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COMPARISON OF TWO STRENGTHS OF BUTORPHANOL ADDED TO HYPERBARIC BUPIVACAINE GIVEN INTRATHECALLY IN LOWER ABDOMINAL OR LOWER LIMB SURGERY

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ABSTRACT

Aims and objective : To evaluate the effects of addition of two strengths (25 mcg and 50 mcg) of Butorphanol to hyperbaric Bupivacaine on the onset, quality and duration of sensory and motor blockade when administered intrathecally and compare them with control group.To observe the side effects (if any) of Butorphanol when administered intrathecally with hyperbaric Bupivacaine in two different doses.

Methodology: The study was conducted in 60 patients belonging to ASA grade I & II, of either sex and age undergoing subarachnoid block for elective surgeries of 1 – 2 hours duration.Prior permission of Institutional Ethical Committee (IEC) was obtained to conduct the study.Informed consent was obtained from all the patients.All the patients were subjected to thorough pre – anaesthetic evaluation and relevant laboratory investigations.

Results: All the three groups were comparable with respect to the patient's demographic profile.The onset of sensory block did not show any significant difference statistically in all the three groups: Group A control (16.1 6.90sec), Group B Butorphanol 25mcg (18.4 8.25sec), Group C Butorphanol 50mcg (17.75 7.64sec)The motor block was slightly delayed in group B & C (32 8.64 & 28.25 7.30 sec) as compared to control group (23.1 8.01sec), which is practically acceptable.

Conclusion. Thus we conclude from our study that Intrathecal Butorphanol potentiates bupivacaine induced sensory spinal block and reduces the analgesic requirement in the early postoperative period without prolonging motor block recovery time to micturition and without any other major side effects.

INTRODUCTION

A complaint of pain that brings the patient to the physician is a personal sensory experience, unique for the specific individual. Since the experience is subjective, there is a wide variation in the interpretation and reaction to noxious stimulation. In the evaluation of any pain relieving measure, the nature of the pain must be considered. It is at best difficult to evaluate, either by the subject or the physician.

The International association for the study of pain defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage". Term nociception describes the neural response to traumatic or noxious stimuli. Pain is mainly a protective mechanism of the body. With the birth of effective anaesthesia in the middle of the 19th century, it was not long before the Postoperative Pain was recognized as a discipline worthy of attention in its own right. The goal for the postoperative pain management is to reduce an individual patients pain to a tolerable level with minimal or no associated suffering or distress.

Noxious stimuli such as surgical trauma and subsequent postoperative pain results in a broad range of endocrinologic, immunologic and inflammatory responses including increased release of catabolic hormones and inhibited secretion of anabolic mediators. Thousands of spinal anaesthetics are administered daily in hospitals & nursing homes. At low cost, a surgery of up to two hours duration can be performed.

Bupivacaine is the local anaesthetic most commonly used intrathecally. However, the anaesthesia provided by Bupivacaine alone may be too short for certain planned surgical procedures. Therefore many anaesthesiologists are preferring to add opioids like fentanyl, buprenorphine, butorphanol etc or non – opioids like clonidine to the local anaesthetic used in spinal, to give a smoother effect and to provide prolonged pain relief once the action of the spinal has worn off. The addition of adjuvants provides a prolonged anaesthetic action but may be associated with certain undesired effects, which are more prominent with agonist drugs i.e. pruritis, respiratory depression, urinary retention, excessive sedation etc. Butorphanol being an Agonist Antagonist is less likely to cause the above mentioned side effects.

Butorphanol has been in use since 1978 in western countries and a number of studies have been performed establishing its efficacy and safety, but was not available in India till 2002.Since its launch in India (2002), it has been commonly used by intravenous, intramuscular and epidural routes but its intrathecal use is still not explored.

In the present study, we investigated the efficacy and safety of two doses of intrathecal butorphanol (25mcg & 50mcg) added to 17.5 mg (3.5ml) of 0.5% hyperbaric bupivacaine and compared it with a control group using 17.5 mg (3.5ml) of 0.5% hyperbaric bupivacaine with 0.5 ml normal saline.

METHODOLOGY

The study was conducted in 60 patients belonging to ASA grade I & II, of either sex and age undergoing subarachnoid block for elective surgeries of 1 – 2 hours duration.Prior permission of Institutional Ethical Committee (IEC) was obtained to conduct the study.Informed consent was obtained from all the patients.All the patients were subjected to thorough pre – anaesthetic evaluation and relevant laboratory investigations.

INCLUSION CRITERIA

1. Patients of 18 – 60 age group of either sex.
2. Patients belonging to ASA grade I & II
3. Available informed consent.
4. Patients undergoing elective surgeries.

EXCLUSION CRITERIA

1. Patients not willing to get enrolled in the study and not willing for spinal anaesthesia.
2. Age below 18 years and above 60 years.
3. Patients with acute infection like upper respiratory tract infection, urinary tract infection etc.
4. Patients with spinal deformities and local skin infections overlying lumbar vertebral region
5. Patients with bleeding and/or coagulation disorders.

METHODS OF RANDOMIZATION

A statistician was consulted and method of randomization, adequacy of sample size and power of test confirmed.60 patients were divided into 3 equal groups of 20 patients each i.e. Group A, Group B and Group C. The patients were allotted to respective group according to a computer-generated allocation.

GROUP A (CONTROL GROUP):In this group patients were given Injection Bupivacaine 0.5%(17.5mg, 3.5ml) + 0.5 ml normal saline

(Total volume 4ml) Intrathecally.

GROUP B (STUDY GROUP I):In this group patients were given injection Bupivacaine 0.5%(17.5mg, 3.5ml) with injection Butorphanol 25mcg in 0.5ml by intrathecal route (Total volume 4ml)

GROUP C (STUDY GROUP II):In this group patients were given injection Bupivacaine 0.5%(17.5mg, 3.5ml) with injection Butorphanol 50 mcg in 0.5ml by intrathecal route (Total volume 4ml)

The patients were kept fasting overnight prior to the scheduled day of operation. Sedatives and hypnotics, inclusive of Opioids were avoided in pre medication as well as intra operatively.In the operation theatre, all the patients were preloaded with Ringer Lactate solution. @ 8-10ml/kg over 15-20 min. Following baseline parameters were noted down before and after preloading: Pulse rate, Non Invasive Blood Pressure (NIBP), SpO2, Respiratory rate and ECG.

Subarachnoid block was given using 26G Quincke's spinal needle into L_3-L_4 space in sitting position (as this position is shown to cause less hypotension than when given in lateral position) under al aseptic precautions and depending on the group, respective agents were injected intrathecally by keeping the anaesthesiologist blinded about the agent. Patients were made to lie down immediately after the injection and position was adjusted to achieve a level of sensory block up to T6 segment.

The following readings were noted for assessment of onset of blockade:

T0------- Time of Spinal anaesthesia
T1------- Time of onset of sensory block (loss of pinprick sensation)
T2------- Time of onset of motor block (inability to lift the extended leg)

Side effects such as sedation, nausea, vomiting, depression of ventilation etc. were noted. At the end of the study, results in both groups were tabulated, statistically analyzed and compared to draw the conclusions.

OBSERVATION TABLES

The present study, the effect of addition of Butorphanol to 0.5% hyperbaric Bupivacaine (3.5ml, 17.5mg), in two different strengths 25mcg & 50mcg in 0.5ml each was compared to plain 0.5% hyperbaric Bupivacaine (3.5ml, 17.5mg) plus 1ml of normal saline, in 60 adult patients in the age range of 18 to 60 years, undergoing lower abdominal surgeries of medium duration under spinal anaesthesia. The patients were randomly divided into 3 groups of 20 patients each.

A total of 60 patients were divided into three equal groups **A, B** and **C, of 20 each.**Sex wise distribution in all the three groups was compared using "chi-square test" and there was no statistically significant difference found between the three groups.Applying **"ANOVA"** test, mean age in all the three groups was compared and showed **no** statistically significant difference between the three groups.Applying **"ANOVA"** test, mean height in all the three groups was compared and showed **no** statistically significant difference between the three groups.ASA grade wise distribution in all the three groups was compared using "chi-square test" and there was no statistically significant difference found between the three groups.

TABLE 1: COMPARISON OF SENSORY ONSET RESPONSE IN STUDY GROUPS

Onset response (Sec)	Group A Mean SD (n=20)	Group B Mean SD (n=20)	Group C Mean SD (n=20)	F Value	P Value
Sensory (T1)	16.1 6.90	18.4 8.25	17.75 7.64	0.48	>0.05

Applying **"ANOVA"** test, onset of sensory block in all the three groups was compared and showed no statistically significant difference between the three groups

TABLE 2: COMPARISON OF MOTOR ONSET RESPONSE

Onset response (Sec)	Group A Mean SD (n=20)	Group B Mean SD (n=20)	Group C Mean SD (n=20)	F Value	P Value
Motor (T2)	23.1 8.01	32 8.64	28.25 7.30	6.23	<0.01

Onset of motor block in all the three groups was compared applying "ANOVA" test and showed statistically significant difference.The onset of motor block was delayed in-group B (32 ± 8.64 sec) compared to group C (28.25 ± 7.30 sec) and group A (23.1 ± 8.01 sec).However this was not clinically significant as the difference was less than 60 seconds.

TABLE 3: COMPARISON OF 2 SEGMENT REGRESSION IN STUDY GROUPS

Parameters	Group A Mean SD (n=20)	Group B Mean SD (n=20)	Group C Mean SD (n=20)	F Value	P Value
2 Segment Regression	85 20.13	103.5 18.14	94.75 16.82	5.05	<0.01

The time for two-segment regression of sensory level was shorter in Group A (85 ± 20.13 min) compared to group B (103.5 ± 18.14 min) and Group C (94.75 ± 16.82 min).Analysis was done using "ANOVA" test, which showed statistically significant difference between the three groups.Time to 2 segment regression i.e. duration of sensory block was longest in Group B (Butorphanol 25mcg) followed by Group C (Butorphanol 50 mcg) & Group A (Control).

Heart rate in all the three groups was compared applying "ANOVA" test at various time intervals and showed no statistically significant difference between the three groups.

TABLE 4: COMPARISON OF SYSTOLIC BLOOD PRESSURE IN STUDY GROUPS

SBP (mm Hg)	Group A Mean SD (n=20)	Group B Mean SD (n=20)	Group C Mean SD (n=20)	F Value	P Value
Pre op	121.9 14.46	126.65 14.23	121.25 12.24	0.92	>0.05
At 3 min	117.9 16.36	124.55 13.96	112.55 10.44	3.78	<0.05
At 10 min	111.7 15.62	112.5 14.95	106.6 12.64	0.97	>0.05
At 15 min	105.65 13.40	108.15 13.39	104.55 13.68	0.37	>0.05
At 30 min	105 14.18	104.25 10.05	105.6 14.59	0.05	>0.05
At 45 min	107 14.02	109.55 8.75	108 12.85	0.22	>0.05
At 60 min	108.6 12.54	109.7 10.33	110.05 15.51	0.06	>0.05
End of Surgery	109.1 12.31	109.8 10.32	111.55 11.39	0.24	>0.05
Postoperative	109.25 12.24	109.8 10.32	112.3 11.50	0.40	>0.05

Systolic blood pressure in all the three groups was compared applying "ANOVA" test at various time intervals and showed no statistically significant difference except at 3 minutes where fall in systolic blood pressure was more in Group C (112.55 ± 10.44) as compared to Group B (124.55 ± 13.96) and Group A (117.9 ± 16.36)

The intragroup comparison of Systolic Blood Pressure in Group A at various time intervals showed a slight fall from 3mins to 60mins (borderline significant), but was within the normal physiological range (121-105mmHg) at all time intervals.The intragroup

comparison of Systolic Blood Pressure in Group B at various time intervals showed a slight fall from 10mins to 60mins (borderline significant), but was within the normal physiological range (126-104mmHg) at all time intervals.The intragroup comparison of Systolic Blood Pressure in Group C at various time intervals showed a slight fall from 3mins to 60mins (borderline significant), but was within the normal physiological range (120-104mmHg) at all time intervals.

TABLE 5: SIDE EFFECTS IN STUDY GROUPS

Side effects	Group A (n=20)	Group B (n=20)	Group C (n=20)
Bradycardia	1 (5)	4 (20)	5 (25)
Hypotension	4 (20)	3 (15)	6 (30)
None	15 (75)	13 (65)	9 (55)

Bradycardia:In Group C (Butorphanol 50 mcg) 5 patients had bradycardia as compared to 4 patients in Group B (Butorphanol 25 mcg) & 1 patient in Group A (Control), requiring inj. Atropine 0.6 mg i/v.Hypotension: In Group C (Butorphanol 50 mcg) 6 patients had hypotension as compared to 3 patients in Group B (Butorphanol 25 mcg) & 4 patients in Group A (Control), requiring inj. Mephenteramine 6 mg i/v.Hence, intraoperative intervention required for haemodynamic stability was more in Group C as compared to Group B and Group A.

TABLE 6: QUALITY OF SEDATION IN STUDY GROUPS

Quality of block	Group A (%)	Group B (%)	Group C (%)	Total
Irritable	7 (11.67)	0 (0)	0 (0)	7 (11.67)
Awake & comfortable	13 (21.66)	16 (26.67)	15 (25)	44 (73.33)
Sedated & arousable	0 (0)	4 (6.67)	5 (8.33)	9 (15)
Total	20 (33.33)	20 (33.33)	20 (33.33)	60 (100)

On comparison, using **"Chi Square"** test, it was found that more number of patients in Group C (5) were sedated but arousable as compared to Group B (4) and Group A (0) Patients who were sedated but arousable were considered to have the best quality of sedation, followed by patients who were awake and comfortable and the irritable patients were considered to have the least quality.**Therefore best quality of sedation was found in maximum number of patients in Group C.**

RESULTS

It was observed that, All the three groups were **comparable** with respect to the patient's **demographic profile.**The **onset of sensory block** did not show any significant difference statistically in all the three groups: Group A control (16.1 6.90sec), Group B Butorphanol 25mcg (18.4 8.25sec), Group C Butorphanol 50mcg (17.75 7.64sec)The **motor block** was **slightly delayed in group B & C (**32 8.64 & 28.25 7.30 sec) as compared to **control group** (23.1 8.01sec), which is practically acceptable.The **time for two segment dermatomal regression of sensory level** was **prolonged in group B** Butorphanol 25 mcg (103.5 18.14) and **group C** Butorphanol 50mcg (94.75 16.82) as compared to **Group A** Control (85 20.13)The **mean duration of analgesia** in **Group C Butorphanol 50mcg (273 37.57 min)** and in **Group B Butorphanol 25mcg (271.5 44.04 min)** was **significantly** (clinically & statistically) **prolonged** as compared to **control group A (205.5 31.2 min)**.

With respect to quality of block, patients who were sedated but arousable were considered to have the best quality of block, followed by patients who were awake and comfortable and the irritable patients were considered to have the least quality.On comparison, **significant improvement in quality** (sedated but arousable patients) of the block was found more in patients of **Group C** Butorphanol 50mcg (5 patients) when compared to **Group B** Butorphanol 25mcg (4 patients) and **Group A** control (0 patient).Heart rate, Systolic BP, Diastolic BP, Respiratory rate & SpO_2were compared at various time intervals.

STATISTICAL ANALYSIS:

At the end of study, results in the two groups were tabulated and subjected to statistical analysis by applying Statistical Package for Social Sciences (SPSS) software version 11. The Z-test was used for comparisons of the components of the total deviation. The results were considered statistically significant when P value was less that 0.05 and statistically not significant when P value was greater than 0.05. Finally the results in the two groups were compared to draw the conclusion.

DISCUSSION

Spinal anaesthesia is widely used for lower limb and lower abdominal surgeries. It has been the mainstay for regional anaesthesia in developing countries, especially in India. Various local anaesthetics have been injected into the intrathecal space to achieve intrathecal blockade. The quest for searching newer and safer anesthetic agents has always been one of the primary needs in anesthesiology practice. Levobupivacaine, the enantiomer of bupivacaine, has strongly emerged as a safer alternative for regional anesthesia than its racemic sibling, bupivacaine. Levobupivacaine has been found to be equally efficacious as bupivacaine, but with a superior pharmacokinetic profile. Clinically, levobupivacaine has been observed to be well-tolerated in regional anesthesia techniques both after bolus administration and continuous post-operative infusion.[1]

Chari VR, Goyal A et al did a randomized, controlled trial on addition of Inj. Butorphanol to hyperbaric Inj. Bupivacaine given intrathecally to patients undergoing lower segment caesarean section. They compared injection butorphanol and normal saline as an adjuvant to local anesthetic agent in subarachnoid block in lateral position with respect to onset, duration of sensory and motor block and duration of analgesia. Their **aim was t**o evaluate the effect of addition of 25 mg of injection butorphanol to hyperbaric injection bupivacaine 0.5% on onset, quality, duration of sensory and motor block, hemodynamic changes, side effects, and post-operative analgesic effect when administrated intrathecally in patients undergoing elective lower segment cesarean section (LSCS). The principle outcome measures were systolic and diastolic blood pressure changes and the anesthetic and analgesic effects. These were summarized and compared between the two groups. Parametric statistics were used to test the null hypothesis of no difference in the two groups. They concluded that , addition of injection butorphanol gives longer duration of post-operative analgesia compared with control without serious side effects.[2]

In another study Bhosle SS etal used intrathecal Nalbuphine.It is an Effective Adjuvant for Post Operative Analgesia. Nalbuphine is an opioid drug with mixed μ antagonist and agonist properties. Thus we conducted a prospective, randomized study to observe the effect of intrathecal nalbuphine on pain relief after lower limb and lower abdominal surgeries. Sixty patients of ASA grades I and II of either sex in the age group of 18-65 years were randomly allocated to one of the two groups. Group B (n = 30) received 0.5% hyperbaric bupivacaine intrathecally; group N (n = 30) received 0.5% hyperbaric bupivacaine + 0.8 mg nalbuphine (preservative free) intrathecally. The onset of sensory and motor blockade, highest level of sensory blockade, duration of motor blockade and analgesia, VAS score, hemodynamic and respiratory changes, side effects were recorded, tabulated, and analyzed. Onset of sensory and motor blockade was faster in group N. The VAS scores showed that post operative analgesia lasted significantly in patients in group N than in group B. No significant side effects were observed in either of the two groups. Thus the authors conclude that intrathecal nalbuphine improved the quality of intraoperative and postoperative analgesia, with minimal side effects.[3]

Similar studies were done by other authors eg. Tiwari AK, Tomar G et al who used intrathecal bupivacaine in comparison with a combination of nalbuphine and bupivacaine for subarachnoid block. They performed this randomized, prospective double-blind

study to evaluate the effects of 2 different doses of intrathecal nalbuphine (a synthetic opioid agonist–antagonist) on the onset, duration of action, side effects, and complication produced by intrathecal hyperbaric 0.5% bupivacaine in lower abdominal, urologic and lower limb surgeries. Seventy-five patients of ASA grades 1 and 2 of either sex in the age group of 20–60 years were randomly allocated to 1 of 3 groups. The onsets of sensory and motor blockade, highest level of sensory blockade, 2 segment regression time of sensory blockade, duration of motor blockade and analgesia, visual analog scale score, hemodynamic and respiratory changes, side effects were recorded, tabulated, and analyzed. Onsets of sensory and motor blockade and duration of motor blockade were not affected. Two segment regression time of sensory blockade and duration of analgesia were maximally prolonged in group C ($P < 0.05$). The visual analog scale scores were in the following order: group A > group B > group C at 90, 120, and 150 minutes after induction ($P < 0.05$). Hemodynamic and respiratory complications were absent except in 2 patients in groups A and C each, and 1 patient in group B developed bradycardia ($P > 0.05$). Nalbuphine hydrochloride (400 µg) significantly prolongs the duration of sensory blockade and postoperative analgesia without any side effect or complication when introduced intrathecally along with hyperbaric bupivacaine.[4]

Mukherjee A, Pal A et al studied the role of Intrathecal nalbuphine as an adjuvant to subarachnoid block and postulated about the most effective doseVarious adjuvants have been used along with local anaesthetics for prolongation of analgesia post operatively in neuraxial blockade. The frequently used adjuvants are opioids, midazolam, neostigmine, ketamine etc. Neuraxial opioids bind to intrathecal opioid receptors and produce effective pain relief post operatively with minimal untoward effects. However, certain adverse effects like pruritis, post operative nausea and vomiting, urinary retention and respiratory depression have been observed with the use of majority of opioids.[5]

Naaz S, Shukla U did a comparative study of analgesic effect of intrathecal nalbuphine and fentanyl as adjuvant in lower limb orthopaedic surgery.Intrathecal opioids when added to local anaesthetics decrease their dosage and provide haemodynamic stability. Nalbuphine is an agonist-antagonist and acts on kappa receptors providing analgesia.The study aims to compare the analgesic efficacy of fentanyl with that of two doses of nalbuphine when used with injection bupivacaine heavy in spinal anaesthesia.Patients were randomly allocated into three groups (n=30). Each group received 12.5 mg of 0.5% of injection bupivacaine heavy along with either 25 µg of 0.5 ml fentanyl (Group F) or 0.8 mg of 0.5 ml nalbuphine (Group NL) or 1.6 mg of 0.5 ml nalbuphine (Group NH). Characteristics of sensory and motor blocks, haemodynamic changes, duration and quality of analgesia, adverse effects, sedation, VRS score and analgesic requirement were studied at different time interval intraoperatively and till 24 hours of block. The adverse effects of NL Group were least.There was no significant advantage of intrathecal fentanyl or 1.6 mg nalbuphine over low dose 0.8 mg nalbuphine.[6]

In a similar study by Nazir N, Jain S was a Randomized Controlled Trial for Evaluating the Analgesic Effect of Nalbuphine as an Adjuvant to Bupivacaine in Supraclavicular Block under Ultrasound Guidance.This was a prospective, randomized, double-blind study involving sixty patients of either sex undergoing elective orthopedic procedures of upper limb. In control Group C (n = 30), 30 mL of 0.375% bupivacaine + 1 mL normal saline and in study Group N (n = 30), 30 mL of 0.375% bupivacaine + 1 mL (10 mg) nalbuphine were used for giving supraclavicular block under US guidance. Parameters assessed were onset and duration of sensory and motor block, duration of analgesia (DOA), and any adverse events. Data between the groups were analyzed using independent t-test with SPSS 16.0 software.Nalbuphine when added to bupivacaine as an adjuvant in supraclavicular block significantly shortened the onset of sensory and motor block and enhanced the duration of sensory and motor block and DOA.[7]

CONCLUTION

Thus we conclude from our study that Intrathecal Butorphanol potentiates bupivacaine induced sensory spinal block and reduces the analgesic requirement in the early postoperative period without prolonging motor block recovery time to micturition and without any other major side effects. However, from our study, Butorphanol in a dose of 25mcg is found to be optimal for intrathecal administration, as when used in a higher dose of 50mcg, was found to have more haemodynamic side effects and not much difference in the prolongation of the duration of effective analgesia was observed.

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