THE JOURNAL OF OBSTETRICS AND GYNECOLOGY OF INDIA

The Journal of Obstetrics and Gynecology of India (May–June 2019) 69(3):258–265
https://doi.org/10.1007/s13224-018-1189-2

ORIGINAL ARTICLE

Can Epidural Dexamethasone Reduce Patient-Controlled Epidural Consumption of Fentanyl and Levobupivacaine in Laboring Women? A Double-Blind, Randomized, Placebo-Controlled Trial

Ankur Dhal[1] · Sukanya Mitra[1] · Richa Saroa[1] · Jasveer Singh[1] · Reeti Mehra[2]

Received: 4 July 2018 / Accepted: 10 November 2018 / Published online: 22 November 2018
© Federation of Obstetric & Gynecological Societies of India 2018

About the Author

Dr. Ankur Dhal completed his postgraduation (M.D.) in anesthesiology from Government Medical College and Hospital, Chandigarh, India. His area of interest includes obstetric anesthesia and pain management. He takes a keen interest in labor analgesia. He has extracurricular interests as well, particularly in music and singing.

Abstract

Background The efficacy of a single bolus dose of epidural dexamethasone added to levobupivacaine–fentanyl combination for labor analgesia has not been studied. In this randomized double-blind controlled trial, we assessed the effect of epidural dexamethasone in reducing the hourly average consumption of epidural levobupivacaine–fentanyl combination in laboring parturients and to study its effect on pain score, maternal satisfaction, maternal and neonatal outcome.

Ankur Dhal completed his postgraduation (M.D.) in anesthesiology from Government Medical College and Hospital, Chandigarh, India. Sukanya Mitra is a Professor in Department of Anesthesia and Intensive Care, Government Medical College and Hospital, Chandigarh, India. Richa Saroa is Associate Professor, Department of Anaesthesia and Intensive Care, Government Medical College and Hospital, Chandigarh, India. Jasveer Singh is Associate Professor, Department of Anaesthesia and Intensive Care, Government Medical College and Hospital, Chandigarh, India. Reeti Mehra is Associate Professor, Department of Obstetrics and Gynaecology, Government Medical College and Hospital, Chandigarh, India.

✉ Sukanya Mitra
drsmitra12@yahoo.com

Ankur Dhal
ankur_dhal@yahoo.com

Richa Saroa
richajayant@rediffmail.com

Jasveer Singh
drjassy18@gmail.com

Reeti Mehra
drreetidatta@yahoo.co.in

[1] Department of Anaesthesia and Intensive Care, Government Medical College and Hospital, Sector 32, Chandigarh 160030, India

[2] Department of Obstetrics and Gynaecology, Government Medical College and Hospital, Chandigarh, India

Methods Sixty adult ASA I-II single-gestation full-term primigravid laboring parturients with cervical dilation $\leq$ 5 cm were randomly assigned to two equal-sized groups. Combined spinal–epidural block was performed in all the parturients. After placing the epidural catheter in epidural space, 8 mg of preservative-free dexamethasone was administered to the dexamethasone group, and 0.9% saline to the placebo group. All parturients received continuous background infusion of 5 ml of 0.1% levobupivacaine with 2 μg/ml of fentanyl with the provision of patient-controlled bolus of 5 ml of 0.1% levobupivacaine with 2 μg/ml of fentanyl (lockout interval 15 min). The primary outcome measure was the hourly total consumption of levobupivacaine–fentanyl mixture. The secondary outcome measures were maternal satisfaction, pain score, maternal hemodynamic parameters, fetal heart rate, duration of second stage of labor, mode of delivery, Apgar scores and adverse effects.

Results Hourly drug consumption and hourly bolus requirement were significantly lower in the dexamethasone group than placebo group (6.97 ml $\pm$ 1.22 vs. 8.40 ml $\pm$ 2.59 and 0.41 $\pm$ 0.26 vs. 0.72 $\pm$ 0.55, respectively, $P = 0.008$ for both). There were no significant differences in other outcome measures.

Conclusion Epidural dexamethasone significantly decreased average hourly drug consumption and the number of boluses in laboring parturients, thus providing epidural drug dose-sparing effect.

Keywords Dexamethasone · Epidural · Labor analgesia · Randomized controlled trial

Introduction

Ensuring safety and adequacy of analgesia in a laboring parturient has always been a challenge for anesthesiologists. With rapidly advancing knowledge of physiology and pharmacotherapy of pain, newer techniques and pharmacological agents are emerging and broadening the spectrum of labor analgesia.

Neuraxial analgesia is considered as "the gold standard" for labor analgesia. Combined spinal–epidural analgesia (CSEA) and patient-controlled epidural analgesia (PCEA) are among the newer techniques that allow for optimization of labor analgesia [1, 2]. Introduction of newer local anesthetics like levobupivacaine and ropivacaine and the adjuvant drugs like opioids, neostigmine and clonidine has advanced the practice of pain management by partially circumventing the adverse effects like motor blockade and prolongation of duration of labor [3]. Unfortunately, these agents are also not free from adverse effects. Hence, the quest for newer and safer agents continues (Fig. 1).

Dexamethasone is a relatively newer agent in this context. It has been extensively used in clinical practice for surgical pain relief via oral, intravenous (IV) and epidural routes, as summarized in several recent systematic reviews and meta-analyses focusing on efficacy and safety of single use in perioperative settings [4–6]. These systematic reviews and meta-analyses generally indicate its efficacy as an analgesic adjunct as well as safety in the short-term, though the need for further studies has also been emphasized. However, there are very limited data available for its efficacy in labor analgesia. This study assessed the effect of dexamethasone administered epidurally as part of CSEA, on the dose requirement of epidural levobupivacaine–fentanyl combination and also on the pain score, maternal satisfaction, maternal and neonatal outcome.

Methods

This was a prospective, double-blind, randomized placebo-controlled trial following ethics committee approval by the institute and trial registration (CTRI/2015/02/005558 at http://ctri.nic.in). Patients were recruited from July 2015 till June 2016. After obtaining written informed consent from the patients, 60 parturients belonging to American Society of Anesthesiologists (ASA) physical status I and II, more than 18 years of age, primigravida with single gestation and cephalic presentation at $\geq$ 37 weeks of gestation, cervical dilation $\leq$ 5 cm with baseline pain score $>$ 30 (on 0–100 VAS) and requesting epidural analgesia were selected for the study.

Patients who refused labor analgesia and had an administration of oral or parenteral analgesics in last 4 h before the start of neuraxial block, gestational age $<$ 37 weeks, history of obstetric complication, fetus with non-reassuring non-stress test or with a known or suspected congenital abnormality, allergy to study drugs, preexisting or gestational diabetes mellitus, already receiving steroids or any history of immunosuppression, with local infection or deranged coagulation profile were excluded from study. These exclusion criteria were chosen to exclude any high-risk patients and those who received prior analgesics (to avoid confounding).

The primary outcome measure for this study was hourly total consumption of neuraxially administered drugs in terms of ml/h of the levobupivacaine–fentanyl combination. The secondary outcome measures were maternal satisfaction, pain score, maternal hemodynamic parameters, fetal heart rate, duration of second stage of labor, mode of delivery, Apgar scores and adverse effects.

The patients were randomized into two groups of 30 each by using computer-generated random number tables using coded and sealed opaque envelopes to receive one of the following regimens via the epidural route:

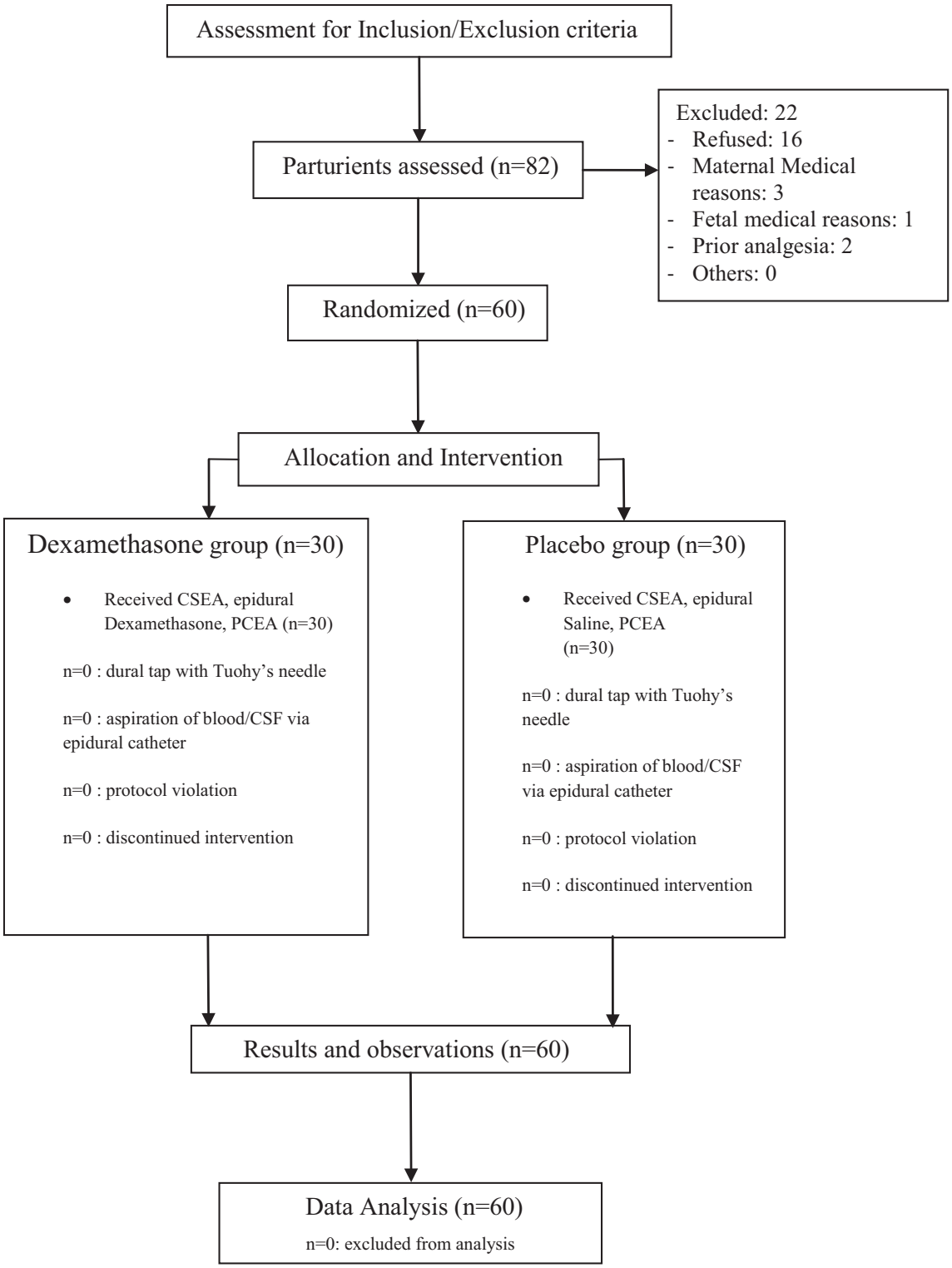

Fig. 1 CONSORT flow diagram of study. *CSEA* Combined spinal–epidural analgesia, *PCEA* patient-controlled epidural analgesia

Group I (dexamethasone group) received bolus of 8 mg preservative-free dexamethasone dissolved in 10 ml of 0.9% saline.

Group II (placebo group) received bolus of 10 ml of 0.9% saline.

A person not involved in the study opened a sealed envelope containing a number, drew the vial corresponding to the number in the sealed envelope and prepared the study solution in similar-looking syringes. The patients as well as the primary investigator who made the various

observations after the epidural catheter placement were blinded to the group allocation of the patients.

For insertion of the epidural catheter, patients were taken to the area adjoining the operation theater located within the labor unit but designated exclusively for cesarean sections. Preloading with Ringer's lactate solution at 10 ml/kg IV was done. Multichannel monitors (Datex Light, Helsinki) were attached, and baseline heart rate (HR), electrocardiogram (ECG), noninvasive blood pressure (NIBP) and oxygen saturation (SPO_2) were obtained. Baseline fetal heart rate (FHR) was also recorded using external cardiotocography to ensure fetal well-being. A baseline visual analog pain score (VAS based on a 0–100 mm scale; 0 mm = no pain and 100 mm = worst pain imagined) was also obtained. Patients were continuously monitored for HR, ECG, NIBP and SPO_2 throughout the study period.

Under all aseptic precautions, CSE block was performed in L3-4 or L4-5 interspace in all the parturients in sitting position using needle-through-needle technique (using "BD Durasafe^{TM} Plus!" CSE kit). The neuraxial block was performed by a resident under the supervision of an experienced anesthesiologist. With 18G Tuohy's needle, epidural space was reached using loss of resistance to air technique. After confirming the free flow of cerebrospinal fluid (CSF) through a 27-G spinal needle, 0.5 ml of 0.5% hyperbaric bupivacaine (2.5 mg) was injected intrathecally. A 20-G epidural catheter was inserted, and 4 cm of the catheter was left in situ. Aspiration test was performed, and if aspirate contained blood or CSF, catheter was taken out and resited and the patient was excluded from the study and was managed according to the departmental protocol. The study solution was administered as per randomization (8 mg preservative-free dexamethasone dissolved in 10 ml of 0.9% saline to the dexamethasone group and 10 ml of 0.9% saline to the placebo group) in a double-blind manner. The syringe containing the study solution was handed over to the anesthesiologist performing the block. After the administration of the study drug, catheter was fixed and the patient was placed in the supine position. All the patients received PCEA infusion after positioning them supine.

Maintenance of PCEA (Master PCA pump, Fresenius Kabi, Finland) was started in both the groups with infusions of levobupivacaine 0.1% with 2 μg/ml of fentanyl at 5 ml/h. The patients were provided with a remote-controlled handheld button, and there was provision of patient-controlled boluses of 5 ml of 0.1% levobupivacaine with 2 μg/ml of fentanyl with a lockout interval of 15 min.

The patients were monitored for HR, ECG, NIBP, SPO_2, visual analog scale (VAS) 0–100 pain score, level of sensory block and motor power using the modified Bromage scale [7] in the operation theater for 20 min before shifting the patient to labor room for monitoring the mother and fetus during the course of labor.

Time of intrathecal drug administration and the delivery of baby were considered as the start (i.e., 0 min) and the end of study period, respectively. HR, NIBP (systolic and diastolic), SPO_2 and FHR were continuously monitored and recorded at 5, 10, 15, 20, 30, 40, 50, 60 min and then every 1 h until delivery. Hypotension was defined as a decrease in systolic BP of more than 20% below baseline and was treated with left uterine tilt, IV fluids and vasopressors (5 mg ephedrine or 50 μg phenylephrine) as necessary. ECG was continuously monitored throughout the study period.

The other variables measured were total consumption of analgesic drugs (background infusion and bolus doses), time of onset of sensory block, time of onset of analgesia (VAS < 30), duration of second stage of labor, mode of delivery, pain score (VAS) which was monitored hourly up to 12 h after delivery, maternal satisfaction (VAS), Apgar scores at 1 and 5 min, adverse effects, if any.

Statistical Analysis

Sample size calculation: From our own previous data on 30 patients undergoing labor epidural analgesia with PCEA in our hospital, it was seen that the mean hourly consumption was 9.69 ml/h, with a standard deviation (SD) of 2.58. Following the example of Ross et al. [8], it was decided that a 20% reduction in hourly consumption of neuraxial analgesic combination would be considered as clinically meaningful difference, yielding a value of 7.75 ml/h with SD of 2.58 as the mean hourly neuraxial drug consumption in the dexamethasone group.

Thus, for this study, sample size analysis with the above assumption and with a beta-error of 0.20 (i.e., power of 80%) and an alpha-error of 0.05 demonstrated that a sample size of 28 per group would allow us to detect a 20% difference in total epidural drug combination volume required per hour. To allow for slight oversampling, it was decided to have a total sample size of 60 patients, with 30 patients per group.

Data analysis was done per protocol, as patients were admitted for up to 48 h following delivery as per our hospital policy, and hence all were available for the study period. For normally distributed data (checked by Kolmogorov–Smirnov test), means of two groups were compared using independent Student's t test (age, height, weight, hemodynamic measures, pain scores, total drug consumed per hour). Mann–Whitney U test was used for skewed data (cervical dilatation, duration of second stage of labor, maternal satisfaction, number of bolus doses). Proportions were compared using Chi-square or Fisher's exact test, depending on their applicability (proportions of ASA-1

patients, mode of delivery, Apgar score bands, adverse effects; for time-related variables of scores, Kaplan–Meier log-rank test was applied (pain scores); for normally distributed data, ANOVA followed by post hoc multiple comparisons test (Dunnett's t test) was carried out (pain scores). All the statistical tests were two-sided and were performed at a significant level of $\alpha = 0.05$. Analysis was conducted using IBM SPSS STATISTICS (version 22.0).

Results

A total of 60 patients, 30 in each group, completed the study. Demographic, obstetric and neonatal measures are shown in Table 1 and incidence of adverse effects is shown in Table 2.

Baseline pain scores recorded just before neuraxial analgesia were similar in both the groups (90.83 ± 13.40 in the dexamethasone group and 90.60 ± 15.48 in the placebo group). Both groups documented a significant improvement in pain as compared with the baseline (Table 3).

Time to onset of analgesia was recorded from the time of administration of intrathecal drug to the time when VAS became less than 30. It was comparable in both the groups (12.27 ± 7.49 min in the dexamethasone group and 14.20 ± 13.93 min in the placebo group).

The hourly consumption of epidural levobupivacaine and fentanyl combination in the dexamethasone group (6.97 ± 1.22 ml/h) was significantly lower compared to the placebo group (8.40 ± 2.59 ml/h; $p < 0.05$). Similar results were obtained while comparing the hourly bolus consumption (0.41 ± 0.26 in the dexamethasone group vs. 0.72 ± 0.55 in the placebo group. $p < 0.05$) (Table 4).

The mean maternal HR, NIBP (systolic and diastolic), SPO_2 and the FHR were found to be comparable and statistically nonsignificant at different time points between the two groups ($p > 0.05$). Based on modified Bromage scale, 15 patients in dexamethasone group and 12 patients in placebo group had motor block, but this was not statistically significant ($p > 0.05$).

On the day after delivery, all women were questioned regarding their satisfaction for analgesia and future desire to use it in subsequent pregnancies. Mothers quantified their overall perception of adequacy of epidural analgesia and its side effects and the aspects of their psychological state during labor on a 0–100 visual analog scale. The mean maternal satisfaction was 95.43 ± 12.04 in the dexamethasone group and 93.00 ± 10.80 in the placebo group. We observed no significant difference in global maternal satisfaction between the two groups ($p > 0.05$).

Table 1 Demographic, obstetric and neonatal measures

Characteristics	Dexamethasone group $N = 30$	Placebo group $N = 30$	P value
Age (years)	24.73 ± 3.11	25.90 ± 3.38	0.169
Height (cm)	159.94 ± 7.41	161.71 ± 5.98	0.311
Weight (kg)	63.20 ± 11.54	66.26 ± 12.08	0.319
No. of ASA-1 patients (%)	21 (70.0%)	14 (46.7%)	0.067
Cervical dilatation (cm)	3.12 ± 0.86	3.08 ± 0.77	0.874
Modes of delivery			
Normal	20 (66.7%)	20 (66.7%)	1.000
Instrumental	7 (23.3%)	7 (23.3%)	1.000
Cesarean	3 (10%)	3 (10%)	1.000
Duration of second stage (min)			
$N = 27$ (in each group)[a]	56.48 ± 37.64	62.78 ± 48.60	0.597
Maternal satisfaction score	95.43 ± 12.04	93.00 ± 10.80	0.166
Apgar score at 1 min			
9	27 (90)	23 (76.7)	0.572
8	2 (6.7)	4 (13.3)	0.414
7	1 (3.3)	2 (6.7)	0.564
< 7	0 (0)	1 (3.3)	1
Apgar score at 5 min			
9	30 (100)	28 (93.3)	0.793
8	0 (0)	1 (3.3)	1
7	0 (0)	1 (3.3)	1

[a]In each group, 27 patients underwent vaginal delivery (20 normal vaginal, 7 instrumental)

Table 2 Incidence of adverse effects

	Dexamethasone group (%)	Placebo group (%)	*P* value (Fisher exact test)
Pruritus	3.3	0	0.313
Nausea	20	13.3	0.488
Vomiting	20	16.7	0.739
Shivering	40	33.3	0.592
Fever	0	3.3	0.313
Hypotension	23.3	20	0.754
Motor block	50	40	0.436
Fetal bradycardia	16.7	16.7	1.000
Urinary retention	0	0	1.000
Postdural puncture headache	0	0	1.000
Nerve injury	0	0	1.000

Table 3 Comparison of mean visual analog scale (VAS) pain scores in the two groups

VAS	Dexamethasone group *N* = 30	Placebo group *N* = 30	*P* value
0 Min	90.83 ± 13.40	90.60 ± 15.48	0.906
5 Min	50.33 ± 19.91	55.60 ± 26.24	0.580
10 Min	27.17 ± 26.48	27.67 ± 32.02	0.666
15 Min	17.17 ± 25.55	15.50 ± 22.45	0.937
20 Min	14.17 ± 22.09	12.27 ± 19.40	0.987
30 Min	9.67 ± 14.74	16.93 ± 22.84	0.298
40 Min	15.83 ± 19.44	22.77 ± 25.87	0.401
50 Min	14.67 ± 16.61	23.53 ± 21.90	0.106
1 H	21.40 ± 25.27	29.87 ± 24.58	0.083
2 H	31.19 ± 27.17	25.23 ± 25.51	0.419
3 H	27.48 ± 28.70	45.45 ± 28.37	0.024
4 H	40.00 ± 28.94	34.12 ± 24.51	0.566
5 H	26.43 ± 28.99	37.69 ± 29.20	0.310
6 H	42.22 ± 40.55	44.44 ± 36.52	0.894
7 H	20.00 ± 6.33	52.86 ± 33.02	0.064
8 H	17.50 ± 9.57	35.00 ± 30.69	0.241
9 H	67.50 ± 35.94	43.33 ± 30.77	0.334
10 H	42.50 ± 33.04	17.50 ± 12.58	0.219
11 H	25.00 ± 7.07	47.50 ± 40.31	0.481
12 H	35.00 ± 7.07	35.00 ± 7.07	1.000
13 H		80.00 ± 28.28	
14 H		25.00 ± 7.07	
15 H		40.00 ± 14.14	
16 H		65.00 ± 21.21	
17 H		30.00	

The data are represented as mean ± standard deviation. *N* number of patients

Discussion

In the present study, when the hourly consumption of levobupivacaine–fentanyl admixture was compared between the two groups, it was found that the dexamethasone group had a significantly lesser consumption of hourly levobupivacaine–fentanyl combination and lesser hourly bolus requirement compared to placebo, thus demonstrating the dose-sparing effect of dexamethasone when used as an adjunct in labor analgesia through the epidural route.

Table 4 Hourly consumption of epidural levobupivacaine–fentanyl combination and number of boluses

Group	Total hourly consumption of levobupivacaine–fentanyl combination (ml/h) $N = 30$	Number of boluses/h $N = 30$
Dexamethasone group	6.97 ± 1.22	0.41 ± 0.26
Placebo group	8.40 ± 2.59	0.72 ± 0.55
P value	0.008	0.008

Various studies have demonstrated the analgesic property of dexamethasone used via oral, IV or neuraxial routes as an analgesic adjuvant [4–6, 9]. Regarding epidural dexamethasone, a number of studies have found epidural dexamethasone to be an effective analgesic adjunct for several conditions [10, 11]. However, there are limited data available for its effectiveness in labor analgesia. Finally, in a meta-analysis of 45 studies involving 5796 patients receiving dexamethasone, the authors concluded that the patients treated with IV dexamethasone experienced less postoperative pain, required less postoperative opioids, had longer time to the first analgesic dose, needed less rescue analgesia and had a shorter post-anesthesia care unit stays. The authors reported small elevations in blood glucose levels at 24 h after operation, but there was no apparent increase in adverse effects because of that. No increased risk of infection or delayed wound healing was reported [12].

Although the exact mechanism of analgesic action of perineural dexamethasone is not known, there is evidence from recent systematic reviews of its analgesic efficacy through the regional analgesia route [13, 14]. It may be related to the anti-inflammatory action, edema reduction or shrinkage of connective tissue, but also suppression of transmission in normal nociceptive C fibers [5, 6]. In a recently conducted experiment on rats, epidural administration of 300 μg of dexamethasone was shown to have an attenuating effect on the peripheral inflammatory tissue injury-induced hyperalgesia, mediated through the inhibition of PLA_2 in the spinal cord [15]. However, it is difficult to extrapolate these findings to the putative action of dexamethasone on labor pain. Labor pain is nociceptive (physiological) in nature, due to severe pressure and stretch arising in the cervix and nearby structures. It has a visceral component and a somatic component. The visceral component of pain sensation is carried by unmyelinated C fibers, whereas the somatic component of pain sensation is carried by myelinated A fibers. The action of dexamethasone of suppression of transmission in normal C fibers may explain its analgesic effect on the visceral component of labor pain. For the component of somatic pain, we can only speculate about a possible role of the cytokine interleukin-6, which is increased during labor pain, and it is attenuated by dexamethasone [16]. Of course, at this stage it is only a conjecture and it needs to be studied further.

In two recently published studies from Egypt, using the same control group but adding epidural dexamethasone to either epidural anesthesia or CSEA in laboring parturients, the authors did not find any difference in adverse effects on the mother, fetus or neonate between the control group and the two dexamethasone groups [17, 18]. These two studies are the only studies currently directly comparable with ours, in terms of patient groups, study design and procedures.

The strength of the present study was its double-blind, randomized, placebo-controlled design with adequate sample size to provide sufficient power to detect significant differences. A limitation of the study was lack of blood level estimation of dexamethasone, although this does not decrease the clinical value of the study findings.

In conclusion, this study demonstrated that epidural administration of 8 mg of dexamethasone significantly decreased average hourly drug consumption (ml/h) and the number of boluses in parturients using PCEA, thus providing the epidural drug dose-sparing effect. Both groups were comparable in maternal satisfaction, mode of delivery, duration of second stage of labor, maternal and fetal parameters and incidence of side effects, thus emphasizing the safety and efficacy of use of epidural dexamethasone as an adjunct in the intrapartum period.

Compliance with Ethical Standards

Conflict of interest All the authors declare that they have no conflict of interest.

Human and Animal Rights All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008.

Informed Consent Informed consent was obtained from all patients for being included in the study.

References

1. Sng BL, Kwok SC, Sia AT. Modern neuraxial labor analgesia. Curr Opin Anaesthesiol. 2015;28:285–9.
2. Wong CA. Labor analgesia: is there an ideal technique? Anesth Analg. 2009;109:296–8.
3. Pandya ST. Labor analgesia: recent advances. Indian J Anaesth. 2010;54:400–8.
4. Albrecht E, Kern C, Kirkham KR. A systematic review and meta-analysis of perineural dexamethasone for peripheral nerve blocks. Anaesthesia. 2015;70:71–83.
5. Li X, Xu G, Xie W, et al. The efficacy and safety of dexamethasone for pain management after total knee arthroplasty: a systematic review and meta-analysis. Int J Surg. 2018;53:65–71.

6. Toner AJ, Ganeshanathan V, Chan MT, et al. Safety of perioperative glucocorticoids in elective noncardiac surgery: a systematic review and meta-analysis. Anesthesiology. 2017;126:234–48.
7. Curry PD, Pacsoo C, Heap DG. Patient-controlled epidural analgesia in obstetric anesthetic practice. Pain. 1994;57:125–7.
8. Ross VH, Pan PH, Owen MD, et al. Neostigmine decreases bupivacaine use by patient-controlled epidural analgesia during labor: a randomized controlled study. Anesth Analg. 2009;109:524–31.
9. Hefni AF, Mahmoud MS, Al Alim AA. Epidural dexamethasone for post-operative analgesia in patients undergoing abdominal hysterectomy: a dose ranging and safety evaluation study. Saudi J Anesth. 2014;8:323–7.
10. Naghipour B, Aghamohamadi D, Azarfarin R, et al. Dexamethasone added to bupivacaine prolongs duration of epidural analgesia. Middle East J Anesthesiol. 2013;22:53–7.
11. Jo YY, Yoo JH, Kim HJ, et al. The effect of epidural administration of dexamethasone on postoperative pain: a randomized controlled study in radical subtotal gastrectomy. Korean J Anesthesiol. 2011;61:233–7.
12. Waldron NH, Jones CA, Gan TJ, et al. Impact of perioperative dexamethasone on postoperative analgesia and side-effects: systematic review and meta-analysis. Br J Anaesth. 2013;110:191–200.
13. Hussain N, Van den Langenbergh T, Sermer C, et al. Equivalent analgesic effectiveness between perineural and intravenous dexamethasone as adjuvants for peripheral nerve blockade: a systematic review and meta-analysis. Can J Anaesth. 2018;65(2):194–206.
14. Zorrilla-Vaca A, Li J. Dexamethasone injected perineurally is more effective than administered intravenously for peripheral nerve blocks: a meta-analysis of randomized controlled trials. Clin J Pain. 2018;34:276–84.
15. Min SH, Soh JS, Park JY, et al. Epidural dexamethasone decreased inflammatory hyperalgesia and spinal cPLA2 expression in a rat formalin test. Yonsei Med J. 2014;55:1631–9.
16. Wang LZ, Hu XX, Liu X, et al. Influence of epidural dexamethasone on maternal temperature and serum cytokine concentration after labor epidural analgesia. Int J Gynaec Obstet. 2011;113:40–3.
17. Wahdan AS, El-Sakka AI, Gaafar HM. The effect of addition of dexamethasone to levobupivacaine in parturients receiving combined spinal-epidural for analgesia for vaginal delivery. Indian J Anaesth. 2017;61:556–61.
18. Ali HM, Wahdan A. Using dexamethasone as an adjuvant to levobupivacaine in epidural anesthesia to change the pain intensity and duration in painless labor. Saudi J Anaesth. 2018;12:209–14.