

SCIENTIFIC ARTICLE

Combined spinal-epidural block for labor analgesia. Comparative study with continuous epidural block

Angélica de Fátima de Assunção Braga, Vanessa Henriques Carvalho*,
Franklin Sarmento da Silva Braga, Rosa Inês Costa Pereira



Universidade Estadual de Campinas (Unicamp), Faculdade de Ciências Médicas, Departamento de Anestesiologia, Campinas,
SP, Brazil

Received 15 January 2017; accepted 8 August 2018

Available online 28 October 2018

KEYWORDS

Spinal anesthesia;
Combined
spinal-epidural;
Continuous epidural;
Labor analgesia;
Fetal and obstetric
outcomes

Abstract

Introduction: Lumbar epidural block is an effective and routinely used technique for labor pain relief, and the combined spinal-epidural block has the benefit of using lower doses of local anesthetics and rapid onset of analgesia. The objective of this study was to evaluate the effectiveness and safety of two anesthetic techniques: combined spinal-epidural block and continuous epidural block in pregnant women for labor analgesia.

Methods: Eighty patients, ASA II and III, with cephalic presentation and cervical dilation between 5 and 6 cm, undergoing labor analgesia, allocated in two groups according to the anesthetic technique: combined spinal-epidural (G1) and continuous epidural (GII). Pain severity before the blockade, time to complete analgesia, degree of motor blockade, time to full cervical dilation, duration of the second stage of labor, pain severity during the 1st and 2nd stage of labor, type of delivery, use of oxytocin during labor, maternal cardiocirculatory and respiratory parameters and adverse events, and neonatal repercussions were recorded.

Results: At the time of anesthesia, pain severity was similar in both groups. Pain relief was faster in G1 (4.5 ± 1.5 min) when compared to GII (11.6 ± 4.6 min) $p = 0.01$; pain scores in the first and second stages of delivery were lower in G1 (0.9 ± 0.3 and 1.8 ± 0.7 , respectively) when compared to GII (1.9 ± 0.6 and 2.2 ± 0.5 , respectively), with $p = 0.01$ only in the first stage of labor; there was need for local anesthetics supplementation in GII; there were more frequent spontaneous deliveries in G1 (80% of patients) than in GII (50%) ($p = 0.045$) and more frequent use of instrumental ($p = 0.03$) in GII (12 patients) compared to G1 (4 patients); the frequency of cesarean deliveries was significantly higher ($p = 0.02$) in Group II than in Group I, with 4 cases in G1 and 8 cases in GII; absence of maternal cardiocirculatory and respiratory changes and neonatal repercussions; more frequent pruritus in G1 (10 patients) and (0 patients in GII) ($p = 0.02$).

* Corresponding author.

E-mail: vanessahcarvalho74@gmail.com (V.H. Carvalho).

Conclusion: The combined blockade proved to be effective with better quality of analgesia and greater comfort for pregnant women, constituting a good option for the practice of obstetric analgesia.

© 2018 Sociedade Brasileira de Anestesiologia. Published by Elsevier Editora Ltda. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

PALAVRAS-CHAVE

Anestesia espinhal;
Raquiperidural combinada;
Peridural contínua;
Analgesia de parto;
Resultados fetais e obstétricos

Bloqueio combinado raquiperidural para analgesia de parto. Estudo comparativo com bloqueio peridural contínuo

Resumo

Introdução: O bloqueio peridural lombar constitui técnica eficaz e rotineiramente empregada para alívio da dor do parto e o bloqueio combinado raquiperidural tem como benefícios o emprego de doses menores de anestésicos locais e rápido início de analgesia. O objetivo do estudo foi avaliar comparativamente a eficácia e a segurança de duas técnicas anestésicas: bloqueio combinado raquiperidural e peridural contínua em grávidas submetidas à analgesia de parto.

Método: Oitenta gestantes, ASA 2 e 3, apresentação céfálica e dilatação cervical entre cinco e seis centímetros, submetidas à analgesia de parto, distribuídas em dois grupos de acordo com a técnica anestésica: técnica combinada raquiperidural (G1) e peridural contínua (GII). Avaliaram-se: intensidade de dor antes do bloqueio; tempo para completa analgesia; grau do bloqueio motor; tempo para dilatação cervical total; duração do 2º estágio do trabalho de parto; intensidade de dor durante o 1º e o 2º estágio do trabalho de parto; tipo de parto; uso de oxitocina durante trabalho de parto; parâmetros cardiocirculatórios, respiratórios e eventos adversos maternos; repercussões neonatais.

Resultados: No momento da anestesia a intensidade de dor era semelhante em ambos os grupos. O alívio da dor foi mais rápido no G1 ($4,5 \pm 1,5$ min) quando comparado com o GII ($11,6 \pm 4,6$ min) $p = 0,01$; os escores de dor no primeiro e segundo estágios de parto foram menores no G1 ($0,9 \pm 0,3$) e ($1,8 \pm 0,7$) quando comparados com o GII ($1,9 \pm 0,6$) e ($2,2 \pm 0,5$) com $p = 0,01$ somente no primeiro estágio de trabalho de parto; houve necessidade de complementação com anestésicos locais no GII; partos espontâneos mais frequentes em G1 (80% das pacientes) do que em GII (50%) $p = 0,045$ e instrumentais mais frequentes ($p = 0,03$) em GII (12 pacientes) quando comparadas com o G1 (quatro pacientes); a frequência de partos cesáreos foi significativamente maior ($p = 0,02$) no Grupo II do que no Grupo I, quatro casos no G1 e oito no GII; ausência de alterações cardiocirculatórias e respiratórias maternas e repercussões neonatais; prurido mais frequente no G1 (10 pacientes) e (0 paciente no GII) $p = 0,02$.

Conclusão: O bloqueio combinado mostrou-se eficaz com melhor qualidade de analgesia e maior conforto às gestantes, constitui boa opção para a prática de analgesia obstétrica.

© 2018 Sociedade Brasileira de Anestesiologia. Publicado por Elsevier Editora Ltda. Este é um artigo Open Access sob uma licença CC BY-NC-ND (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction

Pain relief during labor, in addition to promoting maternal comfort, prevents the undesirable consequences of stress. Among regional anesthesia, lumbar epidural block is an effective and routinely used technique for labor pain relief, regardless of cervical dilatation. However, its slow onset of sensory block is an inconvenience.¹⁻⁷ The Combined Spinal-Epidural (CSE) blockade technique for labor analgesia has the benefit of using lower doses of local anesthetics, rapid onset of analgesia and a lower incidence of motor blockade, in addition to allowing access to the epidural space through a catheter if necessary.¹⁻⁵ The aim of this study was to evaluate the efficacy and safety of two anesthetic

techniques – combined spinal-epidural (CSE) and continuous epidural (CE) – in nulliparous pregnant women undergoing labor analgesia.

Method

Randomized, double-blind, comparative clinical study of two anesthetic techniques for labor analgesia: combined spinal-epidural (Group I) and continuous epidural (Group II). After approval by the Ethics Committee of the Institution and getting written informed consent, term pregnant women, physical status ASA II and III, single gestation, cephalic presentation, and cervical dilation between 5 and 6 cm were included in the study. Exclusion criteria were

diagnosis of fetal distress prior to indication of analgesia, emergency obstetric status, contraindication to regional anesthesia, history of hypersensitivity to the drugs used, and previous administration of opioids.

The sample size calculation was based on the results of Tsen et al.,⁶ considering the difference of 1.3 h in the mean values of time elapsed between the onset of analgesia and obtaining total cervical dilatation between the two groups (CSE = 3.8 h vs. CE = 5.1 h). Assuming this difference using Student's *t*-test, and considering a level of significance of 5% ($\alpha = 0.05$) and 80% power ($\beta = 20\%$), the sample size was 36 subjects in each group, 40 patients were included in each group to allow for possible losses. Randomization was performed with SAS 9.1 software, based on a uniform distribution with $p = 0.50$ (probability of 50% belonging to Group I (CSE) and 50% belonging to Group II (CE).

After obstetric indication of labor analgesia in the operating room, all patients were continuously monitored with cardioscope in DII lead, pulse oximeter and non-invasive blood pressure monitor, venoclysis with 18G catheter, and infusion of Lactated Ringer's solution. One of the authors prepared the solution to be used, which was unknown to the anesthesiologist who evaluated the studied parameters and performed the blockade.

With the patients in the sitting position, Group I (CRP) received an epidural block applied to the L2–L3 interspace with a 16G Tuohy needle and, after identifying the epidural space through the loss-of-resistance method, a 16G epidural catheter was introduced in the cephalic direction. A 25G Quincke needle was introduced in the L3–L4 interspace, with identification of the subarachnoid space by the CSF drip and injection of 0.5% heavy bupivacaine (2.5 mg) plus sufentanil (5 µg). In Group II (CE), after identifying the epidural space as described for Group I, the association of 0.125% bupivacaine with adrenaline (12.5 mg) plus sufentanil (20 µg) was administered and the catheter was introduced.

After blockade, the pregnant women were placed in the horizontal dorsal decubitus; the Crawford wedge was used to move the uterus to the left until the blockade fixation. Subsequently, the patients were placed in the left lateral decubitus and proclivity; the alternation of decubitus was allowed whenever requested. Oxygen supplementation (2–3 L·min⁻¹) was performed through a nasal catheter.

The labor evolution of parturients was monitored by the obstetrician, including uterine contractility and fetal heart rate, clinically and/or with the help of a fetal monitor. In both groups, the return of painful contractions with a score ≥ 3 (Verbal Numerical Scale; VNS) constituted a parameter for local anesthetic injection via catheter (0.25% bupivacaine with adrenaline – 12.5 mg). When perineal dose supplementation was required, it was performed with 0.25% bupivacaine with adrenaline (12.5 mg).

The following parameters were evaluated:

- (1) *Intensity of pain before blockade*: measured with the aid of the verbal numerical scale of pain;
- (2) *Time to complete analgesia*: time elapsed between the end of the initial injection of the anesthetic solution and the presence of painless uterine contraction (0 and 1 – VNS);

- (3) *Degree of motor block*: evaluated using the modified Bromage scale: 0 = lower limbs mobility (nil); 1 = able to flex knees and move feet; 2 = able to flex only the feet; 3 = lower limbs complete immobility, every 5 min during the first 30 min after the anesthetic solution injection and during the expulsive period, before assuming the lithotomy position;
- (4) *Time to total cervical dilation*: time interval (min) elapsed between blockage and total dilation (end of the 1st stage of labor);
- (5) *Length of the second stage of labor*: time between total cervical dilation and birth;
- (6) Severity of pain (VNS) during the 1st and 2nd stages of labor;
- (7) *Type of delivery*: vaginal with or without forceps and cesarean section;
- (8) Use of oxytocin during labor;
- (9) *Maternal cardiocirculatory and respiratory parameters*: systolic and diastolic blood pressure (SBP and DBP), heart rate (HR), oxygen saturation (SpO₂), and respiratory rate assessed at the following times: before blockade, immediately after blockade, each 5 min during the first 30 min, and then at 15 min intervals until the end of the procedure;
- (10) *Adverse maternal events*: nausea, vomiting, pruritus, drowsiness, hypotension, bradycardia, respiratory depression (Sat.O₂ $\leq 90\%$ and respiratory rate < 10 breaths per minute);
- (11) *Neonatal repercussions*: Apgar score in the first and fifth minutes.

Hypotension was defined as a decrease in systolic blood pressure $\geq 20\%$ of baseline values or below 100 mmHg and, if present, treated with rapid infusion of crystalloids and, if persistent, ephedrine (5–10 mg; venous bolus); bradycardia was defined as heart rate below 50 beats per minute and treated with venous atropine (0.01–0.02 mg·kg⁻¹).

Initial cervical dilatation (cm), assessed by the obstetrician at the time of analgesia indication, was considered as pain severity immediately before the blockade (VNS). At the end of each labor stage, pregnant women were asked to report pain severity (VNS) during these periods. In cases where cesarean section was indicated, 0.5% bupivacaine (75 mg) would be administered through the epidural catheter.

The distribution frequencies of the control and dependent variables were analyzed in the groups to assess their comparability. Fisher's exact test was used to assess the categorical variables; for the numerical variables, the Student *t* or the Mann–Whitney test was used; and for the variables with repeated measures, the MANOVA test was used. The level of significance was 5%.

Results

The analysis of anthropometric data and cervical dilatation (cm) at the time of anesthesia showed that there was no significant difference ($p = 0.07$) between groups. The mean values and standard deviations and number of patients are shown in Table 1. Regarding the physical status (ASA), a predominance of ASA II patients was observed in both groups.

Table 1 Patient characteristics and obstetric parameters.

| | Group I (CSE) | Group II (CE) |
|--|---------------|---------------|
| Age (years) ^a | 20.4 ± 5.1 | 19.2 ± 2.3 |
| Weight (kg) ^a | 69.2 ± 9.7 | 69.0 ± 11.3 |
| ASA (2:3) ^b | 32:08 | 30:10 |
| Cervical dilatation (cm) at the time of analgesia ^a | 5.4 ± 0.5 | 5.6 ± 0.6 |

n = 40 in each group, values presented as mean ± SD; number of patients.

^a Student's t-test.

^b Fisher's exact test.

At the time of anesthesia, the pain severity was similar in both groups ($p = 0.08$), with mean values and standard deviations of pain score equal to 9.8 ± 0.8 and 9.2 ± 1.4 in Groups I and II, respectively.

The time between the blockade and reference of painless uterine contraction was significantly lower in Group I compared to Group II ($p = 0.01$). The degree of motor block varied between 0 and 2, with predominance of degree 0 in all stages of labor. The pain scores assessed between the initial dose and total cervical dilation (end of 1st stage of labor) were significantly lower in Group I compared to Group II ($p = 0.01$). The times elapsed between the onset of analgesia and total cervical dilation, total dilatation and delivery, as well as pain scores during the second stage of labor were lower in Group I compared to Group II, but without significant difference ($p = 0.07$; $p = 0.06$ and $p = 0.06$; respectively) (Table 2).

In the second stage of labor, there was a need for local anesthetic supplementation via catheter in eight cases of Group II.

Regarding the types of delivery between groups, spontaneous vaginal delivery was more frequent in Group I (32 patients – 80%) compared to Group II (20 patients – 50%), which was significant ($p = 0.045$). For vaginal deliveries requiring the use of forceps (instrumental deliveries), there was a significant difference between groups, with four cases

Table 3 Maternal side effects.

| | Group I (CSE) | Group II (CE) | p |
|------------|---------------|---------------|------|
| Vomiting | 02 | 01 | 0.40 |
| Pruritus | 10 | 00 | 0.02 |
| Drowsiness | 05 | 03 | 0.40 |

Fisher's exact test; data presented as number of patients.

in Group I and 12 cases in Group II ($p = 0.03$). The frequency of cesarean delivery was significantly higher ($p = 0.02$) in Group II compared to Group I, with four cases in Group I and eight cases in Group II. The indications for cesarean section were cephalopelvic disproportion and secondary arrest. In these cases, 0.5% bupivacaine (75 mg) was added to the catheter. During labor, oxytocin was used in 14 patients of Group I and in 16 of Group II.

In both groups, hemodynamic and respiratory parameters were similar at all measurement times. All patients maintained respiratory rate above 10 breaths per minute and SpO₂ between 95% and 100%. Hemodynamic changes were similar and there was no significant difference between the mean values of SBP, DBP, and HR in the different times studied. The weight in grams of the newborns (3135 ± 358 for G1 and 3175 ± 478.8 for GII) and vitality conditions were similar between groups. The Apgar score ranged from 8 to 9 in the first minute and by the fifth minute all newborns received Apgar 10.

The occurrence of vomiting and drowsiness was higher in Group I, but without significant difference in relation to Group II. Pruritus was observed in 10 patients of Group I (25%) with significant difference ($p = 0.02$) in relation to Group II (Table 3). No case of headache was recorded in Group I (CSE).

Discussion

The introduction of combined spinal-epidural blockade for labor analgesia has gained popularity as an option for conventional epidural blockade due to its rapid onset of

Table 2 Characteristics of spinal block and course of labor.

| | Group I (CSE) | Group II (CE) | p |
|---|---------------|------------------------|-------|
| Pain scores on indication of analgesia ^a | 9.8 ± 0.8 | 9.2 ± 1.4 | 0.08 |
| Complete analgesia time (min) ^a | 4.5 ± 1.5 | 11.6 ± 4.6* | 0.01 |
| Total dilation analgesia time (min) ^a | 87.4 ± 12.41 | 96.5 ± 8.90 | 0.075 |
| Time between total dilatation – delivery (min) | 29.05 ± 3.6 | 33.1 ± 2.5 | 0.068 |
| Analgesia time – childbirth (min) ^a | 116.45 ± 9.63 | 129.6 ± 9.23 | 0.065 |
| Degree of motor block ^b | | | |
| 0 | 32 | 36 | |
| 1 | 6 | 2 | |
| 2 | 2 | 2 | |
| 3 | 0 | 0 | |
| Pain scores during first stage of labor ^a | 0.9 ± 0.3 | 1.9 ± 0.6 ^a | 0.01 |
| Pain scores during second stage of labor ^a | 1.8 ± 0.7 | 2.2 ± 0.5 | 0.068 |

Mean ± SD, number of patients.

^a Mann-Whitney test.

^b Fisher's exact test.

analgesia and minimal motor block which allows comfort and ambulation to the pregnant woman.^{1,8} Although the epidural blockade is still widely used in clinical practice and with recognized benefits regarding pain relief it is important to be aware of its effects on the course of labor.

There are controversial results in the literature, with reports of decrease, increase or no influence on the duration of the labor stages with epidural block.⁸⁻¹³ In this study, considering the time elapsed between analgesia up to total cervical dilatation and delivery, it was found that in the CSE Group these were clinically minor. However, the statistical analysis showed no significant difference between groups, a result similar to that reported by Singh et al., who compared the analgesia provided by combined (spinal-epidural) block with 0.5 mL of 0.2% ropivacaine associated with 0.5 mL of 25 µg intrathecal fentanyl (followed by continuous infusion of 0.0625% ropivacaine associated with 2 µg·mL⁻¹ of fentanyl in an infusion pump 8 mL·h⁻¹) with that provide by using inhaled N₂O/O₂ (50%/50%) or pethidine (50 mg) associated with promethazine (12.5 mg) intramuscularly.¹² The authors then compared the combined spinal-epidural block with pharmacological techniques of labor analgesia via inhaled and IM routes and did not obtain a significant difference in duration of the two stages of labor.

Regarding the types of delivery, our results differ from those reported by Singh et al., since these authors did not obtain a difference between groups regarding spontaneous and instrumental delivery rates, and in our study our groups showed a significant difference. Regarding the frequency of cesarean sections, our groups also presented a difference, higher for GII, which diverged from that described by Singh et al.¹²

Leighton et al.⁹ showed a decrease in the labor stages of pregnant women undergoing epidural block (EB) compared to parenteral opioid analgesia,⁹ differing methodologically from our study.

A study carried out in Australia, which extrapolated to other methodologies and evaluated the duration of labor with epidural analgesia,¹⁰ demonstrated that the results regarding obstetricians' perception of labor evolution are antagonistic, as 21% of obstetricians, study subjects, reports reduced duration of first stage and 29% of obstetricians believe that EB prolongs the first stage of labor. These last findings resemble those observed by Taneja et al.,¹³ who showed that 30% of obstetricians describe a longer duration of labor, but did not specify at what stage this occurs.

In our study, although the labor stages were slightly longer in the epidural block group compared to the combined spinal-epidural block group, they were not statistically different. This result was similar to that published recently by other authors who compared systemic methods of labor analgesia with combined blockade followed by continuous infusion of local anesthetic associated with opioid in the epidural space.¹² However, these results are contrary to those described by Tsen et al.,⁶ who described faster cervical dilatation in nulliparous pregnant women undergoing early delivery analgesia with the CSE technique, when compared to that observed in pregnant women undergoing epidural block.

Although the mechanism of this event is unclear, it may be related to the use of a lower mass of local anesthetic in the combined blockade, in relation to that used in

the epidural block. The increased duration of labor, the increased need for oxytocin, and the greater frequency of instrumental vaginal deliveries, described when using the conventional epidural technique in labor analgesia, may be due to motor block, perineum premature relaxation, and reflex damage in the second stage of labor, which is necessary for birth, and which are related to the higher concentration of local anesthetics used.⁷

In vitro studies¹⁴ demonstrated local anesthetic effect on uterine activity expressed by an increase in tone, but with a decrease in frequency and strength of uterine contraction. Another hypothesis is related to the rapid relief of pain in pregnant women undergoing combined blockade. Evidence indicates that maternal levels of epinephrine and norepinephrine increase during painful labor and the rapid onset of analgesia with consequent reduction in maternal epinephrine levels observed with combined blockade may justify shorter labor times.^{6,15} Laboratory and clinical studies suggest that changes in uterine activity resulting from decreased epinephrine levels are due to its tocolytic activity and its reduction may be able to stimulate uterine contraction.^{16,17}

In this study, the lower frequency of instrumental vaginal deliveries in pregnant women who received combined blockade may be associated with a shorter time to complete analgesia, lower amount of local anesthetic used, and less need for supplementation with local anesthetics during the course of labor. Although controversial, our results are similar to those achieved by other authors,¹⁸ who respectively described a higher and lower incidence of spontaneous and instrumental delivery in pregnant women undergoing CSE compared to those undergoing CE. In other studies, the anesthetic technique did not influence the outcome of childbirth.^{7,12}

Considering reports in the literature¹⁹ that labor and, consequently, the rate of cesareans may be increased when continuous epidural analgesia is used primarily during labor; in this study, the statistically significant incidence that 10% of cesarean sections occurred in CSE group and 20% in CE group contradicted other authors who found no increase in these rates.^{7,20}

However, regarding pain control, in contrast to the results reported by Nageotte et al.,¹⁸ our results showed better analgesic quality in CSE group, expressed by lower pain scores during the first stage of labor and no need for local anesthetic supplementation during the second stage of labor, compared with CE group. The low pain scores seen in CE group during the second stage of labor, with no significant difference in relation to the CSE group, may be attributed to the local anesthetic supplementation via catheter, necessary for pain relief in this period.

The distribution of side effects was similar in both groups, except for pruritus, which was significantly more frequent in CSE group. Although transient, it can cause great discomfort to patients, the opioid dose is the determining factor for this effect. However, adverse effects such as nausea, vomiting, and pruritus can be minimized when smaller doses of these drugs are used.²¹

The results of this study demonstrate a better efficacy of combined blockade during labor, with faster pain relief, greater comfort for pregnant women, better quality of analgesia, and greater frequency of spontaneous delivery and it

may be recommended as a good option for the practice of obstetric analgesia.

Conflicts of interest

The authors declare no conflicts of interest.

References

1. Ranasinghe JS, Birnbach DJ. Progress in analgesia for labor: focus on neuraxial blocks. *Int J Womens Health*. 2010;1:31–43.
2. Cambic CR, Wong CA. Labour analgesia and obstetric outcomes. *Br J Anaesth*. 2010;150:i50–60.
3. Collis RE, Davies DWL, Aveling W. Randomised comparison of combined spinal-epidural and standard epidural analgesia in labour. *Lancet*. 1995;345:1413–6.
4. Van de Velde M, Mignolet K, Vandermeersch E, et al. Prospective, randomized comparison of epidural and combined spinal epidural analgesia during labor. *Acta Anaesthesiol Belg*. 1999;50:129–36.
5. Gambling D, Berkowitz J, Farrell TR, et al. A randomized controlled comparison of epidural analgesia and combined spinal-epidural analgesia in a private practice setting: pain scores during first and second stages of labor and at delivery. *Anesth Analg*. 2013;116:636–43.
6. Tsen LC, Thue B, Datta S, et al. Is combined spinal-epidural analgesia associated with more rapid cervical dilation in nulliparous patients when compared with conventional epidural analgesia? *Anesthesiology*. 1999;91:920–5.
7. Simmons SW, Taghizadeh N, Dennis AT, et al. Combined spinal-epidural versus epidural analgesia in labour. *Cochrane Database Syst Rev*. 2012;10:CD003401.
8. Arendt KW. The 2015 Gerard W Ostheimer lecture: what's new in labor analgesia and cesarean delivery. *Anesth Analg*. 2016;122:1524–31.
9. Leighton BL, Halpern SH. The effects of epidural analgesia on labor, maternal, and neonatal outcomes: a systematic review. *Am J Obstet Gynecol*. 2002;186:S69–77.
10. Vandendriesen NM, Lim W, Paech MJ, et al. Obstetricians' knowledge and attitudes toward epidural analgesia in labour. *Anaesth Intensive Care*. 1998;26:563–7.
11. Sohaib M, Ismail S. Does labour epidural slow the progress of labour and lead to complications? Obstetricians' perception working in private and public sector teaching hospitals in a developing country. *Indian J Anaesth*. 2015;59: 779–84.
12. Singh SK, Yahya N, Misiran K, et al. Combined spinal-epidural analgesia in labour: its effects on delivery outcome. *Braz J Anesthesiol*. 2016;66:259–64.
13. Taneja B, Nath K, Dua CK. Clinical audit on the existing attitudes and knowledge of obstetricians regarding labour analgesia. *Indian J Anaesth*. 2004;48:185–8.
14. McCaughey HS Jr, Corey EL, Eastwood D, et al. Effects of synthetic anesthetics on the spontaneous motility of human uterine muscles in vitro. *Obstet Gynecol*. 1962;19:233–40.
15. Cascio M, Pygon B, Bennett C, et al. Labour analgesia with intrathecal fentanyl decreases maternal stress. *Can J Anaesth*. 1997;44:605–9.
16. Lederman RP, Lederman E, Work BA, et al. The relationship of maternal anxiety, plasma catecholamines, and plasma cortisol to progress in labor. *Am J Obstet Gynecol*. 1978;132: 495–500.
17. Segal S, Csavoy AN, Datta S. The tocolytic effect of catecholamines in the gravid rat uterus. *Anesth Analg*. 1998;87:864–9.
18. Nageotte MP, Larson D, Rumney PJ, et al. Epidural analgesia compared with combined spinal-epidural analgesia during labor in nulliparous women. *N Engl J Med*. 1997;337:1715–9.
19. Thorp JA, Parisi VM, Boylan PC, et al. The effect of continuous epidural analgesia on cesarean section for dystocia in nulliparous women. *Am J Obstet Gynecol*. 1989;161:670–5.
20. Ohel G, Gonon R, Vaida S, et al. Early versus late initiation of epidural analgesia in labor: does it increase the risk of cesarean section? A randomized trial. *Am J Obstet Gynecol*. 2006;194:600–5.
21. Armstrong S, Fernando R. Side effects and efficacy of neuraxial opioids in pregnant patients at delivery: a comprehensive review. *Drug Saf*. 2016;39:381–99.