Comparative Evaluation between intrathecal sufentanil with bupivacaine to fentanyl with bupivacaine and bupivacaine alone for intraoperative and postoperative analgesia in infraumblical surgeries

N Saraswat, A Mishra, T Chand, S Saxena, I Khan, G Saurabh

Citation

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Abstract

This study was conducted to compare sufentanil & fentanyl in combination with bupivacaine for infra-umbilical surgeries. Sixty ASA I and II patients for elective intra-umbilical surgeries under spinal anaesthesia were divided into three groups to receive 15 mg bupivacaine alone, 10 μg sufentanil & 25 μg fentanyl in combination with 15mg bupivacaine. Onset time of sensory blockade, Duration of side effects, surgical conditions, and quality of the anaesthesia was assessed. The duration of effective analgesia of bupivacaine alone was prolonged with the addition of sufentanil and fentanyl by 179% and 141% respectively. No patient is the sufentanil and fentanyl groups required additional intra-operative analgesics compared with 17.6% of patients in the bupivacaine alone group. There was an increase in incidence of desaturation in the sufentanil group (45%) and fentanyl group (5.6%) compared with the bupivacaine only group (0%). The incidence of pruritus was 35% with sufentanil, 27.8% with fentanyl against 0% with bupivacaine alone. The addition of 10 μg of sufentanil and 25 μg of fentanyl to improved intraoperative analgesia. However, the incidence of pruritus and episodes of desaturation were increased more with 10 μg sufentanil than with 25 μg fentanyl.

INTRODUCTION

Spinal anesthesia has increasingly become the technique of choice [12] for infra-umbilical surgery especially cesarean section. Spinal anesthesia has the advantages of simplicity of technique [34], rapid onset of action and reliability in producing uniform sensory and motor blockade when compared to epidural anaesthesia [568]. Its main disadvantage relates to its limited duration of action and hence lack of long-lasting post-operative analgesia.

To address the problem of limited duration of action and to improve the quality of analgesia both intra-operatively and post-operatively, intrathecal opiates have been given in addition to bupivacaine [712].

Abboud [13] reported the use of mini-dose Intrathecal morphine for the relief of post-caesarean section pain in 1988. 0.25 mg morphine given intrathecally with bupivacaine provided a mean duration of analgesia of approximately 28 hours. The risk of delayed respiratory depression of relatively hydrophilic opioids has prevented the widespread use of intrathecal morphine.

The use of intrathecal fentanyl, a lipophilic opioids, and bupivacaine for caesarean delivery was described by Hunt [7]. The addition of 6.25 μg fentanyl to bupivacaine for spinal anaesthesia was shown to improve intrapoerative analgesia and to provide analgesia into the immediate postoperative period with no adverse effects on the mother or neonate.

Recently there has been interest in using intrathecal sufentanil, an even more lipophilic opioid, either alone or in combination with bupivacaine for labour analgesia [1416]. Sufentanil alone provided analgesia in the first stage of labour for between 1-3 hours [151617]. The use of intrathecal sufentanil in combination with bupivacaine for infra – umbilical surgeries has not been reported.

The aim of this study was to evaluate the addition of intrathecal sufentanil to bupivacaine for infra-umbilical surgeries and to compare its use to that of intrathecal fentanyl and bupivacaine.

METHODS

We studies 60 ASA I and II patients undergoing elective infra-umbilical surgeries (Table 1) under spinal anaesthesia. Informed consent was obtained from all patients and the study was approved by the Hospital Ethics Committee. The patients were randomly assigned, in a prospective double-blind fashion, to receive the study solution, which was prepared by a colleague who was not part of the study. After the administration of the study solution, the patients were evaluated by an investigator blinded to the test solution given.

In study group F, a solution consisting of 15 mg bupivacaine (3 mLs of 0.5% hyperbaric bupivacaine) and 25 μg of fentanyl (0.5 mLs), a total volume of 3.5 mLs was given by the anesthetist performing the block.

In study group S, a solution consisting of 15 mg bupivacaine (3 mLs of 0.5% hyperbaric bupivacaine) and 10 μg of sufentanil (made up to 0.5mL) was diluted with 0.9% saline to a total volume of 3.5 mLs.

In study group B, a solution consisting of 15 mg bupivacaine (3 ml of 0.5% hyperbaric bupivacaine) was diluted with 0.9% saline to a total volume of 3.5 mLs.

The patients were pre-loaded through a 18 G cannula with 500-700 mLs of Hartman's balanced salt solution. The procedure was then preformed under aseptic conditions with the patients in the right lateral or sitting position. The inter-space between lumbar vertebrae 3 and 4 (L3/4) was chosen. After identification of clear, free flowing cerebrospinal fluid, the chosen study solution was injected slowly(15-20sec) through the 25 G Quincke's babcock spinal needle bevel facing in cephalad direction. Then the patient was turned supine and position of table was kept horizontal.

The level of sensory blockade was assessed by pin prick method; response to cold was assessed with an ice pack in the mid-clavicular line. The time for the sensory blockade to reach T8 and T6 levels were recorded.

Surgery was only allowed to proceed when a sensory level of T6 was attained. None of the patient was excluded from the study. The patients were monitored continuously with ECG and pulseoximetry. The blood pressure was recorded every 5 minutes for 120 minutes. Any fall in blood pressure greater than 20% decrease in mean arterial pressure or a systolic arterial pressure less than 90 mmHg systolic was treated with boluses of 6 mg of ephedrine and fluids. All episodes of hypotension, nausea and vomiting, shivering, somnolence, respiratory depression, inadequate analgesia and purities were recorded. Any treatment given for side-effects was noted. The duration of surgery was noted.

The quality of the surgical conditions afforded was assessed by the operating surgeon on a three point scale. (1 – insufficient if unable to proceed with surgery; 2 – adequate if able to proceed but with some difficulty, and 3 - optimal operating conditions).

At 120 mins after the block was given, the patients were assessed for their degree of sedation using the Campbell score [17] (1 – wide awake; 2 – sedated but easily arousable; 3 – drowsy and difficult to arouse, and 4 – unarousable). Residual motor blockade was assessed with modified bromage scale.

On the first post-operative day, the patients were interviewed to check for headache, backache, nausea and vomiting and pruritis. The presence of urinary retention was also assessed (if patient was not routinely catheterized for surgical reasons). Effective duration of analgesia, defined as the time to request for the first dose of analgesia, was recorded.

STATISTICS

A pre study power analysis for sample size estimation was done, based on previous studies a difference of 40% was sought between study & control groups with respect to onset of analgesia and a sample size of 20 was obtained to provide $\alpha = 0.2$ & $\beta = 0.05$ at 95% confidence interval.

Parametric data were assessed for statistical significance using analysis of variance and Student –Newman – Kewls test for comparison between groups. Non-parametric data were assessed with the Chi – square test with pearson correction. Differences were considered statistically significant when $p<0.05$. SPSS for MS windows Release 10.0 was used for statistical analysis.

Figure 1

Table 1: Type of infraumblical surgeries.

Hysterectomy	15
Hysterotomy with ligation	1
Myomectomy	6
Hermiorrhaphy	16
Tibial interlocking	8
D.H.S	5
K nailing Femur	2
Reterograde nailing of femur	4
Open I/L femur	3

Figure 2

Table 2: Demographic Data

Group	Bupivacaine(15 mg)	Bupivacaine(15 mg)+Sufentanil 10	Bupivacaine(15mg)+ Fentanyl 25
Number of patients (n)	18	20	17
Age (Yr)	41.2±4.6	42.2 ± 6.4	41.9 ± 4.6
Weight (Kg)	62.6± 9.3	72.9±8.4	70.6± 12.2
Height (cm)	161.2±5.1	160.9± 7.0	166.7±5.3
ASA			
I	14	11	11
II	4	9	6
Surgical time (min)	59.7±13.7	57.1±10.7	58.2±17.7

Figure 3

Table 3

Group	Bupivacaine (15mg)	Bupivacaine (15mg)+Sufentanil 10	Bupivacaine (15mg)+Fentanyl 25
Number of patients	17	20	18
T8(seconds)	183.6 ± 49.3	145 ± 62.2	151.6 ± 76.4
T6(seconds)	245.8± 91.0	196.9± 105	225.5±123.7
Duration of effective analgesia (min)	229.38±26.38	409.36±40.68	322.67±42.09

Figure 4

Table 4: Side effects

Group	Bupivacaine(15 mg)	Bupivacaine(15 mg)+Sufentanil 10	Bupivacaine(15mg)+ Fentanyl 25
Number of patients	17	20	18
Desaturation	0%	9(45%)	1(5.6%)
Pruritis	0%	7(35%)	5(27.8%)
Hypotension	3(17.6%)	4(20%)	3(16.7%)
Nausea	0%	5(25%)	4(22.2%)

RESULTS

There were no significant differences in patient age, weight, height, ASA status or duration of surgery between the three groups (table 2).

There was no significant difference in onset of sensory blockade to T8 and T6 levels (Table 3). All patients included in the study attained a T6 sensory level within 10 min of intrathecal injection to allow surgery to proceed.

The duration of effective analgesia was defined as the time from the onset of action to the time of first request for analgesia. The duration of effective analgesia was 322.67□42.09 min with 25 □g of fentanyl added and 409.36 □ 40.68 mins with 10 □g sufentanil compared to 229.38 □ 26.38 mins for the bupivacaine 15 mg alone group. This represented an increase in the mean duration of effective analgesia of 141% for the fentanyl group and 179% for the sufentanil group compared to the bupivacaine alone group.

QUALITY OF INTRA-OPERATIVE ANALGESIA

Three of the 17 (17.6%) patients in the bupivacaine alone group complained of pain intra-operatively and required intravenous ketamine 0.5mg/kg intra-operatively. Those patients who belonged to bupivacaine group were given ketamine supplementation when surgery lasted for longer duration (>3hrs) and effect regressed. No patients in the other two groups required additional analgesics intra-operatively.

Side effects (Table 4) .There was a significant increase in the incidence of pruritus with the addition of 10 □g of sufentanil to bupivacaine (p-0.028). Thirty-five percent (7/20) of patients who received sufentanil complained of itching affecting the face and the upper body. Of these 7 patients, 2 required treatment for the itch. 27.8% (5/18) of patients who received 15 □g of fentanyl complained of itching affecting mainly the nose and face. No patients in the bupivacaine alone group complained of pruritus.

The incidence of desaturation, defined as saturation below 94% with the patient breathing room air after the delivery of the baby, was significantly increased (p=0.0005) with the addition of sufentanil. Forty-five percent (9/20) of patients in the sufentanil group had episodes of desaturation compared with 5.6% (1/18) in the fentanyl group and 0% in the bupivacaine only group.

Hypotension was defined as any fall greater than 20% in the mean arterial pressure or a systolic pressure less than 90 mmHg. These episodes of Hypotension were treated with boluses of 6 mg of ephedrine and fluid loading. There was no significant difference between the three groups with respect to the incidence of Hypotension.

Nausea was reported in 25% (5/20) in the sufentanil group, 22.2% (4/18) in the fentanyl group and 11.8% (2/17) in the bupivacaine alone group. There was no significant difference between the three groups.

There was no significant difference in the degree of sedation or motor blockade 120 mins after intrathecal injection of the study solutions using the Kruskal-Wallis one-way Anova test. There was also no significant difference in the surgical condition offered by the three test solutions as assessed by the principal operating surgeon.

DISCUSSION

In this study it was demonstrated that the addition of 25 □g of fentanyl and 10 □g of sufentanil to bupivacaine intrathecally significantly prolonged the mean duration of effective analgesia by 141% and 179% respectively. 25 □g of fentanyl added to 15 mg bupivacaine provided effective analgesia for 5 ½ hours and 10 □g of sufentanil added to 15 mg

bupivacaine provided effective analgesia for 6 ¾ hours. This provided improved patient comfort and reduced the need for intra-muscular and intravenous analgesia in the immediate post-operative period.

There was a prolongation of effective analgesia and a significant improvement in intra-operative patient comfort with the addition of fentanyl and sufentanil to bupivacaine. Three patients in the bupivacaine only group companied of pain and were given additional intra-operative analgesics compared to no patients in the fentanyl and sufentanil groups. Intra-operative analgesia in the bupivacaine only group could be improved by using a higher dose of bupivacaine but this would increase the level of sensory blockade and the incidence of hypotension. The duration of motor blockade would also be prolonged. The synergistic, potentiating effect of fentanyl (an opiod) on bupivacaine (a local anesthetic) in spinal anesthesia is presented; fentanyl is able to reduce the dose of bupivacaine and therefore its harmful effects. [24]

Both fentanyl and sufentanil possess local anaesthetic properties which have reported with the use of intrathecal sufentanil and fentanyl [1522]. This local anaesthetic property may contribute to the synergistic effect between fentanyl, sufentanil and bupivacaine.

Systemic opioids potencies correlate directly with opioid lipophilicity reflecting the need to cross the blood brain barrier to gain access to the receptor site. Therefore sufentanil (octanol/water partition coefficient 1778) is considered 10 times as potent as fentanyl (octanol/water partition coefficient 813) when systemically administered [1720]. Intrathecal drug bypass the blood brain barrier and therefore their systemic potencies do not predict intrathecal potency. There have been few human studies on the potency ratios of intrathecal sufentanil and fentanyl, but Honet et al [20] estimated that after intrathecal injection, sufentanil is only twice as potent as fentanyl. The findings of this study support this estimate with the duration of effective analgesia provided by the addition of 10 mg of sufentanil being 1.4 times that 25 mg of fentanyl compared to the expected 1.3 times if intrathecal sufentanil was twice as potent as fentanyl.

Recently, there has been an increase in the popularity of using intrathecal sufentanil in a combined spinal epidural technique for labour analgesia. The incidence of desaturation to below 94% was 45% for the sufentanil group and 5.6 % for the fentanyl group with the patient's breathing room air. Hays and Palmer [22] reported a case of early respiratory depression after administering 15 g of sufentanil and 25 mg of fentanyl in addition to 15 mg of bupivacaine. The plasma concentration of intrathecal sufentanil reaches a peak approximately 39 min after injection. The mean plasma concentration (0.15ng/ml) after intrathecal injection of 15 µg sufentanil is so low that it is unlikely that anything other than the intrathecal sufentanil was responsible for the patient's respiratory symptoms [22]. No patients in the bupivacaine 15 mg group had any episode of desaturation. In all the patients, the episodes of desaturation were easily corrected by asking the patients to take a few deep breaths and by giving supplemental oxygen at 40%. At the end of the recovery monitoring period at 120 mins, no patient experienced any episode of desaturation. This finding is in agreement with Palmer who reported early respiratory depressing occurring after intrathecal Fentanyl & morphine combination [21] and intrathecal sufentanil [22] alone. Delayed onset of respiratory depression has not been reported for the lipophilic opiates sufentanil [912] and fentanyl [9]. There was no difference in the degree of somnolence when the patients were assessed at 120 mins. We conclude that intrathecal sufentanil and fentanyl are safe for use. The patients should have their respiratory rates monitored every 15 mins for the first hour after injection and every 30 mins for the next 2 hours [22] with the addition of pulse oximetry and supplemental oxygen for those patients who have demonstrated episodes of desaturation intra-operatively. Thirty-five percent of those who received 10 g of sufentanil and 15 mg of bupivacaine had pruritus involving the face and upper body. The pruritus was mild and transient in the fentanyl group, which did not require treatment. In the group who receive sufentanil, 2 of the 7 patients who complained of pruritus required treatment with ondansetraon. Pruritus was the most common side-effect and had a significantly higher incidence when a dose of sufentanil >7.5 µg was used. [25]

In our study, the addition of fentanyl and sufentanil did not increase the incidence of hypotension. The episodes of hypotension were transient and responded to fluid loading or boluses of 6 mg of ephedrine.

In summary, the addition of 10 g of sufentanil and 15 g of fentanyl to 15 mg of bupivacaine prolonged the duration of effective analgesia and improved intra-operative analgesia. However, the incidence of pruritus and episodes of

desaturation were increased more with 10 g sufentanil than with 25 g fentanyl.

CORRESPONDENCE TO

Dr. Namita Saraswat Post Graduate student, Deptt. of Anaesthesia and Critical Care S.N. Medical College, Agra. Telephone number : 09412254295 E–mail address: namita_saraswat@yahoo.com

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Author Information

Namita Saraswat, MD
Postgraduate student, Department of Anaesthesiology & Critical Care, S N College, Agra

Abhijeet Mishra, MD
Postgraduate student, Department of Anaesthesiology & Critical Care, S N College, Agra

Trilok Chand, MD
Assistant Professor, Department of Anaesthesiology & Critical Care, S N College, Agra

Surekha Saxena, MD
Head of Department, Department of Anaesthesiology & Critical Care, S N College, Agra

Imran Khan, MD
Postgraduate student, Department of Anaesthesiology & Critical Care, S N College, Agra

Gyan Saurabh, MS
Pool Officer, Deptt of Surgery, JPNA Trauma Centre AIIMS