Comparative Study of Intrathecal Dexmedetomidine versus Fentanyl as an Adjuvant to 0.5% Heavy Bupivacaine in Lower Abdominal Surgeries

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ABSTRACT

Introduction: Neuraxial anesthesia is a popular technique of anesthesia. The most frequently performed neuraxial blocks are subarachnoid, epidural, and caudal blocks. The objective of this study was to compare the effect of intrathecal dexmedetomidine and fentanyl on the characteristics of block when given intrathecally as an adjuvant to bupivacaine in lower abdominal surgeries.

Methods: Total 100 patients of ASA grade I and II undergoing lower abdominal surgery under spinal anesthesia were divided into two groups: group F and group D. Group D received intrathecal 0.5% bupivacaine heavy 3 ml with 5µgm of dexmedetomidine in 0.5 ml normal saline (100 µgm/ml dexmedetomidine diluted in 10 ml normal saline). Group F received intrathecal 0.5% bupivacaine heavy 3 ml with 0.5 ml ie 25 µgm fentanyl (50 µgm/ml fentanyl). Time to achieve T6 level sensory block, highest level of block achieved, time to achieve the highest level, time of onset of motor block of Bromage 3, time of first analgesia request in the postoperative ward and time to regression of motor block to Bromage 0 was noted in both the groups.

Results: Time to achieve a sensory level of T6 dermatome was 6.96 ± 1.641min in group D and 8.20 ± 1.62 min in group F. The time to achieve a sensory level of T6 dermatome was significantly shorter in group D. The highest level achieved was similar in both the groups. Time to achieve the highest sensory level was 10.90 ± 2.88 min in group D and 12.60 ± 2.29 min in group F. Time to achieve a motor block of Bromage 3 was 8.80 ± 1.525 min in group D and 9.68 ± 1.362 min in group F. The time to first analgesia required was 261.5 0 ± 116.054 min in group D and 167.64 ± 44.50 min in group F. Regression of motor block to Bromage 0 was 240.18 ± 112.290 min in group D and 114.28 ± 42.931 min in group F.

Conclusions: We found that 5 microgram of dexmedetomidine significantly shortens the onset time of sensory and motor block, prolongs the duration of motor block and the duration of analgesia as compared to 25 microgram of fentanyl when given intrathecally as an adjuvant to bupivacaine.

Keywords: *bupivacaine; dexmedetomidine; fentanyl; intrathecal.*

INTRODUCTION

Neuraxial anesthesia is a popular technique of anesthesia. The most frequently performed neuraxial blocks are subarachnoid, epidural, and caudal blocks. For lower abdominal surgeries subarachnoid block is the most preferred technique because of the advantages like rapid onset of action, cost effectiveness, easy administration and shorter post-anesthesia care unit stay.[1] Spinal anesthesia with sole 0.5% bupivacaine heavy has a relatively shorter duration of block thereby lacking effective postoperative analgesia. Fentanyl is a synthetic opioid

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widely used as an adjuvant to bupivacaine in spinal anesthesia. Addition of fentanyl to local anesthetic has been reported to improve the quality and duration of block.[2]

Coombs et al[3] were the first one to introduce the analgesic properties of alpha 2 receptor agonists during intrathecal injection. Although Clonidine was the first one to be used intrathecally,[4] Dexmedetomidine, a highly selective alpha 2 adrenergic receptor agonist, has been shown to be a better adjuvant for neuraxial blocks.[5-7] It has been found that when used as an adjuvant to local anesthetics for neuraxial blocks, dexmedetomidine leads to reduced onset time of sensory and motor block, increased duration of sensory block, delayed motor regression, prolonged postoperative analgesia and reduced total dose of analgesic, delayed need of first rescue analgesic and decreased postoperative shivering.[8- 12]

Fentanyl is being frequently used as an adjuvant to bupivacaine in subarachnoid block in our institute. But the effect of dexmedetomidine as an adjuvant in spinal anesthesia has not been studied in our institute. This study was designed with the aim of comparing this newer drug with the conventionally used fentanyl as an intrathecal adjuvant.

METHODS

It was a randomized double blind study conducted at Nepal Medical College Teaching Hospital from January, 2018 to July, 2018. After obtaining ethical approval of the institute and informed written consent, 100 patients of ASA physical status I and II, both male and female, aged 18- 65 years, height 145 to 180 cm, weight 40-80 kgs, scheduled for inguinal hernia repair or total abdominal hysterectomy were included in this study. Exclusion criteria were patient allergic to the drug, heart block/dysrrhythmia or on therapy with adrenergic receptor antagonist, calcium channel blockers and or ACE inhibitor, opium addiction or history of chronic analgesic consumption and any contraindication to spinal anesthesia.

All patients received 0.2 mg/kg diazepam orally night before surgery. On the day of surgery an intravenous access was opened. All the patients were preloaded with 15 ml/kg of lactated ringer's solution. Monitors attached were automated noninvasive blood pressure, pulse oximetry and ECG. Under all aseptic precautions, subarachnoid block was done at L3-L4 interspace with 25 G Whitacre needle in sitting position, midline approach. Patients were randomly divided into two groups by sealed envelope technique: Group D and group F. Group allocation and drug preparation was done by a third year resident. Group D received intrathecal 0.5% bupivacaine heavy 3 ml with 5 µgm of dexmedetomidine in 0.5 ml normal saline (100 µgm/ml dexmedetomidine diluted in 10 ml normal saline). Group F received intrathecal 0.5% bupivacaine heavy 3 ml with 0.5 ml ie 25 µgm fentanyl (50 µgm/ml fentanyl). Subarachnoid block was performed by a consultant anesthesiologist who was also involved in monitoring the patient and data collection. Intrathecal injection was given slowly over 10-15 secs. Immediately after injection patient was made to lie supine. Sensory testing was done by bilateral loss of pin prick sensation to a hypodermic needle in midclavicular line every 2 min. Modified Bromage scale was used to assess motor block (Bromage 0: The patient is able to move the hip, knee, and ankle; Bromage 1: The patient is unable to move the hip but is able to move the knee and ankle; Bromage 2: The patient is unable to move the hip and knee but able to move the ankle; and Bromage 3: the patient is unable to move the hip, knee, and ankle). The time to reach sensory block upto T6 dermatome level and motor block of Bromage 3 was recorded. Once the sensory level reached T6 surgery was allowed. The highest level of block achieved was noted as the sensory level stabilized by consecutive tests. Both the highest level and time taken to achieve the highest level was noted. Failure to achieve motor block of Bromage 3 or sensory block of T6 till 15 minutes of intrathecal injection was considered as failed spinal anesthesia. Such patients were given General anesthesia and were excluded from the study.

Hypotension was defined as decrease of blood pressure more than 30% from baseline, and was treated with IV fluid and inj. Ephedrin 5 mg iv in incremental doses. Bradycardia defined as heart rate of less than 50 and was treated with inj. Atropine 0.6 mg. Intraoperative nausea, vomiting, hypotension, bradycardia, respiratory depression, pruritus if present were also recorded. Total duration of surgery was recorded. After completion of surgery, patient was transferred to post anesthesia care unit (PACU). Time to first rescue analgesia and time to regression of motor block to Bromage 0 postoperatively was recorded. All durations were calculated considering the time of spinal injection as time zero.

Statistical analysis was done using Statistical Package for Social Sciences (SPSS), version 16

Based on the study done by Nayagam HA et al, the mean standard deviation of duration of analgesia was 2.55 hour and the difference in mean was 1.56.[13]

Using the following formula sample size was calculated

Number of cases in each group (n)=

$$\frac{2(z_{\alpha}+z_{\beta})^2 S^2}{d^2}$$

The minimum sample size required was 43 in each group. We conducted the study with 50 patients in each group.

RESULTS

Among 100 patients recruited in the study, block level was adequate in all the patients, none of the patients were excluded from the study. The demographic data (age, weight, height and gender) and ASA physical status were comparable in both the study groups (Table 1).

Table 1. Patient characteristics.

Parameters	Group D	Group F	P
Age (years)	52.22 ± 6.26	50.50 ± 6.32	.175
Gender (M:F)	13:37	14:36	1
Weight(kgs)	65.96 ± 4.05	62.58 ± 6.7	.003
Height(cm)	156.45 ± 3.65	154.25 ± 3.5	.003
ASA PS (I/II)	38:12	34:16	.504

Duration of surgery (93.58 ± 20.13 min in group D and 87.50 ± 17.93 min in group F) was statistically similar in both the groups. The distribution of type of surgery was also statistically similar in both the groups (Table 2).

Table 2. Type and duration of surgery.

Parameters	Group D	Group F	P
Type of surgery (IHR: TAH)	13:37	14:36	1
Duration of surgery(min)	93.58 ± 20.13	87.50 ± 17.93	.114

The results of the onset time to achieve a sensory block of T6 (6.96 ± 1.64 min in group D versus 8.20 ± 1.62 min in group F) was significantly shorter in group D as compared to group F. Highest level of sensory block achieved was similar in both the groups. Time taken to achieve highest level of block (10.90 ± 2.88 min in group D versus 12.60 ± 2.29 min in group F) was significantly shorter in group D. Time taken to achieve motor block of Bromage 3 (8.80 ± 1.525 min in group D versus 9.68 ± 1.362 min in group F) was significantly shorter in group D (Table 3).

Table 3. Onset of block

Parameters	Group D	Group F	P
Time to achieve T6 level (min)	6.96 ± 1.64	8.20 ± 1.62	.000
Highest block level T4:T5:T6	22:21:7	28:15:7	.42
Time to highest block level(min)	10.90 ± 2.88	12.60 ± 2.29	.002
Onset to Bromage 3 Motor block (min)	8.80 ± 1.525	9.68 ± 1.362	.003

Duration of analgesia (261.50 ± 116.054 min in group D versus 167.64 ± 44.50 min in

group F) was significantly prolonged in group D as compared to group F. Regression time of motor block to a Bromage score 0 (240.18 ± 112.290 min in group D versus 114.28 ± 42.931 min in group F) was again significantly prolonged in group D (Table 4).

Table 4. Duration of block.

Parameters	Group D	Group F	P
Time to rescue analgesia (min)	261.50 ± 116.054	167.64 ± 44.50	.000
Regression to Bromage0(min)	240.18 ± 112.290	114.28 ± 42.931	.000

The number of episodes of hypotension, bradycardia, nausea and vomiting were comparable in both the groups. There was no respiratory depression and pruritus in any of the patients in both the groups (Table 5).

Table 5. Side effects.

Parameters	Group D (n=50)	Group F (n=50)	P
Hypotension	4	2	0.678
Bradycardia	2	0	0.495
Nausea	2	4	0.678
Vomiting	0	2	0.495
Respiratory depression	0	0	
Pruritus	0	0	

DISCUSSION

In 1999, dexmedetomidine was approved by the Food and Drug Administration (FDA) for short term sedation and analgesia (< 24 hr) in the intensive care units. Since then it has been widely used in anesthesia, both intravenously as well as in neuraxial and peripheral nerve blocks. In neuraxial anesthesia, dexmedetomidine mediates its analgesic effects via spinal alpha 2 receptors by depressing the release of C-fiber neurotransmitters and hyperpolarization of postsynaptic dorsal horn neurons7 Binding of alpha 2 adrenoceptor agonists to motor neurons in the dorsal horn explains its motor effect.

Various studies have been conducted with different doses of dexmedetomidine. It has been studied in doses of 3, 5, 10 and 15 mcg.[14,15] Zhang Y et al. conducted a meta analysis on the effect of different doses of intrathecal dexmedetomidine on spinal anesthesia. They concluded that the action of spinal anesthesia may be prolonged by increasing the dose of intrathecal dexmedetomidine but the risk of bradycardia is also increased with higher dose.[16] Similarly Nayagam HA et al13 in their study have also concluded that dexmedetomidine in a dose of 5 µg is ideal for use as an additive in spinal anesthesia. In order to achieve a longer duration of analgesia after subarachnoid block with minimal side effects a dose of 5µg was chosen for our study.

In our study, onset time to reach T6 level (6.96 ± 1.641 minutes in group D vs 8.20 ± 1.629 min in group F) was found to be significantly shorter in dexmedetomidine group (p-value .000). Though the highest block level was comparable in both the groups, time to achieve the highest level was significantly shorter in group D (10.90 ± 2.88 mins in group D vs 12.60 ± 2.29 in group F). Motor block onset to Bromage 3 was 8.80 ± 1.525 minutes in group D as compared to 9.68 ± 1.362 minutes in group F. The onset of motor block to Bromage 3 was significantly faster in dexmedetomidine group than in fentanyl group (P= 0.003).

Our results are comparable to the result of Farhad S et al.[17] who compared 5µg of intrathecal dexmedetomidine with 25µg fentanyl added to bupivacaine. The dose of the additives they used was similar to the dose used in the present study. They found the onset time of sensory block as well as motor block was significantly shorter in dexmedetomidine group as compared to fentanyl group. Saadalla AT et al studied the influence of addition of dexmedetomidine or fentanyl to bupivacaine in lumbar spinal subarachnoid anesthesia for inguinal hernioplasty and concluded that dexmedetomidine as adjuvant to spinal bupivacaine produces earlier onset of sensory and motor blockade.[18]

Gupta R et al studied the effect of intrathecal dexmedetomidine and fentanyl as adjuvants to bupivacaine.[19] The dose of dexmedetomidine and fentanyl compared was similar to the dose used in our study. Their results regarding the onset time of sensory and motor block was different from ours. In their study the time to highest sensory level and the onset time of motor block of Bromage 3 was statistically similar in both the groups. In their study they used 0.5% bupivacaine 2.5 ml and the volume of the adjuvant was 0.5 ml. Total 3 ml of drug was injected intrathecally. But in our study we used 3 ml of 0.5% bupivacaine heavy and volume of adjuvant was 0.5 ml. A total of 3.5 ml of the drug was injected intrathecally which may be the reason for the difference in the onset of block.

In our study time of regression of motor block to Bromage 0 was 240.18 ± 112.290 min in dexmedetomidine group and 114.28 ± 42.931 min in fentanyl group. In our study the regression time was significantly longer in dexmedetomidine group. Time to rescue analgesia was 261.50±116.054 min in dexmedetomidine group and 167.64 ± 44.50 min in fentanyl group. Both the duration of motor block and the duration of analgesia was significantly longer in dexmedetomidine group than in fentanyl group. (P= 0.000 and P= 0.000 respectively)

The findings of our study correlate with the findings of study done by Farhad S et al.[17] They also found a significantly longer duration of block with 5µg of intrathecal dexmedetomidine as compared to 25µg fentanyl added to bupivacaine. Gupta R et al in their study found the duration of motor block and the duration of analgesia to be significantly longer in dexmedetomidine than in fentanyl group which is again comparable to our study.[19]

In our study hypotension and bradycardia was more in the dexmedetomidine group than in the fentanyl group, but it was not statistically significant. The lower incidence of hypotension and bradycardia in dexmedetomidine group in our study may be because of the lower dose of dexmedetomidine used. Episodes of nausea vomiting were more in the fentanyl group but again it was not statistically significant. None of the patients had respiratory depression and pruritus in both the groups.

CONCLUSIONS

We found that dexmedetomidine (5µg) significantly shortens the onset time of sensory and motor block, prolongs the duration of motor block and the duration of analgesia as compared to fentanyl (25µg) when given intrathecally as an adjuvant to bupivacaine in lower abdominal surgeries.

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