A PROSPECTIVE STUDY TO COMPARE SINGLE DOSE INTRATHECAL COMBINATION OF BUPIVACAINE AND MORPHINE WITH FENTANYL, BUPIVACAINE AND MORPHINE FOR LABOUR ANALGESIA

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ABSTRACT

BACKGROUND

Advances in the field of labour analgesia have tread a long journey from the days of inhalation to the present-day practice. Low dose neuraxial blocks with local anaesthetic or opioids or combination of two give superior analgesia with lesser side effects and facilitate ambulation.

MATERIALS AND METHODS

This study was a non-randomised, controlled trial. There were 50 parturients of ASA physical status I or II with a term singleton foetus in a vertex position without any comorbidity were randomly divided into two groups of 25 each. Spinal analgesia was administered at L3-L4 or L4-L5 using a pencil point 25-G spinal needle in sitting position. Group I received injection Morphine 100 mcg + Inj. Bupivacaine 2.5 mg (.25%) and Group II received Inj. Fentanyl 15 mcg + 50 mcg Morphine + Inj. Bupivacaine 2.5 mg (.25%) intrathecally. We monitored changes in haemodynamics, duration of labour and degree of pain using VAP score (0-100 mm). Neonatal outcome was assessed by Apgar score at 1, 5 and 10 minutes interval. Maternal satisfaction and side effects like pruritus, nausea and hypotension were monitored. Since the calculated sample size was too high and thereby not feasible to include in this limited period of study, we had to limit the sample size for convenience.

RESULTS

Pain score was significantly less ('P' < 0.5) in Group II at 5, 60 and 120 minutes in both primigravida and multigravida. Mean duration of labour is comparable in active 1st and 3rd stage in both groups and it is significantly prolonged in 2nd stage of labour in Group I, i.e. 90.00 +/_ 41.23 minutes as compared to 58.55 +/_ 24.27 minutes in Group II. Apgar score was between 9 and 10 at 0, 1, 5 and 10 minutes in both groups. Pruritus was the most frequent side effect in 76% and 72% in Group I and II respectively. 32% patients in Group I and 24% patients in Group II were unsatisfied.

CONCLUSION

We conclude that a single dose spinal block with Fentanyl 15 mcg + 50 mcg Morphine + Inj. Bupivacaine 2.5 mg (.25%) provide a rapid onset, profound analgesia with less side effects and good maternal satisfaction without affecting neonatal outcome.

KEY WORDS

Central Neuraxial Block, Labour Analgesia, Intrathecal, Pruritus.

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BACKGROUND

One of the most severe pain experienced by a woman is that of child birth. Providing analgesia for labour has always been a challenge, more so because of the myths and controversies. Advances in the field of labour analgesia have tread a long journey from the days of inhalation to the present day practice of comprehensive approach including neuraxial block which include spinal, epidural and Combined Spinal Epidural block (CSE). Low dose neuraxial blocks with local anaesthetic or opioids or combination of two give superior analgesia with lesser side effects and facilitate ambulation. These also allow mother to participate in active labour. All these reasons make neuraxial block the gold standard for intrapartum labour analgesia. Multiple controlled trials comparing neuraxial analgesia with systemic analgesia have demonstrated lower maternal pain scores and higher maternal satisfaction as well as better maternal cardiovascular, pulmonary physiology and acid base status of foetus. In many rural communities, epidural anaesthetic is unavailable as well as there are many patients who come in advance labour; so as epidural and CSE are more time consuming procedure, a single shot spinal block with low dose opioids and local anaesthetic is more feasible option which can provide early onset of effective analgesia for adequate time. Due to all these benefits, the number of parturients choosing neuraxial labour analgesia increased significantly. Several drugs have been used in spinal analgesia. Large doses of lipid soluble opioids produce rapid and profound analgesia, but are associated with significant side effects. Because of the synergistic effect of combining local anaesthetic, the dose of opioid required to provide effective labour analgesia can be significantly reduced. Indeed, studies have shown that reducing the dose of spinal medication reduced the duration of analgesia, but does not affect the quality of pain relief. Intrathecal morphine when used in large doses produces long-lasting pain relief, but with slow onset and significant side effects. Because the side

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effects associated with morphine seem to be dose depended, so a smaller dose may be desirable. We hypothesised that an intrathecal injection of a smaller combined dose of Fentanyl, Bupivacaine and Morphine provide rapid and effective analgesia.

MATERIALS AND METHODS

This study non-randomised controlled trial with 50 parturients of ASA physical status I or II with a term singleton foetus in a vertex position, without any comorbidities presenting for delivery and requesting for analgesia were asked to participate in this prospective study. There was no exclusion in relation to maternal age, parity or gestational age. After approval from Institutional Ethical Committee, all patients provided an informed written consent before taking part in this study and randomly divided in two groups of 25 each. Spinal analgesia was administered at L3-L4 or L4-L5 using a pencil point 25-G spinal needle in sitting position. Group I received injection Morphine 100 mcg + Inj. Bupivacaine 2.5 mg (.25%) and Group II received Inj. Fentanyl 15 mcg + 50 mcg Morphine + Inj. Bupivacaine 2.5 mg (.25%). Patients were then placed in the left lateral position to minimize aorto-caval compression and hypotension. Hypotension was defined as a decrease in systolic BP more than 30% of baseline or less than 90 mmHg and treated with IV fluids and 5 - 10 mg boluses of Inj. Ephedrine. A 1 - 2 mcg/ kg dose of Naloxone Hydrochloride was administered intravenously as needed to limit pruritus or nausea. Patient assessment before spinal block included vital signs, pain score and cervical dilation. After spinal injection vital signs, pain score, sensory and motor block evaluated at 5, 30 and 60 minutes interval in first hour and then every 2 hourly till delivery. We monitored changes in haemodynamics, duration of labour and degree of pain using VAP score (0 – 100 mm). The quality of analgesia was considered effective i.e. no pain when VAPS was between 0-30, partially effective i.e. painful but bearable, when the VAPS was between 40 - 60 and ineffective, unbearable pain when the VAPS was between 70 - 100. Neonatal outcome was assessed by Apgar score at 1, 5 and 10 minutes interval. Maternal satisfaction and side effects like pruritus, nausea, vomiting and hypotension were monitored. Since the calculated sample size was too high and thereby not feasible to include in this limited period of study, we had to limit the sample size for convenience.

Statistical Analysis

The data were entered into the computer and analysed by using the Statistical Package for Social Sciences (SPSS) version 10.0 programs for Windows. Unpaired student's t-test, the means and SD was calculated. The significance value was achieved at $p < 0.05$.

RESULTS

Parameter	Group-1 (n=25)	Group-2 (n=25)	'P' value
Age (in years)	23.48 ± 3.15	24.56 ± 4.10	P > .05
Weight (in kg)	64.72 ± 3.57	64.805.28	P > .05
Height (in cm)	159.32 ± 3.56	160.28 ± 4.79	P > .05

Table 1. Demographic Profile

Demographically both groups are comparable. Mean age in GP 1 is 23.48 years and GP 2 is 24.56 years. The mean weight and height in Group 1 and Group 2 are 64.72 kg, 64.80 kg, 159.32 cm and 160.28 cm respectively.

At Duration (in Minutes)	Mean VAPS					
	Primigravida			Multigravida		
	Group 1	Group 2	'P' value	Group 1	Group 2	'P' value
5	45.83 ± 9.96	21.00 ± 5.67	P<.05	42.31 ± 11.65	18.00 ± 8.60	P<.05
60	39.16 ± 13.11	22.00 ± 7.37	P<.05	36.15 ± 10.43	18.60 ± 8.33	P<.05
120	29.00 ± 10.44	29.00 ± 7.37	P>.05	30.00 ± 12.90	23.33 ± 6.17	P>.05
At Delivery	35.00 ± 7.07	40.00 ± 23.19	P>.05	41.66 ± 22.89	35.71 ± 12.22	P>.05

Table 2. VAP Score in Group 1 and Group 2

In primigravida 5 minutes VAP score is 45.83 ± 9.96 in Group 1 and 21.00 ± 5.67 in Group 2, while in multigravida VAP score is 42.30 ± 11.65 in Group 1 and 18.00 ± 18.6 in Group 2. The difference between VAP score is significant in both primigravida and multigravida at 5 minutes and at 60 minutes. In primigravida at delivery, VPA score is 35.00 ± 7.07 in Group 1 and 40.00 ± 23.19 in Group 2, while in multigravida 41.66 ± 22.89 in Group 1 and 35.71 ± 12.22 in Group 2. The difference between VAP score is not significant at 120 minutes and at the time of delivery.

Stages	Mean Duration of Labour (in Minutes)					
	Primigravida			Multigravida		
	Group 1	Group 2	'P' value	Group 1	Group 2	'P' value
Active 1st stage	292.27 ± 27.82	276.00 ± 22.25	P>.05	223.84 ± 6.94	228.33 ± 55.95	P>.05
Active stage 2nd	90.00 ± 41.23	58.55 ± 24.27	P<.05	49.09 ± 23.32	24.33 ± 12.65	P<.01
Active stage 3rd	17.00 ± 4.21	16.50 ± 7.47	P>.05	11.25 ± 2.26	13.92 ± 5.60	P>.05

Table 3. Mean duration of active 1st Stage, 2nd Stage and 3rd Stage in Group 1 and Group 2

Mean duration of Stage 2 in primigravida is 90.00 ± 41.23 minutes and 58.55 ± 24.27 minutes in Group 1 and Group 2 respectively, while in multigravida Stage 2 is 49.09 ± 23.32 minutes in Group 1 and 24.33 ± 12.65 minutes in Group 2. The difference between mean duration of 2nd Stage of Group 1 and Group 2 is significant (CP < 0.5). The difference between mean duration of 1st stage and 3rd stage is not significant in both primigravida and multigravida.

Pruritus	Group 1	Group 2
None	6 (24%)	7 (28%)
Mild	4 (16%)	4 (16)
Moderate	8 (32%)	9 (36%)
Severe	7 (28%)	5 (20%)
Total	**25 (100%)**	**25 (100%)**

Table 4. Incidence of Pruritus

28% patients complained of severe pruritus and it was moderate in 32% and mild in 16% patients in Group 1; 20% patients complained of severe pruritus and it was moderate in 36% and mild in 16% in Group 2.

Maternal Satisfaction	Primigravida		Multigravida	
	Group 1	Group 2	Group 1	Group 2
Highly Satisfactory	0 (0%)	1 (10%)	1 (7.69%)	2 (13.33%)
Satisfactory	8 (66.66%)	6 (60%)	8 (61.53%)	10 (66.66%)
Unsatisfactory	4 (33.33%)	3 (30%)	4 (30.76%)	3 (20%)
Total	**12 (100%)**	**10 (100%)**	**13 (100%)**	**15 (100%)**

Table 5. Maternal Satisfaction

In Group 1, 8 primigravida patients were satisfied and 4 were unsatisfied. While one multigravida was highly satisfied, 8 patients were satisfied, and 4 patients were unsatisfied. In Group 2, 6 primigravida were satisfied in comparison to 10 multigravida.

Side Effects	Group 1	Group 2
Nausea	8 (32%)	5 (20%)
Vomiting	3 (12%)	2 (8%)
Hypotension	2 (8%)	1 (4%)
Others	0 (0%)	0 (0%)

Table 6. Other Side Effects

42% patients in Group 1 and 32% patients in Group 2 experienced minor side effects as illustrated in the above table.

DISCUSSION

A clinically relevant findings in our study showed that addition of Fentanyl 15 mcg to a small dose of 2.5 mg (.25%) Bupivacaine and 50 mcg of Morphine significantly reduced the VAP score from 45.83 ± 9.96 in Group I to 21.00 ± 5.67 in Group II primigravida patients and from 42.30 ± 11.65 in Group I to 18.00 ± 8.60 in Group II multigravida patients at 5 minutes. Results coincide with Hui-Ming et al,[1] where the VAPS at 5 mins was less than 10 in all patients. Several factors could explain why we did not find a result of similar magnitude. Our smaller doses of Bupivacaine and Fentanyl had significantly shortened duration of pain relief. Thus, it is possible that the Morphine-induced analgesia did not reach full effectiveness, secondly the smaller dose of Morphine used in our study may not have had as significant effect. This shortened duration would be consistent with pharmacokinetic explanation. We conclude that intrathecal dose of 2.5 mg (0.25%) Bupivacaine with 50 mcg Morphine and 15 mcg Fentanyl provide a rapid onset of analgesia with effective duration of pain relief till delivery. Mean duration of the active 1st stage, 2nd stage and 3rd stage of labour in primigravida in Group I were 292.27 ± 27.82, 90.00 ± 41.23 and 17.00 ± 4.21 minutes respectively and for Group II 276.00 ± 22.25, 58.55 ± 24.27 and 16.50 ± 7.47 minutes respectively. Mean duration of the active 1st stage, 2nd stage and 3rd stage were 223.84 ± 86.94, 49.09 ± 23.32 and 11.25 ± 2.26 minutes respectively in Group I multigravida and for Group II multigravida 228.33 ± 55.95, 24.33 ± 12.65 and 13.92 ± 5.60 minutes respectively. So mean duration of active 1st stage and 3rd stage in both primigravida and multigravida is comparable, but in cases of 2nd stage of labour the mean duration was significantly prolonged in Group I. Oxytocin used to augment the labour in 3 patients in Group I, while it was used only in one patient in Group II. These results are in accordance with Medline observations that Fentanyl injected into the intrathecal space seems to cause rapid cervical dilatation and shortening of 1st stage of labour. There was no adverse effect on neonatal outcome in both the groups. Apgar score ranged between 9 and 10 at 0, 1, 5 and 10 minutes in both groups. There were no haemodynamic changes or respiratory depression in infants. It is concluded that the safety is offered by the poor diffusion of substance between the foetus and the mother. These clinical findings correlate with the result of Eriksson SL, Blomberg I and Olofsson[2] who reported high Apgar score. In the study of Pace MC et al,[3] the Apgar was also between 7 and 10.

Pruritus is the most frequent side effect of intrathecal opioids and incidence of this in our study is within the range of others.[4] In our study, 76% patients in Group I and 72% patients of Group II complained of pruritus of various degree. In both groups most of the patients had Bromage score zero and only 4 (16%) patients in Group I and 3 (12%) patients in Group II had Bromage score of 1. This low incidence of modified Bromage score in both groups were due to low dose of Bupivacaine (2.5 mg, 0.25%). No active intervention was needed for this and all the patients took full participation in labour. Our findings coincide with various studies.[2] There was no other major maternal and neonatal complications like respiratory depression and sedation. Large dose of lipid soluble opioids are associated with significant side effects,[5-10] which can be significantly reduced[11-12] by using combinations of low dose of local anaesthetic with low dose of opioids. Studies have shown that reducing these doses do not affect the quality of pain relief.[6,11,13-15] At the end one of the 25 patients (4%) in Group I was highly satisfied, 64% patients were satisfied and 29% were unsatisfied. In Group II out of 25 patients 12% were highly satisfied, 64% were satisfied and 29% were unsatisfied. So in our method Group II provide effective analgesia in labour, especially in the active first stage. Our method is comparable to Eriksson SL, Blomberg I and Olofsson[2] and Philip E. Hus.[16] This method is very effective in patients with rapidly progressive labour and important reason for dissatisfaction in primigravida seems to be due to anxiety and inexperience. Our study confirms the results of previous studies that the use of low-dose Bupivacaine with combination of opioids in low dose provide effective mean of prompt and satisfying labour analgesia without increasing the duration of labour and significant side effects with acceptable neonatal outcome and maternal satisfaction. We can identify several limitations to our study. The subjects in our study consisted of both multiparous and primiparous women. This limits the ability to compare the results with studies that use a homogeneous population.

CONCLUSION

We conclude that a single-dose spinal block with Fentanyl 15 mcg + 50 mcg Morphine + Inj. Bupivacaine 2.5 mg (.25%) provide a rapid onset, profound analgesia with less side effects and good maternal satisfaction without affecting neonatal outcome.

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