
SPECIAL REPORT

THE AMERICAN SOCIETY OF REGIONAL ANESTHESIA AND PAIN MEDICINE GUIDELINES FOR PATIENTS RECEIVING MEDICATIONS THAT AFFECT HEMOSTASIS: A CLINICAL PERSPECTIVE

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Abstract

It is always challenging in regards to deciding for-or-against neuraxial interventions among the patients who are receiving medications that affect hemostasis. In the year 2015, the American Society of Regional Anesthesia and Pain Medicine (ASRA) released their collaborative guidelines updated specifically for interventional pain physicians with focus on clinical and procedural implications of antiplatelets and anticoagulants. This was to address the persistent voids and to accommodate the call of changing times since the year 2010 when ASRA had last released their practice advisory's third edition for regional anesthesiologists and pain clinics in regards to concerns for antithrombotics or thrombolytics. However, some concerns still remain unanswered and unclear. Firstly, the intermediate-risk interlaminar epidural steroids injections should have been clarified to be similar as regional epidural insertions that are most commonly performed by median approach. Secondly, the guidelines are deficient by failing to comment the precautions that need to be followed when manipulating (incompletely withdrawing by few centimeters) the in-situ neuraxial catheters. Thirdly, in regards to time-interval between subcutaneous heparin (8-hourly or 12-hourly subcutaneous dosing) and the planned pain procedures, the 8-10hrs timeframe clearly specified in the 2015 guidelines was documented only indistinctly as advice to perform the neuraxial intervention just prior to the heparin injection in the 2010 guidelines. Fourthly, with the inclusion of 12-hourly and 8-hourly subcutaneous dosing under same umbrella at least for needle insertion, 8-10hrs for withholding the dose would affect the dosing schedule when 8-hourly subcutaneous dosing is being followed. Fifthly, although it is assumed by default that 8-hourly subcutaneous dosing would mean heparin 15,000 units per day, pregnant patients are often recommended to receive $\geq 10,000$ units 12-hourly heparin dosing. Sixthly, secondary to inclusion of recommendations in regards to aspirin when performing intermediate risk procedures, labor analgesia with epidural might raise questions of safety among pregnant patients on aspirin because there are proponents for universal prophylaxis with aspirin in all pregnant patients for cost savings in terms of improved maternal and perinatal outcome, and there can be a boom in the number of pregnant patients presenting to labor and delivery rooms with the immediate history of being on aspirin. Finally, discouraging the readers' utilizing cookbook approach of these guidelines may reflect the inadequacy of the guidelines to state and formulate the minimum time limits across all patients. In

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summary, the 2015 guidelines guide providers' steps in the right direction from 2010 guidelines although are not yet completely clear in few but important avenues of neuraxial anesthesia-analgesia for patients on medications affecting their hemostasis.

Perspective

It is always challenging in regards to deciding for-or-against neuraxial interventions among the patients who are receiving medications that affect hemostasis. In the year 2015, the American Society of Regional Anesthesia and Pain Medicine (ASRA) released their collaborative guidelines updated specifically for interventional pain physicians with focus on clinical and procedural implications of antiplatelets and anticoagulants¹. This was to address the persistent voids and to accommodate the call of changing times since the year 2010 when ASRA had last released their practice advisory's third edition for regional anesthesiologists and pain clinics in regards to concerns for antithrombotics or thrombolytics². However, some concerns still remain unanswered and unclear.

Firstly, even though they may seem exclusive to each other in regards to their applicability, the intermediate-risk interlaminar epidural steroids injections¹ should have been clarified to be similar as regional epidural insertions that are most commonly performed by median approach. This becomes more important because compared to fluoroscopically performed epidural steroid injections, the regional epidural insertions are performed blindly and almost always involve additional "trauma" of catheter blindly traversing the epidural spaces. That clarification in the 2015 guidelines¹ would have been able to guide the regional anesthesiologists to follow the updated guidelines for intermediate risk procedures rather than the 2010 guidelines² at least for deciding when to insert epidural needles in neuraxial space including for the indications of epidural anesthesia/analgesia and epidural blood patch. However, spinal anesthesia/analgesia seems to be left open to individual interpretations for the readers of 2015 guidelines in regards to procedure risk-category that may presumably be different for smaller gauge needle spinal puncture

vs. inadvertent dural puncture by epidural needle vs. intrathecal catheter placement that has been graded as high-risk procedure in the 2015 guidelines¹. As a regional anesthesiologist, it is difficult to pick and choose whether to follow (or not follow) the old 2010 guidelines when the new 2015 guidelines are trying to only address interventional pain physicians' concerns despite those concerns overlapping regional anesthesiologists' concerns too.

Secondly, even though the 2015 guidelines¹ (after they are hopefully acclaimed by ASRA as formally applicable for regional anesthesiologists too) can guide when to insert epidural needles in neuraxial space, the readers would still have to follow the old 2010 guidelines² to decide when to remove the neuraxial catheters. However, herein also, the guidelines are deficient by failing to comment that same precautions and guidelines need to be followed when manipulating (incompletely withdrawing by few centimeters) the in-situ neuraxial catheters. Though the research is lacking to consider catheter manipulation same as catheter removal in regards for following the appropriate timed-precautions, this appears to be a very simple logic wherein intentional/iatrogenic catheter movements by the healthcare providers irrespective of whether incomplete withdrawal or complete removal of the catheter should assumingly be entailing the same level of risk for the patients.

Thirdly, in regards to time-interval between subcutaneous heparin (8-hourly or 12-hourly subcutaneous dosing) and the planned pain procedures, the 8-10hrs timeframe clearly specified in the 2015 guidelines¹ was documented only indistinctly as advice to perform the neuraxial intervention just prior to the heparin injection in the 2010 guidelines² wherein the recommendations had been made only for heparin 5,000 units 12-hourly subcutaneous dosing. Moreover, even in the 2015 guidelines¹, the time-frames for removing and manipulating the neuraxial catheters were not addressed for patients on 8-hourly dosing schedule of heparin.

Fourthly, with the inclusion of 12-hourly and 8-hourly subcutaneous dosing under same umbrella at least for needle insertion, 8-10hrs for withholding the dose would affect the dosing schedule when 8-hourly subcutaneous dosing is being followed. Herein the

timing of heparin administration would need to be altered to accommodate neuraxial intervention. This has the potential for skipped heparin dose (or at a minimum, delayed heparin dose resumption by 2hrs post-pain procedure). This is avoidable in the 12-hourly dosing schedule wherein scheduled time of heparin administration could remain unaltered while allowing neuraxial intervention without the need for skipped heparin dose or delayed heparin dose.

Fifthly, although 2015 guidelines do NOT specifically address pregnant patients and neuraxial procedures and moreover it is assumed by default that 8-hourly subcutaneous dosing would mean heparin 15,000 units per day, pregnant patients are often recommended to receive $\geq 10,000$ units 12-hourly heparin dosing³ to accommodate its “prophylactic” (“low” dose) and/or “therapeutic” (“high” dose) effects^{3,4} against thromboembolism during pregnancy⁵. As only laboratory investigation namely activated partial thromboplastin time (aPTT) can determine if the “low” dose is in the “prophylactic” range (non-elevated aPTT) or the “high” dose is in the “therapeutic” range (1.5-2.5 times elevated aPTT 6hours post-heparin)^{3,4}, the increased daily requirements of heparin among pregnant patients can further complicate the adherence to ASRA guidelines (2010 version) and may prompt time-consuming laboratory investigations prior to attempting any neuraxial intervention in the urgent scenarios of labor analgesia and cesarean section deliveries.

Sixthly, secondary to inclusion of recommendations in regards to aspirin when performing intermediate risk procedures¹, labor analgesia with epidural might raise questions of safety among pregnant patients on aspirin, prompting conservative providers to explore alternative methods to attain pain relief because decision to withhold aspirin for 4-days may often preclude labor epidurals except in the scenarios of elective obstetrical management wherein obstetric teams would have had ample time to plan discontinuation of aspirin for 4-days or so. Although the year 1994 CLASP (Collaborative Low-Dose Aspirin Study in Pregnancy)⁶ had only explored 60mg aspirin use in high-risk pregnancies wherein increased bleeding was not observed during preparation for epidural and recent 2013 guidelines by American

College of Obstetricians and Gynecologists (ACOG)⁷ suggested 60-80mg daily dose of aspirin for pregnant patients at-risk for preeclampsia and pre-term delivery, the 2014 recommendations by U.S. Preventive Services Task Force (USPSTF)⁸ include 81-mg daily dose of aspirin for all asymptomatic patients at risk for preeclampsia. Additionally, there are proponents for universal prophylaxis⁹ with aspirin in all pregnant patients for cost savings in terms of improved maternal and perinatal outcome. Consequently, there can be a boom in the number of pregnant patients presenting to labor and delivery rooms with the immediate history of being on aspirin.

Finally, discouraging the readers’ utilizing cookbook approach of these guidelines^{1,2} may reflect the inadequacy of the guidelines to state and formulate the minimum time limits across all patients as similar to minimum 2-hours wait-time recommendation after clear liquids (with what constitutes clear liquids being clearly defined and most likely based on better studied, investigated and documented scenarios in the medical literature) per nothing-by-mouth guidelines¹⁰. Moreover, if down the line, evidence crops up suggesting lowering the time limits further, then the future guidelines can be accordingly updated; however, till then, minimum time limits rather than the range would have been more appropriate and advisable in the current guidelines^{1,2}. The safest way of formulating the guidelines would have been to recommend to wait at least certain number of hours corresponding to each among the commented medications while prohibiting the clinical considerations for lowering the limits unless for the sake of medical research evaluating to generate evidence for future updates in the practice guidelines.

The concept underlying all guidelines is that the designated societies recommend minimum standards based on evidence-based medicine that guide formulation of local institutional policies while allowing adjustments for individual patient case scenarios although superseding personal preferences based on personal knowledge, understanding and experiences. Individual basis means to assess and evaluate the greater risk (and not presume for lower risk) and increased severity of complications when cumulative factors co-exist about which guidelines

were not have been able to clearly state in their current editions. Individual basis is not about blurring the minimum standards (unless if not clearly quoted in the guidelines) to accommodate adventurous providers performing neuraxial interventions in the expectation of uneventful peri-procedural period while intentionally contrasting the guidelines, assuming those guidelines to be limited in application by being based on incomplete evidence.

Neuraxial interventions are elective non-emergent procedures as far as when meant for regional anesthesia and/or acute/chronic pain management; including even for labor analgesia wherein though under-explored, yet definitive alternative analgesic methods are always available when neuraxial access cannot be waited for per guidelines' time-frames. Exploration of known yet under-explored alternatives to neuraxial interventions should not be deterred in the scenarios where patients' medication profile do not allow neuraxial access by

anesthesia providers or pain practitioners without breaching the minimum standards accrued by evidence based guidelines or recommendations. Even though the incidence of neurological complications post-neuraxial access is inherently very rare (<1:10,000)¹¹, the risk for incidence of complications certainly increases with anticoagulants coming into the play^{2,12,13} and it is this risk that the well-informed patients, well-conscientious providers and well-aware payers would willingly take only based on the available clear-cut minimum time-line standards' guidelines for neuraxial interventions in patients receiving medications that affect their hemostasis.

In summary, the 2015 guidelines¹ guide providers' steps in the right direction from 2010 guidelines although are not yet completely clear in few but important avenues of neuraxial anesthesia-analgesia for patients on medications affecting their hemostasis.

References

1. NAROUIZE S, BENZON HT, PROVENZANO DA, BUVANENDRAN A, DE ANDRES J, DEER TR, RAUCK R, HUNTOON MA: Interventional spine and pain procedures in patients on antiplatelet and anticoagulant medications: guidelines from the American Society of Regional Anesthesia and Pain Medicine, the European Society of Regional Anaesthesia and Pain Therapy, the American Academy of Pain Medicine, the International Neuromodulation Society, the North American Neuromodulation Society, and the World Institute of Pain. *Reg Anesth Pain Med*; 40:182-212, 2015.
2. HORLOCKER TT, WEDEL DJ, ROWLINGSON JC, ENNEKING FK, KOPP SL, BENZON HT, BROWN DL, HEIT JA, MULROY MF, ROSENQUIST RW, TRYBA M, YUAN CS: Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy: American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines (Third Edition). *Reg Anesth Pain Med*; 35:64-101, 2010.
3. JAMES A: Committee ON Practice Bulletins-Obstetrics: Practice bulletin no. 123: thromboembolism in pregnancy. *Obstet Gynecol*; 118:718-729, 2011.
4. HARDER KA, BLOOMFIELD JR, SENDELBACH SE, SHEPHERD MF, RUSH PS, SINCLAIR JS, KIRSCHBAUM M, BURNS DE: Improving the Safety of Heparin Administration by Implementing a Human Factors Process Analysis. In: *Henriksen K, Battles JB, Marks ES, Lewin DI (editors). Advances in Patient Safety: From Research to Implementation (Volume 3: Implementation Issues)*. Rockville (MD): Agency for Healthcare Research and Quality (US); 2005 Feb. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK20570/>
5. KATZ D, BEILIN Y: Disorders of coagulation in pregnancy. *Br J Anaesth*; 115:ii75-88, 2015.
6. Clasp (Collaborative Low-Dose Aspirin Study In Pregnancy) Collaborative Group: Clasp: a randomised trial of low-dose aspirin for the prevention and treatment of pre-eclampsia among 9364 pregnant women. *Lancet*; 343:619-629, 1994.
7. American College of Obstetricians and Gynecologists; Task Force on Hypertension in Pregnancy: Hypertension in pregnancy. Report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy. *Obstet Gynecol*; 122:1122-1131, 2013.
8. LEFEVRE ML: U.S. Preventive Services Task Force: Low-dose aspirin use for the prevention of morbidity and mortality from preeclampsia: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med*; 161:819-826, 2014.
9. WERNER EF, HAUSPURG AK, ROUSE DJ: A Cost-Benefit Analysis of Low-Dose Aspirin Prophylaxis for the Prevention of Preeclampsia in the United States. *Obstet Gynecol*; 126:1242-1250, 2015.
10. American Society of Anesthesiologists Committee: Practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration: application to healthy patients undergoing elective procedures: an updated report by the American Society of Anesthesiologists Committee on Standards and Practice Parameters. *Anesthesiology*; 114:495-511, 2011.
11. MOEN V, DAHLGREN N, IRESTEDT L: Severe neurological complications after central neuraxial blockades in Sweden 1990-1999. *Anesthesiology*; 101:950-959, 2004.
12. STAFFORD-SMITH M: Impaired haemostasis and regional anaesthesia. *Can J Anaesth*; 43:R129-141, 1996.
13. NEAL JM, BARRINGTON MJ, BRULL R, HADZIC A, HEBL JR, HORLOCKER TT, HUNTOON MA, KOPP SL, RATHMELL JP, WATSON JC: The Second ASRA Practice Advisory on Neurologic Complications Associated With Regional Anesthesia and Pain Medicine: Executive Summary 2015. *Reg Anesth Pain Med*; 40:401-430, 2015.

