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COMPARISON OF INTRATHECAL BUPIVACAINE AND BUPIVACAINE WITH BUTORPHANOL FOR POST-OPERATIVE ANALGESIA IN PATIENTS UNDERGOING LOWER ABDOMINAL SURGERY

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ABSTRACT

Background and Aim: Opioids, like butorphanol, have been widely used for providing pain relief postoperatively and the advantages of neuraxial narcotics over systemic narcotics are well established. When compared to local anaesthetics, they offer good analgesia while allowing early ambulation of the patient by sparing sympathetic and motor nerves. The aim of the study was to compare the safety and efficacy of anaesthesia and analgesia of intrathecal bupivacaine-butorphanol mixture with intrathecal bupivacaine alone.

Methods: This randomized prospective double-blind active-control study was performed on 60 female patients, aged between 18 and 60 years of ASA physical status I and II undergoing various elective lower abdominal surgeries under spinal anaesthesia. Patients were randomized in two groups, with 30 patients in each group. Patients in the Group B received 3ml (15mg) of 0.5% hyperbaric Bupivacaine plus 25 microgram of Butorphanol (0.25 ml) making a total volume of 3.25 ml and Group C received 3ml (15mg) of 0.5% hyperbaric Bupivacaine plus 0.25 ml of normal saline making a total volume of 3.25 ml intrathecally. Onset and duration of analgesia were recorded. The efficacy of analgesia was recorded based on VAS score. Side effects, time of recovery also were noted.

Results and observations: The two groups were comparable regarding the demographic profile. The onset of sensory block was delayed in group C (3.4 ± 1.3 min) when compared to group B (2.73 ± 0.78 min). The duration of sensory block as well as motor block was prolonged in butorphanol group (376.53 ± 10.32 mins) and (149.47 ± 6.76 min) respectively as compared to bupivacaine group (144.37 ± 25.32 min) and (135.63 ± 30.74 min) respectively. Both the findings were significant. Butorphanol provided a significantly longer duration of postoperative analgesia (432.60± 12.04 vs 140.03 ± 26.46 mins). No drug related side effects were observed in either group.

Conclusions: Intrathecal bupivacaine-butorphanol mixture provides longer duration of sensory blockade and superior analgesia than intrathecal bupivacaine alone.

KEYWORDS : Intrathecal, bupivacaine, butorphanol, post-operative analgesia

INTRODUCTION

Pain is one of the most common and uncomfortable consequences of a surgery, feared by all.[1] Effective and rapid relief from pain is always a challenge, but is necessary for alleviating nociception – induced responses like endocrine metabolic responses to surgery, autonomic reflexes with adverse effects on organ function, reflexes leading to muscle spasm, and other undesirable results.[2] Spinal anesthesia using local anesthetics like cocaine, procaine, lignocaine, bupivacaine, ropivacaine is one of the most popular techniques for both elective and emergency surgical procedures.[3] . In the recent past, the use of intrathecal adjuvants have gained a lot of acclaim as they prolong the duration of block, there is a better success rate, better patient satisfaction and faster recovery as well as being cost effective. This enables the patients to return to their normal activity more quickly.[4]

Neuraxial opioids are widely used in conjunction with local anesthetics (LA) as they permit the use of lower dose of LA while providing adequate anesthesia and analgesia.[5] Neuraxial opioids also allow prolonged analgesia in the postoperative period and faster recovery from spinal anesthesia.[6] Antinociceptive synergism between LA and intrathecal opioids has been demonstrated in various animal studies.[7]

Butorphanol is a lipophilic opioid agonist-antagonist analgesic with a published affinity for opioid receptors in vitro of 1:4:25 (mu: delta: kappa).[8] Abboud et al have reported a dose-dependent increase in the duration of analgesia provided by epidural butorphanol for relief of post-cesarean section pain.[9] The present study was undertaken to compare the safety and efficacy of intrathecal bupivacaine-butorphanol mixture with intrathecal bupivacaine alone to provide post-operative analgesia in patients undergoing lower abdominal surgery.

MATERIALS AND METHODS

This prospective, randomized, comparative, double blind study was conducted at a tertiary level teaching hospital in Eastern India over a period of one year (January 2014-June 2015) after approval of the Ethical cum Screening Committee. We included randomly selected 60 (sixty) female patients (determined by power analysis study) in between the age of 18-60 years with American Society of Anaesthesiologists (ASA) physical status (PS) I and II, weighing between 40 and 70 kg posted for elective lower abdominal surgical procedures under spinal anaesthesia.

They were divided randomly (as per computerised randomization table) into 2 groups of 30 each, Group B and C (n=30). For the purpose of sample size calculation, duration of effective post-operative analgesia had been taken as the primary outcome measure. It had been estimated that 23 subjects (recruitment target being 30 subjects per group) would be required per group in order to detect the difference of 1 hour in this parameter between the 2 groups with 90% power and 5% probability of type 1 error. The calculation assumed standard deviation of 1 hour.

Group B received 3ml (15mg) of 0.5% hyperbaric Bupivacaine plus 25 microgram of Butorphanol (0.25 ml) making a total volume of 3.25 ml intrathecally and Group C received 3ml

(15mg) of 0.5% hyperbaric Bupivacaine plus 0.25 ml of normal saline making a total volume of 3.25 ml. intrathecally.

Each patient received a written and verbal description of the research protocol and written informed consent was taken from all the patients in their language for inclusion in the study. Exclusion criteria for the study were patient undergoing emergency surgery, allergy to amide local anesthetics, history of drug and alcohol abuse, patient contraindication to spinal anesthesia ,inadequate block (sensory block < T8 segment), body mass index >30 kg/m2, patient with severe systematic disorders like diabetic , musculoskeletal and neurological disease and patient refusal.

Parameters to be studied:

- Onset and duration of sensory block.
- Onset and duration of motor block.
- Visual Analogue Scale Score.
- Incidents of adverse effects.

The level of sensory block evaluated by pin prick method using 20-gauge hypodermic needle. The test was performed every 5 minutes till loss of discrimination to pin prick for the first 10 to 15 minutes and then every 10 minutes after operation until its full recovery. We checked bilaterally T_{12}, T_{10}, T_8, T_6 or higher (T_4) dermatomes by pin prick and we used forehead as baseline point for normal sensation.

Motor blockade was assessed using a modified Bromage scale (0 = no motor block, 1 = hip blocked, 2 = hip and knee blocked, 3 = hip, knee and ankle blocked). The maximum Bromage score reached and duration of the motor block (from spinal injection until Bromage 1 and/or 0 score) were registered every 5 minutes after injection of study drug for 10 to 15 minutes and every 10 minutes in post-operative period until full recovery.

Duration of analgesia was calculated by the time gap between onset of sensory block and administration of subsequent analgesia. Pain was assessed by Visual Analogue Scale which was measured from 0 to 10, score 0= no pain, score 10= worst pain. When VAS score was > 4, analgesia was supplemented.

Study Techniques

Prior to the scheduled operations, patients were fasted for a minimum of 8 hours and were not premedicated with analgesics and sedatives. Blood pressure (systolic, diastolic and mean), heart rate, respiratory rate and oxygen saturation were recorded.

All patients were preloaded with 500 ml of Ringer's Lactate solution. Under full aseptic conditions, a lumbar puncture was performed at the level of L4-L5 interspace using 25 gauze Whitacre needle by a senior anaesthesiologist not involved in the study. Correct needle placement was identified by free flow of cerebrospinal fluid and study drug was injected over 10 second. Patients in Group B was given 15mg of 0.5% Hyperbaric Bupivacaine along with 25μg of Butorphanol. The patients in Group C received 15mg of 0.5% Hyperbaric Bupivacaine.

Drugs were drawn in similar syringes by a person not involved in the study as per randomization number allocated to the particular patient. Patient and the person administering the drug here were blinded to the study preparation.

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Immediately after the administration, the patient was placed in a horizontal position and onset of analgesia by loss of pain to pin prick and inability to raise the lower limb, degree and level of sensory blockade, degree of motor blockade, duration and quality of post operational analgesia were recorded at specified intervals. Hemodynamic changes like heart rate, blood pressure were recorded every 5 minutes interval for the first 30 minutes, there after every 30 minutes for the rest of the surgical procedure. Post operatively, they were recorded every 2 hours up to 12 hours and at 4 hourly intervals for 24 hours.
Side effects such as sedation, respiratory depression, itching, urinary retention, nausea, vomiting, and headache were also noted.

Statistical Analysis:

The results of the observations thus obtained in each group of patients were tabulated, compiled and statistically analyzed using Stastica version 6 [Tulsa, Oklahoma: StatSoft Inc., 2001] and SPSS version 17 [Illinois, Chicago: SPSS Inc., 2008]. All numerical variables were mostly normally distributed by Kolmogorov-Smirnoff goodness of fits test. Results on continuous measurements were presented on Mean ± SD (Min-Max). Significance was assessed at 5 % level of significance. Paired/unpaired t tests / Fisher Exact test were used to find the significance of study parameters on categorical scale between the groups.

A p value < 0.05 was considered as statistically significant and < 0.01 was considered as highly significant.

RESULTS:

The two groups were comparable with regards to age, weight, height, BMI and ASA status. [Table 1-2]. The mean baseline values of HR, SBP, DBP, RR and SpO2 were comparable among the groups.

Table 1:- Demographic profile

	B		C		
	Mean	Standard Deviation	Mean	Standard Deviation	p value
AGE	48.63	10.93	45.47	9.94	0.221869
WT	53.73	7.46	52.53	7.45	0.333896
HT	150.53	8.13	147.30	8.90	0.157455
BMI	23.50	2.79	24.00	3.14	0.755055

Table 2: ASA status of the patients

		B		C		Total		
		Value	Percentage	Value	Percentage	Value	Percentage	p value
ASA	I	27	90%	25	83%	52	87%	0.4475
	II	3	10%	5	17%	8	13%	
	Total	30	100%	30	100%	60	100%	

Table 3: Perioperative heart rate (HR) of the patients

	B		C		
HEART RATE	Mean	Standard deviation	Mean	Standard deviation	p value
BASE LINE	85.47	12.03	84.73	12.39	0.828
2 MIN	84.60	12.49	84.60	13.26	1.000
5 MIN	85.40	12.29	84.43	12.72	0.776
10 MIN	85.77	12.87	81.50	10.32	0.237
15 MIN	85.67	13.53	82.57	12.46	0.403
20 MIN	85.33	12.93	81.77	12.25	0.347
25 MIN	85.60	13.02	80.67	13.84	0.234
30 MIN	84.97	10.76	79.67	12.41	0.271
60 MIN	86.13	11.98	85.03	12.10	0.733
90 MIN	85.77	11.70	84.93	10.33	0.770
120 MIN	85.10	12.70	85.33	11.98	0.940

From Table 3, the heart rate among the patients in the two groups were comparable with no significant difference throughout the procedure (p>0.05).

Table 4: Perioperative systolic blood pressure (SBP) of the patients

	B	C	

SBP	Mean	Standard deviation	Mean	Standard deviation	p value
BASE LINE	123.80	16.28	123.20	14.67	0.896
2MIN	122.40	16.55	114.53	14.32	0.081
5MIN	119.83	15.48	112.53	16.25	0.099
10MIN	123.13	15.30	116.33	14.18	0.099
15MIN	124.43	16.98	118.57	13.36	0.088
20MIN	124.50	15.69	117.27	15.89	0.098
25MIN	120.70	16.04	114.83	14.20	0.153
30MIN	123.93	15.42	116.07	15.84	0.096
60MIN	124.20	16.75	115.27	11.75	0.087
90MIN	124.70	14.76	118.03	7.92	0.050
120MIN	124.50	15.91	120.20	8.86	0.243

From Table 4, the systolic blood pressure among the patients in the two groups were comparable with no significant difference throughout the procedure ($p>0.05$).

Table 5: Perioperative diastolic blood pressure (DBP) of the patient

	B		C		
DBP	Mean	Standard deviation	Mean	Standard deviation	p value
BASE LINE	77.60	11.00	76.13	8.96	0.618
2 MIN	77.37	13.56	72.17	10.67	0.144
5 MIN	75.70	11.64	71.93	9.57	0.208
10 MIN	77.83	13.86	73.10	10.07	0.163
15 MIN	75.97	10.48	72.50	9.82	0.187
20 MIN	77.53	12.58	71.70	9.18	0.058
25 MIN	78.40	12.61	72.57	10.85	0.093
30 MIN	76.03	11.07	70.20	8.31	0.098
60 MIN	76.70	12.22	71.93	9.67	0.143
90 MIN	77.60	11.05	77.97	7.73	0.885
120 MIN	78.63	12.18	78.93	7.25	0.911

From Table 5, the diastolic blood pressure among the patients in the two groups were comparable with no significant difference throughout the procedure ($p>0.05$).

Table 6: Perioperative mean arterial pressure (MAP) of the patient

	B		C		
MBP	Mean	Standard deviation	Mean	Standard deviation	p value
BASE LINE	93.00	11.39	91.82	9.92	0.713
2 MIN	92.38	12.20	86.29	10.75	0.072
5 MIN	90.41	11.32	85.47	10.52	0.105
10 MIN	92.93	12.61	87.84	9.59	0.098
15 MIN	92.12	11.10	87.52	9.08	0.098
20 MIN	93.19	11.67	88.22	10.08	0.099
25 MIN	92.50	11.44	86.66	10.81	0.077
30 MIN	92.00	10.28	89.82	10.33	0.102
60 MIN	92.53	12.22	88.04	8.83	0.097
90 MIN	93.30	11.10	91.32	6.96	0.426
120 MIN	93.92	11.87	92.69	6.60	0.638

From Table 6, the mean arterial pressure among the patients in the two groups were comparable with no significant difference throughout the procedure ($p>0.05$).

Table 7: Onset & duration of sensory block (in min)

	B		C		
	Mean	Standard Deviation	Mean	Standard Deviation	p value
SENSORY ONSET	2.73	0.78	3.40	1.302	0.024
SENSORY OVER	376.53	10.32	144.37	25.326	0.000

From Table 7, the onset and duration of sensory block among the patients in the two groups were comparable with significant difference throughout the procedure ($p<0.05$).

Table 8: Onset and duration of motor block (in min)

	B		C		
	Mean	Standard Deviation	Mean	Standard Deviation	p value
MOTOR ONSET	4.07	0.87	6.07	1.70	0.000
MOTOR OVER	149.47	6.76	135.63	30.74	0.023

From Table 8, the onset and duration of motor block among the patients in the two groups were comparable with significant difference throughout the procedure ($p<0.05$).

Table 9: Duration of Analgesia

	B		C		
	Mean	Standard Deviation	Mean	Standard Deviation	p value
DURATION OF ANALGESIA	432.60	12.04	140.03	26.46	0.000

From Table 9, the duration of analgesia among the patients in the two groups were comparable with significant difference throughout the procedure ($p<0.05$).

Table 10: Perioperative side effects

Side effects	Group B; n (%)	Group C; n (%)	P value
Hypotension	0	0	1
Bradycardia	0	0	1
Pruritus	0	0	1
Sedation	2 (6.6)	0	0.246
Respiratory depression	0	0	1
Shivering	2 (6.6)	2 (6.6)	1
Nausea	0	0	1
Vomiting	0	0	1
Urinary retention	4 (13.3)	3 (10)	1
Headache	0	0	1

Data is presented as number (%) All the patients in both the groups remained hemodynamically stable throughout the conduct of anesthesia with no significant deviation in heart rate, systolic and diastolic BP and mean arterial pressure.

Sensory blockade onset time and time to attain highest sensory level were rapid and statistically significant with Butorphanol as compared to Bupivacaine alone. The onset of motor block was comparable in both the groups and the difference was statistically significant. Time for two segment regression and motor block duration were significantly prolonged with Group B as compared to Group C and were statistically significant.

Analgesia was prolonged and was statistically significant with Butorphanol as compared to Bupivacaine alone. There were no significant side effects among the groups (Table 10).

DISCUSSION

The principal findings in our study were that addition of 25 g of butorphanol as adjuvant to hyperbaric bupivacaine 0.5% provides a faster onset of sensory block as compared to bupivacaine alone. Butorphanol provided a significantly greater duration of both sensory and motor block and post-operative analgesia.

Also in the present study, there were no statistically significant difference between both groups as regards to the hemodynamics and post-operative side effects.

Any method of post-operative analgesia must meet three basic criteria; it must be simple, safe, clinically appropriate and evidence based.[10] Parenteral or intramuscular

administrations of the opioid drugs are not as effective and the patients are left with unrelieved pain.[11,12] The discovery of opioid receptors in the brain and spinal cord started a new era in the field of postoperative analgesia.[13,14] The first clinical use of opioids was done by Wang et al and since then, the opioids are found to be more beneficial as a single intrathecal injection producing pain relief of sufficient duration.[15] The use of opioids in conjunction with local anesthetic for spinal anesthesia has been associated with decreased pain scores and reduced analgesic requirement in the post-operative period.[16,17] Results of previous studies have demonstrated that intrathecal opioids not only enhance analgesia when added to sub therapeutic doses of local anesthetics but also do not prolong recovery[6,18,19] A study by Shaloo Ipe et al observed that 150mcg buprenorphine was not as effective as 300 mcg buprenorphine given epidurally where the duration of analgesia was highest, though the analgesic effect of buprenrphine given intrathecally was quite effective with 50% patients showing the effect for 6 hours.[20] Some investigators have demonstrated that by using buprenorphine alone epidurally, in doses of 1 to 4 mg, varying durations of pain relief ranging from 2.5 to 9 hours are observed.[21,22]

Weight, height, age and ASA grading of patients showed no significant differences in our study. The onset of sensory block was delayed in bupivacaine alone group (3.4 ± 1.3 min) when compared to butorphanol group (2.73 ± 0.78 min). It was statistically significant. The duration of sensory block as well as motor block was prolonged in butorphanol group (376.53 ± 10.32 mins) and (149.47 ± 6.76 min) respectively as compared to bupivacaine group (144.37 ± 25.32 min) and (135.63 ± 30.74 min) respectively, which were both statistically and clinically significant. Another significant finding was prolong duration of analgesia in butorphenol group (432.60± 12.04 vs 140.03 ± 26.46 mins). Singh V et al., in their study compared intrathecal fentanyl and butorphanol in combination with bupivacaine for lower limb surgeries and concluded that 25μg intrathecal butorphanol is superior to 25μg intrathecal fentanyl in respect to duration of sensory block.[23] Kumar B et al., in their study compared intrathecal bupivacaine-fentanyl and bupivacaine-butorphanol mixtures for lower limb orthopedic procedures, concluded that intrathecal bupivacaine-butorphanol mixture provides longer duration and superior analgesia than intrathecal fentanyl-bupivacaine mixture.[24]

The results of our study are consistent with experimental evidence of synergistic interaction between spinal opioids and local anesthetics, which are characterized by enhanced somatic analgesia without effect on the degree or level of the local anesthetic induced sympathetic or motor blockade.[7,25] The synergism between intrathecal opioids in addition to local anesthetics is due to the drugs' separate mechanism of action; blockade of Na+ channel by local anesthetics[26] and voltage-gated Ca++ channels with opioids.[27] The combination of opioids with local anaesthetic (LA) allows for a reduction in doses of the LA, thus lessening the likelihood of side effects.[26,28] Although two patients had sedation in the group receiving butorphanol-bupivacaine, as compared with none in the group receiving bupivacaine alone; none of them had respiratory depression. Sedation was a reported side effect of neuraxially administered butorphanol.[27] Varassi et al have reported that bupivacaine 15 mg along with 25- g fentanyl did not cause respiratory depression in elderly patients.[29] Two patients (6.6%) in each group had shivering which was mild in nature and did not require any treatment.

Seven patients were catheterized during the post-operative period due to difficulty in voiding, although the average times to voiding were comparable among both the study groups. Previous studies had reported that intrathecal bupivacaine was associated with a clinically significant disturbance of bladder function and spontaneous voiding may not be expected until the sensory blockade has regressed to the S3 level.[30] None of the patients in the study experienced nausea or vomiting. None of the patients reported post dural puncture headache or any neurological deficit.

Limitation of the study

Although inclusion of bupivacaine alone group has supported our findings, we also recognize the fact that the wide variability in the age of the patients included in the study is a confounding factor in relation to perception of pain as pain perception varies for various age groups. We did not record the number of doses and the total dose of rescue analgesic required to relieve pain. Further investigation should be aimed at finding the minimal possible doses of intrathecal butorphanol in conjunction with hyperbaric bupivacaine that will provide adequate anaesthesia and analgesia for lower abdominal surgeries.

CONCLUSION

We conclude that intrathecal butorphanol enhances sensory blockade of the local anesthetic without affecting the sympathetic activity. Addition of 25 mcg of butorphanol to bupivacaine 0.5% heavy in spinal anesthesia provides the advantage of faster onset of sensory block and longer duration of postoperative analgesia as compared to 0.5% bupivacaine alone. The benefits of the opioid are far more than the side effects like vomiting and nausea. It is easily available, easy to perform and most predictable drug.

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Conflicts of interest

There are no conflicts of interest.

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