Original Article

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Comparative Study of Role of Fentanyl and Dexmedetomidine as an Adjuvant to Bupivacaine in Controlling Post-operative Pain

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Abstract

Background: Neural anesthesia is becoming popular because of its ease of practice and multiple advantages. The addition of adjuvants such as fentanyl and dexmedetomidine to drugs like bupivacaine can improve the outcome. However, lack of knowledge limits its acceptance. Various amendments have been done in the technique to curtail the undesirable events and increase the efficiency in a precise direction.

Aim: The aim of the present study was to compare the effect of intrathecal fentanyl and dexmedetomidine as an adjuvant to hyperbaric bupivacaine in the patients admitted for lower abdominal surgeries.

Materials and Methods: The observational study was conducted in the Department of Anesthesiology at Teerthanker Mahaveer Medical College, Moradabad from August 2015 to January 2016. The patients were randomized and divided into two groups each containing 50 members. In Group 1, 2.5 mL of 0.5% hyperbaric bupivacaine was given along with 25 g fentanyl intrathecally. In Group 2, 5 g dexmedetomidine was added to 2.5 mL of 0.5% hyperbaric bupivacaine and given intrathecally. Onset of sensory and motor blockade, duration of analgesia and side effects were noted in both groups.

Results: The combination of dexmedetomidine (5 g) and 0.5% bupivacaine, prolongs the duration of analgesia, decreases total analgesic dose necessity in first 24 h post-operative with unwavering hemodynamic parameters and is also not associated with side effects like pruritus as observed in fentanyl group, hence can be an attractive alternative for being used as the adjuvant to bupivacaine in controlling post-operative pain.

Conclusion: The good post-operative analgesia is to produce a long lasting, continuous effective analgesia with minimum side effects. These requirements are fulfilled by the dexmedetomidine better as compared to fentanyl.

Key words: Adjuvant, Analgesia, Bupivacaine, Dexmedetomidine, Fentanyl

INTRODUCTION

Neural anesthesia is nowadays becoming popular because of its ease of practice and multiple advantages. However, the high failure rate of block, other side effects and lack of knowledge limits its acceptance. Various amendments have been done in the technique to curtail the undesirable events and increase the efficiency in a precise direction.[1] The addition of adjuvants such as fentanyl and dexmedetomidine to drugs like bupivacaine is one of the alterations, which can improve the outcome.[2]

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The blockage of opioid receptors in the spinal cord plays an important role in improving perioperative analgesia. Along with this, the identification of these receptors has also reduced the other supraspinal side effects of systemic steroids such as sedation and respiratory depression.[2]

The opioids which have a rapid mode of onset, slow and steady clearance from cerebrospinal fluid and decreased the

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risk of delayed side effects such as respiratory depression are preferred. Thus lipophilic opioids are more ideal to be used intrathecally as compared to morphine.[3] Various studies[2,4,5] suggest that when the anesthetic drugs such as lidocaine or bupivacaine are given along with the adjuvant fentanyl (15-25 mcg), the drastic improvement is seen in the quality of intra as well as post-operative blocks. However, some studies[1,3] suggest that although fentanyl is one of the most beneficial spinal anesthesia adjuvants, but it is associated with certain side effects such as nausea, pruritus, and retention of urine.

In recent literature,[6] some other drugs such as clonidine and alpha-2 agonist-like dexmedetomidine are becoming popular as adjuvants for spinal anesthesia. These drugs have good sedative, analgesic, and hemodynamic stabilizing property with fewer side effects. They are being used in veterinary anesthesia for several years. Recent literature[5,7] suggests that dexmedetomidine is more specific alpha-2 adrenoceptor agonist with almost eight times more empathy for alpha-2 adrenoceptor as compared to clonidine. Dexmedetomidine has 1:1620 ratio for alpha-2 receptor binding selectivity as paralleled to 1:220 for clonidine. Besides this, this drug also provides good quality intra and post-operative analgesia, stable hemodynamic parameters and nominal side effects. So, this drug can also be considered as adjuvant in spinal anesthesia in humans.

The aim of the present study was to compare the effect of intrathecal fentanyl and dexmedetomidine as the adjuvant to hyperbaric bupivacaine in the patients admitted for lower abdominal surgeries. The important parameters such as the onset of sensory blockade, duration of analgesic effect, dose requirement in first 24 h after surgery, and various side effects of the drug will help in comparing the two drugs.

MATERIALS AND METHODS

It is an observational study which is randomized and prospective. The study was conducted in the Department of Anesthesiology at Teerthanker Mahaveer Medical College, Moradabad from August 2015 to January 2016. The written consent was taken from all the patients, and the study was passed through the Ethical Committee. The sample size was 100 including males and females which were admitted for elective lower abdominal surgeries under spinal anesthesia. The age group ranged from 20 to 50 years. The patients of body weight more than 100 kg, height <140 cm, having any cardiac or respiratory abnormalities, taking medications such as alpha 2 receptor antagonists, calcium channel blocker, and angiotensin converting enzyme inhibitors, allergic to drug, having psychiatric illness or neurological disorder were excluded from the study. The patients were randomized and divided into two groups each containing 50 members. In Group 1 (n = 50), 2.5 mL of 0.5% hyperbaric bupivacaine was given along with 25 μg fentanyl intrathecally. In Group 2 (n = 50), 5 μg dexmedetomidine (dexmedetomidine 100 μg/mL was diluted in 10 ml of normal saline) was added to 2.5 mL of 0.5% hyperbaric bupivacaine and given intrathecally. Pre-anesthetic check-up of the patients was done to assess respiratory tract and spine. Other investigations such as complete hemogram, blood grouping, urine microscopy, blood urea, creatinine, electrocardiogram (ECG), and chest X-ray were done.

In the pre-operative preparation, the patient was kept nil per orally for 6 h before surgery Tablet alprazolam 0.5 mg and tablet ranitidine 150 mg were given in night before surgery. 500 ml of Ringer lactate solution was preloaded intravenously half an hour before the surgery. Preoperatively, all the vitals were recorded.

Proper sterilization was maintained. The patient in lateral decubitus was positioned, and the skin was cleaned with the help of iodine, spirit and was draped properly. A 25 G Quincke spinal needle was introduced into the L2-L3 or L3-L4 intervertebral space until it enters the subarachnoid space which is confirmed by the dripping of cerebrospinal fluid. 2.5 ml of 0.5% hyperbaric bupivacaine with 0.5 ml (25 μg) of fentanyl or 2.5 ml of 0.5% hyperbaric bupivacaine with 0.5 ml (5 μg) of dexmedetomidine was injected in Groups 1 and 2, respectively, at the rate of 0.25 ml/s. The patient was turned supine after withdrawing the needle. 100% oxygen via face mask (at the rate of 4 L/min) was administered.

Hemodynamic checking was done by measuring various parameters such as heart rate (HR), systolic blood pressure (SBP) diastolic blood pressure, mean arterial pressure (MAP), ECG and SpO_2 intraoperatively and postoperatively.

Hypotension

The decrease in SBP more than 30% of baseline is defined as hypotension. The treatment includes giving intravenous fluids and if required injection mephentermine 6 mg.[8]

Bradycardia

The decrease in HR to 60/min is called as bradycardia. Injection atropine 0.6 mg IV is given to treat it.[8]

The following parameters were measured:

a. Onset of sensory blockade
b. Onset of motor blockade
c. Duration of analgesia
d. Side effects if present.

Onset of Sensory Blockade

It is the duration in between the time of injection and absence of sensation of pinprick at tenth thoracic level.[8]

Duration of Analgesia

It is defined as the interval in between the time of injection and rescue analgesic in the post-operative period.[8]

Duration of Sensory Blockade

It is defined as the duration between the time of injection and the presence of sensations at S1 dermatome.[8]

Duration of Motor Blockade

It is defined as time duration in between the time of injection and complete recovery of motor functions.[8]

All the side effects intra and postoperatively were recorded. The vitals (pulse, blood pressure, respiratory rate, and oxygen saturation) were recorded. After evaluating the sensory and motor functions clinically, the patient was transferred to post-operative room.

RESULTS

The least age in Group 1 is 20 years and in Group 2 is 21 years. 50 years are the maximum age in both the groups. The mean age in Group 1 and 2 are 38.74 ± 10.6 and 37.17 ± 10.8 years, respectively. There is no statistical difference between the two ($P > 0.05$).

The mean time of sensory blockade onset in Group 1 is 1.88 ± 0.62 min while in Group 2 is 1.71 ± 0.61 min. There is no statistical significance between Group 1 and Group 2 regarding mean time taken for onset of sensory blockade, with $P = 0.170$ ($P > 0.05$) (Table 1).

The mean duration of analgesia is 172.64 ± 16.2 min in Group 1 and 285.35 ± 32.6 min in Group 2. There is a statistically highly significant difference between Group 1 and Group 2 ($P < 0.05$) (Table 2).

In the Group 1, the basal value of mean HR is 78 ± 7.01 bpm and we observed a decrease in mean HR which is maximum of 6 bpm from basal value at 50th min, whereas in the Group 2 the basal value of mean HR is 78 ± 7.2 bpm and we observed a decrease in mean HR which is maximum of 7 bpm from basal value at 60th min. The greater decrease in mean HR is seen in Group 2, but there is no statistically significant difference between the two groups (Table 3).

In the Group 1, the basal value of mean MAP is 96.68 ± 2.76 mmHg, and we detected a drop in MAP, which is maximum of 9.99 mmHg from mean basal MAP at 20th min. In the Group 2, the basal value of mean MAP is 96.56 ± 2.88 mmHg, and we found a reduction in MAP, which is maximum of 13.34 mmHg from mean basal MAP at 20th min. The mean MAP from basal to 20th min recording is statistically not significant between the two groups. The mean MAP from 20th to 60th min recording is statistically highly significant between Groups 1 and 2 (Table 4).

Table 1: Time taken for onset of sensory blockade (min)

Group	Mean±SD	Maximum	Minimum
1	1.88±0.62	3	1
2	1.71±0.61	3	1

SD: Standard deviation

Table 2: Duration of analgesia in both the groups (min)

Group	Mean±SD	Maximum	Minimum
1	172.64±16.2	205	140
2	285.35±32.6	410	260

SD: Standard deviation

Table 3: Mean HR (beats per min) in two groups at various intervals

HR (min)	Group	Mean±SD	*P* value	Significance
Basal	1	78±7.01	1.0	Not significant
	2	78±7.2		
5	1	80±6.84	1.0	Not significant
	2	80±6.55		
10	1	78±7.3	0.171	Not significant
	2	76±7.21		
15	1	77±7.16	0.487	Not significant
	2	76±7.2		
20	1	76±7.8	0.192	Not significant
	2	74±7.45		
30	1	76±6.86	0.133	Not significant
	2	74±6.34		
40	1	74±5.28	0.572	Not significant
	2	72±5.11		
50	1	72±6.95	1.0	Not significant
	2	72±6.78		
60	1	72±7.19	0.488	Not significant
	2	71±7.2		
90	1	74±5.7	0.399	Not significant
	2	73±6.1		
120	1	76±7.27	0.167	Not significant
	2	74±7.12		

HR: Heart rate, SD: Standard deviation

Table 4: MAP (mmHg) in two groups at various intervals

MAP (min)	Group	Mean±SD	*P* value	Significance
Basal	1	96.68±2.76	0.832	Not significant
	2	96.56±2.88		
5	1	94.62±3.12	0.143	Not significant
	2	93.64±3.52		
10	1	88.54±4.11	0.455	Not significant
	2	87.92±4.16		
15	1	90.68±2.98	0.55	Not significant
	2	91.00±2.32		
20	1	86.69±3.75	<0.0001	Significant
	2	83.22±2.99		
30	1	91.00±3.94	0.004	Significant
	2	88.92±3.23		
40	1	92.45±4.94	<0.0001	Significant
	2	87.93±3.75		
50	1	91.79±2.42	<0.0001	Significant
	2	89.19±2.99		
60	1	92.85±3.1	<0.0001	Significant
	2	89.94±2.22		
90	1	94.79±5.1	0.361	Not significant
	2	93.88±4.82		
120	1	96.46±3.93	0.906	Not significant
	2	96.55±3.67		

MAP: Mean arterial pressure, SD: Standard deviation

In Group 1, 3 out of 50 and in Group 2, 5 out of 50 patients established hypotension which is statistically not significant ($P > 0.05$). Intravenous fluids and vasopressor were used to treat these patients (Figure 1).

In Group 1, 4 out of 50 and in Group 2, 6 out of 50 patients developed bradycardia which is statistically not significant ($P > 0.05$). A single dose of 0.6 mg of atropine was given to cure them (Figure 2).

In Group 1, 6 out of 50 patients, i.e., 18% of patients had developed pruritus, whereas in Group 2 pruritus was absent in all patients. There is a statistically highly significant difference in the incidence of pruritus between the two groups ($P < 0.05$) (Figure 3).

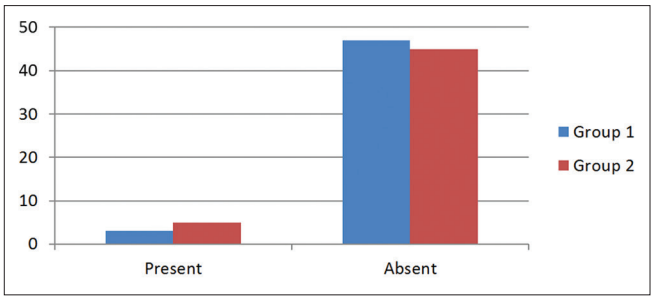

Figure 1: Incidence of hypotension in two groups

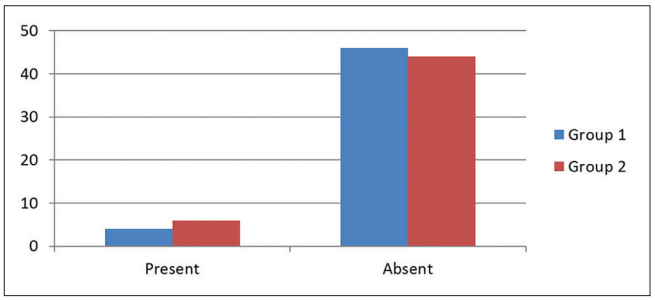

Figure 2: Incidence of bradycardia in two groups

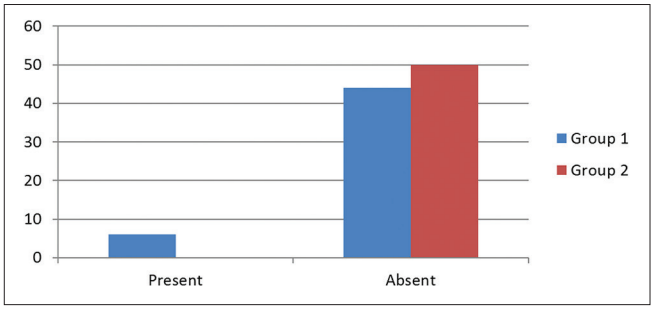

Figure 3: Incidence of pruritus in two groups

DISCUSSION

The good post-operative analgesia is the basic requirement of any surgical intervention. Ideally, the post-operative analgesia should be continuous, long lasting, and with least adverse effects. Nowadays in India, the most commonly used intrathecal local anesthetics are lignocaine and bupivacaine. The post-operative analgesia action of these drugs is limited. Continuous epidural analgesia is used in some places for prolonging the duration of analgesia, but this method is costly and technically difficult. Thus, local anesthetics additives prove to be a better and cheaper method of prolonging analgesic effect.[9]

The most commonly used drugs for this purpose are opioids like fentanyl, which is a lipophilic receptor agonist. Fentanyl blocks the opioid receptors present in the dorsal horn of spinal cord.[10]

Dexmedetomidine is an adrenergic-2 receptor agonist which has been recently approved by the FDA in 1999 for analgesia in humans. The mechanism of action of sensory and motor blockade of alpha-2 adrenoceptors is not clear. They bind to the presynaptic C fibers and decrease the release of C-fiber transmitters. Intrathecal 2-receptor agonists have been found to have antinociceptive action for both somatic and visceral pain.[8]

This study was conducted to weigh and relate the effects of adding fentanyl versus dexmedetomidine with intrathecal hyperbaric 0.5% bupivacaine in elective lower abdominal surgeries. In the study, it was hypothesized that intrathecal bupivacaine and dexmedetomidine mixture provides

prolonged sensory blockade and better analgesia than the intrathecal bupivacaine and fentanyl.

In regard to onset of sensory blockade, no statistically significant difference was found in between fentanyl group and the dexmedetomidine group. The mean duration of analgesia in our study is 172.64 ± 16.2 min in Group 1 (fentanyl) and 285.35 ± 32.6 min in Group 2 (dexmedetomidine group). There is a statistically highly significant difference between the two groups. ($P < 0.05$) In studies conducted by Tarbeeh *et al*.,[11] Gupta *et al*.,[9] and Eid and Shafie[10] authors observed that mean duration of analgesia is more in dexmedetomidine as compared to fentanyl.

In the Group 1, the basal value of mean MAP is 96.68 ± 2.76 mmHg, and we detected a drop in MAP, which is maximum of 9.99 mmHg from mean basal MAP at 20th min. In the Group 2, the basal value of mean MAP is 96.56 ± 2.88 mmHg, and we found a reduction in MAP, which is maximum of 13.34 mmHg from mean basal MAP at 20th min. The MAP from basal to 20th min recording is statistically not significant between the two groups. However, the mean MAP from 20th to 60th min recording is statistically highly significant between Groups 1 and 2. In a study piloted by Tarbeeh *et al*.,[11] authors witnessed no significant difference between the two groups in MAP at 120 min but significantly lower when equated with the basal values, which coincides with our study outcomes.

The greater decrease in mean HR was seen in Group 2, but there is no statistically significant difference between the two groups (1 and 2). Similar findings were also witnessed by other studies such as Al-Ghanem *et al*.,[12] and Tarbeeh *et al*.[11] who found no significant difference in mean value of HR throughout the intraoperative and post-operative period.

In a study conducted by Al-Ghanem *et al*.,[12] authors observed that the hypotension was present in only 10.5% of patients in fentanyl group, whereas this percentage was 23.7% in fentanyl group, but it did not reach a significant difference. Similarly, Tarbeeh *et al*.[11] observed 15% incidence of hypotension in both the groups. In our study, the incidence of hypotension was three out of 50 (6%) in Group 1 and in Group 2, 5 out of 50 patients (10%) established hypotension which is statistically not significant ($P > 0.05$).

In our study, none of the patients developed other side effects such as nausea, vomiting, and respiratory depression. Other complaints such as backache, pain in buttock or leg, and any neurological deficit were also not reported.

Pruritus in fentanyl group is a common side effect, although it is mild in nature and requires no treatment.[13] A study was conducted on spinal anesthesia for ambulatory knee arthroscopy in which the combination of bupivacaine with fentanyl was used resulting in pruritus ranging from 48 to 75% compared with the group getting only bupivacaine.[14] Ackerman *et al*.[15] have also reported that opioids that stimulated-receptors following epidural administration exhibited significantly less pruritus than pure-receptor opioids administered similarly.

CONCLUSION

The combination of dexmedetomidine (5 g) and 0.5% bupivacaine, prolongs the duration of analgesia, decreases total analgesic dose necessity in first 24 h post-operative with unwavering hemodynamic parameters and is also not associated with side effects like pruritus as observed in fentanyl group, hence can be an attractive alternative for being used as an adjuvant to bupivacaine in controlling post-operative pain.

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