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Original Article

Use of intrathecal midazolam or fentanyl as an adjunct to spinal anaesthesia with bupivacaine for lower limb surgery: A randomised controlled study

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ABSTRACT

Background: Intrathecal adjuncts have been used to prolong the quality and duration of subarachnoid anaesthesia. Midazolam given intrathecally is reported to have anti-nociceptive properties. The purpose of this study was to compare intrathecal midazolam with fentanyl for pain relief and patient comfort.

Methods: In this prospective, double-blind, randomised controlled trial, 90 patients for lower limb surgeries were randomly allocated to three groups: “control group” (3 ml 0.5% heavy bupivacaine), “fentanyl group” (3 ml 0.5% bupivacaine + 10 mcg fentanyl) and “midazolam group” (3 ml 0.5% bupivacaine + 1 mg midazolam). Level, duration, and quality of blocks were compared along with the duration and quality of postoperative analgesia. Haemodynamic stability and any associated complications were also noted.

Results: Onset of block was fastest in Group C (28.5 ± 13.48 min) vis-a-vis other groups (35.5 ± 26.05 min for Group “F” and 28.5 ± 23.68 min for Group “M”; $P = 0.51$). Duration of block was comparable in all groups (130.5 ± 39.3 min Group “C”; 126.5 ± 44.0 min Group “F” and 129.5 ± 45.7 min Group “M”; $P > 0.5$).

Addition of adjuncts did not significantly defer the appearance of pain. Intensity of pain was lower in Group “M”. Average VAS scores were lower for Group “M” (3–4) than those for Group “C” (4–5) and Group “F” (4–6).

Majority of patients required at least one dose of rescue analgesic; however, those receiving fentanyl reported better quality of postoperative analgesia than those in midazolam group.

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Conclusion: Adjuvants improve quality of postoperative analgesia (fentanyl better than midazolam).

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Introduction

Intrathecal opiates and sedatives have often been used as adjuncts to the local anaesthetic agent in subarachnoid block (SAB) to improve the quality and prolong the duration of analgesia and have been found effective in enhancing the anaesthetic and analgesic properties of local anaesthetic agents used in SAB.

Patients undergoing lower limb orthopaedic surgery usually suffer considerable postoperative pain and require either parenteral or neuraxial opioids for adequate analgesia in postoperative period. Use of neuraxial opioids in combination with local anaesthetic agents has now become commonplace for postoperative analgesia. However, opioid-induced side-effects, such as respiratory depression, nausea, vomiting, urinary retention and pruritis, are incapacitating to the patients, and there is a felt need to search for an equally effective alternative pharmacological adjunct.

Midazolam, which is a water-soluble benzodiazepine, is mainly a sedative and anxiolytic. Various studies have reported that when administered intrathecally, it had antinociceptive properties, and its intrathecal use has been recommended for postoperative analgesia.

The purpose of this study was to compare the effects of intrathecal midazolam vs intrathecal fentanyl in pain relief and patient comfort when used as an adjunct to intrathecal bupivacaine for lower limb orthopaedic surgery.

Material and methods

This prospective, double-blind, randomised controlled study was conducted over a period of 2 years, from May 2006 to May 2008 at a multispecialty Tertiary Care Centre. Patients posted by the Department of Orthopaedics for elective lower limb surgery under SAB constituted the study population. After obtaining the necessary approval from the Hospital Ethics Committee and informed consent of patients, a total of 132 patients were enrolled for the study. Of these 9 patients were unwilling to enter the study and thus were excluded. Another 33 patients were excluded as they did not conform to the inclusion criteria. Remaining 90 patients were randomly divided into three groups of 30 patients each.

CONSORT 2010 flow diagram

Sample size calculation

The “primary outcome of interest” was to study impact of the proposed intervention on “quality and duration of postoperative analgesia”. The target population for this study was restricted to patients undergoing orthopaedics surgery on lower limbs, although the results were intended to be extrapolated to all patients undergoing surgery under neuraxial block. Sample size was calculated using one of the on-line formulae available for the purpose (Raosoft Online Sample Size Calculator), with a confidence level of 95% and confidence interval of 10%, for a study population of 500 patients (being average annual number of patients undergoing lower limb orthopaedic surgery at the centre).

Randomisation and blinding

Randomisation was carried out on the basis of computer generated numbers. The study was conducted in a double-

blind manner where the actual worker was blinded to the contents of the combination chosen, as well as the post-procedure observations, which were collected and tabulated by an independent team of workers.

The worker instituting SAB was presented with a set of three prefilled syringes, which were prepared by an independent worker, and the contents of the same were not known to the actual worker. These prefilled syringes consisted of one syringe each of the three solutions, solution “C”: 3.0 ml of 0.5% heavy bupivacaine + 0.2 ml normal saline; solution “F”: 3.0 ml of 0.5% bupivacaine + 0.2 ml (10 µg) of fentanyl (with no preservative) and solution “M”: 3.0 ml of 0.5% bupivacaine + 0.2 ml (1 mg) of midazolam (with no preservative) and were numbered randomly. The worker picked up any one of these syringes, instituted the block and recorded the intraoperative observations. Postoperative observations were recorded by a third independent worker.

The decodification of solutions was carried out after all the observations had been collected and the data was being analysed.

Inclusion criteria

- (a) American Society of Anesthesiologists (ASA) Status I/II
- (b) Patient undergoing lower limb orthopaedic surgery.

Exclusion criteria

- (a) All cases which were not suitable for spinal anaesthesia.
- (b) ASA Status III or less.
- (c) High Risk cases with co morbid conditions.

All patients were preloaded with a crystalloid (Ringer Lactate 10 ml/kg) given intravenously. SAB was given via L3–L4 interspace using 25 G or 26 G disposable needle.

Vital parameters were recorded at baseline, after volume preload, after SAB, at 5 min interval for 30 min (till complete fixation of block) and at regular intervals of 15 min till end of surgery. Onset, highest level and duration of SAB were ascertained by testing segmental involvement and regression. Any intraoperative complications/inadequacy of block/patient or surgeon's discomfort was also recorded. Pain scores were recorded postoperatively on visual analog scale (VAS) every hour and any patient experiencing discomforting pain (VAS score more than 5) received rescue analgesia with Inj Diclofenac Sodium 75 mg intra muscular (IM).

The duration of effective analgesic time from the SAB, time to first analgesic use in postoperative phase and total consumption of analgesics in the 24 h after SAB were recorded. Any adverse events were also recorded. At the end of the study, the data for analgesia, duration of block, sedation, and nausea/vomiting were compared for all the three groups and analysed for significant change using IBM SPSS Statistics (version 20).

Results

Average age, weight and sex distribution were comparable in all the three groups. Majority of the patients were young adult males (except one female in Group “F”). Commonest surgical

procedure undertaken was arthroscopy (diagnostic/reparative). Other procedures were bone grafting, implant removal, and ORIF for fractures (Table 1).

Time to onset of block was comparable in all the three groups. Average rise in level of block, measured at 10 min after institution of SAB (from the point of injection), was $6.7 (\pm 2.4)$, $6.3 (\pm 1.7)$ and $5.9 (\pm 2.1)$ vertebral segments in groups “C,” “F” and “M,” respectively. The intergroup difference was statistically insignificant ($P > 0.05$) (Fig. 1).

The mean highest level of block achieved in Group “C” was $8.70 (\pm 2.32)$, in Group “F” was $7.95 (\pm 1.67)$ and in Group “M” was $7.20 (\pm 2.06)$ vertebral segments. The intergroup difference was statistically significant ($P < 0.05$) between Group “C” and Group “M”. However between Group “C” and Group “F,” it was not statistically significant.

In Group “C,” this highest level was achieved in $23.5 (\pm 13.9)$ min, whereas in Group “F,” it was achieved in $22.0 (\pm 11.0)$ min and in Group “M,” in $22.0 (\pm 19.1)$ min. Thus time taken to achieve the highest level of block was comparable in all the three groups, with intergroup differences being statistically insignificant ($P > 0.05$) (Table 4).

Duration of block was measured from the time of injection to the time when the highest level of block regressed by 2 spinal segments. The average duration of block was comparable in all the three groups. In Group “C,” the average duration of block was $130.5 (\pm 39.3)$ min; in Group “F,” it was $126.5 (\pm 44.0)$ min, while in Group “M,” it was $129.5 (\pm 45.7)$ min. The difference amongst the groups was statistically insignificant ($P > 0.05$). No supplementation of block with general anaesthesia (GA) and total intra-venous anaesthesia (TIVA) was required for any of the patients in any group.

Haemodynamics were monitored in the perioperative period, and the results were recorded at predetermined intervals (Table 2). Fall in heart rate was observed in all groups after SAB. Average fall in heart rate was $11.7 (\pm 8.76)$ beats per minute (BPM) in Group “C,” $22.3 (\pm 17.9)$ BPM in Group “F” and $11.7 (\pm 12.7)$ BPM in Group “M”. This change in pulse rate was most profound in Group “F,” and the difference was statistically significant ($P < 0.05$) (Fig. 3).

Systolic blood pressure (SBP), mean arterial pressure (MAP), and diastolic blood pressure (DBP) also fell in all patients after SAB. Mean fall in SBP was $12.5 (\pm 7.3)$ mm Hg in Group “C,” $17.9 (\pm 13.7)$ mm Hg in Group “F” and $10.35 (\pm 19.2)$ mm Hg in Group “M”. As this reduction was less than 20% of the baseline average values, it was not considered to be clinically significant. Also there was no significant intergroup difference noticed in the study population ($P > 0.05$).

Fall in MAP was $11.6 (\pm 9.8)$ mm Hg; $16.5 (\pm 8.8)$ mm Hg; and $11.2 (\pm 10.7)$ mm Hg in groups “C,” “F” and “M,” respectively. The change in MAP and the intergroup differences in averages were not statistically significant ($P > 0.05$).

Fall in DBP was most pronounced in Group “F” ($13.26 (\pm 8.8)$ mm Hg). In the other two groups, it was significantly lesser ($P < 0.05$) being 7.75 ± 5.7 mm Hg in Group “C” and 8.55 ± 7.8 mm Hg in Group “M”. However, the reduction in DBP was clinically insignificant in all the three groups (being less than 20% of the baseline values).

Quality and duration of postoperative analgesia was assessed by observing average VAS scores as well as the pain free interval for 24 hrs in the postoperative period (Table 3;

Table 1 – Characteristics of patients, diagnosis and operative procedures.

Parameter	Description	Group			p-value
		C (n = 30)	F (n = 30)	M (n = 30)	
Age (yrs)	Mean (Min–Max)	34 (21–70)	30 (24–45)	30 (22–43)	—
Sex	F (Count)		1		—
	M (Count)	30	29	30	—
Weight	Mean ($\pm$ SD)	67 ($\pm$ 8)	69 ($\pm$ 6)	66 ($\pm$ 7)	—
Diagnosis	ACL tear	70.0%	65.0%	70.0%	—
	Fracture femur	10.0%	5.0%	5.0%	—
	Fracture tibia/fibula	10.0%	15.0%	5.0%	—
	IDK		15.0%	5.0%	—
	Meniscus tear	5.0%		10.0%	—
	Polytrauma			5.0%	—
	Synovitis (Lt Knee)	5.0%			—
Operation	Arthroscopic ACL Reconstruction	45.0%	60.0%	65.0%	—
	Arthroscopy	30.0%	20.0%	15.0%	—
	Arthroscopy & repair of meniscus	5.0%			—
	Bone grafting	5.0%			—
	Implant removal	5.0%	10.0%	5.0%	—
	ORIF	10.0%	5.0%	15.0%	—
	ORIF + ILN		5.0%		—

SD: Standard deviation, ACL: Anterior cruciate ligament, ILN: Inter locking nail, ORIF: Open reduction and internal fixation, IDK: Internal Derangement of knee.

Fig. 1 – Dynamics of subarachnoid block. (Chart A) Shows the graphic representation of average height of block achieved for each group at periodic intervals during first 4 hrs. Group “C” patients achieved the highest level of block, and those in Group “M” achieved the lowest. This trend was maintained all through the period of observation. (Chart B) Shows the distribution pattern of the highest level of block achieved by patients in different groups, which reiterates the above findings. Thus addition of either fentanyl or midazolam did not significantly improve the quality and dynamics of SAB as compared with the control group. SAB: subarachnoid block.

Fig. 2). Average VAS scores were recorded at predetermined intervals in the postoperative period. In Group “C,” these scores ranged between 0.74 ($\pm$ 1.9) to 4.40 ($\pm$ 2.3). In Group “F,” VAS scores remained between 0.8 ($\pm$ 2.1) and 5.35 ($\pm$ 2.4), while in Group “M,” the average VAS scores were recorded between 0.96 ($\pm$ 1.9) and 4.88 ($\pm$ 2.6). VAS scores peaked around 8–9 hrs after the SAB in all the three groups. Intergroup differences were minor and were statistically insignificant ($P > 0.05$).

Pain free interval was the average duration for which the patient remained pain free after institution of SAB with VAS scores remaining < 5 and was a measure of the time when the first rescue analgesic was given. In Group “C,” this duration was 6.33 ($\pm$ 3:03) hours, in Group “F,” it was 6:05 ($\pm$ 1:29) hours while in Group “M,” the duration of pain free period was 6:19 ($\pm$ 2:31) hours. The intergroup difference was statistically not significant ($P > 0.05$).

Table 2 – Haemodynamics.

Parameter	C (n = 30)	F (n = 30)	M (n = 30)	P-values		
	Mean (SD)	Mean (SD)	Mean (SD)	C vs F	C vs M	F vs M
Pulse (baseline)	82.4 (14.16)	85.3 (11.93)	78.8 (14.96)	0.512	0.462	0.143
Pulse (max difference)	11.7 (8.77)	22.3 (17.95)	11.7 (12.77)	0.023	1.000	0.038
SBP (baseline)	132.1 (11.24)	131.0 (8.67)	124.6 (8.13)	0.724	0.027	0.024
SBP (max difference)	12.5 (7.30)	17.9 (13.55)	10.4 (19.16)	0.128	0.642	0.166
MAP (baseline)	92.3 (10.28)	89.8 (10.61)	90.6 (7.05)	0.475	0.572	0.776
MAP (max difference)	11.6 (9.81)	16.5 (8.22)	11.2 (10.74)	0.099	0.915	0.095
DBP (baseline)	76.5 (13.73)	79.7 (8.49)	79.3 (8.00)	0.396	0.465	0.870
DBP (max difference)	7.8 (5.79)	13.3 (8.82)	8.6 (7.96)	0.026	0.718	0.088

Table in bold a value of 0.05 denoting statistical significance.

MAP: mean arterial pressure; SBP: systolic blood pressure; DBP: diastolic blood pressure.

Table 3 – VAS scores and pain free duration.

VAS (time since SAB)	C (n = 30)	F (n = 30)	M (n = 30)	P-values		
	Mean (SD)	Mean (SD)	Mean (SD)	C vs F	C vs M	F vs M
VAS (3 hrs)	1.4 (2.7)	0.8 (2.1)	1.3 (3.2)	0.404	0.874	0.560
VAS (6 hrs)	4.0 (2.5)	3.9 (2.2)	4.2 (3.2)	0.675	0.773	0.510
VAS (9 hrs)	4.4 (2.3)	5.4 (2.5)	4.7 (3.2)	0.215	0.574	0.614
VAS (12 hrs)	4.4 (3.0)	4.2 (3.4)	3.6 (2.8)	0.986	0.851	0.847
VAS (15 hrs)	3.5 (2.9)	2.8 (2.3)	2.7 (2.5)	0.416	0.388	0.895
VAS (18 hrs)	1.7 (1.9)	2.0 (1.8)	1.6 (2.2)	0.542	0.768	0.812
VAS (21 hrs)	0.7 (1.9)	0.9 (1.9)	1.0 (1.8)	0.683	0.505	0.784
Pain free duration (hrs)	6:20 (3:03)	5:35 (1:29)	6:50 (2:31)	0.574	0.793	0.746

SD: standard deviation, VAS: Visual analog scale.

Table 4 – Block dynamics.

Height of block (time since SAB)	C		F		M		P-values		
	Mean	Standard deviation	Mean	Standard deviation	Mean	Standard deviation	C vs F	C vs M	F vs M
Ht (10 min)	6.7	2.4	6.3	1.7	5.9	2.1	0.598	0.271	0.467
Ht (20 min)	7.3	2.5	6.8	1.7	6.5	2.2	0.514	0.287	0.576
Ht (30 min)	8.0	2.3	7.3	1.9	6.7	2.5	0.269	0.094	0.439
Ht (40 min)	8.3	2.3	7.1	2.0	6.6	2.6	0.103	0.041	0.498
Ht (50 min)	8.3	2.3	6.8	1.9	6.6	2.7	0.031	0.038	0.788
Ht (60 min)	8.4	2.3	6.6	2.1	6.3	2.8	0.014	0.015	0.749
Ht (90 min)	7.3	2.3	5.8	2.3	5.9	2.2	0.049	0.050	0.945
Ht (120 min)	5.8	2.2	5.0	2.6	4.9	1.5	0.339	0.174	0.880
Ht (150 min)	4.1	2.5	3.5	2.2	3.1	1.5	0.423	0.113	0.456
Ht (180 min)	3.2	2.4	2.3	2.0	2.0	1.4	0.233	0.060	0.521
Ht (210 min)	2.3	2.3	1.4	1.7	1.0	1.6	0.169	0.054	0.492
Ht (240 min)	0.9	1.5	0.4	1.2	0.1	1.1	0.203	0.050	0.420
Time for peak Ht	23.50	13.87	22.00	11.05	22.00	19.08	0.707	0.778	1.000
Duration of block	130.50	39.27	126.50	44.04	129.50	45.71	0.763	0.941	0.834

One patient in Group “M” had inadequate block and two patients had delayed onset of block in same group. This complication might be because of dilution effect of additive drug or might be a technical fault. No other complications were observed.

Discussion

This double-blind, randomised controlled trial was carried out to evaluate the effectivity of combining opioid as an adjunct with local anaesthetic (fentanyl + bupivacaine) vis-a-vis that

of combining sedative as an adjunct with local anaesthetic (midazolam + bupivacaine), a third group of patients, where a placebo was combined with local anaesthetic (saline + bupivacaine), acting as a control.

The onset, time to achieve peak level and duration of Sub Arachnoid (SA) block was comparable in all the three groups, with no statistical difference amongst them. This finding is at variance with that reported by earlier studies, which have either reported no change^{1,2} or a faster onset of block with use of adjuncts.^{3,4} However, in a recent study by Singh et al.,⁵ it has been reported that when a combination of fentanyl and clonidine was used as an adjunct, the onset of SAB was faster,

Fig. 2 – Postoperative analgesia. (Chart A) Depicts average VAS scores at periodical intervals for each group. It is evident that the VAS scores peaked between 8 and 11 hrs after the institution of SAB, with highest average scores being reported by the patients of fentanyl group. In other groups, the peak scores remained below 5, however at least one dose of rescue analgesic was given to majority of patients in all the three groups at the peak of pain, which resulted in a downtrend in VAS scores, which remained below 4 between 12 and 24 hrs postoperatively. (Chart B) Shows the box and whiskers charts for “pain free duration” as reported by all patients in the three groups. The median period for which the patients remained pain free, was between 5.5 and 7.0 hrs postoperatively. After that majority of them demanded at least 1 dose of a rescue analgesic, following which they remained pain free for next 16–18 hrs. SAB: subarachnoid block.

Fig. 3 – Haemodynamics. (Chart A) Depicts the changes in average MAP in patients of all the groups after institution of SAB. Although MAP fell in all the groups, but this fall was clinically as well statistically not significant as the fall in MAP observed was less than 20% of the average baseline value. The intergroup differences were also not statistically significant and were managed conservatively with fluid therapy and positioning. (Chart B) shows the changes in average pulse rate in patients of the three groups. The pulse rate also declined after institution of SAB, but again, as in case of arterial pressures, the change observed was not significant, both clinically as well as statistically. MAP: mean arterial pressure; SAB: subarachnoid block.

but when fentanyl alone was used with bupivacaine, the onset of block was slower than the control group, which is in consonance with our findings. This is despite the fact that the workers had used a higher dose of fentanyl (25 µg) for their patients compared to our study (10 µg). In another study by Codero et al.,⁶ the authors report a significantly longer time taken for onset of block when midazolam was added as an adjunct as compared to fentanyl (17.1 min vs. 13.2 min,

respectively, with $P = 0.023$), which again has been demonstrated by our study. In this study, the dose of midazolam used as an adjunct was double than what was used in our study (2 mg vs 1 mg of midazolam).

Our study revealed that the level of block at any point in time was highest in control group, while it was lowest in midazolam group, with the patients where fentanyl was used, it was somewhere in between the two. Difference between

the control group and midazolam group patients was statistically significant. This finding was also at variance with those reported in the existing literature. Previous studies have reported that addition of adjuncts does not significantly affect the peak level of block achieved.¹

The average duration of block was in the range 126.5 ± 44.0 min– 30.5 ± 39.3 min, and the difference amongst the groups was not statistically significant ($P > 0.05$). Only one previous study has reported a similar finding.¹ There are several other authors who have reported an increase in duration of block by using adjuncts with local anaesthetic agents.^{7,8} A comparative study conducted by Chattopadhyay et al., in 2013 showed that addition of 2 mg of midazolam to 4.0 ml of bupivacaine significantly increased the duration of block,⁹ which is at variance to that of our study. On the other hand, there is one study which has also reported a reduction in duration of block with use of adjuncts.¹⁰

Average VAS scores were low for the first 4 h after SAB in all the three groups indicating that there was no significant postoperative pain during this period. Pain free duration was measured as time elapsed between institution of SAB and the time when the rescue analgesic was given and was considered as a surrogate marker for duration of postoperative analgesia.

Our study indicated that there was no significant difference amongst the three groups as far as pain free duration is concerned (Table 3). This finding is at variance from earlier reports which have stated that there is a significant increase in duration of postoperative analgesia when fentanyl or midazolam is used as an additive with local anaesthetic.^{8,9,11–15}

All the patients remained haemodynamically stable across the three groups. A statistically insignificant fall in pulse rate ($P > 0.05$) was observed in all the groups, but this reduction was less than 20% from baseline with this variability being least in midazolam group. SBP, MAP and DBP fell from baseline values in all the three groups; however, this fall in BP (MAP) was clinically insignificant (as the MAP fell less than 20% of baseline). No intergroup difference was also observed amongst the three groups. In a previous study conducted by Ben-David et al. in 2000 on a group of elderly patients, it was reported that if 4.0 mg of isobaric bupivacaine was combined with 20 µg of fentanyl, it provided adequate anaesthesia and analgesia without producing any haemodynamic instability.¹⁶ Our study also has shown that adding fentanyl as an adjunct does not adversely impact the haemodynamic stability in all patients.

No significant complications were noted with only two patients having a delayed onset of block and one patient having an inadequate motor block, all of them belonging to the midazolam group. In other words, adding of either an opioid (fentanyl) or a sedative (midazolam) to local anaesthetic did not adversely affect the safety of patients, and both the combinations were observed to be safe for clinical practice.

Conclusions

This double-blind, randomised controlled trial was carried out to evaluate the effectivity of combining opioid as an adjunct with local anaesthetic (fentanyl + bupivacaine) vis-a-vis that

of combining a sedative as an adjunct with local anaesthetic (midazolam + bupivacaine). Dynamics of SAB, as well as the onset, duration and quality of postoperative analgesia were assessed.

The onset of block, time to achieve peak level, and duration of SA block were comparable in all the three groups, with no statistical difference amongst the groups. Average duration of block was in the range 126.5 (44.0) min– 130.5 (39.3) min, and the difference amongst the groups was not statistically significant.

Level of block at any point in time was highest in control group, lowest in midazolam group, while in patients where fentanyl was used, it was somewhere in between. However these intergroup differences were not statistically significant.

Average VAS scores in the postoperative period were comparable in all the three groups. Also no significant difference was noticed amongst the three groups as far as pain free duration is concerned, indicating that addition of adjuncts did not delay the requirement of a rescue analgesic and did not significantly improve the postoperative analgesia.

Haemodynamically, all the patients remained stable across the three groups with patients in midazolam group exhibiting least variability from the baseline. No significant complications were recorded in all the three groups.

To conclude, this study has been unable to confirm that addition of fentanyl (opioid) or midazolam (sedative) offered any improvement in the “quality and duration of postoperative analgesia” vis-a-vis the patients who received local anaesthetic alone. Their use as an adjunct also does not significantly alter the dynamics of SAB.

Conflicts of interest

The authors have none to declare.

REFERENCES

1. Diana F, Montserrat R, Victoria M, et al. Spinal anesthesia with bupivacaine and fentanyl in geriatric patients. *Anesth Analg*. 1996;83:537–541.
2. Agrawal A, Asthana V, Sharma JP, Gupta V. Efficacy of lipophilic vs lipophobic opioids in addition to hyperbaric bupivacaine for patients undergoing lower segment caesarean section. *Anesth Essays Res*. 2016;10(3):420–424.
3. Yaksh TL, Allen JW. Preclinical insights into the implementation of intrathecal midazolam: a cautionary tale. *Anesth Analg*. 2004;98:1509–1511.
4. Gupta A, Kamat H, Kharod U. Efficacy of intrathecal midazolam in potentiating the analgesic effect of intrathecal fentanyl in patients undergoing lower limb surgery. *Anesth Essays Res*. 2015;9(3):379–383.
5. Singh R, Kundra S, Gupta S, Grewal A, Tewari A. Effect of clonidine and/or fentanyl in combination with intrathecal bupivacaine for lower limb surgery. *J Anaesthesiol Clin Pharmacol*. 2015;31(4):485–490.
6. Codero F, Vitalis M, Thikra S. A randomised controlled trial comparing the effect of adjuvant intrathecal 2 mg midazolam to 20 micrograms fentanyl on postoperative pain for patients undergoing lower limb orthopaedic surgery under spinal anaesthesia. *Afr Health Sci*. 2016;16(1):282–291.

7. Bhattacharya D, Biswas B, Banerjee A. Intrathecal midazolam with bupivacaine increase the analgesic effects of spinal blockade after major gynaecological surgery. *J Anaesthesiol Clin Pharmacol*. 2002 Apr;18(2):183–186.
8. Yegin A, Sanli S, Dosemeci L, Kayacan N, Akbas M, Karsli B. The analgesic and sedative effects of intrathecal midazolam in perianal surgery. *Eur J Anaesthesiol*. 2004;21:658–662.
9. Chattopadhyay A, Maitra S, Sen S, et al. A study to compare the analgesic efficacy of intrathecal Bupivacaine alone with intrathecal bupivacaine-midazolam combination in patients undergoing elective infraumbilical surgery. *Anesthesiol Res Pract*. 2013, 567134.
10. Srivastava U, Kumar A, Saxena S, Saxena R, Gandhi NK, Salar PS. Spinal anaesthesia with lignocaine and fentanyl. *Indian J Anaesth*. 2004;48(2):121–123.
11. Kim MH, Lee YM. Intrathecal midazolam increases the analgesic effects of spinal blockade with bupivacaine in patients undergoing haemorrhoidectomy. *Br J Anaesth*. 2001;86(1):77–79.
12. Khanna MS, Singh Ikwinder KJP. Comparative evaluation of bupivacaine plain versus bupivacaine with fentanyl in spinal anaesthesia in geriatric patients. *Indian J Anaesth*. 2002;46(3):199–203.
13. Valentine JM, Lyons G, Bellamy MC. The effect of intrathecal midazolam on post-operative pain. *Eur J Anaesthesiol*. 2003;13(6):589–593.
14. Malan AJ, Campbell DC, Martel J, Biem S. Efficacy of the addition of intrathecal fentanyl to spinal anesthesia for uterine exteriorization during caesarean delivery. *Can J Anesth*. 2005;52:A51. <https://doi.org/10.1007/BF03023091>.
15. Patra P, Kapoor MC, Nair TGM. Spinal anaesthesia with low dose bupivacaine and fentanyl for endoscopic urological surgeries. *J Anaesth Clin Pharmacol*. 2005;21(2):147–154.
16. Ben-David B, Frankel R, Arzumov T, Marchevsky Y, Volpin G. Minidose bupivacaine-fentanyl spinal anesthesia for surgical repair of hip fracture in the aged. *Anesthesiology*. 2000 Jan;92(1):6–11.