

# Coagulation management in epidural steroid injection

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## Abstract

The objective of this study was to review all published articles in the English language literature about the coagulation management of epidural corticosteroid injections (ESI) in humans. ESI are among the most commonly used procedures to manage chronic spinal pain, yet there is no conclusive review on the coagulation management of this popular procedure. We searched for reports using MEDLINE and EMBASE with the terms 'epidural and steroids', 'corticosteroids' or 'glucocorticosteroids', 'coagulation', and 'haematoma' up to and including the year 2012. Reports were also located through references of articles. We conclude that even though epidural steroid injection is one of the most used techniques in treating radicular pain, correct management of coagulation is necessary.

**Key words:** chronic pain, epidural injections, coagulation, steroids

Anaesthesiology Intensive Therapy 2014, vol. 46, no 3, 195–199

Epidural steroid injections (ESI) are commonly used to temporarily alleviate chronic pain [1]. Despite its acceptance as a relatively safe procedure, an epidural steroid injection is not without risk [1, 2]. An epidural injection delivers steroids into the epidural space around spinal nerve roots to relieve pain caused by irritated spinal nerves. The steroid used in the epidural injection reduces the inflammation of those nerves, which is often the source of the pain [3]. Bleeding into the epidural space is a serious complication after an epidural injection [4, 5]. Particular care is needed in individuals with disturbed clotting either from medical problems, or medication. The benefits and risks of an epidural should be considered on an individual patient basis and after discussion with the cardiologist [2, 6].

The aim of this review was to present the coagulation management of steroids epidural injection, since ESI is a common treatment in a wide variety of patient populations.

In this review, we present all papers that have been published about the systemic effects of steroids following ESI in humans in the English language literature up to and including the year 2012. We looked for published reports using Medline and Embase services, with the search terms 'epidural and steroids', 'corticosteroids' or 'glucocorticosteroids systemic effects'. Reports were also located through references of articles. Only objective findings outside the

epidural space were included, and subjective findings such as the patient's global assessment of the physician and pain following ESI were not included.

## BLEEDING COMPLICATIONS — SPINAL HAEMATOMA

The most feared complications following epidural or intrathecal puncture is spinal haematoma. This event is rare: its commonly quoted estimated incidence is less than 1:150,000 and 1:220,000 [7] after epidural and spinal procedures, respectively [8, 9]. Even if a rare condition, it is particularly serious as the pressure effects of the haematoma can lead to compression and/or ischaemia of the spinal cord and subsequent paralysis [10]. Vandermeulen et al. [11] have compiled 61 cases of spinal haematoma following neuroaxial procedures in patients treated with heparin, antiplatelet agents (nonsteroidal anti-inflammatory drugs NSAIDs, ticlopidine).

The risk of spinal haematoma is increased in anti-coagulated patients who undergo lumbar puncture or neuraxial anaesthesia [12]. The neurologic dysfunction resulting from haemorrhagic complications associated with central neural blockade is unknown [12]. Haemorrhage into the spinal canal most commonly occurs in the epidural space, most likely because of the prominent

**Table 1.** Guidelines to prevent spinal haematoma following epidural/intrathecal/spinal procedures and perineural haematoma following peripheral nerve procedures. Prior to neuraxial/nerve procedure: minimum time between last dose of anticoagulant and spinal injection or neuraxial/nerve catheter placement. While neuraxial/nerve catheter in place: restrictions on use of anticoagulants in patients. After neuraxial/nerve procedure: minimum time between neuraxial/nerve catheter removal or spinal/nerve injection and next anticoagulant dose

Medication	Prior to neuraxial/nerve procedure	While neuraxial/nerve catheter in place	After neuraxial/nerve procedure
Heparin unfractionated 5,000 units q8 or q12 hr	May be given; no time restrictions for catheter placement/removal or spinal injections		
Heparin unfractionated 7,500 units SQ q8 hr	8 hrs	Contraindicated while catheter in place	2 hrs
Enoxaparin 40 mg SQ qday	12 hrs (longer in renal impairment)	May be given. Must wait 6–8 hrs after catheter placement before giving dose. Must wait 18–24 hrs after last dose before removing catheter	2 hrs
Enoxaparin 30 mg SQ q12hr or 40 mg SQ q 12hr	12 hrs (longer in renal impairment)	Contraindicated while catheter in place	2 hrs
Fondaparinux < 2.5 mg SQ qday	48 hrs (longer in renal impairment)		
Warfarin	When INR < 1.5	Contraindicated while catheter in place.	2 hrs
Aspirin/NSAIDs	May be given, no time restrictions for catheter placement or removal		
Abciximab	48 hrs	Contraindicated while catheter in place	2 hours
Clopidogrel	7 days		
Prasugrel	7 days		
Alteplase 2 mg dose for catheter clearance	May be given; no time restrictions for catheter placement or removal (maximum dose 4 mg/24 hours)		
Alteplase full dose for stroke, MI	10 days	Contraindicated while catheter in place	10 days

epidural. Epidural haematoma may be very difficult to diagnose following regional block or in the presence of an epidural infusion, because the signs and symptoms can either be masked or ascribed to the effects of the epidural block or infusion [13].

It is thus crucial to have patients with the following signs and symptoms immediately assessed by medical staff: severe back pain (in the epidural site but may occur in the buttocks or radiate into the legs), tenderness at the epidural site, any severe or prolonged motor block or new sensory block, faecal or urinary incontinence, paraplegia (late sign).

Clinically significant cases are usually seen in the presence of abnormal coagulation of bleeding disorder, and the onset of symptoms is usually faster than that seen with an abscess. Benzon et al. [14] showed acute onset of quadriparesis, weakness of arms and legs, 14 hours after a procedure in a patient in treatment with diclofenac, clopidogrel and acetylsalicylic acid (spinal injection in C2–C7). Ghaly et al. [15] presented a case of haematoma in a patient treated with diclofenac, two hours after epidural steroid injection in C5–C2 and Xu et al. [16] shows an epidural haematoma in a patient despite strict adherence to anticoagulation guidelines.

## GUIDELINES

Guidelines from national societies of anaesthesiologists are expert opinions based on large case series, case reports and pharmacological data of the anticoagulant drugs involved. These guidelines always include: a minimum time interval that should be respected between the last dose of an anticoagulant and insertion of a neuraxial needle/catheter or the removal of that catheter, a minimum time interval that should be respected between the insertion of a neuraxial needle/catheter or the removal of that catheter and the next dose of anticoagulant, and minimal values of clotting times necessary for the performance of a neuraxial technique (if applicable). A summary of the recommended time intervals can be found in Table 1.

## TREATMENTS

### WARFARIN (COUMADIN)

This must be stopped prior to placement and normal coagulation studies confirmed. Chronic warfarin therapy increases the risk of spinal haematoma following lumbar puncture. The addition of agents that affect different parts of the clotting mechanism probably increase the risk for spinal haematoma and do so without further elevation of the prothrombin time (PT) or international normalised ratio (INR).

Warfarin should be discontinued in anticipation of the spinal procedure and normalisation of the INR documented procedure. If a spinal procedure is performed on a patient with an INR > 1.2, close neurologic testing of motor and sensory function should be performed for at least 24 hours to ensure prompt recognition and treatment of spinal haematoma. In emergent cases, the injection of vitamin K or transfusion of fresh frozen plasma may counteract the effects of warfarin. So warfarin must be stopped for seven days prior to a procedure; if INR is < 1.3 the procedure can be performed but if INR is 1.5 the procedure cannot be done [17].

### **UNFRACTIONATED HEPARIN**

Minidose prophylaxis is not a contraindication; blocks may be performed up to one hour prior to heparin administration. Removal of catheters should occur one hr prior to, or four hr after, heparin dosing. It should be avoided in patients on therapeutic doses of heparin or in those with increased PTT. There is no contraindication to spinal puncture in patients receiving subcutaneous heparin as a prophylaxis for deep venous thrombosis providing that the total dose is < 10,000 U. Higher dosing may result in sustained prolongation of the activated partial thromboplastin time (aPTT). These patients are managed similarly to those who are systematically heparinised. Delaying the scheduled heparin injection until after the puncture may reduce the risk of spinal haematoma. The risk of bleeding is probably increased in debilitated patients on prolonged therapy. Patients receiving heparin for longer than four days need to have a platelet count assessment because of the potential for heparin-induced thrombocytopenia. Removal of the epidural catheter occurs at least six hours after the last dose of unfractionated heparin. After removal, the next dose should not be given for at least two hours. Vandermeulen et al. [11] reported 30 cases of epidural haematoma in patients receiving fractionated or unfractionated heparin therapy [18].

### **LOW MOLECULAR WEIGHT HEPARIN**

For patients treated with low molecular weight heparin (LMWH), it is necessary to wait 12–24 hrs prior to performing neuroaxial block, if a bloody needle or catheter placement occurs [19]. LMWH should be delayed until 24 h postoperatively to decrease the risk of spinal haematoma [20]. Early postoperative dosing, twice-daily dosing, and traumatic needle placement have been identified as risk factors for spinal haematoma associated with neuraxial anaesthesia. Because significant anticoagulant activity persists for 12 hours after low-dose injection (and 24 hours for a high-dose injection), these time intervals should be observed before a spinal procedure [21, 22].

### **THROMBOLYTIC/FIBRINOLYTIC THERAPY**

Patients should be asked before starting thrombolytic/fibrinolytic therapy whether there has been a recent spinal procedure such as a lumbar puncture. This will allow for appropriate monitoring in cases where the drug must be administered. Guidelines recommend the avoidance of thrombolytic drugs for ten days following puncture of non compressible vessels. Measurement of fibrinogen level may be helpful in monitoring a patient who has undergone or will undergo a spinal procedure [23, 24].

### **ANTIPLATELET THERAPY**

ASA and NSAIDs should be safe in normal patients with normal coagulation profiles; more potent agents should be stopped and a waiting period observed. The use of NSAIDs alone does not seem to increase the risk of spinal haematoma from spinal puncture. At this time, there do not seem to be specific concerns related to the timing of spinal puncture in relation to the dosing of NSAIDs or post procedure monitoring. Vandermeulen et al. [11] only identified two haematomas related to aspirin and indomethacin in their series of 61 patients.

### **THIENOPYRIDINE DERIVATIVES**

The agents in this class include clopidogrel and ticlopidine. The patient should be carefully assessed for other factors that might lead to bleeding such as easy bruising/bleeding, female sex, and increased age. The addition of other medications affecting different clotting mechanisms will probably increase the chance for spinal haematoma. Clopidogrel should be stopped for seven days prior to a neuraxial procedure [25]. Neuraxial procedures should be avoided for four weeks following a glucoprotein receptor antagonist thienopyridine injection [26].

### **GP IIB/IIIA RECEPTOR ANTAGONISTS**

This class of antiplatelet drugs includes abciximab, eptifibatid, and tirofiban. Normal platelet aggregation is usually achieved eight hours after discontinuation of tirofiban and eptifibatid, and 24–48 hours after discontinuing abciximab. Injections should be delayed for 24–48 h following abciximab and 4–8 h after tirofiban [25].

### **DISCUSSION**

Epidural steroid injections are relatively safe procedures, although the risk of haemorrhagic complications in patients undergoing long-term anticoagulation therapy is higher. Patient management is based on appropriate timing of needle placement and catheter removal relative to the timing of anticoagulant drug administration. The American Society of Regional Anesthesia and Pain Medicine [27] has specific

guidelines for the treatment of these patients when they undergo neuraxial anaesthetic procedures. Long-term anticoagulation with warfarin is often indicated for patients with a history of mechanical heart valves, and atrial fibrillation. In addition, patients with bare metal or coronary stents require antiplatelet therapy with aspirin and thienopyridine derivatives (e.g. clopidogrel) for varying durations [28].

Spinal haematoma, defined as symptomatic bleeding within the spinal neuraxis, is a rare and potentially catastrophic complication of spinal or epidural anaesthesia [25, 29].

Warfarin is a widely used oral anticoagulant. It inhibits the synthesis of vitamin K dependent coagulation factor II, VII, IX and X and anticoagulant proteins C and S. Warfarin is used extensively for prophylaxis and treatment of deep vein thrombosis and pulmonary embolism and thromboembolism prophylaxis in patients with mechanical prosthetic heart valves or atrial fibrillation. The therapeutic range of warfarin typically is at an INR of between 2 and 3. An epidural or spinal needle is placed in patients anticoagulated with warfarin, who had stopped therapy seven days prior to placement and who have been confirmed as having normal coagulation. Removing a catheter from a patient on low dose therapy (5 mg/day) is reported to be safe.

Systemic heparinisation represents an increased risk for spinal bleeding. Heparin infusion should be discontinued and aPTT normalised before the procedure. A subsequent dose of intravenous heparin should not be administered for at least an hour after the procedure.

The combined use of other anticoagulants with unfractionated heparin may increase the risk of spinal haematoma. These include antiplatelets, low molecular weight heparin (LMWH), and oral anticoagulants. Standard unfractionated heparin in minidose prophylaxis is not a contraindication. Blocks may be performed up to one hour prior to heparin administration, removal of catheters should occur one hr prior to, or four hr after, heparin dosing, and avoided in patients on therapeutic doses of heparin or in those with increased PTT.

LMWH is the recommended thromboprophylactic agent following major orthopaedic and general surgical procedures. It is important for there to be a number of dosing regimens for LMWH, including low-dose (thromboprophylactic) and high dose (therapeutic) applications. There are many pharmacological differences between standard unfractionated heparin and LMWH, including prolonged half-life and irreversibility with protamine [30]. The first postprocedural LMWH dose should be administered 18–24 hours later, to allow for adequate haemostasis if a bloody needle or catheter placement occurs. LMWH should be delayed until 24 h postoperatively to decrease the risk of spinal haematoma, removing catheters two hrs prior to first LMWH dose. If the catheter is already present, wait ten hours after the last

dose to pull it, and wait another two hours before restarting it [31]. Monitoring anti Xa level is not recommended. The anti Xa level is not predictive of the risk of bleeding and is not helpful in its management. Preoperative LMWH: altered coagulation, needle placement should occur at least 10–12 hours after the LMWH dose. Post operative: twice daily dosing unsafe, increased risk of spinal haematoma, single daily dosing is safer.

There is no clear definition of how long spinal puncture should be avoided following termination of thrombolytic/fibrinolytic therapy; however, significant defects in haemostasis are present for longer than 24 hours. Patients who have recently had or who are likely to receive thrombolytic/fibrinolytic therapy should be warned against receiving a spinal puncture except in very unusual circumstances. The concomitant use of heparin and/or antiplatelet agents further increases the risk of procedure-related and spontaneous bleeding. The use of these drugs is increasing and vigilance is warranted. Guidelines detailing original contraindications for thrombolytic drugs suggest evidence of these drugs for ten days following puncture of non compressible vessels [32]. Preoperative evaluation should determine whether fibrinolytic or thrombolytic drugs have been used preoperatively. Patients receiving fibrinolytic and thrombolytic drugs should be cautioned against receiving spinal or epidural anaesthetics, except in highly unusual circumstances [33].

The antiplatelet medications include a diverse group of agents in terms of their effects on platelet function; it is not possible to extrapolate between the various groups of drugs regarding spinal procedures [34]. These agents include NSAIDs, thienopyridine derivatives, and GP IIb/IIIa antagonists. Cyclooxygenase inhibitors disrupt the formation of thromboxane A<sub>2</sub>, which disturbs vasoconstriction and secondary platelet aggregation. Aspirin irreversibly inhibits cyclooxygenase for the life of the platelets, whereas non steroidal drugs reversibly inhibit this enzyme. Procedural postponement may not be necessary, except in situations in which bleeding times are excessively prolonged. Another option is to have patients without aspirin for 7–10 days and nonsteroidal antiinflammatory drugs. ASA and NSAIDs should be safe in normal patients with normal coagulation profiles; more potent agents should be stopped and a waiting period observed. Thienopyridine inhibitors, such as clopidogrel, interfere with primary and secondary platelet aggregations. These agents interfere with ADP binding and subsequent activation of the GP IIb/IIIa receptor complex [35].

GP IIb/IIIa receptor antagonists affect platelet-fibrinogen and platelet von Willebrand factor binding to inhibit platelet aggregation. The true risk of spinal haematoma in patients on thienopyridine derivatives or GP IIb/IIIa antagonists is unknown. The concomitant use of aspirin with these agents

may increase the risk for spinal haematoma. The GP IIa/IIIb antagonists have a profound effect on platelet aggregation and spinal puncture should be avoided until platelet function has recovered. These agents are contraindicated within four weeks of surgery [36].

## CONCLUSIONS

Changes in coagulation, fibrinolytic and thrombolytic mechanisms escalate the risks. The increased vigilance regarding thromboembolisms and the introduction of more efficacious antiplatelet agents has introduced a degree of complexity into the performance of spinal procedures. The presence and continued evolution of antiplatelet agents, various heparin derivatives and thrombolytic therapy, requires a thorough investigation of a patient's medication history.

Continued surveillance of the literature will be necessary to stay abreast of the newer agents that are sure to appear, as well as any changes in the recommendations regarding agents currently in use.

## References:

- Bellini M, Barbieri M: Systemic effects of epidural steroid injections. *Anaesthesiol Intensive Ther* 2013; 45: 93–98.
- Abdi S, Datta S, Trescot AM *et al.*: Epidural steroid in the management of chronic spinal pain: a systematic review. *Pain Physician* 2007; 10: 185–212.
- Abram SE, O'Connor TC: Complications associated with epidural steroid injections. *Reg Anesth* 1996; 21: 149–162.
- Horlocker TT, Baiwa ZH, Ashraf Z *et al.*: Risk assessment of hemorrhagic complications associated with nonsteroidal anti-inflammatory medications in ambulatory pain clinic patients undergoing epidural steroid injection. *Anesth Analg* 2002; 95: 1691–1697.
- Shah RV, Kaye A: Bleeding risk and interventional pain management. *Curr Opin Anaesthesiol* 2008; 21: 433–438.
- Kovesi T, Royston D: Is there a bleeding problem with platelet-active drugs? *Br J Anaesth* 2002; 88: 159–163.
- Snarr J: Risk, benefits and complications of epidural steroid injections: a case report. *AANA J* 2007; 75: 183–188.
- Reitman CA, Watters W: Subdural haematoma after cervical epidural steroid injection. *Spine* 2002; 27: E174–E176.
- Linn AJ, Desilva C, Peeters Asdourian C: Thromboembolic stroke: a rare complication associated with periprocedural management of an epidural steroid injection. *Pain Physician* 2009; 12: 159–62.
- Gustafsson H, Rutberg H, Bengtsson M: spinal haematoma following epidural analgesia. Report of a patient with ankylosing spondylitis and a bleeding diathesis. *Anaesthesia* 43: 220–222, 1988.
- Vandermeulen EP, Van Aken H, Vermeylen J: Anticoagulants and spinal-epidural anesthesia. *Anesth Analg* 1994; 79: 1165–1177.
- Horlocker TT, Wedel DJ, Rowlingson JC *et al.*: 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* 2010; 35: 64–101.
- Wulf H: Epidural anaesthesia and spinal haematoma. *Can J Anaesth* 1996; 43: 1260–1271.
- Benzon HT, Wong HY, Sidduqui T, Ondra S: Caution in performing epidural injection in patients on several antiplatelet drugs. *Anesthesiology* 1999; 91: 1558–1559.
- Ghaly RF: Recovery after high-dose methylprednisolone and delayed evacuation: a case of spinal epidural haematoma. *J Neurosurg Anesthesiol* 2001; 13: 323–328.
- Xu R, Bydon M, Gokaslan ZL, Wolinsky JP, Witham TF, Bydon A: Epidural steroid injection resulting in epidural haematoma in a patient despite strict adherence to anticoagulation guideline. *J Neurosurg Spine* 2009; 11: 358–364.
- Endres S, Bogduk N, Schlimgen M, Shufelt A, Endres B: Efficacy/safety of performing fluoroscopically guided spinal interventions in conjunction with anticoagulation therapy. *Pain Med* 2011; 12: 1442.
- Atwater B: The risk of bleeding complications after pain procedures in anticoagulated patients. *Curr Pain Headache Rep* 2005; 9: 30–35.
- Cosmi B, Hirsh J: Low molecular weight heparins. *Curr Opin Cardiol* 1994; 9: 612–618.
- Ain RJ, Vance MB: Epidural haematoma after epidural steroid injection in a patient withholding enoxaparin per guidelines. *Anesthesiology* 2005; 102: 701–703.
- Abram SE, O'Connor TC: Complications associated with epidural steroid injections. *Reg Anesth* 1996; 21: 149–162.
- Bergqvist D, Lindblad B, Matzsch T: Low molecular weight heparin for thromboprophylaxis and epidural/spinal anaesthesia: is there a risk? *Acta Anaesthesiol Scand* 1992; 36: 605–609.
- McEvoy MD, Bailey M, Taylor D, Del Schutte H: Non compliance in the inpatient administration of enoxaparin in conjunction with epidural or spinal anesthesia. *J Arthroplasty* 2000; 15: 604–607.
- Gogarten W, Vandermeulen E, van Aken H, Kozek S, Llau JV, Samama CM: Regional anaesthesia and antithrombotic agents: recommendations of the European Society of Anaesthesiology. *Eur J Anaesthesiol* 2010; 27: 999–1015.
- Odoom JA, Sih IL: Epidural analgesia and anticoagulant therapy. *Anaesthesia* 1983; 38: 254–259.
- Layton KF, Kallmes D, Horlocker T: Recommendations for anticoagulated patients undergoing image guided spinal procedures. *Am J Neuroradiol* 2006 27: 468–470.
- Horlocker T, Wedel DJ, Rowlingson JC *et al.*: 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* 2010; 35: 64–101.
- Ho AM, Chung DC, Joynt GM: Neuraxial blockade and haematoma in cardiac surgery: estimating the risk of a rare adverse event that has not /yet) occurred. *Chest* 2000; 117: 551–555.
- Rao TLK, El AA: Anticoagulation following placement of epidural and subarachnoid catheters: an evaluation of neurologic sequelae. *Anesthesiology* 1981; 55: 618–620.
- Manchikanti L, Boswell MV, Singh V: Comprehensive evidence-based guidelines for interventional techniques in the management of chronic spinal pain. 2009; 12: 699–802.
- Breivik H, Bang U, Jalonen J, Vigfússon G, Alahuhta S, Lagerjanser M: Nordic guidelines for neuraxial blocks in disturbed haemostasis from the Scandinavian Society of Anaesthesiology and Intensive Care Medicine. *Acta Anaesthesiol Scand* 2010; 54: 16–41.
- International Spine Intervention Society. Anticoagulants. In: *Bogduk N (ed): Practice guidelines for spinal diagnostic and treatment procedures*, 2<sup>nd</sup> ed. International Spine Intervention Society, San Francisco, 2013. (In Press).
- Llau JV, De Andres J, Gomann C, Gomez-Luque A, Hidalgo F, Torres LM: Anticlotting drugs and regional anaesthetic and analgesic techniques: comparative update of the safety recommendations. *Eur J Anaesthesiol* 2007; 24: 387–398.
- Horlocker TT, Wedel DJ, Schroeder DR *et al.*: Preoperative antiplatelet therapy does not increase the risk of spinal haematoma associated with regional anesthesia. *Anesth Analg* 1995; 80: 303–309.
- Endres S: Efficacy/safety of performing fluoroscopically guided spinal interventions in conjunction with anticoagulation therapy. Paper presented at the 19<sup>th</sup> Annual Scientific Meeting of the International Spine Intervention Society, Chicago, August 10–13, 2011, ISIS.
- Horlocker TT, Bajwa ZH, Ashraf Z *et al.*: Risk assessment of hemorrhagic complications associated with nonsteroidal anti-inflammatory medications in ambulatory pain clinic patients undergoing epidural steroid injection. *Anesth Analg* 2002; 95: 1691–1697.

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Received: 11.09.2013

Accepted: 15.03.2014