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Research Article

Comparison of Cardiorespiratory Effects during Intrathecal Bupivacaine Combined with Buprenorphine in Lower Limb Surgeries

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Abstract: Intrathecal injections of opioids like buprenorphine have been reported to cause anti-nociception in animals and pain relief in human beings including the potentiation of local anaesthetic action in the spinal cord. The present study was aimed to evaluate the cardiorespiratory and adverse effects of addition of buprenorphine to bupivacaine a local anaesthetic used for spinal anaesthesia. The study was prospective, randomized and observer blinded. It involved 100 patients (50 per group) ASA I and II, age 20-60 years undergoing lower limb surgeries under spinal anaesthesia. Patients were randomized into two groups; the study group received a spinal injection of hyperbaric bupivacaine 0.5% (heavy) 2.5 ml (12.5 mg) plus buprenorphine 1µg/kg (not > 50 ug). which was diluted in 0.5 ml of normal saline and control group receiving injection bupivacaine 0.5% (heavy) 2.5 ml (12.5 mg) plus 0.5 ml normal saline thus making the volume constant around 3 ml. Results of the present study showed that in both the groups the basal heart rate level were almost similar with t-value being 1.39 and p-value being an 0.017 which was not significant, but intraoperatively at 15 minutes, 45 minutes there was an increase in heart rate which is statistically significant and at 180 minutes the heart rate being similar in both the groups with t-value being 0.50 with p-value being 0.62 which is not significant. The basal respiratory rate was compared in the two groups the t-value was 4.01 with the p-value being > 0.05 which was insignificant, at 15 minutes the t-value was 5.10 and p-value being < 0.01 which is highly significant, at 45 minutes the t-value was 2.83 with p-value being < 0.01 which is significant, at 90 minutes the t-value was 1.30 and p-value of 0.20 which is not significant, at 180 minutes the t-value being 2.05 and p-value being 0.04 which is significant. To conclude, intrathecal buprenorphine 1 µg/kg along with bupivacaine for spinal anaesthesia did not showed any major adverse effect on the cardiovascular parameters, respiratory function and gives better and prolonged duration of analgesia with minimal side effects.

Keywords: Intrathecal buprenorphine, Post-operative analgesia, Bupivacaine.

INTRODUCTION

Pain is one of the first sensations known to mankind from the beginning. There are many situations where a subject experiences pain sensations for e.g. post-operative pain being one of them. Thus to minimize or to overcome the adverse effects, the post-operative pain should be adequately treated. The use of neuraxial opioids has increased dramatically in recent years augmenting the analgesia produced by local anaesthetics by binding directly to the opioid receptors [1]. Opioids have been used for allieviation of post-operative pain extensively. Conventional methods include administration of opioids through intramuscular, intravenous, sublingual route. Of late intrathecal route and extra dural administration of opioids is widely studied, thus is a novel approach and may prove advantageous over existing conventional methods [2].

Subarachnoid block is one of the commonest local anaesthetic techniques and would probably maintain its place in the developing countries because of simplicity, minimal skill requirement, onset, economy and minimum post-operative complications. This has the advantage that it is easy to perform and requires small dose of the drug making systemic absorption unimportant and also the patient will be most of the time conscious throughout the procedure [3]. The disadvantage is limited duration of action and lack of post-operative pain relief by these local anaesthetic drugs like bupivacaine where in the analgesic action ends with the regression of the block which means that there is an early post-operative need for analgesia.

Buprenorphine is a long acting, highly lipophilic opioid which proved to be a promising analgesic by epidural and intrathecal route [4]. It is well documented that the dose limiting side effects of systemically administered opioids, such as nausea and

vomiting, sedation and respiratory depression were also mediated by opioid receptors [5]. The present study was aimed to evaluate the cardiorespiratory and adverse effects of addition of buprenorphine to bupivacaine a local anaesthetic used for spinal anaesthesia.

MATERIALS AND METHODS

This study was conducted in Mamata General Hospital, Khammam for over a period of 18 months. After obtaining approval from the ethical clearance committee of the college, 100 patients fulfilling the inclusion and exclusion criteria belonging to American Society of Anaesthesiology (ASA) grade I and II physical status scheduled for elective lower limb surgeries and aged between 20-60 years were included in this study.

Patients were allocated into two following groups

Group A:

Patients of this group received 2.5 ml of hyperbaric bupivacaine heavy (12.5 mg) of 0.5% with 0.5 ml of injection buprenorphine 50 µg.

Group B:

Patients of this group received 2.5 ml of hyperbaric bupivacaine heavy (12.5 mg) of 0.5% with 0.5 ml of normal saline.

The selection of the patients and anesthesia procedure were performed as explained in our earlier [6].

After the various treatments as explained in the above groups, patients were monitored continuously using sphygmomanometer, pulse oximeter and electrocardiogram. Patients pulse rate, blood pressure, respiratory rate were recorded at 0 (basal) 15, 30, 45, 90 and 180 minutes. Postoperatively heart rate, blood pressure, respiratory rate and $SP0_2$ were monitored at 360 and 600 minutes. The side effects of intrathecal buprenorphine like nausea, vomiting, pruritis, shivering, respiratory depression (respiratory rate < 10/min) drowsiness, hypotension (systolic < 90 mm of Hg), bradycardia (heart rate < 60 beats/min), urinary retention were evaluated.

RESULTS

The heart rate of the patients perioperatively in study group (A) was 77.4 beats/rnin as a baseline and 15 minutes after giving the drug intrathecally, the mean heart rate was increased to 90.7 beats/min, then at 45 minutes it slowly decreased to around 86.2 beats/min, at 90 minutes it was around 84.3 beats/min, at around 180 minutes 83.6 beats/min. Whereas in control group (B) the baseline heart rate was 74.2 beats/min and after 15 minutes of giving the drug it increased to around 84.8 beats/min, slowly decreased at 45 minutes to 82.2 beats/min, at 90 minutes it was around 80.8 beats/min, at 180 minutes it increased to 84.6 beats/min. Although in both the groups the basal heart rate level were almost similar with t-value being 1.39 and p-value being an 0.017 which was not significant, but intraoperatively at 15 minutes, 45 minutes there was an increase in heart rate which is statistically significant and at 180 minutes the heart rate being similar in both the groups with t-value being 0.50 with p-value being 0.62 which is not significant. The values were not compared in the 180 and 360 minutes because in the control group the patients had pain with a VAS scale of > 6 which was considered significant and rescue medication was given and thus taken as an end point in the control group. But the heart rate was around 83.1 ± 7.8 at 360 minutes and 92.3 ± 8.7 at 600 minutes in the study group (Table 1).

Table 1: effects on cardiovascular system

Time of assessment (in minutes)	Study group	Control group	Study versus control		
			t-value	p-value	
0	77.4 ± 9.8	74.2 ± 9.7	1.39	0.017	NS
15	90.7 ± 7.4	84.8 ± 10.6	3.20	< 0.05	S
45	86.2 ± 7.9	82.2 ± 8.9	2.37	0.02	S
90	84.3 ± 7.1	80.8 ± 9.7	2.07	< 0.05	S
180	83.6 ± 9.7	84.6 ± 9.6	0.50	0.62	NS
360	83.1±7.8	-	-	-	
600	92.3 ± 8.7	-	-	-	

In the study group (A) patients the mean systolic blood pressure decreased from a baseline value of 125.8 mm of Hg to 102.1 mm of Hg at 15 minutes then it gradually started increasing from 103.4 mm of Hg at 45 minutes to 110.2 mm of Hg at 90 minutes, 110.4 mm of I1g at 180 minutes. In the control group (A) patients the mean systolic blood pressure decreased from a baseline value of 118.8 mm of Hg to 100.6 mm of Hg at 15 minutes then it gradually started decreasing i.e 98.0 mm of Hg at 45 minutes and then it gradually rose to 105.8 mm of Hg at 90 minutes, 128.6 mm of Hg at 180 minutes. The baseline changes in systolic blood pressure had a t-value of 3.05 with a p-value of 0.2 which is clinically insignificant. At 15 minutes the t-value is 0.62 and p-value being 0.54 which is clinically insignificant. Whereas intraoperatively at 45 minutes, 90 minutes there was a fall in systolic blood pressure and it slowly returned back to normal at 180 minutes which is highly significant (p < 0001) systolic blood pressure at 360 minutes and 600 minutes were not

compared between the two groups because at 180 minutes the patients in the control group had a analgesia score of more than 6 wherein they were given rescue medications and that was taken as a end point for comparison, though the systolic blood pressure was 124.0 mm of Hg at 360 min and 140.0 mm of Hg at 600 min in the study group (Table 2).

Table 2: Systolic Blood Pressure

Time of assessment (in minutes)	Study group	Control group	Study versus control		
			t-value	p-value	
0	125.8 ± 12.0	118.8± 11.0	3.05	< 0.01	NS
15	102.1 ± 12.7	100.6 ± 11.5	0.62	0.54	NS
45	103.4 ± 9.8	98.0 ± 7.6	3.08	< 0.01	S
90	110.2 ± 11.5	105.8 ± 10.1	2.03	< 0.05	S
180	110.4±12.3	128.6 ± 12.0	7.51	< 0.001	HS
360	124.0 ± 11.6	-	-	-	
600	140.0 ± 21.3	-	-	-	

In the study group (A) patients the mean diastolic blood pressure was about 79.7 mm of Hg then at 15 min it decreased to 69.0 mm of Hg, at 45 min it was 69.2 mm of Hg, at 90 min it increase to about 73.4 mm of Hg, at 180 min was about 76.2 mm of HG, in the control group *(B)* patients the mean basal diastolic blood pressure was 76 mm of Hg and at 15 min it decrease to 68.8 mm of Hg, at 45 min it was 67.8 mm of Hg, at 90 min it slowly increased to 74.8 mm of Hg, at 180 min it increase to 83.9 mm of Hg when compared at the basal mean diastolic blood pressure, the t-value was around 2.56 and p-value was > 0.05 which was insignificant, at 15 min the t-value was 0.13 and p-value was 0.89 which is "not significant, at 45 min the t-value was 0.98 and p- value was 0.33 which was not significant, at 90 min the t-value is 1.00 and p-value being 0.32 which was not significant. At 180 min t-value was 5.46 and p-value was < 0.001 which was highly significant. Diastolic blood pressure at 360 min and 600 min were not compared between the two groups because at 180 min the patients in the control group had a analgesia score of more than 6 wherein they were given rescue medications and that was taken as a end point for comparision, though the diastolic blood pressure was 81.3 mm of Hg at 360 min and 92.7 mm of Hg at 600 min in the study group (Table 3).

Table 3: Diastolic Blood Pressure

Time of assessment (in minutes)	Study group	Control group	Study versus control		
			t-value	p-value	
0	79.9 ± 7.2	76.0 ± 7.3	2.56	> 0.05	NS
15	69.0 ± 7.9	68.8 ± 6.9	0.13	0.89	NS
45	69.2 ± 7.2	67.8 ± 7.1	0.98	0.33	NS
90	73.4 ±7.2	74.8 ± 6.8	1.00	0.32	NS
180	76.2 ± 6.9	83.9 ± 6.8	5.46	< 0.001	HS
360	81.3 ± 6.8	-	-		
600	92.7 ± 6.2	–	-		

In the present study, the basal respiratory rate was 16.3 breaths/min it increased to 17.8 breaths/min at 15 minutes and slowly came down to 16.7 breaths/min at 45 minutes, 15.9 breaths/min at 90 minutes and it came back to basal level i.e. 16.1 breaths/min at 180 minutes in the study group patients. At the same time the basal respiratory rate was around 14.3 breaths/min increased to 15.7 breaths/min at 15 minutes and then at 45 minutes it was around 15.4 breaths/mill, at 90 minutes it was 15.3 breaths/min, at 180 minutes it increased to 17.1 breaths/min. comparing the two groups at the basal level the t-value was 4.01 with the p-value being > 0.05 which was insignificant, at 15 minutes the t-value was 5.10 and p-value being < 0.01 which is highly significant, at 45 minutes the t-value was 2.83 with p-value being < 0.01 which is significant, at 90 minutes the t-value was 1.30 and p-value of 0.20 which is not significant, at 180 minutes the t-value being 2.05 and p-value being 0.04 which is significant. Respiratory rate at 360 minutes and 600 minutes were not compared between the two groups because at 180 minutes the patients in the control group had a analgesia score of more than 6 wherein they were given rescue medications and that was taken as a end point for comparision, though the respiratory rate was 16.2 breaths/min and 20.2 breaths/min at 600 minutes in the study group. Though the values clearly denote a significant change in the respiratory rate during the time periods it was of no clinical relevance because the respiratory rate did not go less than 10 breaths/min which is a clinical parameter or a criteria to be noted in this study (Table 4).

Table 4: Effect on respiratory system

Time of assessment (in minutes)	Study group	Control group	Study versus control		
			t-value	p-value	
0	16.3±2.5	14.3 ± 2.5	4.01	0.01	S
15	17.8 ± 2.05	15.7 ± 2.10	5.1	< 0.001	HS
45	16.7±2.1	15.4 ± 2.3	2.83	< 0.01	S
90	15.9 ± 2.3	15.3 ± 2.3	1.3	0.2	NS
180	16.1 ± 2.7	17.1 ±2.2	2.05	0.04	S
360	16.2 ± .2.2	-	-	-	
600	20.2 ± 2.0	-	-	-	

The results of the present also shows that saturation of oxygen at the basal level were 98.5% at 15 minutes, 45 minutes, and 90 minutes it was 98% and at 180 minutes it was around 97.9% in the study group. In the control group the saturation of oxygen at the basal level were 98.8% at 15 minutes it was 98.1%, at 45 minutes it was 98.2%, and 90 minutes it was 98.1% and at 180 minutes it was around 98.4% in the control group. Comparing both the groups at basal level or preoperatively the t-value was 2.14 and p-value is > 0.05 which is insignificant. The p-value at 15 minutes, 45 minutes and 90 minutes being 1, 0.48, 0.76 which was not significant and at 180 minutes t-value being 2.58 and p-value being> 0.05 which is significant. Saturation of oxygen at 360 minutes and 600 minutes were not compared between the two groups because at 180 minutes the patients in the control group had a analgesia score of more than 6 wherein they were given rescue medications and that was taken as a end point for comparison, though the saturation of oxygen was 98.1 % and 98.5% at 360 and 600 minutes in the study group. Though the values clearly denote a significant change in the saturation of oxygen during the time periods it was of no clinical relevance because the saturation of oxygen did not go less than 90% which is a clinical parameter or a criteria to be noted in this study (Table 5).

Table 5: Saturation of Oxygen ($SP0_2$)

Time of assessment (in minutes)	Study group	Control group	Study versus control		
			t-value	n-value	
0	98.5 ± 0.9	98.8 ± 0.58	2.14	> 0.05	S
15	98.06 ± 0.9	98.1± 1.0	0.01	1	NS
45	98.0 ± 0.9	98.2 ± 0.8	0.71	0.48	NS
90	98.0 ± 0.9	98.1 ± 1.0	0.31	0.76	NS
180	97.9 ± 0.9	98.4±0.7	2.58	> 0.05	S
360	98.1 ± .0.9	-	-	-	
600	98.5 ± 0.8	-	-	-	

In this study the adverse effects in study group (A) were nausea and vomiting in one patient, shivering in one patient, bradycardia in one patient and hypotension in 5 patients, whereas in control group (B) 4 patients had hypotension. 80 patients out of 100 patients were catherized who had undergone lower limb surgeries. Urinary retention could not be made out because most of the patients undergoing these surgeries were catherized and around 20 patients who underwent lower limb surgeries were not catheterized did not complain of urinary retention (Table 6).

Table- 6: Adverse Effects

Adverse effects	Study group (A)	Control group (B)
Nausea & vomiting	1	0
Pruritis	Nil	Nil
Shivering	1	Nil
Bradycardia	1	Nil
Hypotension	5	4
Urinary retention	Nil	Nil
Respiratory depression	Nil	Nil

DISCUSSION

In our study all the patients were monitored clinically in the intraoperative as well as post-operative period. The pulse rate, systolic blood pressure and diastolic blood pressure were monitored at regular intervals. The incidence of hypotension was noticed in 5 patients of study group and in control group it was in 4 patients. Hypotension was corrected by administration of injection mephenteramine 5 mg I.V in incremental doses alongwith I.V fluids and foot end elevation. The incidence of bradycardia was found in one patient of study group which was adequately treated with injection atropine 0.6 mg I.V. Systolic and diastolic blood pressure in both groups did not vary significantly in two groups uptil 180 minutes, as this was taken as a end point for comparison of both the groups because rescue medication was given to control group patients (VAS score> 6). Laila and co-workers in the year 1997 demonstrated that with 40 µg of buprenorphine no side effects were observed while 80 µg prolonged analgesia with easily manageable side effects and adequate preloading with crystalloids and intravenous atropine premedication can prevent haemodynamic side effects [7]. Similar observation was also seen by Thomas *et al*. in the year 1997 demonstrated that there was no statistical significant change in pulse rate, blood pressure in the two groups [8]. Sen in 1992 demonstrated that blood pressure and pulse rate remained within physiological limits [9]. Our present findings are in accordance with Nalini Damle *et al*. [10] that the incidence of hypotension and bradycardia were comparable in the two groups where in 3 patients from control group and 4 patients in buprenorphine group developed hypotension which was treated by a rapid intravenous fluids and none of them required vasopressors. Capogna et al. [14] in their study demonstrated that heart rate, arterial blood pressure remained within physiological limits during the observation time and there was no significant differences between the groups [11].

Further, present study also demonstrates that effects of intrathecal buprenorphine on respiratory system showed that none of the patients had respiratory rate less than 10 breaths/min or $SP0_2$ less than 90% in either group. Our findings were in agreement with several earlier authors where Laila *et al*. [7] demonstrated in his study that no major side effects such as respiratory depression were observed in the study. Thomas *et al*. [8] demonstrated that buprenorphine being lipid soluble, non-ionized drug rapidly passes through the arachnoid membrane into the venous and lymphatic vessels which minimize the increase of CSF concentration with minor risk of respiratory depression. Sen [9] demonstrated that the tidal volume, blood gas analysis did not show any significant differences between the two groups. Varma [12] in his study demonstrated that they did not observe respiratory depression in any patients. Rudra *et al*. [13] showed that there were no significant changes in respiration in any of the patients. Nalini Damle *et al*. [10] demonstrated that no patients had respiratory rate below 10 breaths/min and there was no significant differences between preoperative and postoperative tidal volumes in two groups as they had used Wrights respirometer for measuring the tidal volumes in all the patients. Capogna *et al*. [14] in their study demonstrated the mean respiratory rates in all the groups during the first 12 hours after surgery did not differs significantly and remained within the physiological limits.

The visual analogue pain scale at 90 minutes were in study group (A)and 1 in control group (B) at 180 minutes it was 1 in study group and 6.6 ± 2 for the control group which was statistically significant. In the study group the VAS score was lower at 180 minutes, 360 minutes and 600 minutes in the post-operative period which indicates the quality of analgesia was better in group (A) patients. In group (B) patients since the VAS score was> 6 rescue medications were given and this was taken as end point for comparison of parameters between the two groups. The present results are also in agreement with several studies [7, 13, 14].

In this study the adverse effects in study group (A) were nausea and vomiting in one patient, shivering in one patient, bradycardia in one patient and hypotension in 5 patients, whereas in control group (B) 4 patients had hypotension. 80 patients out of 100 patients were catherized who had undergone lower limb surgeries. Urinary retention could not be made out because most of the patients undergoing these surgeries were catherized and around 20 patients who underwent lower limb surgeries were not catheterized did not complain of urinary retention which are in agreement with other authors where there was no major demonstrable side effects [7,13,14]. Thomas *et al*. in his study showed that drowsiness was the major side effect of buprenorphine which could be desirable intraoperatively and all patients were arousable on verbal command and other than this there was no major side effects [8]. Varma [12] studying the effects of various doses of buprenorphine intrathecally i.e. 0.15 mg, 0.3 mg, 0.45 mg, 0.6 mg and 0.9 mg showed that the mean side effects observed in group 1, 2, and 3 were nausea, vomiting, headache, but with increasing concentration of buprenorphine as in groups 4 and 5 other side effects like urinary retention, drowsiness were observed.

CONCLUSION

To conclude, use of low dose buprenorphine along with bupivacaine for spinal anaesthesia showed no or minimal adverse effect on the cardiovascular parameters, respiratory function and also gives better and prolonged duration of analgesia.

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