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TO COMPARE THE EFFICACY OF (0.5%) BUPIVACAINE ALONE & IN COMBINATION WITH (5 µG) SUFENTANYL FOR SPINAL ANAESTHESIA

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ABSTRACT

To compare onset & duration of sensory & motar blockade, highest level of sensory block, analgesia & side effects of bupivacaine alone and in combination with sufentanyl for spinal anaesthesia. 100 patients in the age group of 18-60yrs belonging to ASA I & II undergoing elective lower abdominal, urologic & lower limb surgeries were randomly allocated to two groups of 50 each. Gp A received 2.5ml of 0.5% bupivacaine &Gp B received 2.5 ml of 0.5% bupivacaine with 5 µg sufentanyl. There was no difference in onset of sensory & motar block. Time to achieve peak sensory level was 2 minutes earlier in Gp B & higher level (T6) of sensory block was attained in Gp B. Duration of complete & effective analgesia was prolonged by 40 min-1hr & time to requirement of first dose of analgesia was delayed by 1-2hrs in Gp B. Sufentanyl potentiates bupivacaine in spinal anaesthesia by increasing duration &improviing quality of analgesia with minimal side effects.

Key words: Spinal anaesthesia, Bupivacaine, Sufentanyl, analgesia.

INTRODUCTION

Spinal anaesthesia was first introduced in clinical practice by August Bier [1]. Since then, it is being widely utilized for both elective & emergency surgical procedures in orthopaedics, obstetrics and lower abdominal surgeries [2]. It is simple to institute, rapid in its effect and produces excellent operating conditions.

Spinal anaesthesia is defined as Regional anaesthesia obtained by blocking nerves in sub-arachnoid space. Simplicity to perform, rapid onset of action, minimal drug cost, minimal stress response, awake patient, relatively lesser side effects & rapid patient turnover are some of the advantages of spinal anaesthesia over general anaesthesia [3].

One disadvantage of spinal anaesthesia using local anaesthetic alone is a relatively short duration of action and hence lack of long-lasting postoperative analgesia. Another disadvantage, although infrequent is intraoperative nausea particularly during manipulation of peritoneum. To overcome this problem, many adjuvants have been used to prolong the duration of analgesia. These include various opioids and non-opioid drugs like clonidine. The adjuvants most commonly used in combination with bupivacaine are opioids and clonidine. The rationale behind adding opioids to intrathecal local anaesthetics is that opioids act synergistically with local anaesthetics.Opioids reduce the onset time to blockade, improves perioperative analgesia, and extends postoperative analgesia up to 7 hours.

Morphine has been used to control postoperative pain, as it is ionized and highly hydrophilic. Thus, as a result of its pharmacokinetic effects when applied into the subarachnoid space, morphine has a slow onset of action but long duration of analgesia.

Sufentanyl, synthetic congener of fentanyl is 100 times more potent than morphine.[4]It has been the latest tool in the armory of modern day anaesthesiologists.Sufentanil added to intrathecal bupivacaine for spinal anaesthesia has shown to improve intraoperative and postoperative

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analgesia with no adverse effects.

The aim of our study was to compare intrathecal hyperbaric Bupivacaine with Sufentanil and intrathecal hyperbaric Bupivacaine alone with respect to sensory and motor block characteristics, intraoperative Haemodynamic variables, postoperative analgesia.

MATERIAL AND METHODS

The present study was carried out in 100 patients in the age group of 18-60yrs undergoing elective lower abdominal, urological or lower limb surgeries after obtaining permission from institutional ethical committee and obtaining written informed consent from the patients.
Following inclusion and exclusion criteria were used to select the study subjects.

Inclusion criteria

Patients undergoing elective lower abdominal surgeries such as appendicectomy, hernioplasty, herniorrhaphy, ovariectomy, hysterectomy etc.
●ASA I and II

Exclusion criteria

ASA III or more.

Patients with poor myocardial contractility, coagulopathy, back problems, spine deformity.

Patients on potent antiplatelets, or on anticoagulants.
Known allergy to the trial drugs.

Patient refusal

A detailed preanaesthetic examination including history, general physical examination, systemic examination, spine examination for deformity was performed. Detail information about the patients was noted on a prestructured proforma. Routine investigations like hemogram, BT,CT, RBS & RFT were done. ECG & Chest X-Ray were done wherever necessary.

All patients were kept nil orally for 8-10hrs. Premedication was standardized with Tab. Diazepam 0.2mg/kg preoperatively on the night before surgery.
Patients were allocated into 2 groups.

BUPIVACAINE GP-Gp A- 50 Patients receiving intrathecal bupivacaine 0.5% heavy (2.5ml).
SUFENTANYL GP- Gp B- 50 Patients receiving intrathecal sufentanyl 5 µg (0.1ml) with intrathecal bupivacaine 0.5% heavy (2.5ml).

PROCEDURE

Patient was shifted to OT table. IV access with 18 G cannula done. Lactated Ringer's Solution 500ml was infused IV before the block.

Monitors applied. NIBP/SPO2/ECG. Baseline vitals recorded.

Under strict aseptic precautions, in left lateral position, lumbar puncture was performed by midline approach using disposable Quinke's spinal needle 23G at L3-4 intervertebral space.
After giving spinal anaesthesia, O2 (4L/MIN) was given by face mask.
IV fluids- Lactated Ringer's Solution given intraoperatively. (10ml/kg/hr).

Following parameters were observed Vitals- HR, BP, SPO2 & RR were observed at 0, 1, 2, 3, 5, 10, 15, 20, 25, 30, 45, 60, 120 & 180 minutes.

Assessment of sensory blockade

Onset of sensory blockade was tested by pin-prick method using hypodermic needle. The time of onset was taken from time of injection of drug into sub-arachnoid space to loss of pin-prick sensation. The highest level of sensory block & time required to achieve it was noted.

Assessment of motar blockade-

Time interval between injection of drug into sub-arachnoid space to patient's inability to lift straight extended leg was taken as onset time. (Br 3)

Duration of motar blockade was taken from time of injection of drug to complete regression of motar block. (ability to lift extended leg/ Br 0).

Bromage Scale

0- Full flexion of knee & feet.
1- Just able to flex knee, full flexion of feet.
2- Unable to flex knee but some flexion of feet possible.
3- Unable to move legs or feet.

Assessment of analgesia

Pain was assessed by **VAS** (visual analog scale). VAS consists of a 10 cm line anchored at one end by a label such as 'no pain' and at other end by label such as ' pain as bad as can be'. Patient marks the line to indicate intensity of pain & then the provider measures the length of line to mark a point scale. All patients were instructed about VAS & to point intensity of pain on scale.
0- No pain.
1- Worst pain ever.

Quality of intraoperative analgesia
It was assessed by **Belzarena Scale.**

Belzarena Scale

1. Unable to tolerate pain.
2. Able to tolerate discomfort with additional analgesia.
3. Some discomfort but no additional analgesia required.
4. Completely satisfied.

Side Effects

Side effects of intrathecal bupivacaine with sufentanyl like nausea, vomiting, pruitis, shivering, respiratory depression (RR< 10/min), arterial oxygen desaturation : SPO2< 90%, drowsiness, hypotension, euphoria, chest tightness, urinaty retention were noted.

Hypotension defined as decrease in SBP more than 20% of baseline value & was treated with inj. Mephetermine 6 mg iv increments & bradycardia defined as PR< 60/min was treated by inj. Atropine 0.6mg iv stat.

OBSERVATION AND RESULTS

Table 1 shows that both groups were comparable with respect to age, height, weight & sex ratio without any statistically significant difference. (p> 0.05).

Table 2 shows there was no significant difference with regard to onset of sensory block (p value >0.05) &motar block (p value >0.05) between the two groups.

Table 3 shows time to achieve peak sensory level was lesser in GROUP B as compared to GROUP A and the difference was statistically significant**.**

Table 4 shows that Gp B (Sufentanylgp) achieved highest level of sensory block. (T6 in 56% subjects).

Table 5 shows that duration of sensory &motar block was longer in sufentanylgp& the difference was statistically significant. (p<0.001).

Table 6 shows that duration of complete analgesia and time to first analgesic dose was higher in gp B & the difference was statistically significant. (p<0.001).

Table 7 shows that Gp B had better pain control intraoperatively as well as post operatively as compared to Gp A.

Table 8 shows that there is no significant difference in pulse rate between the two groups. (P>0.005).

Table 9 shows that there was no statistically significant difference in mean blood pressure between the two groups.(P>0.05).

Table 10 shows that sufentanyl did not cause any major side effects when it is given intrathecally along with bupivacaine.

Table 1. Demographic Data

Parameter	Group A	Group B	P-Value
Age (years) Mean±S.D	42 ± 9	40± 10.9	0.18
Sex (Male: Female)	30:20	28:22	0.42
Height(feet) Mean±S.D	4.42 ±1.32	5.49 ±0.13	0.39
Weight(Kg) Mean±S.D	56.18 ±7.5	59 ±9.01	0.96

Table 2. Onset of Sensory &Motar blockade

Onset	Group A	Group B	P-Value
Sensory block (time in seconds) Mean±S.D	134.2±15.3	132.4±8.2	0.81
Motar block (time in seconds) Mean±S.D	230±20.1	217±10.7	0.062

Table 3. Time to achieve peak sensory block

Time to achieve peak sensory level	Group A	Group B	P-Value
Time in minutes (Mean ± S.D)	8.20 ±1.40	5.30 ±1.20	<0.01

Table 4. Highest level of sensory block

Level of Sensory Block	Group A	Group B
T6	14 (28%)	28 (56%)
T8	24 (48%)	16 (32%)
T10	12 (24%)	6 (12%)

Table 5. Recovery parameters

Recovery Parameters	Group A	Group B	P-Value
Time to 2 segment regression (in minutes)	88±18.9	138±12	P<0.001
Time to complete sensory recovery (in minutes)	216±12	256±16	P<0.001
Time to complete motar recovery (in minutes)	196±14	218±10	P<0.001

Table 6. Duration of analgesia

Duration of Analgesia (in Minutes)	Group A	Group B	P-Value
Duration of complete analgesia(Mean±S.D)	180±32	278±19	P<0.001
Time to first dose of analgesic(Mean±S.D)	256±24	348±32	P<0.001

Table 7. Visual analog scale (vas) scores

VAS Score	Group A	Group B	P-Value
Intraoperatively(Mean±S.D)	0.46±0.8	0.2±0.6	P<0.001
3 HRS(Mean±S.D)	1.2±0.66	0.8±0.2	P<0.001
6 HRS(Mean±S.D)	4.1±1.1	2.2±0.8	P<0.001
12 HRS (Mean±S.D)	6±2.2	3.2±1.2	P<0.001

Table 8. Pulse rate

Duration (in minutes)	Group A	Group B	P-Value
0 (Baseline)	78.3±7.8	78.4±9.4	0.721
5 (Mean±S.D)	80.2±8.2	81.2±8.7	0.990
10(Mean±S.D)	79.6±8.6	82.4±9.2	0.748
20(Mean±S.D)	81.8±8.8	81.4±10.2	0.410
30(Mean±S.D)	80.2±7.8	79.3±8.1	0.062
60(Mean±S.D)	81.3±7.6	77.4±8.6	0.743
120(Mean±S.D)	78.2±8.6	82.4±8.8	0.605
160(Mean˙±S.D)	80.6±8.8	80.6±9.6	0.316

Table 9.Mean BP

Duration (in minutes)	Group A	Group B	P-Value
0 (Mean±S.D)	90.04±5.64	89.36±6.43	0.360
5 (Mean±S.D)	90.14±5.64	89.47±6.13	0.312
10(Mean±S.D)	90.47±5.27	88.2±6.67	0.107
20 (Mean±S.D)	90.1±5.34	87.7±7.09	0.066
30 (Mean±S.D)	89.3±5.64	88.10±6.6	0.063
60 (Mean±S.D)	84.6±6.83	84.8±5.14	0.109
120 (Mean±S.D)	88.3±9.01	89.6±6.42	0.103
180 (Mean±S.D)	89.3±5.13	89.2±6.35	0.067

Table 10. Perioperative complications

Adverse Effects	Group A	Group B
Nausea/vomiting	6(12%)	8(16%)
Pruitis	0(0%)	16(32%)
Shivering	8(16%)	0(0%)
Bradycardia	0(0%)	0(0%)
Hypotension	10(20%)	4(8%)
Drowsiness	2(4%)	3(6%)
Chest tightness	0(0%)	0(0%)

Fig 1. Duration of Analgesia

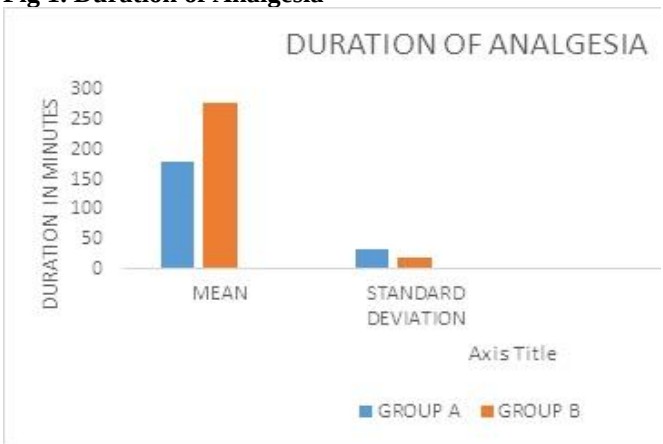
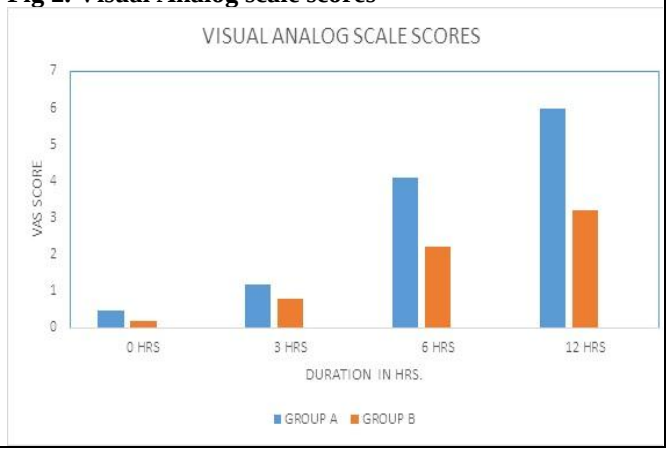


Fig 2. Visual Analog scale scores



DISCUSSION

"Cocainization of the spinal cord" was first described by August Bier in 1899 [1]. The technique has been refined since that time and has evolved into the modern concept of subarachnoid block (SAB). The safety of well-conducted spinal analgesia was supported by reports of thousands of carefully followed-up cases by the recognized authorities [5]. However, the use of local anesthetics in this technique, too, is not without complications such as hypotension, bradycardia, urinary retention and neurological injuries etc., Most of these complications are found to be dependent on the volume and dose of injected drug and the height of SAB [6]. By adding opioid as adjuvants, the dose of local anesthetics can be reduced to half thereby reducing the side-effects without unduly compromising the quality of analgesia. "Combination Wisdom" allows the use of a lower dose of the local anesthetic agent with adjuvants, which offers hemodynamic stability. Opioids in conjunction with local anesthetics improve the quality of intraoperative analgesia and prolong the duration of postoperative analgesia [7].

Morphine was the first opioid to be used intrathecally, but a wide variety of clinically relevant side-effects, especially respiratory depression limited its utility [8]. A favorable pharmacokinetic and pharmacodynamic profile of lipophilic opiates e.g. fentanyl and sufentanil, makes them better alternatives, because of a rapid uptake, faster onset and shorter duration of action. This minimizes the rostral migration of the drug to the respiratory center, avoiding delayed respiratory depression [9]. Sufentanil, a pure agonists is an N-4 thienyl derivative of fentanyl. It is considered to be more lipid soluble, a better receptor ligand and is 7-10 times more potent analgesic than fentanyl [10].

Local anesthetics such as bupivacaine act mainly by blockade of voltage-gated Na+ channels in the axonal membrane and presynaptic inhibition of calcium channels [11]. The μ-agonists sufentanil exert it's action by opening the K+ channels and reducing the Ca++ influx, resulting in inhibition of transmitter release [12-13]. A combination of these effects may explain the observed synergism between bupivacaine and sufentanil. The synergism is characterized by enhanced somatic analgesia without an effect on the degree or level of local anesthetic-induced sympathetic or motor blockade [13].

In our study, mean time for onset of sensory block in sufentanylgp was 132.4 seconds & 134.2 seconds in plain bupivacaine gp. The mean time for onset of motar block in sufentanylgp was 217 seconds and in bupivacaine gp was 230 seconds. There was no statistically significant difference with regard to onset of sensory &motar block between the two groups. Aussucao and associates evaluated the effects of sufentanyl with three different doses of bupivacaine & concluded that onset of action was clinically & statistically insignificant between the groups [4]. Cheng *et al.*, and Palmer *et al.*, in their studies observed that onset of sensory block was faster in fentanyl group as compared with sufentanil, when given intrathecally along with bupivacaine in labor analgesia [14-15]. Our study corroborates with the above mentioned studies, Hence we conclude that addition of sufentanyl has no variation in onset of sensory &motar block.

In our study, mean time to achieve peak sensory level was 3-4minutes earlier in sufentanylgp as compared to bupivacaine gp. ($p<0.05$).). However, Kim *et al*., showed no significant difference in time to peak block level (15.4 min in fentanyl group and 15.1 min in sufentanil group) [16]. Varying results have been seen regarding the highest level of sensory blockade by various studies conducted until date. Lo *et al*., reported a significant higher blockade with sufentanil as compared to fentanyl and plain bupivacaine. In our study, 56% patients in sufentanylgp attained T6 level as compared to 48% in bupivacaine gp. This implies sufentanyl when added to bupivacaine achieves higher level of sensory block [17].

The duration of effective analgesia as defined by the time from intrathecal injection to the time of the first request for analgesia was 179.17 min in bupivacaine group & 370.33 min in bupivacaine-sufentanil group. Mean duration of complete analgesia was prolonged by 50-80 minutes & time to first requirement of analgesic postoperatively was also prolonged in sufentanyl group. Trend toward longer analgesia with sufentanil than with fentanyl has also been supported by Ngiam *et al*., Lo *et al*., Nelson *et al*., in laboranalgesia and cesarean section [18]. In a comparative trial in urological patients Donadoni *et al*., observed that intrathecalsufentanil (5 g) as a supplement to lignocaine provided a significant longer period of post-operative analgesia [19].

Post-operatively, the VAS was significantly of higher values at all-time intervals in group receiving bupivacaine alone. Campbell *et al*., has also shown that VAS scores for pain were significantly higher in the bupivacaine alone group when compared to both sufentanil alone group and the bupivacaine-sufentanyl group in labour analgesia [20]. Addition of opioids to low dose bupivacaine definitely improves the analgesic effect and also leads to a significant beneficial effect of early ambulation because of minimal motor block. Kararmaz *et al*., demonstrated significantly prolonged motor block in plain bupivacaine group as compared to fentanyl with low dose bupivacaine in elderly patients undergoing TURP [21]. Lo *et al*., observed no significant variation in motor block characteristics in their study groups of combination of low dose bupivacaine (2.5 mg) with sufentanil (10 μg) and with fentanyl (10 μg) in combined spinal epidural [17]. Soni *et al*., also concluded that low dose intrathecalropivacaine (3 mg) with sufentanil (10 μg) improved quality and duration of analgesia without impairing the motor strength during labor, to facilitate early ambulation [22].In our study, the two groups did not differ significantly with respect to heart rate at any interval.

There was non episode of bradycardia in either of the two groups.

The cardiovascular responses observed by Donadoni in his study groups of plain 5% heavy lignocaine (1.5 ml) with 1.5 ml normal saline and lignocaine (1.5 ml) in combination with sufentanil (5 μg), revealed a significant decrease in heart rate in the sufentanil group as compared to control group [19]. This difference, in their study was merely the result of a higher pre-operative rate in sufentanil group.

Wang *et al*., explored the clinical efficacy of intrathecally administered low dose sufentanil - bupivacaine in TURP. They observed a significant decrease in heart rate in the combination group of sufentanil 5 μg with bupivacaine 7.5 mg in comparison to plain bupivacaine group and group administered sufentanil 7.5μg and bupivacaine 7.5 mg intrathecally [23]. The changes in MBP at any time interval were statistically & clinically insignificant.. This is in accordance with the earlier study by Atallah *et al*., the combination of intrathecal low dose bupivacaine and fentanyl offers a reliable neuraxial block with stable hemodynamics [24].

Campbell *et al*., also reported no episode of hypotension when sufentanil in combination with bupivacaine was administered intrathecally [20]. Lo *et al*., in their study showed consistently lower blood pressure in sufentanil as compared to fentanyl group, which was statistically significant [17]. Olofsson*et al.*, reported that low dose bupivacaine (7.5 mg) with sufentanil has shown to provide reliable anesthesia for the repair of hip fracture in the aged patients with few events of hypotension and little need for vasopressor support to maintain blood pressure [24].

The administration of intrathecal opioids may provide the benefit in augmenting intraoperative and post-operative analgesia, but carries a risk of respiratory depression and oxygen desaturation. Many studies in the past have shown oxygen desaturation and respiratory depression as a frequent side effect of intrathecalsufentanil. There have been a several case report of respiratory arrest associated with intrathecalsufentanil [25-26]. However, in our study, no episode of respiratory depression or oxygen desaturation, occurred in any of the two groups. Many studies on sufentanil as well as fentanyl have shown pruritus as the major side-effect [27]. Pruritus was noted in16 patients of sufentanil group in our study. Lo *etal*., also reported a higher incidence of pruritus in parturient receiving sufentanil (80%) than those receiving fentanyl (47%) intrathecally.

CONCLUSION

From the above clinical comparative study, we conclude that spinal anesthesia with bupivacaine (12.5 mg) when combined with 5μ g sufentanil provides adequate anesthesia and is associated with a lower incidence of hemodynamic instability as compared to spinal anesthesia with 12.5 mg bupivacaine (0.5%) alone. We recommend sufentanil as an adjuvant to bupivacaine in spinal anesthesia as it provides more effective and prolonged analgesia with less degree of motor block and a better hemodynamic stability as compared to bupivacaine (0.5%) alone.

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