirin/dipyridamole, 25 on dabigatran, 23 on cilostazol, 18 on ticagrelor, and one on prasugrel [21].

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 [22]. 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 [23], 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. [21,24] 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 1000 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.

Anticoagulants and Antiplatelet Agents for Lumbar Medial Branch Radiofrequency Neurotomy

Clark Smith, MD, MPH; David C. Miller, MD, MA; Mathew Saffarian, DO; and Zachary L. McCormick, MD on behalf of the Spine Intervention Society's Patient Safety Committee.

Myth: Therapeutic anticoagulation (AC) and antiplatelet agents (APT) should be discontinued prior to lumbar radiofrequency neurotomy (RFN) due to serious hemorrhagic risks.

Fact: A clinically significant hemorrhagic complication has never been reported in the medical literature in association with a lumbar RFN procedure.

Lumbar RFN is a procedure to treat painful lumbar facet joints. It involves placing an electrode parallel to the medial branch nerve [MBN] where it crosses the neck of the superior articular process. During properly performed procedures [29], the needle and electrode remain entirely extra-spinal confirmed by multiplanar fluoroscopy. At no time does the electrode enter the central spinal canal or intervertebral foramen. The electrode passes through skin, subcutaneous tissue, and muscle along the trajectory to the MBN or L5 dorsal ramus. Therefore, from an anatomical perspective, the primary bleeding complications that could be associated with RFN performed according to technique supported by clinical practice guidelines [29] are paraspinal hematoma or bleeding at the needle puncture site.

No clinically significant hemorrhagic complications occurring during a lumbar RFN have been reported in the current medical literature. Large observational studies [30–32] and systematic reviews [33] have reported no bleeding complications associated with lumbar RFN. Endres et al. performed lumbar RFN for 35 patients on AC and 22 patients on APT, none of whom experienced any bleeding complications [30]. A follow-up

2020 study by Endres et al. encountered no bleeding complications among 145 patients undergoing lumbar RFN on AC and APT medications. This included 47 patients on warfarin, 56 on clopidogrel, 6 on rivaroxaban, and 46 on apixaban [34]. Ehsanian et al. reported no bleeding complications among 18 patients continuing aspirin (n = 12), non-steroidal anti-inflammatory drugs (NSAIDs) (n = 3), and Cyclooxygenase-2 (COX-2) selective NSAIDs [35]. Although these studies report a zero risk, their sample sizes were small, and do not exclude a risk of up to 3%. Reports on larger patient cohorts will be needed to accurately define a more accurate (rare or non-existent) incidence of such events. Nonetheless, published evidence of a serious hemorrhagic complication associated with lumbar RFN has yet to emerge.

Myth: The risk of a cardiovascular or cerebrovascular event resulting from temporary discontinuation of AC and APT medications for the purposes of a lumbar RFN procedure is negligible.

Fact: Discontinuing AC or APT agents, even for a short period of time, may lead to an increased incidence of cardiovascular and cerebrovascular events.

There are significant documented medical risks of discontinuing AC agents for spinal interventions [30]. Cardiovascular and cerebrovascular events, including pulmonary embolism, stroke, and myocardial infarction have been reported prior to interventional spine procedures when AC agents are withheld [30,32,36,37]. Bernstein et al. reported 15 cases of ischemic events in the peri-procedure period. Of these, nine had stopped AC medication and six had continued it [32]. Endres et al. reported on 3827 procedures in which anticoagulants were discontinued [34]. Nine patients suffered serious morbidity, including five patients with non-fatal stroke, one with a pulmonary embolism, and one with a myocardial infarction. There were two deaths (one fatal stroke, one fatal myocardial infarction) [34]. The prevalence of these complications was 0.48% (95% CI: 0.2–0.9%).

Risk of thrombotic complications due to withholding APT prior to spinal interventions has not yet been clearly established. Risks of cardiovascular or cerebrovascular events due to stopping antithrombotic agents have been estimated to be 0.4% (0.2–0.7%) [30,32]. Though this may be perceived as a relatively small number, the complications are serious and have, in some cases, resulted in death. These figures warn that clinical decisions regarding the cessation of antithrombotic agents need to be balanced with the risk of hemorrhagic complications. A recent Cochrane Review concluded that continuation or discontinuation of APT prior to surgery had little or no effect on outcomes; however, they report absolute effect of 17 fewer participants per 1000 with an ischemic event in the continuation group [38]. In the case of lumbar RFN, the medical literature suggests that the predicted frequency of a serious thrombotic event (approximately 0.4%) is greater than the risk of a serious hemorrhagic event (yet to be reported).

Recommendations

* Physicians should weigh the relative risk of serious thrombotic versus hemorrhagic complications when making the decision to stop or continue AC or APT medications prior to lumbar RFN.
* Although larger studies are needed to provide a more confident estimate of zero risk of continuing AC or APT prior to lumbar RFN, there is currently no evidence that continuing AC or APT prior to this procedure carries risk of clinically significant bleeding.
* The rate of serious thrombotic complications associated with stopping AC for the appropriate time period prior to spinal intervention is approximately 0.4%.

Conclusion

Current evidence suggests that the risk of cerebrovascular and cardiovascular complications from stopping AC or APT outweighs the risks of serious hemorrhagic complications associated with lumbar RFN.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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