

Original Article

# Comparison of Intrathecal Midazolam and Fentanyl Added to Bupivacaine for Spinal Anesthesia in Patients Undergoing Appendicectomy

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## ABSTRACT

**Introduction:** Hyperbaric Bupivacaine is the extensively used local anesthetic but the major disadvantage is profound sympathetic blockade leading to hypotension and prolonged duration of motor block. The addition of Fentanyl or Midazolam can provide excellent quality and prolong the duration of analgesia. The study aims to compare the effect of intrathecal Fentanyl with that of intrathecal Midazolam in combination with 0.5% hyperbaric Bupivacaine on the duration and quality of spinal anesthesia in patients undergoing appendicectomy.

**Materials and Methods:** This is a prospective, comparative and interventional study where patients were randomized into two equal groups. The study was conducted in a tertiary referral hospital from July 2018 to December 2018 after ethical approval. Group BF received Fentanyl and group BM received Midazolam. The outcomes measured were, peak sensory level, quality of intraoperative analgesia and motor block, duration of effective analgesia, intraoperative and postoperative complications.

**Results:** A total of 44 patients were studied with 22 in each arm. The two groups were comparable in terms of age, weight, height, duration of surgery, and ASA status of the patients. Peak sensory level and degree of motor block were not statistically different in the two arms. Duration of effective analgesia was 293.16±35 min in the BF group and 267.80±32 min in the BM group (p=0.01). Increased incidence of pruritus was recorded during the postoperative period in the Fentanyl group.

**Conclusions:** Fentanyl and Midazolam both are equally efficient adjuvant added to hyperbaric Bupivacaine for intrathecal use to improve the quality of spinal anesthesia in patients undergoing appendicectomy.

**Keywords:** Appendicectomy; Bupivacaine; Fentanyl; Midazolam

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## INTRODUCTION

Spinal anesthesia for its numerous advantages over general anesthesia makes it the anesthesia of choice in the present surgical practice.<sup>1</sup> Hyperbaric Bupivacaine is the most widely used local anesthetic but the major disadvantage is profound sympathetic

blockade leading to hypotension and prolonged duration of motor block.<sup>2</sup> Despite achieving an adequate block, some patients under spinal anesthesia may experience some degree of visceral discomfort during appendicectomy under spinal anesthesia.<sup>3</sup>

Several additives (opioids, clonidine, neostigmine, ketamine, midazolam, etc) used as an adjunct with intrathecal injection of local anesthetic solutions are aimed at improving the quality and duration of spinal block and postoperative analgesia, or to minimize the dose of a local anesthetic to reduce the extent and effects of sympathetic blockade.<sup>4</sup>

Intrathecal Fentanyl in low doses is associated with minimal side effects as compared to other opioids (morphine and pethidine).<sup>5</sup> Intrathecal administration of midazolam has been associated with various side effects.<sup>6</sup> Addition of Fentanyl or preservative-free midazolam to Bupivacaine for spinal anesthesia has shown promising results in various studies at improving the duration and quality of anesthesia and analgesia with smaller doses of Bupivacaine.<sup>7-10</sup> But there are very few studies done in our part of the world to compare Midazolam and Fentanyl used as adjuncts with spinal Bupivacaine to evaluate the superiority of one over the other.

The aim of the study is to compare the effectiveness of intrathecal Fentanyl with intrathecal Midazolam added with Bupivacaine on improving the quality of intraoperative analgesia and duration of postoperative analgesia in patients undergoing elective as well as emergency appendicectomy.

**MATERIALS AND METHODS**

This was a hospital-based prospective, randomized, double-blind, comparative, interventional study. The study was conducted in the Department of Anaesthesiology of Shree Birendra Hospital, Kathmandu from July 2018 to December 2018. Ethical approval was taken from the institutional review board and the trial was registered in the UMIN database as UMIN000043105.

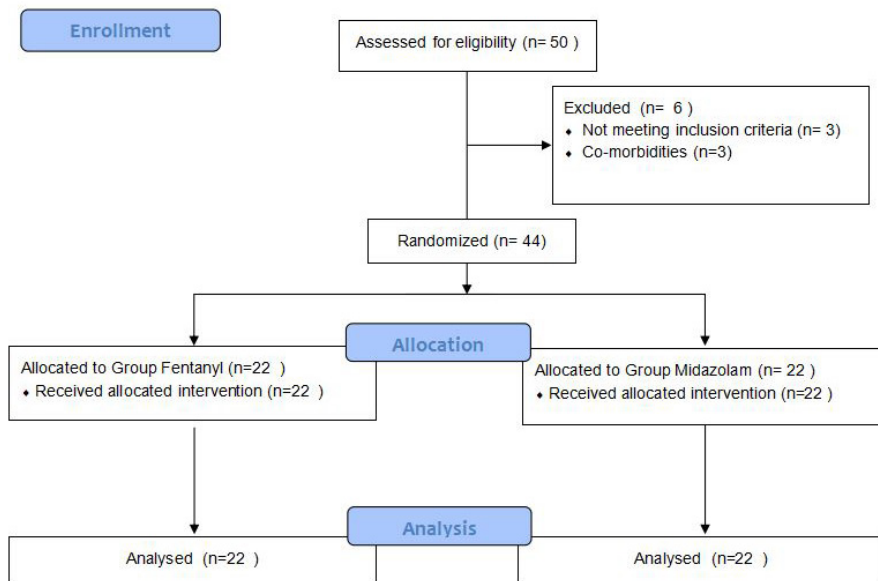
It was calculated that 22 patients in each group would be required to have a 95% confidence interval and a power of 80% in the study. After obtaining informed written consent, the patients

undergoing open appendicectomy meeting the inclusion criteria were randomized. Exclusion criteria were patient refusal, infection at the site of injection, deformities of the spinal column, patient with mental disturbance or neurological disease, and known case of allergic to drugs used.

They were randomly allocated into two groups identified as BF and BM. BF group received intrathecal 3ml 0.5% hyperbaric Bupivacaine with 0.4mls (20micrograms) Fentanyl. Whereas the BM group received intrathecal 3ml of 0.5% hyperbaric Bupivacaine with 0.4ml (2mg) midazolam. The total volume was made 3.4 ml in both groups. Standard monitoring included pulse oximetry, non-invasive blood pressure (NIBP), and electrocardiography (ECG). The parameters taken into consideration were peak sensory level, degree of motor block, quality of intraoperative anesthesia, duration of effective analgesia, and side effects if any. The peak sensory level was defined as the highest level of loss of sharp sensation by using a pinprick test which is recorded bilaterally at the midclavicular line at 2, 5, 10, 15, 20, 25, and 30 minutes after intrathecal injection. The quality of intraoperative analgesia was evaluated by the patient at 15-minute intervals using a 4-point scale as an excellent, adequate, inadequate, and major discomfort. 4 Degree of motor block was assessed bilaterally using a 4-point Bromage scale as 0, 1, 2, 3.5 in 5, 10 and 15 minutes. Duration of effective analgesia was taken from the time of intrathecal injection till the demand of the first rescue analgesic dose and was assessed by using a visual analogue scale. The occurrence of adverse events like hypotension, bradycardia (heart rate < 60 beats/minute), shivering, pruritus, urinary retention, nausea and vomiting, dizziness, sedation, respiratory depression, or any other side effects were monitored for till 24 hours postoperatively.

Collected data were analyzed by means of statistical software SPSS 20.0. Chi-square was used to see the association between groups for categorical variables. The student's t-test was applied to see significant differences between the groups for continuous variables. The p-value less than 0.05 was taken as significant.

**RESULTS**



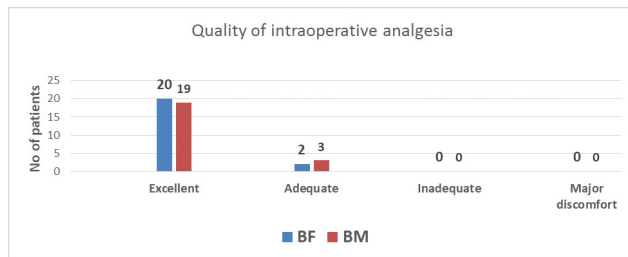
**Figure 1. Flow chart of the participants in the study**

A total of 50 patients was assessed for eligibility and finally, 44 patients were enrolled in the study with 22 in each arm (fig. 1). All cases were completed without any intraoperative major complication, and none of the cases was to be converted to general anesthesia. The study groups did not differ significantly with respect to any demographic variables (Table 1). The ASA physical status of the patients and the mean duration of surgery were similar in both groups.

**Table 1. Baseline characteristics of the participants in the study**

Variables	BF	BM	p value
Age(Yrs)	25.40±6.6	24.20±7.2	0.57
Weight(Kg)	57.84±7.8	59.08±6.8	0.58
Height(Cm)	157.38±14.3	160.36±12.8	0.47
Duration of surgery (minutes)	35.58±14.8	40.12±7.3	0.20
<b>ASA physical status</b>			
ASA PS I	21	22	
ASA PS II	1	0	

The peak sensory level (dermatome) in the BF and the BM group were 4.78± 0.92 and 4.85± 0.86 respectively and were not statistically significant. There was no statistical difference in peak degree of motor block and quality of intraoperative analgesia between the two groups ( Table 2 and fig. 2)



**Figure 2. Quality of intraoperative analgesia**

**Table 2. Degree of motor block (n=44)**

Variable	BF	BM	P-value
Bromage 0	0	0	>0.05
Bromage 1	0	0	
Bromage 2	19	20	
Bromage 3	3	2	

Duration of effective analgesia, defined as the time to demand of first rescue analgesia was significantly longer in the BF group compared to the BM group; 293.16±35 and 267.80±32 ( p=0.01). Two patients from the BF group developed pruritus of which both received intravenous 4 mg Ondansetron. No significant complications were recorded in both groups.

## DISCUSSION

Intrathecal opioids and midazolam are being used as adjuncts with local anesthesia these days to improve the duration and quality of

spinal anesthesia.<sup>11</sup> Fentanyl are shown to produce many of its clinical effects very early after intrathecal administration. In the intraoperative period, it increases surgical analgesia and prolongs the duration of the anesthetic block.<sup>5,12</sup> Midazolam is another adjuvant to hyperbaric bupivacaine for intrathecal administration. Preservative-free midazolam is shown to be effective in prolonging postoperative analgesia without significant adverse effects.<sup>13</sup>

The two groups were matched for comparison. There was no significant difference between the groups in terms of age, weight, height, duration of surgery, and ASA physical status. The peak level of sensory analgesia was similar in both groups. It shows that level of sensory blockade depends upon the dose of Bupivacaine and is not influenced by Fentanyl or midazolam if the volume of the drug is made equal. The results of the present study are consistent with previous studies which have also reported no change in peak sensory level with the addition of fentanyl or midazolam as adjuncts.<sup>14,15</sup>

The degree of motor block was achieved as Bromage 2 in 80% to 90% of the cases in our study and the results were not statistically significant. The degree of the motor block did not increase or decrease with midazolam or fentanyl. Other studies also showed that the synergism of spinal local anaesthetics with fentanyl or midazolam was characterized by enhanced somatic analgesia without effect on the degree or level of the local anesthetic-induced sympathetic or motor blockade.<sup>15,16</sup>

Various studies have shown that the addition of opioids to local anesthetic agents intrathecally was able to relieve visceral pain and discomfort.<sup>17,18</sup> Quality of intraoperative analgesia was excellent in above 90% of patients in both groups. None of the patients complained of any pain or discomfort during surgery. It also agrees with the study performed by Bharti et al<sup>19</sup> who explains that the addition of intrathecal midazolam to bupivacaine significantly improves the quality of spinal anaesthesia.

In this study, the time to first analgesic request was significantly prolonged in the fentanyl group compared with the Midazolam group. In other studies, the duration of effective analgesia, defined as time to demand first rescue analgesia was significantly prolonged in the Fentanyl group.<sup>11,19</sup> A similar observation was also found by Sanna et al<sup>15</sup> who performed the comparative study of intrathecal midazolam versus fentanyl as adjuncts to ropivacaine for lower-limb surgery. Findings were also similar to the study done by Bhure et al<sup>20</sup> where the duration of pain relief was higher in the fentanyl group than the midazolam group. Prakash et al<sup>21</sup> in their study also concluded that intrathecal midazolam 2 mg provided a moderate prolongation of postoperative analgesia when used as an adjunct to bupivacaine.

The commonest side effects of fentanyl are nausea, vomiting, pruritus, and respiratory depression.<sup>22</sup> In our study, pruritus was seen in two patients from the Fentanyl group to whom intravenous Ondansetron (0.1 mg/kg) was given. No significant complications were recorded in both groups. The levels of sedation score were similar in both the groups. None of the patients in our study developed respiratory depression which was measured by pulse oximetry. In our study, none of the patients complained of nausea and vomiting during the intraoperative and postoperative periods.

## CONCLUSIONS

Fentanyl and Midazolam both were equally efficient adjuvant added to hyperbaric Bupivacaine for intrathecal use to improve the quality of spinal anesthesia in patients undergoing appendectomy. Duration of effective postoperative analgesia was prolonged with Fentanyl when compared with Midazolam but with an increased incidence of pruritus.

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