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Evaluation and comparison of Fentanyl and Sufentanil as adjuvants to intrathecal Bupivacaine

KEYWORDS: Fentanyl, Sufentanil, sensory block, analgesia

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ABSTRACT *Objectives: To evaluate Fentanyl and Sufentanil as adjuvants to intrathecal hyperbaric Bupivacaine with respect to: 1. Sensory and motor block characteristics., 2. Analgesia., 3. Haemodynamic variables., 4. Adverse effects.*
Methods: In a prospective, randomized, comparative, double-blind study, 90 patients requiring subarachnoid block were recruited into three groups. Group A received 3ml 0.5%bupivacaine+0.5ml normal saline. Groups B and C received 25µg Fentanyl and 5µg Sufentanil respectively as adjuvants to bupivacaine.
Observations and Results: Onset, time to maximum motor block and duration of motor block were comparable. Onset, highest sensory level and time required to achieve it were comparable. Opioids significantly prolonged duration of regression to T10, duration of sensory block and analgesia and caused significant pruritis.
Conclusion: Opioids prolong duration of sensory block and analgesia without enhancing motor block. Sufentanil provides longer analgesia than Fentanyl. Haemodynamic changes are insignificant. Adverse effects are mild.

INTRODUCTION

Subarachnoid block or spinal anaesthesia is a popular method of administration of anaesthesia for abdominal and lower limb surgeries. It has a fast onset of action, and a predictable duration and offset.

Spinal anaesthesia involves the placement of a local anaesthetic solution in the spinal subarachnoid space. It is considered superior to general anaesthesia with regards to postoperative mortality, intraoperative blood loss, immediate postoperative analgesia, and incidence of nausea and vomiting(8,14,16).

The most commonly used local anaesthetic for subarachnoid block today is Bupivacaine. However, local anaesthetics when used alone have a short duration of action. Hence many adjuvants have been used to prolong the duration of analgesia. The most popular adjuvants , however, remain the opioids.

Morphine being hydrophilic is associated with delayed respiratory depression(5) which limits its usefulness. Today, more lipophilic opioids are used, the most common being Fentanyl. Another opioid gaining popularity in recent times is Sufentanil.

The rationale behind adding opioids to intrathecal local anaesthetics is that opioids act synergistically with local anaesthetics(1,7,17). At the same time they do not produce any motor21 or sympathetic blockade(3,17). Hence, these are the ideal drugs to provide analgesia in the early postoperative period.

This study was conducted to compare Fentanyl and Sufentanil, with respect to their haemodynamic effects, sensory and motor block characteristics, and adverse effects.

AIMS AND OBJECTIVES

To evaluate Fentanyl and Sufentanil as adjuvants to intrathecal hyperbaric Bupivacaine with respect to:

5. Sensory and motor block characteristics.
6. Analgesia.
7. Haemodynamic variables.
8. Adverse effects.

MATERIALS AND METHODS

After approval from the hospital Ethics Committee, a prospective, randomized, comparative, double-blind study was carried out in 90 patients undergoing elective lower abdominal or lower limb orthopaedic surgeries under subarachnoid block.

All patients were subjected to a detailed preoperative assessment a day prior to the surgery, and were investigated for:
- Complete blood counts.
- Serum creatinine and urine analysis
- Fasting and post-prandial sugars.
- Coagulation profile.
- Electrocardiography.
- X-Ray Chest.

1. Inclusion criteria:
- ASA I
- Age: 18 – 60 years.
- Height: 155 – 170 cm.
- Weight: 50 – 75 kg.

2. Exclusion criteria:
- History of back/spine surgery.
- History of backache.
- Presence of spinal deformities.
- Infection at the site of spinal injection.
- Hypersensitivity to local anaesthetics.
- Coagulation disorders.
- Pregnancy.
- Patient's refusal.

The nature of study explained to the patients in detail and a written informed consent taken .Patients kept fasting for six hours. No premedication was given. On arrival in the operation theatre, ECG, NIBP, pulse oximeter applied and baseline readings noted. An intravenous access secured with 20G intravenous cannula on nondominant hand and intravenous fluid started.

All patients were randomly allocated to one of the three groups:
Group A: 3ml 0.5% bupivacaine+0.5ml sterile, preservative-free normal saline.
Group B: 3ml 0.5% bupivacaine+25µg Fentanyl.
Group C: 3ml 0.5%bupivacaine+5µg Sufentanil+0.4ml sterile, preservative-free normal saline.

The total volume injected was kept constant in all as 3.5 ml.

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The local anaesthetic solution was prepared by one anaesthesiologist, while another anaesthesiologist, blinded to the group administered the anaesthetic and monitored the patient intraoperatively and postoperatively.

Lumbar puncture carried out under all aseptic precautions, in sitting position using midline approach with 25G spinal needle in L3-4 interspace and respective solution injected after free and clear flow of cerebrospinal fluid. The patients were then immediately made to lie supine. The time when the spinal injection was completed was taken as T0. The operating table was kept in the neutral position throughout the surgery. In surgeries where position other than supine was required, the respective position was given after the level of anaesthetic was "fixed". All patients received 4 l/min oxygen by mask.

Sensory block assessed every minute for the first 4 minutes, every 2 minutes thereafter for 30 minutes, and every 15 minutes thereafter, by pin-prick method,in the midline. Onset of sensory block defined as achievement of sensory level L1. The highest sensory level and time taken to achieve it recorded. The time taken for the sensory block to regress to T10 recorded. Duration of sensory block recorded as the time taken for the sensory level to regress to S1.

Motor block assessed every minute for the first 4 minutes, every 2 minutes thereafter for 30 minutes, every 15 minutes thereafter using Bromage scale:
0: No impairment of movement of legs and feet.
I: Barely able to flex knees, no impairment of movement of feet.
II: Unable to flex knees, barely able to move feet.
III: Complete motor block.

Onset of motor block defined as the achievement of Bromage I and complete motor block as Bromage III. The duration of motor block defined as time taken for complete regression of the motor block to Bromage 0.

Heart rate, blood pressure, oxygen saturation, and respiratory rate recorded using a multi-channel monitor every 2 minutes for the first 30 minutes, every 5 minutes for the next 30 minutes, and every 15 minutes thereafter.

Bradycardia defined as fall in heart rate below 20% of baseline values or a heart rate less than 60 beats/minute whichever was less and treated with Inj. Atropine IV.

Hypotension defined as fall in systolic blood pressure by more than 20% of baseline values or an absolute fall in blood pressure below 90 mm Hg and treated with fluid boluses of 50 – 100ml, or Inj.Ephedrine IV.

Respiratory depression defined as fall in respiratory rate below 10 breaths per minute and treated with Inj. Naloxone IV.

Pain assessed intraoperatively using the Visual Analogue Scale (VAS). A VAS score of 0 implied complete absence of pain, while a score of 10 implied the worst possible pain. Any intraoperative pain treated with intravenous fentanyl.

Level of consciousness assessed by sedation score:
I = Asleep but easily arousable.
II = Deep sleep but arousable.
III = Unarousable.

Other side-effects were also noted and treated if required. All patients were similarly monitored in post-anaesthesia care unit. Any adverse effects noted and treated appropriately.

Duration of analgesia was defined as time taken for a VAS score of 4, at which point the patients were administered analgesics.

The data obtained was compared using One Way ANOVA and Pearson Chi-square test. A "p" value of less than 0.05 was considered significant.

OBSERVATIONS AND RESULTS

Table 1: Demographic and relevant data

	Group A (n=30)	Group B (n=30)	Group C (n=30)	p Value
Age (yrs)	39.13±10.494	39.97±11.722	41.67±11.257	0.671
Sex (M:F)	12:18	13:17	14:16	0.873
Height (cms)	161.30±4.496	161.27±4.464	160.63±4.148	0.802
Weight (kgs)	63.50±6.575	63.13±6.902	63.13±7.413	0.973
Surgery duration (mins)	90.80±21.382	98.23±17.067	95.53±16.090	0.287
Type of surgery (LA:LL)	14:16	15:15	15:15	0.957

Values are Mean+S.D., LA: Lower Abdominal, LL: Lower Limb.

Table 2: Motor block characteristics

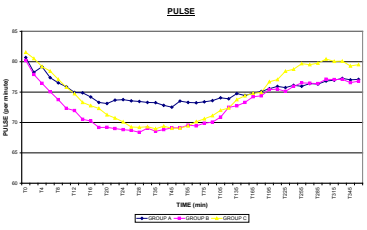
	Group A	Group B	Group C	"p" Value
Onset (min)	3.50±1.075	3.23±0.858	3.33±0.959	0.562
Time to maximum block (min)	8.93±3.095	8.40±2.647	8.20±2.058	0.540
Duration (min)	250±36.175	237±37.865	249.5±22.102	0.230

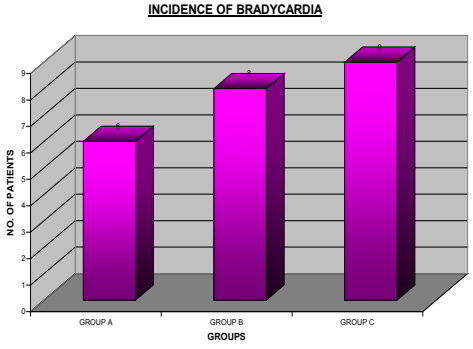
Values are Mean+S.D.

Table 3: Sensory block characteristics

	Group A	Group B	Group C	"p" Value
Onset (min)	3.00±0.742	2.70±0.651	2.66±0.711	0.135
Time for Highest Sensory Level (min)	6.80±1.349	6.73±1.436	6.53±1.382	0.742
Highest Sensory Level (T8:T6:T4)	1:20:9	0:14:16	1:12:17	0.201
Time for Regression to T10(min)	127.5±16.596	143.5±19.570	155.0±21.334	0.000
Duration of sensory block (min)	237.5±14.782	265±16.400	286.5±17.770	0.000
Duration of analgesia (min)	168.93±23.036	257.53±16.548	283.23±31.155	0.000

Values are Mean+S.D. Time for Regression to T10: p= 0.002(Group A Vs Group B), p=0.000(Group A Vs Group C), p=0.023(Group B Vs Group C). Duration: p= 0.000(Group A Vs Group B), p=0.000(Group A Vs Group C), p=0.000Group B Vs Group C). Duration of analgesia: p=0.000(Group A Vs Group B), p=0.000(Group A Vs Group C), p=0.000Group B Vs Group C). p value : 0.664.





p value : 0.832.

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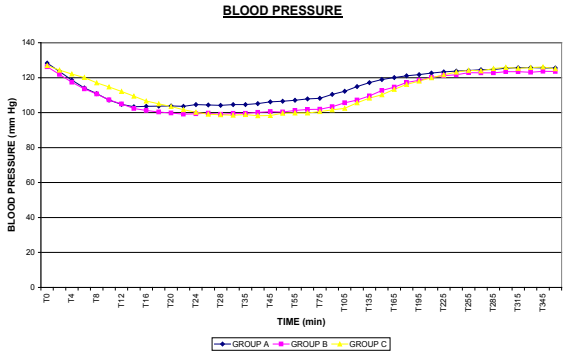
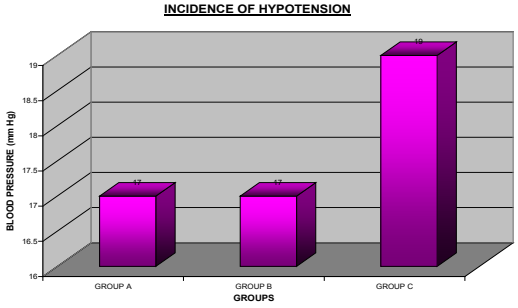
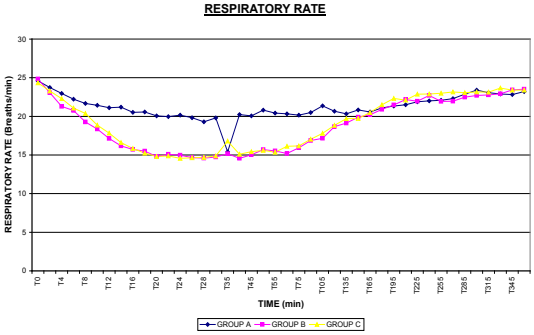
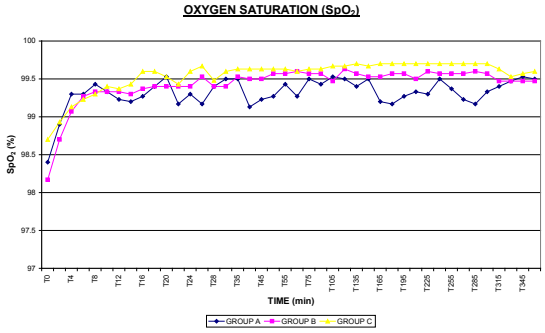
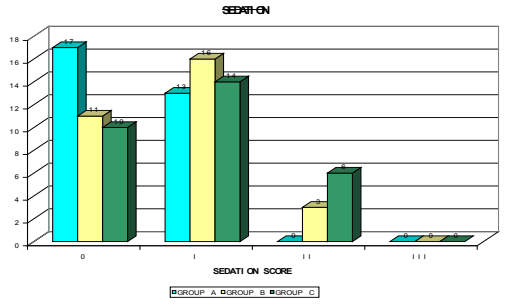




p value: 0.072.







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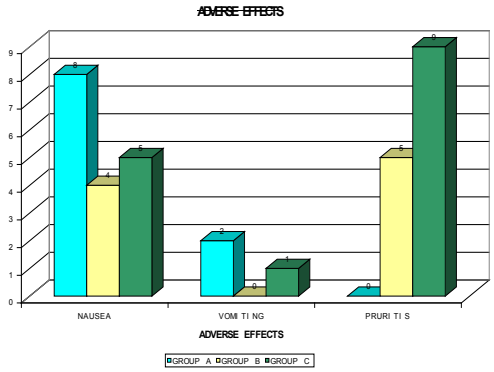

p values: Nausea-0.390, Vomiting-0.355, Pruritis-0.006.

DISCUSSION

Subarachnoid block or spinal anaesthesia is a popular method of providing anaesthesia for surgeries to be performed on the lower abdomen, pelvis and lower limbs. Spinal anaesthesia has been shown to decrease the perioperative risk of deep vein thrombosis and pulmonary embolism1 and is hence often preferred for lower limb orthopaedic surgeries.

The basis of addition of opioids to local anaesthetics is the evidence that local anaesthetics potentiate the antinociception produced by opioids(1,7). Meininger et al(9) demonstrated a prolonged duration of anaesthesia in patients receiving opioid adjuvants. The duration of analgesia was significantly more in the patients receiving sufentanil.

In our study, lipophilic opioids, Fentanyl and Sufentanil are compared. The total volume injected was kept constant in all at 3.5ml as volume of solution for subarachnoid block is shown to affect duration of analgesia,onset and extent of motor blockade(15).

The three groups were comparable in demographic variables and type and duration of surgery.

There was no significant difference in characteristics of motor block. This correlates well with Dahlgren et al(4) and Singh et al(13).

The mean time to onset of sensory block, achievement of highest sensory level, highest sensory level achieved was were not statistically significant, consistent with Dahlgren et al (4).

The mean time for regression of sensory level to T10, duration of sensory block and mean duration of analgesia were highly significant statistically, as also observed by Dahlgren et al (4).

The mean duration of complete analgesia was significantly prolonged in the groups receiving opioids. Dahlgren et al(4) demonstrated that duration of complete analgesia was significantly prolonged in the sufentanil group but not with the fentanyl group. The difference could be attributed to the fact that we used 25µg fentanyl as against 10µg fentanyl used by Dahlgren et al(4).

Intrathecal sufentanil is approximately 4.5 times more potent than fentanyl(10). Hence, fentanyl was used in a dose of 25µg as sufentanil was used in a dose of 5µg.

The µ agonists fentanyl and sufentanil act by decreasing the conductance of voltage gated calcium channels or by opening the inward flowing potassium channels. They also have a post-synaptic effect causing hyperpolarisation and reduction in neuronal activity. The local anaesthetic, bupivacaine, acts by blocking the voltage gated sodium channels, contributing to their synergism.

The mean baseline values of pulse were not statistically

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significant. After spinal anaesthesia, a fall in heart rate was observed in all groups because of blockade of afferent sympathetic fibres T1 – T4 causing loss of chronotropic drive. Opioids cause bradycardia by blocking the preganglionic sympathetic nerves. The incidence of bradycardia was statistically insignificant .

The mean baseline values of systolic blood pressure were not statistically significant . After spinal anaesthesia, a fall in blood pressure was observed in all three groups due to sympathetic blockade resulting in paralysis of vasoconstrictors and dilatation of capillaries and small venules. The incidence of hypotension in the three groups was comparable, consistent with Dahlgren et al(4).

By applying ANOVA test no statistically significant difference was found in baseline respiratory rates and mean baseline oxygen saturation . The respiratory rate decreased in all three groups under spinal anaesthesia due to reduction of sensory input to the respiratory centre. Further, opioids are also known to cause respiratory depression. However, significant respiratory depression i.e. respiratory rate less than 10 breaths per minute was not observed in any of the groups. No patient had an oxygen saturation less than 90%, consistent with Dahlgren et al(4) and Singh et al(12).

Incidence of nausea and vomiting was statistically insignificant. However, incidence of nausea was lower in the groups receiving opioids. Similar results were reported by Dahlgren et al(4), Fournier et al(6) and Biswas et al(2).

Pruritis was seen exclusively in the groups that received opioids and was statistically significant . Pruritis was elicited only after direct questioning and did not require any treatment, consistent with Dahlgren et al(4).

The incidence of sedation was comparable between the three groups, consistent with Ngiam et al(11). No patient had a sedation score of III.

CONCLUSION

In conclusion, the addition of opioids to local anaesthetics prolongs the duration of sensory block and duration of analgesia in the early postoperative period.

The addition of opioids has no effects on the motor block characteristics.

The effect of opioid adjuvants on haemodynamic and respiratory parameters is not significant.

Adverse effects that may occur are mild and can be easily treated.

Intrathecal sufentanil provides a longer duration of analgesia in the early postoperative period as compared to fentanyl without there being any significant difference between the two drugs with regards to haemodynamic parameters and adverse effects.

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