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A Comparative Study of Intrathecal Midazolam vs Fentanyl Along with Hyperbaric Bupivacaine in Below Umbilicus Surgeries

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Abstract

Context: The addition of adjuvant like midazolam or fentanyl has further expanded the advantage of spinal anesthesia. *Aims:* The aim of the present study is to compare the efficacy of intrathecally administered midazolam and fentanyl in combination with hyperbaric bupivacaine with respect to the time of onset of sensory block; Duration of sensory block; Quality of intraoperative anesthesia; Duration of effective postoperative analgesia; Incidence of side effects. *Settings and design:* A comparative study. *Methods and materials:* The study was conducted in 120 ASA Grade I-II patients between age group 20–55 years posted for elective lower abdominal surgeries and gynecological surgeries. We have divided these patients into three groups. Group B — 40 patients received 3 ml (15 mg) intrathecal hyperbaric bupivacaine 0.5% and 0.5 ml of 0.9% normal saline. Group M — 40 patients received 3 ml (15 mg) intrathecal hyperbaric bupivacaine 0.5% and preservative free midazolam 1 mg (0.2 ml) and 0.3 ml of 0.9% normal saline. Group F - 40 patients received 3 ml (15 mg) intrathecal hyperbaric bupivacaine 0.5% and fentanyl 25 micrograms (0.5 ml). *Statistical analysis used: t*-test. *Results:* The patients studied across the groups did not vary much with respect to age, sex. The onset of sensory block was shortened in Group F (4.02 min)when compared to Group M (4.55 min) the two segment regression time was delayed in Group F (190.75 min) when compared to Group M (141.63 min). The addition of fentanyl 25 micrograms and midazolam 1 mg to hyperbaric bupivacaine gives better intraoperative comfort and postoperative analgesia than bupivacaine alone. The Group F (253.63 min) has more comfort and prolonged duration of analgesia than Group M (195.08 min). The Group M has more hemodynamic stability than Group F by fewer incidences of side effects like respiratory depression, hypotension, and bradycardia. The intraoperative comfort without significant hemodynamic changes is a welcome effect in immediate postoperative period in Group M. *Conclusions:* The addition of fentanyl and midazolam to bupivacaine gives better intraoperative comfort and postoperative analgesia than local anesthetic bupivacaine alone.

Keywords: Spinal anaesthesia; Midazolam; Fentany; Bupivacaine.

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Introduction

Spinal anesthesia consists of temporary interruption of nerve transmission within the subarachnoid space produced by injection of a local anesthetic solution into cerebrospinal fluid. Used widely, safely and successfully for almost 100 years spinal anesthesia has many potential advantages over general anesthesia, especially for operations involving the lower abdomen, the perineum and the lower abdominal surgeries.

The main reasons for the popularity of spinal block are that the block has well-defined end points and the anesthesiologist can produce the blocks reliably with single injection.[1]

Local anesthetic agents have been widely used in spinal anesthesia. One of the main disadvantages is the limited duration of block achieved with local anesthetics. To overcome this, various adjuvants have been tried and used successfully. This addition of adjuvant has further expanded the advantage of regional anesthesia over general anesthesia. These may be opioids like morphine, fentanyl, sufentanil or buprenorphine. It may be benzodiazepines alpha-2 agonist clonidine, acetylcholine esterase inhibitors like neostigmine, NMDA receptor antagonist ketamine or nonsteroidal anti-inflammatory agents.

The aim of the present study is to compare the efficacy of intrathecally administered midazolam and fentanyl in combination with hyperbaric bupivacaine with respect to the time of onset of sensory block, duration of sensory block, quality of intraoperative anesthesia, duration of effective postoperative analgesia and side effects.

Subjects and Methods

The study was conducted in 120 patients posted for elective surgeries under spinal anesthesia for lower abdominal and gynaecological surgeries after getting approval of ethical committee of department of Anesthesiology, MGM and CKM, GMH Hospitals and Kakatiya Medical College, Warangal during the period 2011–2013. Adult patients aged 20–55 yrs. ASA physical status I and II, Cases like lower abdominal surgeries and gynecological surgeries were included in this study. ASA physical status III and IV, Allergy to local anesthetics. Pregnancy patients who severe systemic diseases, metabolic disorders, and neurological, congenital and cardiovascular diseases were excluded from this study. On the eve of the surgery all the patients were visited and detailed preanesthetic examination including history and clinical examination.

Once the patient was shifted to the operating room, the patient was connected to the routine monitors which include non-invasive sphygmomanometer, pulse oximeter and electrocardiogram. All the emergency equipment like intubation trolley with airways, laryngoscopes, endotracheal tubes along with drugs like atropine, mephenteramine, adrenaline and other emergency drugs were kept ready. The Boyles anesthetic machine along with oxygen cylinders was also checked. Base line pulse rate, blood pressure and respiratory rate were recorded. Intravenous line was secured with 18G cannula. Preloading was done with 15–20 ml/kg of crystalloid solution.

Patients were put on right lateral position under strict aseptic precaution, subarachnoid block was performed using 25G Quinke Babcock`s needle in L3–L4 intervertebral space. After ensuring free flow of CSF the drug was injected as per the group assigned. After injecting the drug patients were turned supine.

The following parameters were recorded:

1. Time of institution of subarachnoid block.
2. Maximum level of sensory block achieved (which is tested by pinprick).
3. Time of onset of the maximum level of sensory block.
4. Time of onset of the surgery.
5. Pulse rate, blood pressure, respiratory rate and oxygen saturation were monitored every 5 minutes for the first 15 minutes, thereafter every 10 minutes for rest of the surgery and every half an hour in the postoperative period.
6. Analgesia.

Pain in the post operative period was evaluated using word category scale.

Constant worst pain	4
Severe pain	3
Moderate pain	2
Mild pain	1
No pain	0

Supplementary analgesia was given if the patient developed moderate pain during the postoperative period. The duration of analgesia was taken as the time between the institution of subarachnoid block and analgesic requirement.

Results

The three study groups each consist of 40 members were compared with respect to age, sex, baseline, vital parameters and duration of surgery (Tables 1-3).

Table 1: Distribution of Age

Age in Years	B	M	F
20–30	4	8	11
31–40	11	8	13
41–55	25	24	16

Table 2: Distribution of Sex

Sex	B	M	F
Male	19	20	22
Female	21	20	18

Table 3: Base Line Hemodynamic Vitals

Groups	Age (in years)	Baseline vitals	
		PR (pulse rate/min)	BP (blood pressure mm Hg)
B	42.95 ± 8.86	87 ± 4.89	118.25/75.75 ± 18.23/5.04
M	41.48 ± 9.77	87.58 ± 5.44	119.5/75.5 ± 7.68/5.06
F	38.01 ± 10.2	93.00 ± 5.4	118.3/78.7 ± 8.39/5.05

The maximum level of sensory block achieved was elicited with pinprick (Table 4).

Table 4: The Maximum Level Achieved in Each Group

	B	M	
up to T_4	0	2 (5%)	12 (30%)
up to T_5	0	4 (10%)	10 (25%)
block up to T_6	4 (10%)	12 (30%)	10 (25%)
block up to T_7	8 (20 %)	10 (25%)	4 (10%)
block up to T_8	10 (25 %)	8 (20%)	4 (10%)
block up to T_9	16 (40 %)	2 (5%)	0
block up to T_{10}	0	2 (5%)	0

Table 5: Anesthesia Parameters in All Groups

	B	M	F
Average time for maximum sensory blockade (min)	7.35	4.55	4.02
Average two segment dermatomal regression of sensory level in min	96.28	141.63	190.75
Average duration of analgesia	145.55	195.08	253.63

The time taken for maximum sensory blockade when compared in all, both the study groups was less for fentanyl and Bupivacaine combination. When the difference in time taken for maximum sensory blockade was analysed statistically, the p value was which is <0.05 that is statistically significant. Fentanyl—Bupivacaine combination had more effective time of anesthesia when compared to the other group. It is statistically significant (Table 5).

Table 6: Sedation Scale

Score	Group B	Group M	Group F
1	4 (10%)	0	
2	30 (75%)	8 (20%)	2 (5%)
3	6 (15%)	16 (40%)	16 (40%)
4	0	16 (40%)	21 (52.5%)
5	0	0	1 (2.5%)

Table 7: Side Effects

Group	Bradycardia	Hypotension	Respiratory depression	Others
B	2	4	0	0
M	1	4	0	0
F	4	8	1	0

The incidence of bradycardia, hypotension and respiratory depression was more in Fentanyl—Bupivacaine group compared to the other group and this when analyzed statistically showed a p value <0.05 which is statistically significant indicating the higher incidence of side-effects with Fentanyl—Bupivacaine combination compared to Midazolam—Bupivacaine (Table 6 and 7).

Discussion

In this present study the two segment dermatomal regression time is prolonged in both groups compared with the control group in a statistically significant manner.

Lyman A Rust *et al.*[2] conducted a study to examine whether intrathecal opioids like Fentanyl, morphine for labour analgesia offer adequate and cost-effective alternative to epidural analgesia with minimal side effects. They found this technique offered an excellent and cost-effective alternative to epidural analgesia.

Sibel Baris *et al.*[3] conducted study was to evaluate the intensity and effectiveness of 0.75 ml·kg^{-1} bupivacaine 0.25% with the addition of fentanyl or midazolam for caudal block in children undergoing inguinal herniorrhaphy. Seventy-five children were allocated randomly to three groups to receive a caudal block with either 0.25% bupivacaine with fentanyl 1 µg·kg^{-1} (Group BF)

or with midazolam 50 μg·kg^{-1} (Group BM) or bupivacaine alone (Group B) after induction of anesthesia. Hemodynamic parameters, degree of pain, additional analgesic requirements and side-effects were evaluated. There was no difference in additional analgesic requirements between the groups in the first 24h. Sedation score was higher in the midazolam group at 60 and 90 min postoperatively than the other groups.

Intrathecal midazolam causes antinociception by combining with spinal cord benzodiazepine receptors. This effect is reversible with doses of naloxone, suggesting involvement of spinal kappa or delta but not mu opioid receptors. The antinociceptive effects of intrathecally administered drugs in the spinal cord were demonstrated by measurements of the electrical current threshold for avoidance behavior in rats with chronically implanted lumbar intrathecal catheters. A comparision was made of suppression by two opioid selective antagonists (nor-binaltorphimine (kappa selective) and naltrindole (delta selective)) of spinal antinociception caused by equipotent doses of opioids selective for different receptor subtypes [u-50488h (kappa), dslet and dsbulet (delta), fentanyl (mu)] and the benzodiazepine midazolam. Nor-binaltorphimine selectively suppressed the effects of u-50488h but not midazolam or fentanyl. However, the delta selective antagonist, naltrindole, caused dose-related suppression of antinociception produced by both delta opioid agonists and midazolam with the same ed 50 (0.5 nmol). We conclude that intrathecal midazolam caused spinally mediated antinociception.[4–6]

In this present study Duration of analgesia has been shown to be prolonged with the addition of the midazolam and fentanyl. Fentanyl scores over midazolam in duration of analgesia in a statistically significant manner.

Kararmaz A. *et al.*[7], evaluated the effects of low dose Bupivacaine plus Fentanyl administered intrathecally in elderly patients undergoing transurethral prostatectomy. This study showed addition of Fentanyl to local anesthetic provides adequate analgesia with few side effects. Motor block was higher and duration was prolonged.

H. Singh, J Yang *et al.* investigated the effect of intrathecal Fentanyl 25 μg on the onset and duration of Bupivacaine 13.5 mg induced spinal block in adult male patients who underwent urological procedures. Addition of Fentanyl to local anesthetic prolongs the duration of sensory block and reduces the analgesic requirement in the early postoperative period.[8]

Bruce Ben David *et al.* studied 50 patients undergoing ambulatory surgical arthroscopy and found that although small dose Bupivacaine alone is inadequate for this procedure the addition of Fentanyl makes it reliable.[9]

Gulec *et al.*[10] In their study of Comparison of caudal bupivacaine, bupivacaine-morphine and bupivacaine-midazolam mixtures for postoperative analgesia in children included sixty children undergoing inguinal or urogenital surgery were allocated randomly to three groups to receive a caudal injection of either 0.125% bupivacaine 0.75 mol kg^{-1} with 0.5% midazolam 50 μg kg^{-1} (n=20) or with 1% morphine chlorhydrate 0.05 mg kg^{-1} (n=20), or bupivacaine alone (n=20) after surgery under general anesthesia. It is suggested that caudal administration of a bupivacaine-midazolam mixture produces a longer duration of postoperative analgesia than a bupivacaine-morphine mixture and bupivacaine alone with sedation for 8–12h postoperatively.

In this present study on comparing sedation level intraoperatively with midazolam and fentanyl, they are statistically significant. This shows that patients who received fentanyl were more comfortable than those of midazolam group.

Conclude that the use of intrathecal midazolam combined with intrathecal bupivacaine produces a more effective and longer analgesia with a mild sedative effect in perianal surgery.[11,12]

In this study the incidence of bradycardia, hypotension and respiratory depression was more in Fentanyl-Bupivacaine group compared to the other group and this when analyzed statistically showed a p value <0.05 which is statistically significant indicating the higher incidence of side-effects with Fentanyl-Bupivacaine combination compared to Midazolam-Bupivacaine.

In a study administered intrathecal Fentanyl 25 μg with Bupivacaine 2.5 mg in labouring parturients. They found that addition Bupivacaine 2.5 mg to intrathecal fentanyl attenuates the frequency of pruritus on all parts of body except the face. This combination also resulted in rapid and prolonged duration of labor analgesia compared with either drug alone.[13]

Administration of epidural and intraspinal opioids may provide excellent postoperative analgesia, but a minority of patients will suffer from respiratory depression. Etches *et al.* study shows effects of respiratory depression following intrathecal opioid administration.[14]

Rudra Pallab *et al.* in their study the Compared Intrathecal Fentanyl and Midazolam for prevention of Nausea and Vomiting during caesarean delivery under Spinal Anesthesia—Incidence of intraoperative and early postoperative nausea-vomiting was 75% with placebo, 40% with midazolam and 25% with fentanyl (*p* values with placebo <0.05, while that between midazolam and fentanyl >0.05). Adverse events caused by the study agents did not differ significantly. Intrathecal co-administration of midazolam or fentanyl significantly minimize the incidence of nausea-vomiting during intraoperative and early postoperative.[15]

Conclusion

The addition of Fentanyl and Midazolam to Bupivacaine gives better intraoperative comfort and postoperative analgesia than local anesthetic bupivacaine alone. But the Fentanyl gives more comfort and prolonged duration of analgesia compared to Midazolam. The hemodynamic stability was better with Midazolam than that of Fentanyl, with fewer incidences of hypotension, bradycardia and respiratory depression. Though Fentanyl-Bupivacaine combination provided better intraoperative comfort and prolonged analgesia and sedation, Midazolam-Bupivacaine combination has been considered better as it provided good sedation, analgesia and intraoperative comfort though less compared to Fentanyl group but without any side effects.

Conflicting Interest (If present, give more details): Nil

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