

SPECIAL ARTICLE

Labour analgesia in pre-eclampsia: the current perspectives

Sukhminder Jit Singh Bajwa*, Ashish Kulshrestha**, Sukhwinder Kaur Bajwa***

**Professor, Anesthesiology and Critical Care, Gian Sagar Medical College and Hospital, Rajpura, Patiala, Punjab, India*

***Assistant Professor, Anesthesiology and Critical Care, Govt. Medical College and Hospital, Sec-32, Chandigarh, India*

****Professor, Obstetrics and Gynaecology, Gian Sagar Medical College and Hospital, Rajpura, Patiala, Punjab, India*

Correspondence: Dr.Sukhminder Jit Singh Bajwa, House No-27-A, Ratan Nagar, Tripuri, Patiala, Punjab-147001 (India); Phone: 09915025828, +911752352182; E-mail: sukhminder_bajwa2001@yahoo.com

ABSTRACT

Pre-eclampsia is a disease of pregnancy involving various systems with associated high blood pressure and other changes. The pathophysiology of this disease is not well known but the main pathological change is vasoconstriction in the vascular bed of the parturient with abnormalities in the uteroplacental circulation. A multi-disciplinary approach is essential for proper management of this disease. The provision of analgesia during labor significantly reduces the stress response and thus is helpful in reducing the elevated blood pressure and also exerts beneficial effects on uteroplacental perfusion. The neuraxial analgesia technique is considered to be the gold standard and has been found to be effective and safe in pre-eclamptic parturients. The use of lower concentrations of local anesthetic drugs in combination with opioids results in less motor blockade, lesser dose of drugs and lesser incidence of significant side-effects. The patient-controlled epidural analgesia technique is very beneficial with excellent maternal satisfaction. The concern of coagulation abnormalities associated with pre-eclampsia should be kept in mind with the institution of neuraxial techniques with careful monitoring of neurological status. The reduction in stress response with consequent reduction in blood pressure in pre-eclamptic parturient is highly desirable irrespective of the technique of analgesia used.

Key words: Pre-eclampsia; Labor analgesia; Epidural

Citation: Bajwa SJS, Kulshrestha A, Bajwa SK. Labour analgesia in pre-eclampsia: the current perspectives. *Anaesth Pain & Intensive Care* 2014;18(4):419-423

INTRODUCTION

Provision of quality obstetrical care has been the main focus around the globe to decrease the maternal morbidity and mortality resulting from various co-morbid diseases as well as obstetrical complications.^{1,2} Among various obstetric disorders, pre-eclampsia is one of the common ailments which requires timely intervention for better mother and fetal outcome. Pre-eclampsia is a multi-system disorder of pregnancy with accelerated blood pressure and is associated with considerable maternal mortality and morbidity.^[3] The associated complications can be fatal and may include intracranial hemorrhage, acute pulmonary edema, respiratory and hepatic failure. The incidence of pre-eclampsia can range from 5-8% with severe maternal complications and fetal complications which include intrauterine growth retardation and fetal demise.^{4,5} Labour analgesia in

such critical cases becomes all the more essential. Anesthesiologists may frequently be involved in the perioperative care of pre-eclamptic parturients involving provision of effective analgesia for labor to anesthetic management during cesarean delivery. The management of pain during labor is the most important aspect of multi-disciplinary approach to a pre-eclamptic parturient. The recent updates in the management of pain in parturients with pre-eclampsia are presented.

DEFINING THE DISEASE

Pre-eclampsia is included in the broad category of hypertensive disorders of pregnancy with many varied definitions, but some common features like presence of hypertension after 20 weeks of gestation with one or more organ system involvement with resolution of disease by three months postpartum.^[6,7] The term severe pre-eclampsia is applied

to the presence of marked elevation of blood pressure (both systolic and diastolic) with extreme derangement in various organ systems as depicted in Table 1.

Table 1: Features of Severe Pre-eclampsia^{8,9}

System involved	Features
Hypertension	Systolic \geq 140 mmHg \geq 160 mmHg—Severe Hypertension \geq 180 mmHg—Hypertensive Crisis And/ or Diastolic \geq 90 mmHg \geq 110 mmHg—Hypertensive Crisis
Central Nervous System	Seizures Headache Visual disturbances Papilledema Clonus/ Hyperreflexia
Cardiovascular System	Pulmonary edema
Gastrointestinal System	Elevated liver transaminase enzyme \geq 70 IU/l Liver tenderness Nausea and vomiting Epigastric pain
Hematological System	Hemolysis Thrombocytopenia $<$ 100,000 Disseminated intravascular coagulation
Renal System	Proteinuria $>$ 5 gms in 24 hr urine Protein/ creatinine $>$ 0.5 g/ mmol Urine output $<$ 500 ml in 24 hours Renal failure
Uteroplacental Circulation	Placental abruption Intrauterine growth retardation Umbilical/ Uterine artery blood flow abnormality—absent or reversed end-diastolic flow

PATHOPHYSIOLOGICAL MECHANISMS

The main pathophysiological mechanisms in pre-eclampsia involve the placenta with the triad of vasospasm, plasma volume contraction and local or disseminated intravascular coagulation.¹⁰ There is associated endothelial dysfunction due to release of factors from placental hypoperfusion. There is increased sensitivity to the vasoconstrictors leading to plasma volume contraction, increased capillary permeability and low plasma oncotic pressure. There is resulting peripheral tissue edema with intravascular coagulation due to reduced antithrombin III and activation of platelets. The various risk factors associated with pre-eclampsia include obesity, chronic hypertension, chronic renal disease, gestational diabetes, connective tissue disorders and multiple gestations.

MERITS AND ESSENTIALS OF LABOUR ANALGESIA

The pain of labor induces various metabolic and biochemical changes in mother leading to release of stress hormones like catecholamines, cortisol and adrenocorticotrophin hormone.¹¹ It causes reduction of uteroplacental perfusion which is already reduced in parturients with pre-eclampsia, thus affecting fetal well-being. The various metabolic changes create fetal acidosis thus increasing fetal oxygen requirements. Pain relief reduces the stress response and helps maintain the uteroplacental perfusion and fetal well-being. This is more important in pre-eclamptic parturients where the fetus is more exposed to the changes in uteroplacental perfusion. Thus the various characteristics of an ideal analgesic technique in labor may be described as:

- It should have a documented and established safety for both mother and fetus
- It should be easily administered
- It should provide analgesia through all stages of labor
- It should preserve the maternal efforts of expulsion of fetus
- It should not produce any motor blockade of lower limbs thus ensuring ambulation of parturient
- It should allow facilitation of supplemental analgesia without any additional invasive procedure
- It should facilitate the initiation of anesthesia for operative delivery by allowing conversion of analgesia into anesthesia

RELIEVING PAIN DURING LABOUR

A. Non-Pharmacological:

The various non-pharmacological techniques used are transcutaneous electrical nerve stimulation (TENS), acupuncture, intradermal sterile water injections, warm water bath and hypnosis. All these methods have been found to be promising but lack scientific evidence.¹²

B. Parenteral Medications:

It includes use of intravenous analgesics by repeated boluses or by continuous infusions. The advent of specially designed infusion pumps has led to the use for patient controlled analgesia (PCA) allowing patients to administer

analgesic drug boluses, mainly the opioids. This method has been found to be safe and effective in laboring parturients. The literature supports the use of short-acting opioids like remifentanyl through PCA with a loading dose of 0.5 $\mu\text{g}/\text{kg}$ with lockout interval of 5 min with continuous background infusion of 0.05 $\mu\text{g}/\text{kg}/\text{min}$ and has been found to be effective in laboring parturients with no adverse effects on fetus.^{13,14} Recently, use of dexmedetomidine has been reported in laboring women for analgesia with fair degree of success, but it is still not recommended to be used in pregnant patients.¹⁵

Although the intravenous opioids are efficacious in controlling labor pain but a small probability of significant maternal respiratory depression exists with their use which should be reversed with the opioid antagonist naloxone in the dose of 0.4 mg IV. But care should be taken as this dose also reverses the analgesic effects of opioids.

C. Inhalational Methods:

The most common agent used for providing labor analgesia is 50:50 mixture of oxygen and nitrous oxide (Entonox). However, studies show that it may not be a potent analgesic and its role is limited to places with no practice of regional techniques or in situations of short labor.¹⁶

Another potent inhalational agent used for labor analgesia is sevoflurane owing to its short onset and offset of action and also it has been given as patient-controlled inhalational analgesia. But there are few concerns associated with it like loss of protective airway reflexes and environmental pollution.¹⁷

D. Regional Analgesia:

Neuraxial techniques remain the gold standard and most accepted techniques of providing analgesia in labor. This technique is especially favourable in pre-eclamptic parturients as it maintains the uteroplacental perfusion which is compromised and it reduces the hypertensive response to labor pain.¹⁸ The commonest techniques employed are lumbar epidural and combined spinal epidural analgesia. The literature supports the use of epidural analgesia in pre-eclamptic patients with favourable outcomes in pain relief with no increase in operative delivery. This technique also results in upto 20% reduction in maternal blood

pressures and can be easily combined with the conventional anticonvulsant therapy.^{19,20}

The use of patient-controlled epidural analgesic technique (PCEA) have been found to be advantageous over the continuous infusion technique with less amount of local anesthetic drug usage, higher maternal satisfaction and reduced number of unscheduled top-ups due to maintenance of continuous level of analgesia.²¹ The data for advantages of PCEA in pre-eclamptic parturients is scarce but its advantages in normotensive females can be extrapolated to the pre-eclamptic females also.

Various anesthetic drugs which are used through PCEA are ropivacaine (0.1-0.2%) or bupivacaine (0.0625-0.125%) along with an opioid like fentanyl (2 $\mu\text{g}/\text{ml}$). A continuous background infusion of 5-10 ml/hr with controlled boluses of 5 ml is used with lockout interval of 15 minutes.

The use of combined spinal epidural technique (CSEA) has been found to be advantageous in labor analgesia with combination of rapid, reliable and profound analgesia resulting from spinal with longer duration of epidural technique.²² The hypotension associated with the intrathecal local anesthetic can be managed by the conventional methods like intravascular volume enhancement, use of adjuvants etc.^{23,24} The Obstetric Anesthetists Association, United Kingdom guidelines have restricted the use of CSEA technique in parturients in very early stage of labor where use of local anesthetics is avoided, in advanced stages of labor in which rapid analgesia is desired and in cases with difficult epidural placement.

Recently, an adaptation of the conventional epidural drug delivery pump technology with integration of computer to the infusion pump, has been introduced. This computer integrated-PCEA technology continuously changes the rate of background infusion depending on the previous hour's demand boluses. However, the studies have not found any significant difference between the local anesthetic drug consumption thus suggesting scope of further advancement in the technology.²⁵

The use of newer local anesthetic drugs like ropivacaine and levobupivacaine with reduced cardiac toxicity has been found to be advantageous in laboring women. But the studies have failed to demonstrate any clinical

significance with higher motor blockade with bupivacaine.^{26,27}

Ultrasound Imaging

The use of ultrasound imaging to facilitate identification of spinal or epidural space in parturients with difficult or abnormal lumbosacral anatomy has been found to be advantageous. Its use in pre-eclamptic women may be beneficial as these women tend to be more obese and edematous thus making it more beneficial and reducing the spinal or epidural failure rates.²⁸

Operative or Instrumental Delivery and its Association with Epidural Analgesia

It has long been held that institution of epidural analgesia in labouring women leads to increased incidence of operative or instrumental delivery. But recently, a systemic trial has emphasized that no significant increase in incidence of operative delivery is associated with epidural analgesia and there is no direct relationship between them.^[29] The duration of labor and incidence of instrumental delivery has been found to increase with epidural analgesia but use of low concentration of local anesthetics along with opioids has reduced the incidence of instrumental vaginal delivery by 25%.^[30]

Complications Associated With Neuraxial Analgesia

The local anesthetic drug cardiotoxicity has been the most dreaded complication mainly associated with bupivacaine but with the advent of lipid emulsion it has been found to effectively treat the toxicity by chelation of bupivacaine from systemic circulation. However, with the use of more cardiostable local anesthetics like ropivacaine and levobupivacaine, the incidence of such complications has been reduced.

The nerve damage due to intraneural injection of local anesthetic can be reduced by avoiding any bolus injections if the patient experiences pain or paresthesia during the injection

The infective complications of neuraxial techniques

(meningitis) have not found to be different from non-pregnant population, if the complete asepsis is taken care of during the technique.

The knotting or looping of epidural catheter within the epidural space can also be seen but the incidence is not different from normal population.

In patients with pre-eclampsia, the presence of coagulation abnormalities places them at higher risk of major neuraxial hematoma. It has been found by various studies that the platelet count of more than $100 \times 10^9/l^p$ is safe and not associated with major bleeding complication, however, platelet counts less than $100 \times 10^9/l^p$ in patients with pre-eclampsia needs further investigation of coagulation status.³¹ However, in general, the risk of developing neuraxial hematoma with platelet counts more than $75 \times 10^9/l^p$ in women with pre-eclampsia have been found to be low.

These parturients may land in intensive care unit due to multitude of reasons and should be managed accordingly, focussing mainly on the maintenance of uteroplacental circulation and maternal hemodynamic parameters.³²

CONCLUSION

In conclusion, pre-eclampsia is a multi-system disorder of pregnancy associated with high blood pressure and other changes and the management is multi-disciplinary with main focus on reducing any stress on the mother. The provision of analgesia in labouring pre-eclamptic women reduces this stress response and thus prevents precipitous rise in blood pressure. The neuraxial technique (epidural and combined spinal epidural) remains the gold standard in these parturients as it provides reliable and effective analgesia. The advent of patient-controlled epidural analgesia has been found to reduce the consumption of local anesthetic drug as well as enhance the overall satisfaction of mother. However, the association of coagulation abnormalities with pre-eclampsia places these patients at a higher risk of neurological complications and thus a strict monitoring of coagulation profile as well as neurological monitoring is essential in these patients.

REFERENCES

1. Bajwa SS, Bajwa SK, Ghuman GS. Pregnancy with co-morbidities: Anesthetic aspects during operative intervention. *Anesth Essays Res* 2013;7:294-301 [Online]
2. Bajwa SS, Bajwa SK. Improving Obstetrical critical care in developing nations. *ICU Management* 2013;12(4):18-21
3. Cantwell R, Clutton-Brock T, Cooper G, Dawson A, Drife J, Garrod D, et al. 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. *BJOG*. 2011 Mar;118 Suppl 1:1-203. doi: 10.1111/j.1471-0528.2010.02847.x. [PubMed]
4. Lewis G (ed). The Confidential Enquiry into Maternal and Child Health (CEMACH). Saving Mothers' Lives: Reviewing Maternal Deaths to Make Motherhood Safer – 2003–2005. The Seventh report on Confidential Enquiries into Maternal Deaths in the United Kingdom. London: CEMACH, 2007 [Online]
5. European Society of Gynecology (ESG); Association for European Paediatric Cardiology (AEPC); German Society for Gender Medicine (DGesGM), Regitz-Zagrosek V, Blomstrom Lundqvist C, Borghi C, et al. European Society of Cardiology Guidelines on the management of cardiovascular diseases during pregnancy: the Task Force on the Management of Cardiovascular Diseases during Pregnancy of the European Society of Cardiology (ESC). *Eur Heart J* 2011;32:3147–97 [PubMed][Free full text] doi: 10.1093/eurheartj/ehr218.
6. Khan KS, Wojdyla D, Say L, Gulmezoglu AM, Van Look PF. WHO analysis of causes of maternal death: a systematic review. *Lancet* 2006;367:1066–74 [PubMed]
7. ACOG Committee on Obstetric Practice. American College of Obstetricians and Gynecologists practice bulletin. Diagnosis and management of preeclampsia and eclampsia. Number 33, January 2002. *Int J Gynaecol Obstet* 2002;77:67–75 [PubMed]
8. Magee LA, Helewa M, Moutquin JM, von Dadelszen P; Hypertension Guideline Committee; Strategic Training Initiative in Research in the Reproductive Health Sciences (STIRRH) Scholars. Diagnosis, evaluation, and management of the hypertensive disorders of pregnancy. *J Obstet Gynaecol Can.* 2008 Mar;30(3 Suppl):S1-48. [PubMed]
9. Bajwa SJ, Kwatra IS, Bajwa SK, Kaur M. Renal diseases during pregnancy: Critical and current perspectives. *J Obstet Anaesth Crit Care* 2013;3:7-15 [Free full text]
10. Bajwa SK, Singh A, Bajwa SS. Contemporary issues in the management of abnormal placentation during pregnancy in developing nations: An Indian perspective. *Int J Crit Illn Inj Sci* 2013;3:183-9 [PubMed] doi: 10.4103/2229-5151.119197.
11. Bajwa SS, Bajwa SK. Anaesthetic challenges and management during pregnancy: Strategies revisited. *Anesth Essays Res* 2013;7:160-7 [Free full text]
12. Simkin PP, O'hara M. Nonpharmacologic relief of pain during labor: Systemic reviews of five methods. *Am J Obstet Gynecol* 2002;186 (5):S131-59 [PubMed]
13. El-kerdawy H, Farouk A. Labour analgesia in pre-eclampsia: Remifentanyl patient controlled intravenous analgesia versus epidural analgesia. *Middle East J Anesthesiol* 2010;20:539-45 [PubMed]
14. D'Onofrio P, Novelli AM, Mecacci F, Scarselli G. The Efficacy and Safety of Continuous Intravenous Administration of Remifentanyl for Birth Pain Relief: An Open Study of 205 Parturients. *Anesth Analg* 2009;109:1922-4 [PubMed] doi: 10.1213/ane.0b013e3181acc6fc.
15. Abu-Halaweh SA, AlOweidi AKS, Abu-Malooch H, Zabalawi M, Alkazaleh F, Abu- Ali H, et al. Intravenous dexmedetomidine infusion for labour analgesia in patient with preeclampsia. *Eur J Anaesth* 2009;26:86-7 [PubMed] doi: 10.1097/EJA.0b0000e000000f3fb.
16. Rosen MA. Nitrous oxide for relief of labor pain: A systematic review. *Am J Obstet Gynecol* 2002;186:S110-26 [PubMed]
17. Yeo ST, Holdcroft A, Yentis SM, Stewart A, Bassett P. Analgesia with sevoflurane in labour. II. Sevoflurane compared with entonox for labour analgesia. *Br J Anaesth* 2007;98:110-5 [PubMed]
18. Singh J, Kaur M, Kulshrestha A, Bajwa SJS. Recent advances in pre-eclampsia management: an anesthesiologist's perspective! *Anesth Pain & Intensive Care* 2014;18(2):209-214 [Free full text]
19. Patel P, Desai P, Gajjar F. Labor epidural analgesia in pre-eclampsia: a prospective study. *J Obstet Gynaecol Res* 2005;31:291-5 [PubMed]
20. Moir DD, Victor-Rodrigues L, Willocks J. Epidural analgesia during labour in patients with pre-eclampsia. *J Obstet Gynaecol Br Commonw.* 1972 May;79(5):465-9. [PubMed]
21. Hodnett ED. Pain and women's satisfaction with the experience of childbirth: a systematic review. *Am J Obstet Gynecol.* 2002 May;186(5 Suppl Nature):S160-72. [PubMed]
22. Bajwa SS, Kulshrestha A, Jindal R. Co-loading or pre-loading for prevention of hypotension after spinal anaesthesia! a therapeutic dilemma. *Anesth Essays Res* 2013;7:155-9 [Free full text]
23. Bajwa SJ, Bajwa SK, Kaur J, Singh A, Singh A, Parmar SS. Prevention of hypotension and prolongation of postoperative analgesia in emergency cesarean sections: A randomized study with intrathecal clonidine. *Int J Crit Illn Inj Sci* 2012;2:63-9 [PubMed] doi: 10.4103/2229-5151.97269.
24. Sng BL, Sia AT, Lim Y, Woo D, Ocampo C. Comparison of computer integrated patient controlled analgesia and patient controlled epidural analgesia with a basal infusion for labour and delivery. *Anaesth Intensive Care* 2009;37:46-53 [PubMed]
25. Simmons SW, Cyna AM, Dennis AT, Hughes D. Combined spinal-epidural versus epidural analgesia in labour. *Cochrane Database Syst Rev* 2007;3CD003401 [PubMed] doi: 10.1002/14651858.CD003401.pub3.
26. Bajwa SJ, Bajwa S, Jasbir Kaur. Comparison of epidural ropivacaine and ropivacaine clonidine combination for elective cesarean sections. *Saudi J Anaesth* 2010;4:47-54 [PubMed]
27. Atiénzar MC, Palanca JM, Torres F, Borràs R, Gil S, Esteve I. A randomized comparison of levobupivacaine, bupivacaine and ropivacaine with fentanyl, for labor analgesia. *Int J Obstet Anesth* 2008;17:106-11 [PubMed]
28. Arzola C, Davies S, Rofaeel A, Carvalho JC. Ultrasound using the transverse approach to the lumbar spine provides reliable landmarks for labour epidurals. *Anesth Analg* 2007;104:1188-92 [PubMed]
29. Leighton BL, Halpern SH. The effect of epidural analgesia on labor, maternal and neonatal outcomes: A systematic review. *Am J Obstet Gynecol* 2002;186: S69-77 [PubMed]
30. Comparative Obstetric Mobile Epidural Trial (COMET) Study Group UK.2001. Effect of low-dose mobile versus traditional epidural techniques on mode of delivery: a randomised controlled trial. *Lancet* 2001;358:19-23 [PubMed]
31. Head BB, Owen J, Vincent RD Jr, Shih G, Chestnut DH, Hauth JC. A randomized trial of intrapartum analgesia in women with severe preeclampsia. *Obstet Gynecol* 2002;99: 452–7
32. Bajwa SK, Bajwa SJ, Kaur J, Singh K, Kaur J. Is intensive care the only answer for high risk pregnancies in developing nations? *J Emerg Trauma Shock* 2010;3:331-6

