Journal of Cardiovascular Disease Research

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 07, 2023

Original research article

Addition of neostigmine on dose requirement of Ropivacaine 0.1% in labouring patients: APGAR score and Maternal Satisfaction

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Abstract

Clinically significant motor block may occur after repeated bolus doses or continuous infusion of local anaesthetic for a long time into epidural space. Extensive motor blockade may impair maternal expulsive efforts during the second stage of labour and increase the likelihood of instrumental delivery. Patients were randomized into two groups using computer generated random numbers:

Group A: Received 0.1% Ropivacaine with fentanyl 2µg/ml in 10 ml total volume.

Group B: Received 0.1% Ropivacaine with fentanyl 2µg/ml and neostigmine 500µg in 10 ml total volume.

The APGAR score of newborn at 1 min in both group A and group B was statistically significant (p value 0.044), while the APGAR score of newborn at 5min in both groups A and B was statistically insignificant (p value 0.136).4% patients in group A and 20% patients in group B had an excellent satisfaction with regard to their experience of birth process and labour analgesia, which was statistically significant (p value 0.012).

Keywords: APGAR score, maternal satisfaction, neostigmine

Introduction

Epidural anaesthesia can cause local anaesthetic induced systemic toxicity primarily through inadvertent administration of drug into an epidural vein. In obstetrics, incidence of intravascular injection is reduced by placing the patient in lateral position (rather than sitting) during needle and catheter insertion, administering fluid through the epidural needle before catheter insertion, using a single-orifice catheter or a wire embedded polyurethane compared with polyamide epidural catheter, and advancing the catheter less than 6 cm into the epidural space [1].

Epinephrine (15 µg) in 3 mL of local anaesthetic remains the best pharmacological method of detecting intravascular placement in non-pregnant adult patients. However, use of epinephrine is controversial in obstetric patients, as intravascular injection of epinephrine may compromise the blood supply to fetoplacental unit. Also, the cardiovascular changes occurring during active labour may represent a false-positive response to epinephrine. Systemic toxicity can be prevented by aspiration of the catheter and incremental administration of the local anesthetic [2].

An unexpectedly high level of anaesthesia may occur after unintentional injection of local anaesthetic (via a needle or catheter) into either the subarachnoid or subdural space during initiation of epidural analgesia or anaesthesia. Alternatively, the epidural catheter may migrate into subarachnoid or subdural space during the course of labour and delivery. Finally, high spinal blockade may result from an overdose of local anaesthetic in the epidural space. High or total spinal anaesthesia results in agitation, profound hypotension, dyspnoea, inability to speak, and loss of consciousness. Loss of consciousness usually results from cerebral hypoxia secondary to cerebral hypo perfusion. Aspiration alone is not a completely reliable method of excluding subarachnoid placement of the catheter. Administration of an appropriate test dose and careful assessment of the patient's response to the test dose minimizes the chance of inadvertent injection of a large dose of local anaesthetic into the subarachnoid space [3].

Clinically significant motor block may occur after repeated bolus doses or continuous infusion of local anaesthetic for a long time into epidural space. Extensive motor blockade may impair maternal expulsive efforts during the second stage of labour and increase the likelihood of instrumental delivery [4].

Epidural haematomas may present as neurological deficits in the postoperative period due to cord compression. On insertion of catheter in an area at high risk for contamination such as sacral hiatus may increase the risk of abscess formation, emphasizing the importance of meticulous aseptic precaution.

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 07, 2023

Methodology

Source of data: The study was conducted in 50 Primiparous patients in active phase of labour in the labour ward of Department of Obstetrics and Gynecology.

Study design: Prospective, randomized, double blinded, controlled study.

Sample size: 50.

Inclusion criteria

1. ASA II, Consenting primigravida in labour, gestational age ≥ 36 weeks.
2. Age 18-35 years, singleton pregnancy with vertex presentation.

Exclusion criteria

1. Allergy to any of the study drugs.
2. Significant coagulopathy.
3. Patients with history of significant disorders (Pregnancy induced hypertension, diabetes mellitus, obstetric haemorrhage, other cardiovascular, respiratory, central nervous system or renal system disorders).
4. Other contraindications: localized sepsis, raised ICP etc.

Methods of collection of data

Patients were explained about the procedure and informed/written consent was obtained.

- Thorough pre anaesthetic evaluation was performed.
- Routine investigations obtained.
- Foetal status, labour status (frequency and duration of labour pain and cervical dilatation) assessed and noted both clinically and with Cardiotocography (CTG).

Patients were randomized into two groups using computer generated random numbers:

- **Group A:** Received 0.1% Ropivacaine with fentanyl 2µg/ml in 10 ml total volume.
- **GROUP B:** Received 0.1% Ropivacaine with fentanyl 2µg/ml and neostigmine 500µg in 10 ml total volume.
- Baseline hemodynamic parameters like maternal heart rate, oxygen saturation, ECG, non-invasive blood pressure, were recorded.
- Under strict aseptic precautions epidural space identified with patient in left lateral position by midline approach using 18 G Tuohy's needle in L_{3-4} or L_4-L_5 interspace with loss of resistance to saline technique and catheter is threaded cephalad 3 to 4 cms into epidural space. After negative aspiration for blood and CSF, a test dose of 3ml of lignocaine 2% with 1:2, 00, 000 adrenaline was administered through the catheter.
- Ten ml of study drug of either 0.1% Ropivacaine with fentanyl 2µg/ml or 0.1% Ropivacaine with fentanyl 2µg/ml and Neostigmine 500µg was administered as per group allotment.
- Analgesia maintained by top up of 5 ml solution of 0.1% Ropivacaine with fentanyl 2µg/ml with NRS≥4, not earlier than 15 min of previous dose.
- Patients who experienced inadequate analgesia (NRS≥4) during the process were supplemented with additional 5 ml solution at least 15min later.

Results

Table 1: Comparison of mode of delivery among the two groups

MOD	Group A, n=25	Group B, n=25
	Frequency (%)	Frequency (%)
Instrumental	3 (12%)	2 (8%)
Normal	22 (88%)	23 (92%)

P value: 1

The percentage of instrumental delivery was 12% in group A and 8% in group B, while that of normal delivery was 88% in group A and 92% in group B, which was not significant (p value 1).

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 07, 2023

Table 2: Comparison of APGAR scores of newborn among the two groups

APGAR score	Group A, n=25	Group B, n=25	P value
	Frequency (%)	Frequency (%)	
APGAR at 1 min			
5	0	1 (4%)	0.044
6	0	2 (8%)	
7	20 (80%)	22 (88%)	
8	5 (20%)	0	
APGAR at 5 min			
8	11 (44%)	6 (24%)	0.136
9	14 (56%)	19 (76%)	

The APGAR score of newborn at 1 min in both group A and group B was statistically significant (p value 0.044), while the APGAR score of newborn at 5min in both groups A and B was statistically insignificant (p value 0.136).

Table 3: Comparison of maternal satisfaction among the two groups

Satisfaction	Group A, n=25	Group B, n=25
	Frequency (%)	Frequency (%)
Excellent	1 (4%)	5 (20%)
Good	18 (72%)	20 (80%)
Fair	6 (24%)	0

p value: 0.012

4% patients in group A and 20% patients in group B had an excellent satisfaction with regard to their experience of birth process and labour analgesia, which was statistically significant (p value 0.012).

Discussion

Ross VH and his colleagues [5] in a randomized control trial tested the hypothesis that epidural neostigmine in combination with Bupivacaine by continuous infusion during labour would reduce the amount of Bupivacaine required. They found that epidural neostigmine infusion reduced Bupivacaine requirement by 19% in all patients and 25% in those with >4 h of treatment (P 0.05 for both) but might have contributed to the incidence of mild sedation. Mode of delivery, incidence of maternal nausea, and FHR abnormality were similar between groups. They concluded that adding epidural neostigmine 4 µg/mL reduces the hourly bupivacaine requirement by 19% with patient-controlled epidural analgesia during labor. In the present study we found that total dose requirement of local anaesthetic was reduced by 12% when Neostigmine was added to Ropivacaine, though we used an intermittent bolus technique for maintenance of analgesia in comparison to continuous infusion technique used in the above mentioned study.

Owen *et al*. determined whether the addition of clonidine and neostigmine to intrathecal bupivacaine-fentanyl would increase the duration of analgesia without increasing side effects for patients in labour. Forty-five healthy parturient in active labour were randomized to receive a 2-ml intrathecal dose of one of the following dextrose-containing solutions using the combined spinal-epidural technique:

1. Bupivacaine 2.5 mg and fentanyl 25 µg (BF).
2. BF plus clonidine 30 µg (BFC).
3. BFC plus neostigmine 10 µg (BFCN).

Patients administered BFCN had significantly longer analgesia (165 ± 32 min) than those who received BF (90 ± 21 min; P <0.001) or BFC (123 ± 21 min; P< 0.001). They concluded that the addition of clonidine and neostigmine significantly increased the duration of analgesia from intrathecal bupivacaine-fentanyl during labour, but neostigmine caused more nausea, although serious side effects were not observed [6]. We observed similar findings in our study, wherein the addition of neostigmine significantly increased the duration of analgesia in group B when compared to group A.

Determining the duration of labour requires that investigators document start and end times. The end of the first stage of labour is defined as the time of full (10 cm) cervical dilation. Clinically, full cervical dilation is diagnosed when a cervical examination is performed because the patient complains of rectal pressure. It is likely that women with effective epidural analgesia will complain of rectal pressure at a later time than women who received systemic opioid analgesia. There is no evidence that a particular local anaesthetic or opioid used for neuraxial analgesia directly or indirectly affects the duration of labour. Roelants and his colleagues [7] studied the effect of epidural neostigmine combined with Ropivacaine and Sufentanil on neuraxial analgesia during labour. The parturient were randomly allocated to one of the study groups. Patients in the first group received Ropivacaine 0.2% 10 mL. In the other groups, 10 mL of Ropivacaine 0.1% was combined with Sufentanil 10 µg, Sufentanil 10 µg and

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 07, 2023

Neostigmine 2 μg/kg, Sufentanil 10 μg and neostigmine 4 μg/kg, or neostigmine 4 μg/kg. All the parturient received the first epidural bolus in a total volume of 14 mL. They found that epidural Neostigmine in the dose of 4 μg/kg did not significantly affect the duration of labour and thought that the dose of Neostigmine administered was too low. But in our study we found that addition of Neostigmine 500 μg to Ropivacaine 0.1% significantly reduced the duration of labour which can be attributed to the dose we administered in the study.

Decca *et al*. studied the association of epidural analgesia with operative vaginal delivery in a cohort of 207 women with no risk factors who delivered with epidural analgesia and found that epidural analgesia does not affect the rate of caesarean delivery. But the rate of instrumental vaginal delivery was increased in their study due to longer second stage of labour in the subjects [8]. The rate of instrumental delivery was clinically insignificant in our study and none of the patients in both the study groups underwent caesarean delivery.

Hasegawa J *et al*. [9] conducted a retrospective case-control study to evaluate the relationship between epidural analgesia, labour length, and perinatal outcomes. A total of 350 pregnant women at term who delivered under epidural analgesia (cases) were compared with 1400 patients without epidural analgesia (controls). They found that the Apgar scores were significantly lower in the neonates delivered by vacuum extraction compared with those in the neonates delivered by spontaneous delivery or caesarean section, regardless of whether epidural analgesia was performed. In our study we assessed the neonatal outcome by taking the APGAR score into consideration and found that the APGAR scores at 1 min and 5min were better in group B.

The incidence of hypotension after initiation of neuraxial analgesia during labour is approximately 14% [55]. In our study, the mean systolic BP and diastolic BP in both the groups recorded at different intervals was statistically insignificant and there was no profound hypotension in both the groups. Similarly, Palmer *et al*. found no difference in blood pressure in women randomly assigned to receive intrathecal fentanyl combined with either 1.25 or 2.5 mg of bupivacaine. The incidence of mild sedation and nausea was reported when neostigmine was administered along with local anaesthetic epidurally. However, we did not observe any of these side effects in the present study.

Bawdane *et al*. [10] compared 0.1% Ropivacaine vs. 0.1% bupivacaine for extradural analgesia, at the end of the study parturients were asked to rate overall satisfaction as either excellent, good, fair, poor or absent, to know the quality of labour analgesia and observed that majority of the parturient rated the experience of labour analgesia as excellent. We found that in our study, about half of the study subjects had an excellent satisfaction with regard to epidural labour analgesia.

Conclusion

- The APGAR score of newborn at 1 min in both group A and group B was statistically significant (p value 0.044), while the APGAR score of newborn at 5min in both groups A and B was statistically insignificant (p value 0.136).
- 4% patients in group A and 20% patients in group B had an excellent satisfaction with regard to their experience of birth process and labour analgesia, which was statistically significant (p value 0.012).

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ISSN:0975 -3583,0976-2833 VOL14, ISSUE 07, 2023

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