Epidural Hematoma After Epidural Blockade in the United States: It's Not Just Low Molecular Heparin Following Orthopedic Surgery Anymore

Terese Horlocker, MD and Sandra Kopp, MD

pidural hematoma is a rare, but serious complication of neuraxial blockade, the frequency of which is affected by patient and practice variables. Recent publications have been epidemiologic series (typically from Europe) or included only cases of epidural hematoma (without overall population demographics).1-7 In this issue, Bateman et al.8 report the frequency of epidural hematoma within a multicenter North American consortium of academic anesthesia departments. Their findings are relevant in that they represent current applications for epidural analgesia as well as risk for epidural hematoma. Specifically, the frequency is similar to that of other recent epidemiologic series (and is higher than reported 2 decades ago when thromboprophylaxis was less aggressive); epidural analgesia for labor and delivery is associated with less risk of symptomatic neuraxial bleeding than epidural analgesia for a non-obstetric surgical indication; and the demographics of the patients reflect the diminished utilization of epidural analgesia for major orthopedic surgery and continued application among high-risk patients undergoing major abdominal, thoracic, or open vascular surgery.

Before the introduction of potent antithrombotic drugs and routine thromboprophylaxis, the risk of neuraxial bleeding after epidural blockade was assumed to be a rare event. For example, in a meta-analysis published in 1993, **Tryba'** identified 13 cases of epidural hematoma following 850,000 epidural anesthetics and calculated the incidence to be <1 in 150,000. The following year, Vandermeulen et al.¹⁰ reported 46 cases of epidural hematoma associated with epidural anesthesia/analgesia occurring between 1906 and 1994, representing the first century of neuraxial block. Importantly, 60% of cases occurred in the **last decade** of the study period. The authors stated that it was unclear whether these results represented an increased frequency of epidural hematoma, an increased number of patients undergoing epidural blockade and/or increased reporting of anesthetic complications. On the basis of the meta-analysis performed by Tryba⁹ and their case series, the authors concluded:¹⁰

Knowledge of the pharmacologic properties of the different anticoagulants and their combination with strict patient selection, individual risk-benefit analysis, appropriate regional anesthetic techniques, respecting proper time intervals separating anticoagulant and epidural or spinal anesthesia, and continuous awareness of the possibility that a compressing neuraxial hematoma may develop should enable us to make anesthetic practice safer without withholding anesthetic techniques from patients who would most certainly benefit from them.

It was into this climate of cautious optimism that neuraxial blockade was performed in the presence of low molecular weight heparin (LMWH). Enoxaparin, the first LMWH approved for general use in the United States, was released in 1993. Labeled applications included thromboprophylaxis after total knee and hip replacement, a procedure in which patients are known to have moderate to severe postoperative pain that was successfully treated with epidural analgesia. Safety was not a concern in that >10 years' experience in Europe. Pharmaceutical companies estimated that several million patients had received LMWH while undergoing neuraxial block with only a single epidural hematoma.^{11,12} However, in the United States, 40 cases of neuraxial hematoma (over half of which involved an epidural technique) were voluntarily reported through the MedWatch system over a 5-year period (May 1993-May 1998), representing an estimated risk of neuraxial hematoma of approximately 1 in 3000 epidural anesthetics. However, this is most likely an underestimation, because additional epidural hematomas occurred but were not reported to the MedWatch system at the time of the risk calculation.¹³ The marked disparities in frequencies in the North American and European reports were attributed to differences in dosing, timing of LMWH administration, and preference for spinal (rather than continuous epidural) techniques in Europe.14 The increased risk of epidural hematoma in patients anticoagulated with LMWH prompted a reevaluation of the relative risks and benefits of neuraxial blockade. For example, American Society of Regional Anesthesia and Pain Medicine guidelines recommended *against* the administration of twice daily LMWH in a patient with an indwelling epidural catheter,

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noting that improved analgesia was not balanced with the risk of paraplegia.^{13,14}

Not surprisingly, the complication of epidural hematoma became almost synonymous with LMWH administration and epidural analgesia after major orthopedic surgery. However, in the 5 following years, few were described.¹³ The decline in the number of cases voluntarily reported was ascribed to decreased reporting, publication of national recommendations by the German Society for Anaesthesiology and Intensive Care in 1997¹⁵ and American Society of Regional Anesthesia and Pain Medicine¹⁶ in 1998, and/or avoidance of neuraxial blockade in patients receiving LMWH. However, during this same time frame, and almost certainly associated with the decrease in reported cases, the analgesic superiority of peripheral techniques for patients undergoing total hip and knee replacement was determined.¹⁷

It would seem logical that with the number of LMWHassociated cases decreasing, the overall frequency of neuraxial hematoma associated with epidural analgesia would also fall. Unfortunately, that was not the case. More recent series and epidemiologic studies suggest that epidural hematoma after epidural blockade occurs more frequently than initially estimated, ranging from 1:2700 to 1:19,505 patients (1–4, 7, 8), and that there are patient populations at significantly higher risk. For example, Moen et al.⁷ reported the overall frequency of neuraxial hematoma after epidural block to be 1:18,000, with bleeding occurring rarely in parturients (1:200,000) compared with elderly female patients undergoing total knee replacement (1:3800).⁷ Similar results by Pöpping et al.¹ reported the overall risk of symptomatic epidural hematoma to be 1:4741, but increased to approximately 1:1000 for elderly women undergoing lower extremity surgery.

Bateman et al.⁸ confirm the findings of Moen et al.⁷ that obstetric patients undergoing epidural catheterization are at significantly lower risk for spinal hematoma compared with perioperative (non-obstetric surgical) patients undergoing epidural catheterization. There were 7 epidural hematomas among 142,287 patients undergoing epidural anesthesia/ analgesia, for an overall risk of 1 in 20,326 epidural catheterizations. However, none of the 79,837 obstetric patients who underwent epidural placement developed a neuraxial hematoma requiring decompressive laminectomy (upper limit of 95% confidence interval, 1:21,643), compared with 7 of 62,450 patients who received perioperative epidural catheter placement (1:9000; 95% confidence interval, 1:22,189-1:4330). This difference in incidence is even more striking when considering that bloody taps are more common in the obstetric population and have been reported to occur in approximately 3% of all obstetric epidural placements.⁵ The relatively hypercoagulable state of pregnancy may be protective and offers one possible reason for the lower rate of neuraxial hematomas in this population. The normal anatomic changes that occur in the aging spine may provide another explanation for the differing incidence. Both Moen et al.⁷ and Pöpping et al.¹ cited osteoporotic deformities as likely contributing to the risk of symptomatic vertebral canal bleeding after epidural blockade in elderly women. The prevalence of vascular disease, osteoporosis, and degenerative changes of the spine increase with age,

ultimately resulting in a decrease in the volume of the epidural space.¹⁸ In contrast, the **younger obstetric** patient has a **more compliant** epidural space, with the ability to **accommodate** a larger volume of blood before the onset of symptoms. Magnetic resonance imaging after epidural blood patch revealed blood leaking out through the intravertebral foramina after injection in young individuals.¹⁹ To date, all case reports of neuraxial hematomas in obstetric patients have occurred in parturients with an **existing** coagulopathy (hemorrhage, **preeclampsia**, hemolysis-elevated liver enzymes-low platelets) either at the time of epidural placement or **removal**. There have been no published cases associated with antithrombotic/antiplatelet therapy.¹⁶

Finally, the surgical procedures of the patients in the series by Bateman et al.8 reflect the diminished utilization of epidural analgesia for major orthopedic surgery. Current evidence suggests that benefits of epidural analgesia are probably limited to high-risk patients undergoing major abdominal, thoracic, or open vascular surgery.²⁰ There is increasing evidence that alternative analgesic techniques, such as wound infiltration with sustained release (liposomal) bupivacaine, wound catheter infusions, and single injection peripheral blocks are as effective as epidural analgesia for many patients undergoing these procedures. Nearly 2 decades ago, peripheral techniques replaced epidural analgesia as the gold standard for patients undergoing major lower extremity surgery. As the prevention and treatment of thromboembolism progresses, we must continue to evaluate less invasive analgesic methods recognizing, "When you're at the cutting edge, someone's going to bleed."

RECUSE NOTE

Dr. Terese Horlocker is the section Editor for Regional Anesthesia for the Journal. This manuscript was handled by Dr. Steven L. Shafer, Editor-in-Chief, and Dr. Horlocker was not involved in any way with the editorial process or decision.

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The Risk and Outcomes of Epidural Hematomas After Perioperative and Obstetric Epidural Catheterization: A Report from the Multicenter Perioperative Outcomes Group Research Consortium

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BACKGROUND: In this study, we sought to determine the frequency and outcomes of epidural hematomas after epidural catheterization.

METHODS: Eleven centers participating in the Multicenter Perioperative Outcomes Group used electronic anesthesia information systems and quality assurance databases to identify patients who had epidural catheters inserted for either obstetrical or surgical indications. From this cohort, patients undergoing laminectomy for the evacuation of hematoma within 6 weeks of epidural placement were identified.

RESULTS: Seven of 62,450 patients undergoing perioperative epidural catheterizations developed hematoma requiring surgical evacuation. The event rate was 11.2×10^{-5} (95% confidence interval [CI], 4.5×10^{-5} to 23.1×10^{-5}). Four of the 7 had anticoagulation/antiplatelet therapy that deviated from American Society of Regional Anesthesia guidelines. None of 79,837 obstetric patients with epidural catheterizations developed hematoma (upper limit of the 95% CI, 4.6×10^{-5}). The hematoma rate in obstetric epidural catheterizations was significantly lower than in perioperative epidural catheterizations (*P* = 0.003).

CONCLUSIONS: In this series, the 95% CI for the frequency of epidural hematoma requiring laminectomy after epidural catheter placement for perioperative anesthesia/analgesia was 1 event per 22,189 placements to 1 event per 4330 placements. Risk was significantly lower in obstetric epidurals. (Anesth Analg 2013;116:1380–85)

D pidural hematoma is a recognized complication of epidural catheterization. Recent studies examining this complication have been generally limited by being single-center, survey-based, lacking clear denominators, derived from European rather than North American experience, or having incomplete clinical detail about the affected patients.^{1–5} The Multicenter Perioperative Outcomes Group (MPOG) is a consortium of academic anesthesia departments with electronic Anesthesia Information Management Systems (AIMS). MPOG pools perioperative data for research purposes. The consortium studied the event rate for epidural hematomas requiring laminectomy after epidural catheterization for perioperative or obstetric anesthesia/analgesia.

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METHODS

This study was reviewed and approved by the IRBs of each of the contributing institutions. The study was a retrospective, observational study conducted at academic medical centers that are part of the MPOG consortium. Eleven institutions contributed data regarding epidural catheterization for perioperative anesthesia/analgesia and 6 institutions contributed data regarding obstetric epidural catheterization. Details regarding the characteristics of the institutions participating in the study are available in Online Appendix 1 (see Supplemental Digital Content 1, http://links.lww.com/AA/A382).

Investigators queried their AIMS and quality assurance databases for all epidural catheter insertions in operative patients or obstetric labor patients. The study dates varied by institution, depending on when deployment of their AIMS or quality assurance databases was complete. The cohort of all patients who underwent epidural catheterization was then automatically screened for patients undergoing operations within 6 weeks of the catheter placement using AIMS and/or billing records. This subset of patients and secondary operations was reviewed to identify patients undergoing a laminectomy for the evacuation of epidural hematoma.

Information from each patient requiring a decompressive laminectomy, including demographic characteristics, comorbidities, details of epidural catheterization, pre-, intra-, and postoperative coagulation variables, and antiplatelet and anticoagulant medication usage, were manually collected through use of electronic and paper medical chart review.

Author affiliations are provided at the end of the article.

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Table 1. The Total Number of Perioperative EpiduralPlacements and Laminectomies for Hematoma,by Institution

Institution	Dates of query	No. of epidurals placed	No. of decompressive laminectomies for hematoma
1	11/99-3/09	13,764	1
2	8/03-8/09	9123	0
3	1/99-12/10	7616	0
4	1/01-6/08	7110	1
5	10/03-10/09	6179	1
6	4/04-2/08	6101	1
7	1/03-12/08	5539	2
8	7/06-6/09	3912	0
9	1/05-6/09	1778	1
10	2/07-4/09	760	0
11	1/07-1/10	568	0
Total		62,450	7

Data were also collected on the presenting signs and symptoms of the hematoma, imaging findings, time to imaging and laminectomy, and neurological outcome. The data collection form is available in Online Appendix 2 (see Supplemental Digital Content 2, http://links.lww.com/AA/A383).

The point estimate and 95% confidence interval (CI) on the summary event rate across institutions was calculated using the Pearson-Clopper method. Comparisons of the risk between perioperative and obstetric epidural use were performed using the Fisher exact test; a 95% CI on the difference of proportions was also estimated. Calculations were performed using the binom package version 1.0-5 running in R version 2.14.0 (R: A Language and Environment for Statistical Computing; R Foundation for Statistical Computing, Vienna, Austria) and StatXact 9 (Cytel Inc., Cambridge, MA). As a sensitivity analysis, random effects meta-analysis and Bayesian models were obtained (Online Appendix 3, see Supplemental Digital Content 3, http://links.lww.com/AA/A384).

RESULTS

Six institutions reported a total of 79,837 obstetric epidural placements. There were no reported cases of hematoma requiring decompressive laminectomy for obstetric patients. Eleven institutions reported 62,450 epidural catheters inserted for perioperative anesthesia and analgesia.

Table 2. Demographic and Clinical Characteristics of Patients Who Developed Epidural Hematomas Requiring Decompressive Laminectomy After Epidural Catheterization

Patient	Surgery	Age (y)	Comorbidities	ASA physical status	Туре	Level	No. of attempts
1	Sigmoid colectomy	72	DM, HTN, PVD, ESRD (dialysis dependant)	Ш	Epidural	T9–10	Not documented
2	Hepatectomy	62	Metastatic malignancy	II	Epidural	Thoracic	1
3	Renal artery aneurysms repair	86	HTN, osteoporosis, CAD	Ш	Epidural	T10-11	3 by resident, 2 by faculty
4	Revision of total hip replacement	55	DM, ankylosing spondylitis	Ш	Combined spinal/ epidural	L3–4	Multiple (exact number not recorded)
5	Endovascular aortic aneurysm repair	78	COPD, pulmonary hypertension, HTN, CAD, leukemia	IV	Planned epidural; spinal catheter placed	L2-3	Not documented
6	Single lung transplant	67	Pulmonary fibrosis, CAD, osteoporosis	III	Epidural	T8–9	1
7	Infrarenal abdominal aortic aneurysm repair	76	Atrial fibrillation, hypertension, osteoporosis, multiple kyphoplasties for spinal compression fracture, mildly elevated liver function tests	III	Epidural	Low thoracic	Multiple (exact number not recorded)

bid = twice daily; CAD = coronary artery disease; COPD = chronic obstructive pulmonary disease; DM = diabetes mellitus; ESRD = end-stage renal disease; heparin = unfractionated heparin; HTN = hypertension; INR = international normalized ratio (prothrombin time); L = lumbar; NGT = nasogastric tube; PTT = partial thromboplastin time; PVD = peripheral vascular disease; q = every; SQ = subcutaneously; T = thoracic; tid = 3 times daily.

Among these patients, there were 7 decompressive laminectomies for hematoma for an unweighted risk of 1 laminectomy for hematoma per 8921 epidural placements. One institution had 2 events, 5 institutions had 1 event each, and 5 institutions had no events (Table 1).

Patient characteristics, details regarding epidural catheterization, and information on perioperative anticoagulant/ antiplatelet exposure for each case of hematoma requiring laminectomy are reported in Table 2. Five of the 7 epidurals were thoracic, the other 2 were lumbar. One case occurred in the setting of a combined spinal/epidural, another followed accidental dural puncture and placement of a spinal catheter. In all cases, the neuraxial catheter was in situ at the time that signs and symptoms of epidural hematoma were recognized. In 2 instances, the epidural catheters were inserted in the setting of elevated international normalized ratio (1.6 in both cases). In 5 cases, the patients received standard heparin in the perioperative period, and in 4 cases, the patients received aspirin.

Presenting symptoms, timing of the symptoms after epidural catheterization, timing of imaging and laminectomy after first symptoms, and neurological outcome are noted in Table 3. Motor deficits in the lower extremity were present in all 7 cases. The time to first symptoms after placement ranged from 11 to 71 hours. The timing of laminectomy after symptoms varied widely from 6.5 to 54 hours. There was no apparent relationship between the time to laminectomy and neurological recovery (in the 2 cases of complete recovery, laminectomy occurred at 7 hours and 54 hours after symptoms).

The risk of decompressive laminectomy for epidural hematoma among perioperative epidural catheter placement was 11.2×10^{-5} (95% CI, 4.5×10^{-5} to 23.1×10^{-5}); the lower and upper bounds may also be stated as 1 event in 22,189 and 1 event in 4330 epidural placements. The risk of decompressive laminectomies for epidural hematoma among obstetric epidural catheter placements was 0 (95% CI, 0 to 4.6×10^{-5}); the upper bound may be stated as 1 event in 21,643 epidural placements. The risk difference between perioperative and obstetric epidural catheter placement was also 11.2×10^{-5} (95% CI, 5.4×10^{-5} to 23.1×10^{-5}) and was significant (Fisher exact test, P = 0.003).

Placement complications	Preoperative antiplatelet/ anticoagulation therapy (time stopped)	INR/PTT/platelet abnormality when catheter placed	Intraoperative antiplatelet/ anticoagulation therapy	Postoperative antiplatelet/ anticoagulation therapy	INR/PTT/platelet abnormality when hematoma noted
None None	Warfarin (unknown) Heparin 5000 U SQ, dose held for epidural, previous dose 14 h before catheter placement	INR = 1.05 INR = 1.6 (attributed to factor deficiencies from liver dysfunction or inability to absorb vitamin K secondary to biliary obstruction); PTT = 50		— Heparin 5000 U SQ tid (started 7 h postplacement)	 INR = 5.3; PTT = 56.8
None	Aspirin 81 mg daily (7 d before surgery)	_	Aspirin 325 mg down NGT, heparin 15,000 U IV 156 min after catheter placed	_	_
None	-	-	· _	Aspirin 325 mg daily (started day of surgery)	_
Unintended dural puncture with epidural needle	_	—	Heparin 9000 U IV (administered 101 min after catheter placed)	_	_
None	Aspirin 81 mg daily (not stopped)	_		Heparin 5000 U SQ q 12 h (started 5 h postplacement; second dose given 8 h postplacement), aspirin 81 mg daily	_
None	Warfarin (4 d before surgery)	PTT = 37.1, INR = 1.6 on evening before surgery	Heparin 5000 U IV (approximately 2 h postplacement), reversed with protamine at the end of the operation	Aspirin 325 mg daily, heparin 5000 U SQ bid (started day of surgery)	INR = 1.5; PTT = 44

Table 3. Clinical Course of Patients Who Developed Epidural Hematomas Requiring Decompressive Laminectomy After Epidural Catheterization

Patient	Presenting symptoms	Time of first symptoms after epidural placement	Time to imaging after first symptoms	Time to laminectomy after first symptoms	Imaging modality and findings	Neurological outcome
1	No sensation or motor strength below T8	32 h	20 h	22 h	MRI; very large epidural hemorrhage and fluid collection causing severe cord compression in lower cervical and upper and mid thoracic spine	No motor power/ sensation below T8
2	Bilateral inability to move lower extremities despite decreased epidural rate	71 h	10 h	12 h	MRI; large, extensive epidural collection with the most mass effect exerted from T10–11 inferiorly to L5 with severe compression on the spinal cord and thecal sac	T9 paraplegia
3	Bilateral lower extremity dense paraplegia	11 h	4 h	7 h	MRI; hematoma noted from T6 to T10 with extradural collection displacing spinal cord anteriorly against vertebrae. No spinal cord signal changes	Complete recovery
4	Bilateral lower extremity sensory and motor deficits	45 h	5 h	6.5 h	MRI; significant posterior epidural fluid collection from the upper aspect of T11 to the L4 level	Wheelchair bound with urologic dysfunction
5	Bilateral motor and sensory deficit, absent deep tendon reflexes	14 h	3 h	9 h	CT myelogram; high-density collection posteriorly in the spinal canal, displacing the spinal contents anteriorly. This is seen in the lower thoracic and upper lumbar regions.	2/5 left lower extremity strength, 0/5 right lower extremity, patchy lower extremity sensation
6	Left leg weakness and loss of sensation	29 h	52 h	54 h	MRI; large complex dorsal epidural collection extending from T6 through T12–L1 with compression of the thoracic cord from T7 through T9. No definite cord signal abnormality	Complete recovery
7	Bilateral lower extremity weakness/ decreased sensation	55 h	7 h (first scan, which was limited because of agitation), 12 h (second scan)	13 h	MRI; hematoma noted from T8 to L1 with ventral displacement of the thecal sac and cord compression. No spinal cord signal changes. Congenitally small central canal	Partial recovery of lower extremity strength

CT = computed tomography; MRI = magnetic resonance imaging.

DISCUSSION

We report herein the risk and outcomes of epidural hematomas requiring decompressive laminectomy from a large series of perioperative and obstetric epidural catheterizations at 11 academic medical centers. The unweighted event rate of epidural hematoma requiring laminectomy that we report is 1 per 8921 epidural catheterizations for perioperative anesthesia/analgesia. Five of the 7 patients with hematoma had neurological deficits on discharge, so the rate of neurological injury is approximately 1 in 12,000 epidural catheterizations. These estimates are comparable with other studies.^{1,2,4} In the obstetric series, we report 79,837 epidural catheterizations without a single case of hematoma requiring laminectomy.

Although the number of cases of hematoma in our series is small, several interesting observations emerge. Patient 1 may have been at increased risk because of the deleterious effect of dialysis on platelet function. Four of 7 patients had perioperative anticoagulant management that clearly deviated from current American Society of Regional Anesthesia guidelines.⁶ Patients 2 and 7 had placements with international normalized ratios of 1.6. Patients 3, 6, and 7 all received concurrent aspirin and heparin. The final 2 cases (patients 4 and 5) both occurred in the setting of a dural puncture: one after combined spinal/epidural (after difficult placement in a patient with ankylosing spondylitis) and a second in the setting of an inadvertent dural puncture and spinal catheter. The time to development of symptoms after catheter insertion varied widely from 11 to 71 hours, with 5 of 7 cases presenting beyond the first 24 hours. This underscores the need for vigilance in monitoring for signs and symptoms of hematoma as long as the catheter is in place. In contrast to previous analyses,⁷ we observed no relationship between time to laminectomy and

neurological outcome in our small sample. Although it is clearly prudent to proceed to decompression as rapidly as possible once the diagnosis is made, predictors of neurological recovery are likely multifactorial.

Despite the inclusion of 79,837 obstetric epidurals in our study, we did not detect a single case of hematoma requiring laminectomy, and the risk was significantly lower than that observed in perioperative epidural catheter placement. It is possible that these patients are at decreased risk compared with the general population because of the relatively hypercoagulable state associated with pregnancy. Obstetric patients are also less likely to have canal or foraminal stenoses or receive a combination of antiplatelet and anticoagulant drugs (although in certain situations, including history of venous thromboembolism, antiphospholipid antibody syndrome, and mechanical heart valves, anticoagulation during pregnancy may be required).⁸

Our study has certain limitations. Because our methods only detect patients who underwent decompressive laminectomies, we do not identify those hematomas that were managed non-operatively. Our data provide only a lower bound of the true risk, because patients conceivably could be discharged, develop symptoms, and undergo treatment at another hospital. Our data on neurological outcome are limited to that which is documented at the time of hospital discharge and therefore may overestimate the degree of ultimate neurological impairment. We did not collect information of attempted epidural placements that were aborted because of bleeding or difficult placement; therefore, we might have underestimated the risk of hematoma associated with attempted placement. Likewise, information was not uniformly available for all patients on the type of epidural catheters used and whether spinal stenosis was present.

In conclusion, epidural hematoma is a rare but serious complication after epidural catheterization. In our series, the frequency of epidural hematoma requiring laminectomy after epidural catheterization instituted for perioperative anesthesia/analgesia was between 1 event per 22,189 and 1 event per 4330 epidural catheter placements. In addition, the risk was significantly lower in obstetric patients.

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Intermittent Epidural Bolus Compared with Continuous Epidural Infusions for Labor Analgesia: A Systematic Review and Meta-Analysis: Erratum

In the article by George et al. in the January 2013 issue of *Anesthesia & Analgesia*, the authors were made aware of an error in Table 1 on page 136, "Subject Characteristics and Risk of Bias Assessment of Included Studies." The epidural solution for Wong et al. is presented as "Bupivacaine, 0.625%" where in fact it should be "Bupivacaine, 0.0625%." The authors apologize for this misprint and the confusion in the interpretation of their results this may have caused.

Reference:

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