



SPINAL ANAESTHESIA IN THE PARTURIENT WITH SEVERE PREECLAMPSIA

Obstetrics & Gynaecology

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ABSTRACT

Preeclampsia is a significant, multifactorial, multiorgan disease affecting 6%-8% of all pregnancies in the United States and is the third leading cause of maternal mortality. As such, it is incumbent upon any anaesthesia provider involved in obstetric cases to be familiar with the varied manifestations of the disease, management goals from an obstetric standpoint, and the implications for provision of anaesthesia in this patient group. Despite improvements in the diagnosis and management of preeclampsia, severe complications can occur in both the mother and the fetus. A systematic approach to the anaesthetic evaluation is therefore necessary to reduce morbidity and mortality and to improve outcomes. The potential pitfalls of general anaesthesia, including failed intubation, in these complicated patients make regional anaesthesia the preferred choice in many cases. Recent studies have shown that spinal anaesthesia is often appropriate for preeclamptic patients, even in severe cases. Nevertheless, it is important to be aware of the potential contraindications to neuraxial anaesthesia and to prepare for the possibility of encountering a difficult airway.

KEYWORDS

INTRODUCTION:

Preeclampsia, which affects 5% to 7% of pregnancies, is a significant cause of maternal and neonatal morbidity and mortality¹. Characterized by hypertension and proteinuria after 20 weeks' gestation, the pathophysiologic basis of preeclampsia is deranged angiogenesis with incomplete trophoblastic invasion leading to small, constricted myometrial spiral arteries with exaggerated vasomotor responsiveness, superficial placentation, and placental hypoperfusion. Symptomatic preeclampsia reflects widespread endothelial dysfunction, in which placenta-derived mediators cause multisystem organ dysfunction.³

Preeclamptic parturients whose hypertension has been treated antepartum generally present for delivery with contracted plasma volume, normal or increased cardiac output, vasoconstriction, and hyperdynamic left ventricular function (although left ventricular systolic and diastolic dysfunction may develop). Additional manifestations include increased airway edema, decreased glomerular filtration, platelet dysfunction, and a spectrum of hemostatic derangements (typically accentuated hypercoagulability).^{4,5} In severe preeclampsia, chronic placental hypoperfusion is often significant. Since the uteroplacental circulation is not autoregulated, further decreases in perfusion may be poorly tolerated by the fetus. Primary peripartum goals in the severely preeclamptic parturient are the optimization of maternal blood pressure, cardiac output, and uteroplacental perfusion and the prevention of seizures and stroke.

Historically, a pervasive belief that spinal anesthesia in patients with severe preeclampsia causes severe hypotension and decreased uteroplacental perfusion prevented the widespread use of spinal anesthesia in these patients. However, studies show that parturients with severe preeclampsia experience less frequent, less severe hypotension than healthy parturients. Among patients with severe preeclampsia, spinal anesthesia may cause a greater degree of hypotension than epidural anesthesia; however, this hypotension is typically easily treated and short lived, and no studies have demonstrated clinically significant differences in outcomes when spinal anesthesia is compared with epidural or general anesthesia. Risk-benefit considerations strongly favor neuraxial techniques over general anesthesia for cesarean delivery in the setting of severe preeclampsia as long as neuraxial anesthesia is not contraindicated. Therefore, spinal anesthesia is a reasonable anesthetic option in severe preeclampsia when cesarean delivery is indicated, and there is no indwelling epidural catheter or contraindication to spinal anesthesia.

Spinal Anesthesia And Hypotension In Severe Preeclampsia

Hypotension after spinal anesthesia in severely preeclamptic patients may reflect the rapid onset of sympathetic blockade, underlying intravascular volume depletion, and possible left ventricular dysfunction. Longstanding obstacles to widespread use of spinal anesthesia for patients with preeclampsia were concerns about (1) precipitous spinal anesthesia-induced hypotension, superimposed on (2) preexisting uteroplacental hypoperfusion and (3) the risk of inducing hypertension or pulmonary edema with subsequent efforts to correct the hypotension.⁶ While there was evidence as early as 1950 that preeclampsia actually attenuates spinal anesthesia-induced hypotension,^{7,8} it was not until the mid-1990s, when clinical trials demonstrated the safety of spinal and combined spinal-epidural (CSE) anesthesia in this patient population,⁹⁻¹¹ that spinal anesthesia gained acceptance as an alternative to epidural and general anesthesia for preeclamptic patients.

Most trials assessing the severity of hypotension after spinal anesthesia among severely preeclamptic parturients exclude patients in active labor because labor itself attenuates the frequency and severity of the hypotensive response to neuraxial anesthesia during cesarean delivery.¹² Most studies are relatively small ($n < 150$), and the details of preoperative antihypertensive and magnesium regimens vary.

Three prospective trials have demonstrated that preeclamptic parturients experience less frequent and less severe hypotension and require smaller doses of vasopressors than normotensive controls after the initiation of spinal anesthesia. A potential limitation of an initial study by Aya et al.¹⁴ was that mean gestational age and fetal weight were significantly lower in the severely preeclamptic group compared with the normotensive group. Resulting intergroup differences in degree of aortocaval compression could have contributed to the finding that hypotension was less severe in the preeclamptic group.

Similarly, a study by Clark et al.¹⁵ did not control for fetal weight or gestational age. To correct for this limitation, a follow-up study by Aya et al.¹³ studied preterm parturients presenting for nonemergency cesarean delivery and matched the normotensive and preeclamptic patients for gestational age (neonatal and placental weights were also comparable). The severely preeclamptic group experienced a lower incidence of hypotension requiring treatment (25% vs 41%, $P = 0.044$) and received a lower mean cumulative ephedrine dose (10 vs 16 mg, $P = 0.031$) compared with the normotensive control group. These findings indicate that spinal anesthesia can be safely administered to

severely preeclamptic parturients undergoing nonemergency cesarean delivery and that spinal anesthesia-induced hypotension can generally be treated safely.

Spinal Versus General Anesthesia

For most of the severely preeclamptic population, the risk-benefit profiles of spinal anesthesia and general anesthesia strongly favor the use of spinal anesthesia when feasible. Important factors to consider are the risks of clinically significant maternal hemodynamic derangements, difficult airway management, stroke, spinal/epidural hematoma, and adverse neonatal outcomes. As described earlier, in severely preeclamptic patients, spinal anesthesia-induced hypotension is typically easily treated, the risk of spinal/epidural hematoma is low, and there is no evidence that neonatal outcomes are compromised. In contrast, potential complications of general anesthesia, such as hypertensive crisis, stroke, and difficult airway management, are leading causes of morbidity and mortality in the preeclamptic population. Therefore, in the majority of severely preeclamptic patients, who are not coagulopathic or thrombocytopenic, the risk of difficult or failed airway management and delayed recognition of maternal stroke during a general anesthetic are felt to exceed the risk of adverse outcomes from spinal anesthesia-induced hypotension or spinal/epidural hematoma.¹⁹

Peripartum pharyngeal and glottic edema are accentuated in preeclamptic parturients,²⁴ and the risks of difficult/failed laryngoscopy and intubation are greater among preeclamptic parturients than healthy parturients.²⁵ Traumatic laryngoscopy may trigger pharyngeal or hypopharyngeal bleeding, further obscuring visualization of the airway. Although the absolute risks of general anesthesia (failed/difficult airway management, hypertension with direct laryngoscopy, delayed recognition of stroke under general anesthesia, and aspiration) are low even among preeclamptic parturients, the risk of difficult airway management is a compelling reason to favor neuraxial anesthesia. Closed claims analysis from the United Kingdom from 2006 to 2008 identified poor management of preeclampsia as one of the main categories in which poor perioperative management may have contributed to maternal death.²⁶

Severe preeclampsia is also a leading cause of peripartum hemorrhagic stroke.²⁷ During direct laryngoscopy and intubation, severely preeclamptic parturients experience significantly larger increases in arterial blood pressure and middle cerebral artery velocity compared with healthy parturients.²⁸ Cerebral hypertension may, in turn, precipitate hemorrhagic stroke. Hemorrhagic stroke was the leading direct cause of mortality in patients with severe preeclampsia according to the most recent analysis by the United Kingdom Center for Maternal and Child Enquiries.²⁹ If general anesthesia is necessary, equipment should be immediately available to manage a difficult airway, and every effort should be made to blunt the hemodynamic response to laryngoscopy (e.g., via a bolus of an antihypertensive drug or remifentanyl).^{30,31}

One study has been designed to detect differences in maternal or neonatal outcomes associated with the use of spinal anesthesia compared with general anesthesia in severe preeclampsia. Dyer et al.³² prospectively compared umbilical arterial fetal base deficit and other markers of maternal and neonatal well-being in 70 preeclamptic patients undergoing cesarean delivery due to nonreassuring fetal heart rate tracings, randomized to receive either spinal or general anesthesia (Table 4). The study was powered to detect an intergroup difference in the primary outcome, the incidence of umbilical arterial base deficit >8 mEq/L. In both groups, mean umbilical arterial base deficit values were within the range considered normal for vaginal delivery (<10), although the spinal group had a higher mean umbilical arterial base deficit (7.1 vs 4.7 mEq/L, $P = 0.02$) and a lower median umbilical arterial pH (7.20 vs 7.23, $P = 0.046$). There were no significant intergroup differences in other markers of neonatal compromise, including requirement for neonatal resuscitation, Apgar score <7, umbilical arterial pH <7.2, and need for neonatal intermittent positive pressure ventilation. Maternal heart rate and arterial blood pressure values were also acceptable in both groups.

Notably, in the Dyer et al.³² study, the mean ephedrine dose (14 vs 3 mg, $P = 0.002$) was significantly higher in the spinal anesthesia group. The authors point out that there was no correlation between ephedrine use and neonatal base deficit in either group. Of note, post hoc analysis showed that unless diastolic blood pressure exceeded 110 mm Hg,

there was no intergroup difference in neonatal base deficit. However, the clinical significance of this observation remains unknown, especially since the study was not powered to assess this subset of patients. The trend toward lower umbilical arterial pH in the spinal group, in which ephedrine doses were higher, has prompted some authors³³ to recommend phenylephrine as the first-line vasopressor in severe preeclampsia. This recommendation is consistent with the finding that, in some studies, ephedrine is associated with greater fetal acidemia than phenylephrine among healthy parturients presenting for cesarean delivery.³³

Hemodynamic Monitoring During Spinal Anesthesia In Severe Preeclampsia

The spectrum of hemodynamic profiles observed in severe preeclampsia reflects disease severity,³⁷ whether hypertension has been treated^{38,39} and varied approaches to antihypertensive therapy and comorbidities. Among nonlaboring, term preeclamptic parturients, the incidence of global diastolic dysfunction, typically mild, is 40%.⁴⁰ The ASA practice guidelines for obstetric anesthesia state that the literature is silent or insufficient to determine whether invasive hemodynamic monitoring improves outcomes in women with pregnancy-related hypertensive disorders. No specific monitor has been proven to impact maternal or fetal outcomes in the setting of preeclampsia.³⁰ An arterial catheter can facilitate detection and treatment of blood pressure changes, especially in patients with severe or volatile hypertension. Echocardiography can provide information about volume status and cardiac function. In preeclampsia, central venous pressure often does not correlate with pulmonary capillary wedge pressure,⁴¹ which in turn may not reflect left ventricular stroke work.³⁹ Also, pulmonary artery and central venous catheters confer a reported 4% risk of complications among hypertensive parturients.⁴² Proponents of less invasive monitors that estimate stroke volume, such as arterial waveform analysis⁴³ and impedance cardiography, highlight the favorable risk-benefit ratio and the correlation of these data (in the early postpartum period among severely preeclamptic patients)⁴⁴ with thermomodulation-derived measurements. Further evaluation of these monitors in the peripartum management of severe preeclampsia is ongoing.^{45,46}

REFERENCES

1. Steegers EA, von Dadelszen P, Duvekot JJ, Pijnenborg R. Pre-eclampsia. *Lancet*. 2010;376:631-44
2. Heron MP, Hoyert DL, Murphy SL, Xu J. Deaths: final data for 2006. *National Vital Statistics Reports*; vol 57, No 14. Available at: http://www.cdc.gov/nchs/data/nvsr/nvsr57/nvsr57_14.pdf. Accessed December 11, 2010
3. Gogarten W. Preeclampsia and anaesthesia. *Curr Opin Anaesthesiol*. 2009;22:347-51
4. Diagnosis and management of preeclampsia and eclampsia. ACOG Practice Bulletin No. 33. American College of Obstetricians and Gynecologists. *Obstet Gynecol*. 2002;99:159-67
5. Lindheimer MD, Taler SJ, Cunningham FG. Hypertension in pregnancy. *J Am Soc Hypertens*. 2008;2:484-94
6. Pritchard JA, Cunningham FG, Pritchard SA. The Parkland Memorial Hospital protocol for treatment of eclampsia: evaluation of 245 cases. *Am J Obstet Gynecol*. 1984;148:951-63
7. Assali NS, Prystowsky H. Studies on autonomic blockade. I. Comparison between the effects of tetraethylammonium chloride (TEAC) and high selective spinal anesthesia on blood pressure of normal and toxemic pregnancy. *J Clin Invest*. 1950;29:1354-66
8. Jones GR, Ware HH, Garber EC, McElrath PJ. Continuous spinal anesthesia in the treatment of severe preeclampsia and eclampsia. *Southern Med J*. 1952;45:34-41
9. Wallace DH, Leveno KJ, Cunningham FG, Giesecke AH, Shearer VE, Sidawy JE. Randomized comparison of general and regional anesthesia for cesarean delivery in pregnancies complicated by severe preeclampsia. *Obstet Gynecol*. 1995;86:193-9
10. Karinen J, Rasanen J, Alahuhta S, Jouppila R, Jouppila P. Maternal and uteroplacental haemodynamic state in pre-eclamptic patients during spinal anesthesia for cesarean section. *Br J Anaesth*. 1996;76:616-20
11. Hood DD, Curry R. Spinal versus epidural anesthesia for cesarean section in severely preeclamptic patients: a retrospective survey. *Anesthesiology*. 1999;90:1276-82
12. Brizgys RV, Dailey PA, Shnider SM, Kotenko DM, Levinson G. The incidence and neonatal effects of maternal hypotension during epidural anesthesia for cesarean section. *Anesthesiology*. 1987;67:782-6
13. Aya AG, Vialles N, Tanoubi I, Mangin R, Ferrer JM, Robert C, Ripart J, de La Coussaye JE. Spinal anesthesia-induced hypotension: a risk comparison between patients with severe preeclampsia and healthy women undergoing preterm cesarean delivery. *Anesth Analg*. 2005;101:869-75
14. Aya AG, Mangin R, Vialles N, Ferrer JM, Robert C, Ripart J, de La Coussaye JE. Patients with severe preeclampsia experience less hypotension during spinal anesthesia for elective cesarean delivery than healthy parturients: a prospective cohort comparison. *Anesth Analg*. 2003;97:867-72
15. Clark VA, Sharwood-Smith GH, Stewart AV. Ephedrine requirements are reduced during spinal anesthesia for caesarean section in preeclampsia. *Int J Obstet Anesth*. 2005;14:9-13
16. Visalyaputra S, Rodanant O, Sombonviboon W, Tantivitayatan K, Thienthong S, Saengchote W. Spinal versus epidural anesthesia for cesarean delivery in severe preeclampsia: a prospective randomized, multicenter study. *Anesth Analg*. 2005;101:862-8
17. Sharwood-Smith G, Clark V, Watson E. Regional anesthesia for cesarean section in severe preeclampsia: spinal anesthesia is the preferred choice. *Int J Obstet Anesth*. 1999;8:85-9
18. Chiu CL, Mansor M, Ng KP, Chan YK. Retrospective review of spinal versus epidural anesthesia for caesarean section in preeclamptic patients. *Int J Obstet Anesth*. 2003;12:23-7

19. Santos AC, Birnbach DJ. Spinal anesthesia for cesarean delivery in severely preeclamptic women: don't throw out the baby with the bathwater! *Anesth Analg*. 2005;101:859-61
20. American Society of Anesthesiologists Task Force on Obstetric Anesthesia. Practice guidelines for obstetric anesthesia: an updated report by the American Society of Anesthesiologists Task Force on Obstetric Anesthesia. *Anesthesiology*. 2007;106:843-63
21. Hägerdal M, Morgan CW, Sumner AE, Gutsche BB. Minute ventilation and oxygen consumption during labor with epidural analgesia. *Anesthesiology*. 1983;59:425-30
22. Joupila P, Joupila R, Hollmén A, Koivula A. Lumbar epidural analgesia to improve intervillous blood flow during labor in severe preeclampsia. *Obstet Gynecol*. 1982;59:158-61
23. Abboud T, Artal R, Sarkis F, Henriksen EH, Kammula RK. Sympathoadrenal activity, maternal, fetal, and neonatal responses after epidural anesthesia in the preeclamptic patient. *Am J Obstet Gynecol*. 1982;144:915-8
24. Izci B, Riha RL, Martin SE, Vennelle M, Liston WA, Dundas KC, Calder AA, Douglas NJ. The upper airway in pregnancy and pre-eclampsia. *Am J Respir Crit Care Med*. 2003;167:137-40
25. Munnur U, de Boisblanc B, Suresh MS. Airway problems in pregnancy. *Crit Care Med*. 2005;33:S259-68
26. McClure J, Cooper GLewis Gon behalf of the Centre for Maternal and Child Enquiries. Chapter 8: Anaesthesia. Saving Mothers' Lives: Reviewing Maternal Deaths to Make Motherhood Safer: 2006-2008. The Eighth Report of the Confidential Enquiries into Maternal Deaths in the United Kingdom *Br J Obstet Gynecol*. 2011;118(Suppl 1):1-203
27. Bateman BT, Schumacher HC, Bushnell CD, Pile-Spellman J, Simpson LL, Sacco RL, Berman MF. Intracerebral hemorrhage in pregnancy: frequency, risk factors, and outcome. *Neurology*. 2006;67:424-9
28. Ramanathan J, Angel JJ, Bush AJ, Lawson P, Sibai B. Changes in maternal middle cerebral artery blood flow velocity associated with general anesthesia in severe preeclampsia. *Anesth Analg*. 1999;88:357-61
29. Neilson JLewis Gon behalf of the Centre for Maternal and Child Enquiries. Chapter 3: Pre-eclampsia and eclampsia. Saving Mothers' Lives: Reviewing maternal deaths to make motherhood safer: 2006-2008. The Eighth Report of the Confidential Enquiries into Maternal Deaths in the United Kingdom *Br J Obstet Gynecol*. 2011;118(Suppl 1):1-203
30. Park BY, Jeong CW, Jang EA, Kim SJ, Jeong ST, Shin MH, Lee J, Yoo KY. Dose-related attenuation of cardiovascular responses to tracheal intubation by intravenous remifentanyl bolus in severe pre-eclamptic patients undergoing Caesarean delivery. *Br J Anaesth*. 2011;106:82-7
31. Yoo KY, Jeong CW, Park BY, Kim SJ, Jeong ST, Shin MH, Lee J. Effects of remifentanyl on cardiovascular and bispectral index responses to endotracheal intubation in severe pre-eclamptic patients undergoing caesarean delivery under general anesthesia. *Br J Anesth*. 2009;102:812-9
32. Dyer RA, Els I, Farbas J, Torr GJ, Schoeman LK, James MF. Prospective, randomized trial comparing general with spinal anesthesia for cesarean delivery in preeclamptic patients with a nonreassuring fetal heart trace. *Anesthesiology*. 2003;99:561-9
33. Smiley RM. Burden of proof. *Anesthesiology*. 2009;111:470-2
34. Habib AS. A review of the impact of phenylephrine administration on maternal hemodynamics and maternal and neonatal outcomes in women undergoing cesarean delivery under spinal anesthesia. *Anesth Analg*. 2012;114:377-90
35. Ramanathan J, Vaddadi AK, Arheart KL. Combined spinal and epidural anesthesia with low doses of intrathecal bupivacaine in women with severe preeclampsia: a preliminary report. *Reg Anesth Pain Med*. 2001;26:46-51
36. Rawal N, Schollin J, Westström G. Epidural versus combined spinal epidural block for cesarean section. *Acta Anaesthesiol Scand*. 1988;32:61-6
37. Bosio PM, McKenna PJ, Conroy R, O'Herlihy C. Maternal central hemodynamics in hypertensive disorders of pregnancy. *Obstet Gynecol*. 1999;94:978-84
38. Groenendijk R, Trimpos JB, Wallenburg HC. Hemodynamic measurements in preeclampsia: preliminary observations. *Am J Obstet Gynecol*. 1984;150:232-6
39. Visser W, Wallenburg HC. Central hemodynamic observations in untreated preeclamptic patients. *Hypertension*. 1991;17:1072-7
40. Melchiorre K, Sutherland GR, Baltabaeva A, Liberati M, Thilaganathan B. Maternal cardiac dysfunction and remodeling in women with preeclampsia at term. *Hypertension*. 2011;57:85-93
41. Bolte AC, Dekker GA, van Eyck J, van Schijndel RS, van Geijn HP. Lack of agreement between central venous pressure and pulmonary capillary wedge pressure in preeclampsia. *Hypertens Pregnancy*. 2000;19:261-7
42. Young P, Johanson R. Haemodynamic, invasive and echocardiographic monitoring in the hypertensive parturient. *Best Pract Res Clin Obstet Gynaecol*. 2001;15:605-22
43. Montenij LJ, de Waal EE, Buhre WF. Arterial waveform analysis in anesthesia and critical care. *Curr Opin Anaesthesiol*. 2011;24:651-6
44. Dyer RA, Piercy JL, Reed AR, Strathie GW, Lombard CJ, Anthony JA, James MF. Comparison between pulse waveform analysis and thermodilution cardiac output determination in patients with severe pre-eclampsia. *Br J Anaesth*. 2011;106:77-81
45. Pauca AL. Pressure wave analysis is useful to understand the pathophysiology of preeclampsia, but perhaps not the rapid changes during cesarean delivery. *Anesthesiology*. 2008;108:773-4
46. Dyer RA, Piercy JL, Reed AR. The role of the anaesthetist in the management of the pre-eclamptic patient. *Curr Opin Anaesthesiol*. 2007;20:168-74
47. Moen V, Dahlgren N, Irestedt L. Severe neurological complications after central neuraxial blockades in Sweden 1990-1999. *Anesthesiology*. 2004;101:950-9
48. Bateman BT, Mhyre JM, Ehrenfeld J, Khetarpal S, Abbey KR, Argalious M, Berman MF, Jacques PS, Levy W, Loeb RG, Paganelli W, Smith KW, Wethington KL, Wax D, Pace NL, Tremper K, Sandberg WS. Brief report: the risk and outcomes of epidural hematomas after perioperative and obstetric epidural catheterization: a report from the multicenter perioperative outcomes group research consortium. *Anesth Analg*. 2013;116:1380-5
49. Cook TM, Counsell D, Wildsmith JARoyal College of Anaesthetists Third National Audit Project. Major complications of central neuraxial block: report on the Third National Audit Project of the Royal College of Anaesthetists. *Br J Anaesth*. 2009;102:179-90
50. 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*. 2010;35:64-101
51. Horlocker TT, Wedel DJ, Schroeder DR, Rose SH, Elliott BA, McGregor DG, Wong GY. Preoperative antiplatelet therapy does not increase the risk of spinal hematoma associated with regional anesthesia. *Anesth Analg*. 1995;80:303-9
52. Douglas MJ. Platelets, the parturient and regional anesthesia. *Int J Obstet Anesth*. 2001;10:113-20
53. van Veen JJ, Nokes TJ, Makris M. The risk of spinal haematoma following neuraxial anaesthesia or lumbar puncture in thrombocytopenic individuals. *Br J Haematol*. 2010;148:15-25
54. Neuner C, Lim W, Crowther M, Cohen A, Solberg LJr, Crowther MA American Society of Hematology. The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. *Blood*. 2011;117:4190-20
55. Douglas MJ. Platelets, the parturient and regional anesthesia. *Int J Obstet Anesth*. 2001;10:113-120
56. Ledue L, Wheeler JM, Kirshon B, Mitchell P, Cotton DB. Coagulation profile in severe preeclampsia. *Obstet Gynecol*. 1992;79:14-8