Retrospective Study

Continuing Anti-thrombotic Medication During Low-to-Intermediate Risk Spinal Procedures: A Retrospective Evaluation

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Background: The current American Society of Regional Anesthesia (ASRA) guidelines recommend discontinuing anti-thrombotic therapy prior to any interventional spine procedures to decrease the incidence of bleeding complications. However, discontinuing anti-thrombotics may pose considerable danger in terms of cerebrovascular and cardiovascular events. Recent evidence suggests that some spinal interventions may still be performed safely with anti-thrombotics on board and some practitioners thus elect to continue certain anti-thrombotics for these procedures.

Objective: To assess the rate of adverse events in patients undergoing spine procedures that are currently classified by the ASRA guidelines as "low-to-intermediate bleeding risk," while being on continued anti-thrombotic therapy.

Study Design: Retrospective cohort study.

Setting: Interventional pain management practice.

Methods: A retrospective chart review was performed on patients who underwent low-to-intermediate risk spine procedures with variable anti-thrombotic medications continued throughout the course of treatment.

Results: Between October 2015 and May 2016, out of 2,204 patients who underwent low-to-intermediate risk spine procedures, we identified 490 patients on anti-thrombotic medications. These included aspirin (N = 275), $P2Y_{12}$ inhibitors (N = 129), warfarin (N = 62), heparin (N = 10), factor Xa inhibitors (N = 55), and dipyridamole (N = 1). Forty-two patients were on multiple anti-thrombotics. Anti-thrombotics were continued throughout the procedure for 467 of 490 patients (88%). One bleeding complication (injection site bleeding) occurred in a patient that continued clopidogrel and aspirin during a lumbar radiofrequency ablation. We encountered no bleeding complications attributable to anti-thrombotics in the other 466 procedures in which anti-thrombotics were continued during lumbar (N = 260), thoracic (N = 18), and cervical (N = 40) medial branch injections, sacroiliac injections (N = 47), and during lumbar (N = 87) thoracic (N = 2), and cervical (N = 12) medial branch radiofrequency ablations.

Limitation: The retrospective nature of the study and its reliance on electronic medical records are potential limitations.

Conclusion: Continuing anti-thrombotic medication during medial branch and sacroiliac injections may be possible.

Key words: Interventional pain management, thrombotic complications, hemostasis, anti-coagulation, bleeding complications

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The level of bleeding risk one spinal procedure holds over another is poorly understood. In 2015, the American Society of Regional Anesthesia (ASRA) (1) published guidelines rating the level of risk imposed by variable, commonly performed interventional pain procedures. Those considered 'intermediate risk' for bleeding complications included epidural injections (interlaminar and transforaminal), facet blocks, sympathetic block, radiofrequency neurotomy, and lumbar intradiscal injections. The authors recommend discontinuing anti-thrombotic medications for these procedures and further delineate the length of time certain medications must be stopped in advance to limit the risk of complications such as an epidural hematoma.

This is contrary to a 2013 Spine Intervention Society guideline (2) which suggested that lumbar transforaminal epidural, posterior-approach facet joint, radiofrequency neurotomy, sacroiliac, lumbar sympathetic, and lumbar intradiscal injections may be performed safely while continuing certain anti-thrombotic agents. In addition, in 2013 Manchikanti et al (3) performed a comprehensive systematic review on periprocedural antithrombotic management and provided recommendations specific for interventional pain techniques, which were adapted for the 2013 American Society of Interventional Pain Physicians (ASIPP) guidelines (4). The ASIPP guidelines distinguish "high risk" (interlaminar epidural injections, percutaneous adhesiolysis, disc decompression, sympathetic blocks, placement of implantables) and "low risk" (caudal epidural injection, paravertebral interventional techniques, peripheral joint injections) interventional techniques, and contrary to the ASRA guidelines do not include an "intermediate risk" category. The ASIPP guidelines recommend continuing non-steroidal anti-inflammatory drugs (NSAIDs), aspirin, and phosphodiesterase inhibitors for any procedure and provide more room for choice for the physician to continue or stop other anti-thrombotics for high risk and low risk procedures. They also provide a higher INR requirement (2.0) for low risk procedures (4).

The practice of discontinuing anti-thrombotic medication prior to spinal interventions is mostly based on several case reports of epidural hematomas in patients undergoing spine procedures under continued anti-thrombotic medications (5-7). However, discontinuing anti-thrombotics may pose considerable danger in terms of cerebrovascular and cardiovascular events (8). The risk of epidural hematomas or other bleeding complications would appear to be low in patients undergoing procedures that are currently classified as low-to intermediate risk for bleeding by ASRA guidelines (8,9). As a result, some practitioners elect to continue certain anti-thrombotics for these procedures (8,10). It has been suggested to modify the latest ASRA guidelines to recommend continuation of most anti-thrombotics for low-to-intermediate risk procedures (9). The aim of this study was to assess the risk of bleeding complications in patients undergoing several low-to-intermediate risk spine interventions during which anti-thrombotic medications were continued.

Methods

Study Population

The study was conducted in a private practice in which some practitioners routinely continued anti-thrombotics while others discontinued anti-thrombotics in keeping with the currently accepted ASRA guidelines for spine interventions. To assess the risks associated with continuation of anti-thrombotic therapy, we performed a retrospective chart review on all patients who underwent certain low-to-intermediate risk spine interventions between October 1, 2015, and May 31, 2016. We chose this time window because we estimated from a preliminary analysis that this would include ~400 patients on anti-thrombotics in our analysis. A previous study on bleeding risk associated with spine interventions and anti-thrombotics reached reliable results including ~200 patients (9). We included medial branch blocks (lumbar, thoracic, and cervical), sacroiliac joint injections, and medial branch radiofrequency ablations (lumbar, thoracic, and cervical). Medial branch blocks and medial branch radiofrequency ablations are currently classified as intermediate-risk by the ASRA guidelines (1), whereas sacroiliac joint injections are classified as low risk. We did not include epidural injections because all practitioners in our office discontinue anti-thrombotics prior to epidural injections. This study was approved by the Northwell Institutional Ethical Review Board (number: 16-675) on September 13, 2016. Requirement of informed consent and HIPAA authorization was waived. All spinal procedures were performed under fluoroscopic guidance. Most injections were performed with 25 gauge spinal needles. For radiofrequency medial branch ablations, 20 gauge or 22 gauge needles were used.

Anti-thrombotic Medications

The following medications were considered anti-thrombotic medications: aspirin (Ecotrin), warfarin (Coumadin or Jantoven), dabigatran etexilate (Pradaxa), apixaban (Eliquis), rivaroxaban (Xarelto), clopidogrel (Plavix), prasugrel (Effient), ticagrelor (Brilinta), heparin, enoxaparin (Lovenox), and dipyridamole (Persantine).

Data Retrieval

Patient characteristics, medication information, performed interventions, and past complications were collected retrospectively from medical records. We checked for complications from procedures by looking at the notes of follow-up telephone calls 48 hours post-procedure, or notes from a follow-up appointment (~2 to 4 weeks post-procedure). During follow-up calls and follow-up visits patients are specifically asked whether they have experienced any complications as a result of the procedure.

Study Outcome

Bleeding complication from a spine procedure was the main outcome of this study. We screened medical records for clinically evident bleeding complications such as a hematoma or injection site bleeding.

Statistical Analysis

Patients with incomplete follow-up were excluded from the analysis. Continuous data are displayed as mean ± standard deviation. Outcome incidences are reported with adjusted Wald confidence intervals within 95% (11). Analysis was performed using JMP version 12 (SAS Institute Inc., Cary, NC, USA).

Results

During the study period, 2,204 of the predetermined low-to-intermediate risk spinal procedures were performed; 53 patients did not return for a follow-up visit nor could they be reached by phone. Of the 2,151 patients with complete data, 490 patients (260 men, and 230 women) were found to be on anti-thrombotic medication. The mean age of patients on ant-thrombotic medication was 69 ± 11 years. In 467 patients, anti-thrombotic therapy was continued throughout the procedure – Table 1. If anti-thrombotic medication was discontinued for the procedure, it was halted for the duration recommended in the 2015 ASRA guidelines (1).

Study Outcome

A 59-year-old woman developed injection site bleeding after undergoing a lumbar radiofrequency ablation while on aspirin and clopidogrel throughout the procedure. She presented at the emergency department where the bleeding was stopped by applying pressure. Of note, no bleeding complications occurred in 466 other patients in which anti-thrombotics were continued during the different low-to-intermediate risk interventional spine procedures – Table 2.

The corresponding 95%-confidence intervals for bleeding complications were 0.0 – 1.0% for medial branch injections, 0.0 – 5.9% for medial branch radiofrequency ablations, and 0.0 – 6.5% for sacroiliac injections – Table 2.

No clinically evident bleeding events were observed in the 1,661 patients not on anti-thrombotics.

Discussion

This retrospective cohort study describes a significant number of chronic pain patients that underwent low-to-intermediate risk spinal interventions under continued anti-thrombotics. We observed one bleeding complication in this cohort of 467 patients that were on anti-thrombotics throughout their procedure. The 95% confidence intervals of bleeding risk were 0.0 – 1.0%, 0.0 – 6.5%, and. 0.0 – 5.9% for medial branch injections, sacroiliac injections, and medial branch radiofrequency ablations, respectively.

Bleeding Risk of Continuing Anti-thrombotics for Spine Interventions Currently Classified as Low-to-Intermediate Risk by ASRA Guidelines

Management of anti-thrombotics during procedures requires balancing the risk of bleeding complications vs. thromboembolic events. The ASRA consensus guidelines recommend discontinuing most anti-thrombotic medications for low-to-intermediate risk procedures (1), but are mostly based on circumstantial evidence from spinal anesthesia for surgical procedures because no better evidence was available at the time the guidelines were adopted. Recently several studies were conducted in attempts to address this dilemma. A study by Endres et al (8) reported no bleeding complications after 1,836 medial branch injections and 261 sacroiliac injections in patients continuing anti-thrombotics. Similarly, another study (9) found no hemorrhagic complications in patients continuing anti-thrombotics undergoing 62 medial branch injections, 5 sacroiliac injections, and 26 medial branch radiofrequency ablations. These results confirmed an earlier study by

Table 1. *Periprocedural anti-thrombotic therapy.*

Procedure	LMB Inj. N (%)	TMB Inj. N (%)	CMB Inj. N (%)	Sacroiliac Inj. N (%)	LMB RFA N (%)	TMB RFA N (%)	CMB RFA N (%)	Total N (%)
Aspirin								
Discontinued	1 (1)	0	2 (7)	1 (3)	5 (9)	2 (66)	3 (33)	14 (5)
Continued	136 (99)	11 (100)	28 (93)	29 (97)	50 (91)	1 (33)	6 (67)	261 (95)
Clopidogrel								
Discontinued	15 (21)	0	2 (33)	5 (45)	6 (25)	0	0	28 (23)
Continued	58 (79)	4 (100)	4 (67)	6 (55)	18 (75)	1 (100)	1 (100)	92 (77)
Ticagrelor								
Discontinued	0	0	0	0	0	0	0	0
Continued	2 (100)	0	1 (100)	1 (100)	0	0	0	4 (100)
Prasugrel								
Discontinued	0	0	0	0	0	0	0	0
Continued	3 (100)	0	0	0	2 (100)	0	0	5 (100)
Dipyridamole								
Discontinued	0	0	0	0	0	0	0	0
Continued	1 (100)	0	0	0	0	0	0	1 (100)
Warfarin								
Discontinued	4 (12)	1 (100)	1 (14)	2 (20)	1 (10)	0	0	9 (15)
Continued	28 (88)	0	6 (86)	8 (80)	9 (90)	0	2 (100)	53 (85)
Rivaroxaban								
Discontinued	4 (29)	0	0	0	1 (25)	0	0	5 (26)
Continued	10 (71)	0	0	1 (100)	3 (75)	0	0	14 (74)
Dabigatran								
Discontinued	0	0	1 (50)	0	0	0	0	1 (8)
Continued	4 (100)	2 (100)	1 (50)	1 (100)	3 (100)	0	0	11 (92)
Apixaban								
Discontinued	3 (18)	0	0	0	2 (50)	0	0	5 (21)
Continued	14 (82)	1 (100)	0	1 (100)	2 (50)	0	1 (100)	19 (79)
Heparin								
Discontinued	1 (100)	1 (100)	0	0	0	0	0	2 (40)
Continued	3 (100)	0	0	0	0	0	0	3 (60)
Enoxaparin								
Discontinued	0	0	1 (100)	0	0	0	0	1 (20)
Continued	1 (100)	0	0	0	1 (100)	0	2 (100)	4 (80)
Total								
Discontinued	28 (9)	2 (10)	7 (15)	8 (15)	15 (15)	2 (50)	3 (20)	65 (12)
Continued	260 (91)	18 (90)	40 (85)	47 (85)	88 (85)	2 (50)	12 (80)	467 (88)

L, lumbar, T, thoracic, C, cervical, MB, medial branch, Inj., injection, RFA, radiofrequency ablation

Manchikanti et al (10) that found no serious bleeding complications in patients continuing anti-thrombotics undergoing 1,116 facet joint interventions. Our study adds to this fund of safety data for interventional spine procedures. After combining our data with the data from these earlier studies, the upper 95% CI limits for bleeding complications rates with continued anti-thrombotics during medial branch injections, sacroiliac injections, and medial branch radiofrequency ablations are 0.15%, 1.0%, and 4.7%, respectively. Previous stud-

ies that declared epidural or spinal anesthesia safe in patients taking anti-platelet drugs did so on the basis of a zero percent prevalence of complications in 386 (12) and 383 (13) patients, respectively. In those studies the upper confidence limits of 0% were reported as 1.1% (12) and 0.96% (13), which are greater than or relatively equal to the upper limits that are observed with medial branch injections (0.15% upper limit of complication risk) and sacroiliac injections (1.0% upper limit of complication risk). Applying the same safety standard to the present study means that medial branch injections and sacroiliac injections can be regarded as safe in patients on anti-thrombotics. The upper limit of complication risk for radiofrequency ablations is substantially greater (4.7%) than previously used safety thresholds and further research is needed to reliably estimate its associated bleeding risk under continued anti-thrombotics.

In the current study, we did not include epidural injections because all practitioners in our office discontinue anti-thrombotics prior to epidural injections. Manchikanti et al (10) described patients continuing anti-thrombotics during 466 interlaminar epidurals, 630 caudal epidurals, and 170 lumbar transforaminal epidurals. Surprisingly, when they combined data for all epidurals they found an increased risk of local bleeding for the patients that discontinued anti-thrombotics vs. the patients that continued anti-thrombotics (68.3% vs. 60.2%) and no differences regarding intravascular entry, profuse bleeding, local hematoma, oozing, and bruising. Of note, they encountered no epidural hematomas in patients continuing anti-thrombotics, which is consistent with the studies by Endres et al (8) and Goodman et al (9) that found no epidural hematomas in 1,633 and 90 patients, respectively, undergoing transforaminal epidural injections under continued anti-thrombotics. Continuing anti-thrombotics during epidural injections may thus be safe in selected patients. However, in our office all practitioners choose to discontinue anti-thrombotics before epidural injections given the potential serious consequences if an epidural hematoma were to occur, and we were thus unable to assess an event rate in the current study. Studies with very significant sample size are needed to assess whether the risk of epidural hematoma following epidural injection under continued anti-thrombotics is acceptably low in selected patients (8).

Table 2. *Low- and intermediate-risk spine interventions and incidence of bleeding complications.*

	Bleeding complications % (95CI)	Anti-thrombotic continued N (%)
Procedure		
LMB Inj.	0 (0.0 – 1.2)	260 (91)
TMB Inj.	0 (0.0 – 15)	18 (90)
CMB Inj.	0 (0.0 – 7.6)	40 (85)
Total MB Inj.	0 (0.0 – 1.0)	318 (90)
LMB RFA	1.1 (0.0 – 6.8)	88 (85)
TMB RFA	0 (0.0 – 63)	2 (50)
CMB RFA	0 (0.0 – 22)	12 (80)
Total MB RFA	1.0 (0.0 – 5.9)	102 (80)
Sacroiliac Inj.	0 (0.0 – 6.5)	47 (85)
Total	0.2 (0.0 – 1.3)	467 (88)

L, lumbar, T, thoracic, C, cervical, MB, medial branch, Inj., injection, RFA, radiofrequency ablation

Thromboembolic Risk with Discontinuing Anti-thrombotics

We did not encounter any thromboembolic complications in the 63 patients who discontinued their anti-thrombotics in our study (Table 1). However in the study by Endres et al (8), 9 out of 4,766 patients in which anti-thrombotics were discontinued as recommended by guidelines (1) suffered thromboembolic complications (myocardial infarction, stroke, pulmonary embolism). Two patients in that study died as a result of these complications. Although small, this prevalence of serious complications (0.4%, 95% CI: 0.2 – 0.7%) means that there is a risk associated with temporary discontinuation of anti-thrombotics. Outside the current study period of interest, we have previously also experienced a complication of discontinuation of anti-thrombotics in our practice. In that case, a patient undergoing an epidural injection died as a result of an acute myocardial infarction after Plavix was discontinued.

Clinical Implications

Practicing interventional pain management physicians face a dilemma when they need to choose between discontinuing and continuing anti-thrombotics for interventional spine procedures. As mentioned earlier, both choices carry risks: discontinuing anti-thrombotics is associated with a slight increased risk of thromboembolic events such as myocardial infarction and stroke while continuing anti-thrombotics may render patients more vulnerable to bleeding complications. The decision of continuing or discontinu-

ing anti-thrombotics will always need to be made on a case-by-case basis by factoring in individual patient characteristics and the planned procedure. The risks of discontinuing anti-thrombotics should also be discussed with the prescribing physician. In the case of medial branch injections and sacroiliac injections, it may be advisable to continue anti-thrombotics in a majority of patients given the apparent low incidence of bleeding complications with these interventions, and the greater risk of serious thromboembolic complications occurring when anti-thrombotics are discontinued. Of note, the bleeding complications that can occur with these procedures are relatively minor (bruising, injection site bleeding) compared to the potential thromboembolic complications (stroke, myocardial infarction) when anti-thrombotics are discontinued.

Methodological Considerations

Several limitations pertain to this study. First, the retrospective nature of this study means that a small number of patients were lost to follow-up. Second, we did not analyze INR values for this study, which could have provided some more insight into the physiological effects of discontinuation of coumadin. Third, continuation and discontinuation of NSAIDs other than aspirin and selective serotonin reuptake inhibitors were not monitored. However, the ASRA guidelines (1) recommend continuing both NSAIDs and selective serotonin reuptake inhibitors medications during the procedures we investigated in this study. Fourth, we did not analyze bleeding risk for individual anti-thrombotic medications because our sample size did not allow for such an analysis. However, it is safe to assume that some anti-thrombotic medications will convey a higher bleeding risk than others. Fifth, this study utilized a patient sample from a large private practice in which each interventional pain management physician performs large volumes of the studied interventions each year. Additionally, most injections were performed with 25 gauge spinal needles and for radiofrequency medial branch ablations 20 gauge or 22 gauge needles were used to minimize the risk of bleeding. Some physicians use 22 gauge and 18 gauge for these respective procedures instead and bleeding complication rates may thus be different in a different setting. Continued multicenter studies on this topic are therefore warranted to further improve patient safety.

Conclusion

Medial branch injections and sacroiliac joint injections appear to be safe to perform in patients who continue anti-thrombotics throughout the procedure. Continuing anti-thrombotics during these spine interventions will likely prevent the increased risk of thromboembolic complications that might otherwise occur as the result of their discontinuation.

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