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To Evaluate the Efficacy of Butorphanol as an Adjuvant to Bupivacaine Intrathecally in Infraumbilical Surgeries in Terms of Haemodynamic Variables

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ABSTRACT

Background: 0.5% heavy bupivacaine is one of the commonest drugs used intrathecally for spinal anaesthesia. Opioids are commonly used as adjuvants with local anaesthetics. We compared butorphanol as an adjuvant to local anaesthetic agent and local anaesthetic alone in subarachnoid block in infraumbilical surgeries.
Aim: To evaluate how efficacious is butorphanol as an additive to bupivacaine intrathecally in infraumbilical surgeries in terms of haemodynamic stability.
Methodology: The study was done on sixty patients of ASA I & II between 18-65 years posted for elective infraumbilical surgeries and two equal groups were made. In Group A patients received bupivacaine 0.5% (2.5 ml i.e. 12.5 mg) + 0.5 ml normal saline (total volume 3ml) intrathecally and in Group B they received bupivacaine 0.5% (2.5 ml i.e. 12.5mg) + injection butorphanol 25 microgram (1 mg/ml of preservative-free injection butorphanol which was diluted to 20 ml by normal saline , 0.5 ml of this solution was taken) making total volume 3 ml intrathecally. Haemodynamic parameters were summarized and compared between both the groups.
Results: A statistically significant decrease in mean arterial blood pressure occurred in Group A in comparison to Group B. However, patients didn't require any clinical intervention.
Conclusion: Addition of injection butorphanol with bupivacaine gives haemodynamic stability as compared to bupivacaine alone intrathecally.

Key words: Intrathecally, Bupivacaine, Butorphanol, Efficacy, Infraumbilical, Haemodynamic variables

INTRODUCTION

August Bier in 1898 first introduced spinal anaesthesia in clinical practice. [1] Spinal anaesthesia is performed in most of the procedures on the lower half of the body i.e. for infraumbilical surgeries. The various side effects of spinal anaesthesia like hypotension, bradycardia and decreased cardiac output are due to blockade of the sympathetic system.

Of all the local anaesthetics available now a days 0.5% bupivacaine is most commonly used intrathecally as it provides good sensory and motor blockade. [2] Adjuvant drugs are agents used in small doses so that they have no intrinsic pharmacological action but they potentiate the action of other drugs. Intrathecal adjuvants to local anaesthetics are known to increase the quality and duration of spinal anaesthesia along with providing haemodynamic stability. Various drugs which are frequently used as adjuvants are alpha$_2$ agonists (clonidine and dexmedetomidine), fentanyl, butorphanol, morphine, adrenaline, midazolam, ketamine and neostigmine. Each of these have their own advantages and disadvantages.

Butorphanol is a lipophilic opioid and has been used safely in intrathecal space. Cephalic spread of butorphanol is slow due to its high molecular weight and lipophilic nature. It acts by opening potassium channels and decreasing calcium influx which results in transmitter release inhibition .Butorphanol is a partial agonist and antagonist at μ receptors. [3] It is also a competitive antagonist and partial agonist at κ opioid receptors. [4]

We wish to compare the haemodynamic effects of adding an adjuvant butorphanol to bupivacaine and bupivacaine alone intrathecally in infraumbilical surgeries under spinal anaesthesia.

Aim and Objectives

To assess the haemodynamic stability of intrathecal butorphanol with bupivacaine compared to bupivacaine alone in infraumbilical surgeries.

MATERIAL AND METHODS

Approval from Institution Ethics Committee was taken. The study was done on 60 patients, ASA Grade I & II belonging to either sex, between 18-65 years, who were posted for elective infraumbilical surgeries under spinal anaesthesia in the Department of Anaesthesiology in a tertiary care hospital. The following patients were excluded from the study: those with bleeding disorders or on anticoagulant therapy, with increased intracranial tension, any sign of infection at puncture site, disease and deformity of spine ,known sensitivity to drugs like local anaesthetics and butorphanol, those with severe hypovolemia and dehydration, with preexisting neurological disorders and mental disorders

Pre anaesthetic check up was done a day before surgery. Detailed history, physical examination, heart rate, blood pressure, oxygen saturation, routine investigations (Haemoglobin, BT, CT, Complete urine examination) were done. Fasting blood sugar or any other special investigation depending upon the disease process, were recorded in all cases preoperatively and a written consent taken.

They were kept fasting overnight & premedicated with tablet alprazolam 0.25mg & tablet ranitidine 150mg at bed time on the night prior to surgery and in the morning of surgery with a sip of water.

In preoperative ward i/v line was secured with 18G cannula. Preloading was done with 10-20 ml /kg ringer lactate solution. Further fluid was administered at the rate 4-5ml/kg /hr of ringer lactate.

All the patients were given injection midazolam 1mg intravenously, 30 minutes before surgery. Systemic narcotics were not administered so as to avoid analgesic effect of any other drug that might interfere with the study.

After shifting the patients to the operation theatre, monitoring of following parameters were established - heart rate, systolic and diastolic blood pressure, oxygen saturation using pulse oximeter and electrocardiography.

To calculate the sample size a software NCAA PASS 2000 was used. To get a power of 80% and an α error of 0.05 a total of 60 patients was taken and two groups of 30 patients each were made.

The patients' position was lateral decubitus. In the $L_3 – L_4$ intervertebral space skin wheal was raised with subcutaneous injection of lignocaine 2% (2cc) and under strict aseptic precautions spinal was performed through midline approach. A 25G Quincke spinal needle was used. Syringe loaded with drug was attached to the hub of the needle and the drug was injected slowly into CSF by an anaesthetist who was blinded to the drug injected and patient allocation. The patients were randomly divided into two groups as follows:

GROUP A -Patients received intrathecally Bupivacaine 0.5%, 2.5 ml ie12.5mg +0.5ml Normal Saline. Total volume of 3ml

GROUP B- Patients received intrathecally Bupivacaine 0.5%, 2.5ml i.e. 12.5mg +25 mcg Butorphanol (1 mg/ml of preservative-

free injection butorphanol which was diluted up to 20 ml by normal saline and 0.5 ml of this solution was taken). Total volume of 3ml

The patients were observed for the following parameters – Heart rate, SBP, DBP, SpO_2 (Oxygen saturation by pulse oximeter)-every 2 min after injection till 10 min thereafter every 5 min till the end of surgery and ECG continuously.

Rescue Criteria and Interventions

Any fall in the mean arterial pressure of more than 30% of pre induction value was treated with fluids and if mean arterial pressure still did not improve then intravenous bolus of 3 mg of injection Mephentermine was given. For any episode of bradycardia, HR < 60/min bolus of 0.5 mg injection Atropine i.v. was given. All the observations and particulars of each patient were recorded.

STATISTICAL ANALYSIS

SPSS 21 version for Microsoft Windows was used for statistical calculations. For categorical variables, Chi square (χ^2) test was used. Data was expressed as Mean±S.D. p value <0.05 was taken as statistically significant.

OBSERVATIONS AND RESULT

Age, weight and gender distribution were comparable to each other in the two groups (Table 1,2).

TABLE 1 MEAN DISTRIBUTION FOR AGE AND WEIGHT

	Group A		Group B		p- Value
	MEAN	SD	MEAN	SD	
AGE	41.10	13.15	38.80	15.33	0.535
WEIGHT	66.93	9.74	68.13	11.69	0.667

TABLE 2 GENDER DISTRIBUTION OF PATIENTS

Gender	Group A		Group B		p value
	No.	%age	No.	%age	
Male	24	80.0%	25	83.3.0%	0.739
Female	6	20.0%	5	16.7%	

TABLE 3 COMPARISON OF PREOPERATIVE HEMODYNAMIC VARIABLES

Gender	Group A	Group B	P value
HR (/min)	77.77 ± 8.81	77.93 ± 7.64	0.938
SBP (mmHg)	127. ± 9.17	130.13 ± 8.92	0.185
DBP (mmHg)	78.20 ± 6.71	76.93 ± 7.54	0.495
SPO_2 (%)	99.53 ± 0.83	99.87 ± 0.35	0.064

The mean preoperative heart rate in group A was 77.77±8.81beats per min where as in group B it was 77.93±7.64 beats per minute. The difference between two groups when compared statistically was not significant p value >0.05 (Table 3). On comparison of intraoperative mean heart rate in group A and group B at various time intervals both the groups were comparable to each other with no statistically significant difference between them. p value>0.05.(Table 4)

TABLE 4 COMPARISON OF INTRAOPERATIVE MEAN HEART RATE

HR	Group A		Group B		t	p-value
	Mean	SD	Mean	SD		
2 MINS	84.40	15.65	82.73	7.68	0.524	0.603
4	81.73	11.73	83.10	8.24	-0.522	0.603
6	79.23	9.56	81.27	7.08	-0.936	0.353
8	76.77	8.09	79.53	6.64	-1.448	0.153
10	75.37	7.87	78.47	6.87	-1.625	0.110
15	72.53	7.54	75.50	6.48	-1.634	0.108
20	72.00	7.73	73.30	6.29	-0.714	0.478
25	72.83	9.09	72.17	6.12	0.333	0.740
30	72.40	9.13	71.00	6.16	0.696	0.489
35	73.00	9.51	69.86	5.66	1.533	0.131
40	72.38	9.79	68.57	6.05	1.759	0.084
45	72.62	10.17	69.07	5.27	1.646	0.106
50	73.24	9.11	70.54	5.97	1.285	0.204
55	73.93	7.00	72.50	6.73	0.722	0.474
60	73.52	6.33	74.33	6.22	-0.284	0.779

TABLE 5 COMPARISON OF INTRAOPERATIVE MEAN ARTERIAL PRESSURE

MAP	Group A		Group B		t	p-value
	Mean	SD	Mean	SD		
2 MIN	86.53	8.56	89.60	10.34	-1.252	0.016
4	83.47	6.71	86.17	7.48	-1.471	0.047
6	81.30	8.07	84.57	5.93	-1.787	0.049
8	79.17	7.41	82.30	6.72	-1.715	0.092
10	77.80	6.39	80.40	5.97	-1.628	0.109
15	78.00	5.87	79.53	6.84	-0.932	0.355
20	77.93	6.25	78.10	6.83	-0.099	0.922
25	77.43	6.72	77.07	7.83	0.195	0.846
30	77.40	6.54	75.77	7.44	0.904	0.370
35	76.50	5.98	74.93	7.60	0.883	0.381
40	75.55	4.87	73.68	7.12	1.163	0.250
45	76.86	4.95	74.25	6.83	1.656	0.103
50	76.38	4.91	74.78	6.07	1.089	0.281
55	77.04	4.61	75.00	4.65	1.532	0.132
60	79.60	4.68	77.17	1.33	1.246	0.223

Mean preoperative systolic blood pressure in group A was 127 ±9.17 mm Hg where as in group B it was130.13±8.92 mm Hg . The difference between group A and B was not statistically significant. p value >0.05. Mean preoperative diastolic blood pressure in group A was 78.20 ±6.71 mm Hg where as in group B it was76.93±7.54 mm Hg. Difference between them was not

statistically significant, p value>0.05.(Table 3)

TABLE 6 COMPARISON OF INTRAOPERATIVE MEAN SATURATION OF OXYGEN

SPO2	Group A		Group B		Z	p-value
	Mean	SD	Mean	SD		
2 MIN	100.00	.000[a]	100.00	.000[a]	0.000	1.000
4	99.93	0.25	99.93	0.25	0.000	1.000
6	100.00	.000[a]	100.00	.000[a]	0.000	1.000
8	100.00	.000[a]	100.00	.000[a]	0.000	1.000
10	100.00	.000[a]	100.00	.000[a]	0.000	1.000
15	99.97	0.18	99.97	0.18	0.000	1.000
20	99.93	0.25	99.93	0.25	0.000	1.000
25	99.87	0.35	99.87	0.35	0.000	1.000
30	99.93	0.25	99.93	0.25	0.000	1.000
35	99.80	0.48	99.79	0.49	-0.058	0.954
40	99.97	0.19	99.96	0.19	-0.025	0.980
45	99.93	0.26	99.93	0.26	-0.036	0.971
50	99.97	0.19	100.00	0.00	-0.965	0.335
55	99.81	0.40	99.83	0.39	-0.102	0.918
60	99.96	0.20	100.00	0.00	-0.519	0.604

On comparing intraoperative mean arterial blood pressure in group A and group B at various time intervals a statistically significant difference between them was found at 2, 4 and 6 minutes after spinal anaesthesia p<0.05. From 8 minutes till the end of the procedure, no statistical difference occurred between them, p value >0.05.(Table 5)

Mean preoperative Spo2 in group A was 99.53 ±0.83 where as it was 99.87±0.35 mm Hg in group B. Difference between the two groups was not statistically significant, p>0.05.On comparing of intraoperative mean Spo2 in group A and group B at various time intervals both the groups were comparable to each other. No statistically significant difference occurred between them, p>0.05. (Table 6).

DISCUSSION

The advantages of regional anaesthesia over general anaesthesia include decrease in the incidence of deep vein thrombosis, pulmonary embolism, blood loss, respiratory complications and superior intraoperative analgesia. [5] Hypotension, bradycardia, urinary retention, post dural puncture headache and neurological symptoms are some of the complications of intrathecal anaesthesia. [6]

Bupivacaine is one of the most common local anaesthetic used for spinal anaesthesia. It acts by blocking the Na^+channels which are voltage gated in axon membrane and also causes presynaptic inhibition of the calcium channels. [7]

Intrathecal adjuvants are used to enhance the efficacy and prolong the analgesic effect of local anaesthetics. The various adjuvants used are opioids like butorphanol, morphine and fentanyl;α_2 agonists like clonidine and dexmedetomidine, and NMDA receptor antagonist like ketamine. [8] Butorphanol opens the K^+ channels and decreases the Ca^{++} influx which causes inhibition of the transmitter release. [9] The combination of local anaesthetics and opioids act synergistically and their addition may have benefits in providing analgesia long after the effects of local anaesthetic have seized. [10][11]

Of all the opioids which are used in spinal anaesthesia as adjuvants there are very few studies on intrathecal butorphanol. The choice of dosage of bupivacaine and butorphanol in our study was based on a previous study by Binay Kumar et al who also used 12.5 mg of 0.5% bupivacaine and 25mcg of butorphanol intrathecally in lower limb orthopaedic procedures. [12]

The bradycardia after spinal anaesthesia is due to the sympathetic blockade which is more likely if the block is high (T5 and above). The present study showed no statistically significant difference in intraoperative heart rate in both the groups p value >0.05. Ashem JM et al in 2016 did a study on 90 patients who underwent caesarean section by dividing them into three groups. GroupB got bupivacaine (0.5%)2 ml +0.5 ml normal saline; group BB got bupivacaine (0.5%)2 ml+25mcg butorphanol in 0.5ml NS; group BD got bupivacaine (0.5%)2 ml+2.5mcg dexmedetomidine in 0.5ml NS and found no significant change in intraoperative heart rate in all the three groups. Finding of our study are comparable to Ashem et al. [13] Vinita et al also reported no increase in incidence of bradycardia with 25µg butorphanol. [2]

The fall in blood pressure is due to the thoracolumbar sympathectomy produced by the local anaesthetic solution which produces a decrease in systemic vascular resistance and an increase in venous pooling. [1] The mean arterial blood pressure in bupivacaine group decreased significantly at 2 minutes, 4 minute and 6 minutes after spinal as compared to the bupivacaine and butorphanol group. This could because butorphanol increases systemic blood pressure, pulmonary artery blood pressure and cardiac output [14] and also the sympathetic block due to intrathecal butorphanol did not decrease the blood pressure as the block due to bupivacaine was nearly maximum. [15] Subrata N et al in 2014 did a study on 46 patients who received spinal anaesthesia and divided them into two groups. Group A received bupivacaine 15mg &1ml of NS (total volume 4ml) and group B bupivacaine 15mg & 0.5mg butorphanol (total volume 4ml) and found that bupivacaine and butorphanol group was more haemodynamically stable as compared to bupivacaine alone. Findings of our study were comparable to study conducted by Subrata Nag et al. [16] Manpreet K et al in 2011 also found less hypotension in butorphanol group as compared to bupivacaine alone intrathecally. [17]

Even though intrathecal opioids can cause respiratory depression in our no statistically significant difference in intraoperative SpO2 in both the groups p value >0.05. Findings of our study are consistent with those of Ranga Chari VR et al who did a study on 60 patients who underwent elective caesarean section and divided them into two groups and found no significant fall in Spo2 in both the groups. [18]

The only limitation in this study is a small sample size and that the study was limited to one centre only, but it had significantly important results and future studies with a larger sample size can be undertaken.

CONCLUSION

We conclude from our study that addition of butorphanol to bupivacaine intrathecally produces less hypotension as compared to bupivacaine alone and is more haemodynamically stable in infraumbilical surgeries.

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