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SPINAL-EPIDURAL ANALGESIA;

EFFECTIVENESS OF DIFFERENT DOSES OF INTRATHECAL BUPIVACAINE COMBINED WITH FENTANYL FOR SPINAL-EPIDURAL ANALGESIA IN LABOR

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ABSTRACT… Objectives: To compare the efficacy of bupivacaine 2.5 mg and fentanyl 25 µg with bupivacaine 1.25 mg and fentanyl 25µg for spinal-epidural analgesia in the first stage of labor. **Study Design:** Double-blind randomized controlled trial. **Setting:** Anesthesia Department, Surgical Intensive Care Unit, and Pain management clinic, Peoples Medical College Hospital Nawabshah. **Period:** August 2014 to July 2015. **Methodology:** All the participants meeting the eligibility criteria were randomly allocated into two groups i.e. intervention (I) and control (II), with the allocation ratio of 1:1. Patients in the Group I (intervention) received intrathecal Inj. Bupivacaine 1.25 mg (0.5% Bupivacaine 0.25ml) and Inj. Fentanyl 25 µg whereas the Group II (control) was given intrathecal Inj. Bupivacaine 2.5 mg (0.5% Bupivacaine 0.5ml) and Inj. Fentanyl 25 µg for combined spinal epidural analgesia, both made up of total volume of 2 ml of normal saline. Mean±SD (standard deviation) was computed for continuous data (age, weight, VAS). Frequency and percentages was calculated categorical data. Independent t test and Chi square test were used for the differences between the groups. **Results:** The age of all the cases was 27.64±4.07 years. Moreover, groups were homogenous at baseline ($p<0.05$) in terms of mean age, weight, cervical dilatation, gravida, and ASA classification. Mean pain score on VAS was not significant between groups at 0 min and 15 min however mean pain score was found significantly low ($p<0.05$) in group-I. Likewise, efficacy of Bupivacaine 1.25 mg and Fentanyl 25 µg (group-I) was significantly higher than the other group. **Conclusion:** Low-dose bupivacaine 1.25 mg was significantly more effective than high-dose (2.5 mg) bupivacaine when added to 25 µg of fentanyl for combined spinal-epidural analgesia in the first stage of labor, having fewer chances of sensory and motor block, and hypotension.

Key words: Analgesia, Bupivacaine, Fentanyl, Labor, Spinal-Epidural.

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INTRODUCTION

Labor is the most painful experience in a woman's life which, if not adequately controlled, will produce fear and anxiety leading to adverse maternal and fetal outcome.[1] Pain free labor is widely practiced in developed countries, however in Pakistan, the knowledge about pain free labor is very low accounting for only 9.1%.[1,2] Analgesia is requested by most of the women in labor, and for this purpose, several pharmacological and non-pharmacological interventions are employed.[3] Epidural analgesia is the most commonly used procedure worldwide, with 90% of UK population using it to relieve labor pain but the complications like prolonged labor in nulliparous and increase the incidence of instrumental vaginal delivery, especially if administered early in labor, have led to its decreased acceptance.[2,4,5]

Another approach, combined spinal epidural (CSE), is a conventional method for providing analgesia during labor with rapid speed of onset and better sacral analgesia.[6,7] However, it is more complicated, expensive, and there was an increased association of nausea, vomiting, hypotension and pruritus.[8] Comparatively use of other anesthetics like Bupivacaine, most commonly used local anesthetics in obstetric practice, is limited due to significant motor blockade; thus, such anesthetics are used in combination with opioid analgesics such as fentanyl or sufentanil.[9]

According to a randomized controlled trial, it was found that there was a significant reduction (p value <0.001) in pain score in the first stage of labor with CSE analgesia.[10] A Cochrane review of over 19 randomized trials also found rapid onset of analgesia and decreased need for additional boluses of analgesia.[6] Similarly, Goodman et al found lower scores on visual analogue scale (VAS) in CSE group compared to epidural analgesia.[11] Another randomized controlled study compared different doses of intrathecal bupivacaine with fentanyl in CSE and no significant variation was noticed between the groups (p=0.47) in pain scores on VAS during the first 30 minutes. Additionally, the group who received higher dose of bupivacaine (120 min) demonstrated a longer median time to request for additional analgesia compared to the low dose group (75 min) (p=0.013).[12]

Although a few studies have been conducted globally exploring effectiveness of local anesthetics introducing combined spinal epidural in labor but with inconsistent findings and the data from Pakistan is not available.[6-14] Therefore, this is the first study in this region especially in our setting that aims to compare the two different doses of intrathecal bupivacaine with fentanyl in first stage labor.

METHODOLOGY

Study and Participants

This double-blind randomized controlled trial was conducted at the Anesthesia Department, Surgical Intensive Care Unit, and Pain management clinic, Peoples Medical College Hospital Nawabshah during the period of August 2014 to July 2015. Participants were recruited using the non-probability consecutive sampling technique and were then randomly selected for the intervention or control group. Inclusion criteria for the study were: 1) Age group 18-35 years; 2) healthy primigravida and gravida 2 patients at term, American Society of Anesthesiologists (ASA) classification grades ASA I and ASA II requested for labor analgesia; and 3) women in active labor having a cervical dilatation of about 4-5cm in primigravida and 3-4 cm in second gravida. Participants were excluded from the study because: 1) a parturient with ≥3 gravida, with multiple pregnancies, severe anemia, pregnancy-induced hypertension, cephalopelvic disproportion, fetal distress; 2) Previous Lower segment Cesarean section (LSCS), history of ante-partum hemorrhage, local anesthetic allergy, cardiovascular/respiratory system disease, bleeding disorders, psychiatric/neurologic disease, diabetes mellitus; and 3) patient refusal. Sample size required for the study was 80 (40 patients in each group), calculated using the power of 80%, confidence level of 5%.

Procedure

All the participants meeting the eligibility criteria were randomly allocated into two groups i.e. intervention (I) and control (II), with the allocation ratio of 1:1. Patients in the Group I (intervention) received intrathecal injection of Bupivacaine 1.25 mg (0.5% Bupivacaine 0.25ml) and 25 µg Fentanyl injection whereas the Group II (control) was given intrathecal injection of Bupivacaine 2.5 mg (0.5% Bupivacaine 0.5ml) and 25 µg Fentanyl injection for combined spinal epidural analgesia, making a total volume of 2 ml of normal saline. Blinding of participants was ensured since the drug was enclosed in an opaque envelope.

After obtaining a detailed history of the patients, complete physical examination and routine investigations were performed. Blood pressure (BP), peripheral oxygen saturation (SpO_2), and heart rate (HR) was also noticed. Intravenous (IV) line was maintained by 18G IV cannula, and patient was pre-loaded with Hartmann's solution (500ml). In 10 seconds, injection of intrathecal drug was completed, followed by threading of 20G epidural catheter into the epidural space by epidural needle and securing it with plaster. Pain score was recorded on VAS on 0, 15, 30, 45, 60 minutes (i.e. every 15 minutes for 1 hour). Efficacy was labeled when pain score on VAS was ≤2 and epidural analgesia was given with bupivacaine (0.125%) + fentanyl (2µg) in each ml. Moreover, the progress of labor was also monitored.

Statistical Analysis

The data collected was analyzed by SPSS 20.0 (SPSS Inc., Chicago, IL). Mean±SD (standard deviation) was computed for continuous data

(age, weight, VAS). Frequency and percentages was calculated categorical data. Independent t test and Chi square test were applied for the differences between groups, with a p value <0.05 was taken as significant.

Ethical Considerations

Approval of the work was taken from ethical committee review of the Peoples University of Medical & Health Sciences Nawabshah. All of the patients meeting the inclusion criteria gave informed consent in written. Moreover, participation in the study was voluntary and anonymity and confidentiality was ensured.

RESULTS

A total of 80 women in active labor with approximately 4-5cm of cervical dilatation in primigravida and 3-4 cm in second gravida were included in this study. The average age detected was 27.64±4.07 years. Moreover, groups were homogenous at baseline i.e. no significant difference between groups was noticed between the participants in either group in terms of mean age, weight, cervical dilatation, gravida, and ASA classification as shown in Table-I.

Variable	Group-I n=40	Group-II n=40	P-value
Age(Years)	27.45±3.88	27.83±4.31	0.68
Weight (kg)	63.49±5.97	61.23±6.88	0.06
Cervical Dilatation (cm)	4.25±0.77	4.18±0.78	0.65
Primigravida	28 (70%)	12 (30%)	-
Second gravida	22 (55%)	18 (45%)	-
ASA-I	22 (55%)	18 (45%)	-
ASA-II	23 (57.5%)	17 (42.5%)	-

Table-I. Baseline characteristics of the participants

Mean pain score on VAS was not significant between groups at 0 min and 15 min however mean pain score was found significantly low (p<0.05) in group-I in comparison to group-II at 30min, 45min and 60min as shown in Table-II. Similarly, efficacy in group-I was found significantly higher than group-II for combined spinal-epidural analgesia during the first stage of labor (87.5% vs. 60%; p<0.05) as shown in Table-III.

Time	Group-I n=40	Group-II n=40	P-value
0 min	0.38±0.49	0.53±0.78	0.31
15 min	1.18±0.78	1.40±0.93	0.24
30 min	1.58±0.98	2.20±1.32	0.019*
45 min	1.90±0.92	2.58±1.39	0.013*
60 min	1.15±1.14	3.23±2.04	0.0005*

Table-II. Comparison of pain scores between the groups *Significant at p<0.05

Efficacy	Group-I n=40	Group-II n=40	p-value
Positive	35 (87.5%)	24 (60%)	0.005*
Negative	5 (12.5%)	16 (40%)	0.24

Table-III. Comparison of efficacy between the groups *Significant at p<0.05

DISCUSSION

Women report severe pain during childbirth describe more frequently, such women particularly those from the developing countries have fewer or no options for pain free labor during childbirth.[15] In many poor resource settings, the most frequently prescribed agents for women in labor are the parenteral opioids and sedatives.[16] However, little to no effect of this analgesic method has been demonstrated on labor pain.[17] It may be noticed that the pain relief not only serves as a source of comfort for a patient, but it simultaneously reduces the release of stress hormones, thereby exhibiting positive effects on mother and the fetus.[15] Recently combined low-dose spinal–epidural (CSE) analgesia is gaining popularity for widespread labor analgesia as it has prompt onset of analgesia and minimal motor blockade.[18,19] Although previous studies have advocated the effectiveness of intrathecal bupivacaine combined with fentanyl for labor, there is no consensus about its dosage contributing to limited evidence of its overall effectiveness of analgesia.[20,21] Additionally, a combination of 2.5 mg of bupivacaine and 25 µg fentanyl, for instance, has been proved successful for analgesia during labour.[20,22] However, it has been suggested that dynamic analgesia can be possible with small doses but the duration of action will be shorter.[23,24]

In context to the use of intrathecal drugs during labor, dose–response studies have been conducted for sufentanil alone,[25,26] for fentanyl,[27,28]

or in combination with neostigmine.[29] Moreover, it has been suggested that the combination of bupivacaine and fentanyl increases response and duration of analgesia in comparison to the fentanyl alone,[23,30] however evidence base about their combination is limited. In our study we divided total 80 patients in two groups of 40 each. Bupivacaine 1.25 mg (0.5% Bupivacaine 0.25ml) was given intrathecally to Group I (intervention) and 25 µg Fentanyl injection while the Group II (control) was given intrathecal injection of Bupivacaine 2.5 mg (0.5% Bupivacaine 0.5ml) and 25 µg Fentanyl injection for spinal epidural analgesia in combination. In our study, mean pain score on VAS was not significant between both doses of bupivacaine at 0 min and 15 min but group I (Bupivacaine 1.25 mg) showed significantly low mean pain score as compared to group II (Bupivacaine 2.5 mg) at 30min, 45min and 60min. According to Herman et al, marked reduction in VAS score with in 15 minutes can be possible by lowest (5µg) intrathecal injection of fentanyl.[28] The major advantage of spinal-epidural analgesia when given in combination is the 'rapid response of analgesia', with increased maternal satisfaction.[26]

Using 2.5 mg bupivacaine and 25 µg fentanyl, previous studies have explored the effectiveness of combined spinal epidural analgesia, and reported that it leads to early onset, less chances of motor block, and a higher level of maternal satisfaction in comparison to epidural analgesia maintained using intermittent doses of bupivacaine (0.25%).[26,29] In our study we found that efficacy in group-I (1.25 mg of Bupivacaine with 25 μg of Fentanyl) was significantly higher than group-II (2.5 mg of Bupivacaine with 25 μg of Fentanyl) for combined spinal-epidural analgesia during the first stage of labor (87.5% vs. 60%; p=0.05). This was supported by several researches of combined spinal-epidural analgesia that reported that using sufentanil or fentanyl with 2.5 mg of intrathecal bupivacaine shows variable rates of motor block.[20,31,32,33]

CONCLUSIONS

Low-dose bupivacaine (1.25 mg) was more effectual than high-dose bupivacaine (2.5 mg) when combined with 25 µg of fentanyl for combined spinal-epidural analgesia during the first stage of labor. However, motor block avoidance can be beneficial in either those who opt to remain ambulatory or those who may deliver early.

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The worst thing about being lied to is simply knowing you weren't worth the truth.

– Unknown –

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