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Research Article

Comparison of Fentanyl and Nalbuphine as an Adjuvant to Bupivacaine for Spinal Anesthesia in Lower Limb Surgeries

Imran Mehdi, Mohd Sameer Ahmad*, Madhulika Dubey, Danish Ahmad, Surendra Singh, Mohammad Tanweeruddin

Department of Anaesthesiology& Critical care, Era's Lucknow Medical College, ECR Hospital Danapur, Lucknow, India.

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ABSTRACT

Background: Opioids commonly used as adjuvant anaesthetics during spinal anesthesia, are favored technique for lower limb surgeries. Nalbuphine is an opioid adjuvant that acts as antagonist at μ-receptors and agonist at k-receptors that work reasonably potent analgesia. In this study we compare the efficacy of epidural Fentanyl with bupivacaine versus Epidural Nalbuphine with Bupivacaine for post-operative pain relief in lower limb surgeries.

Methods: Altogether 80 patients of lower limb surgeries were randomly allocated into two groups. 40 patients in Group I (Inj. 0.5% Bupivacaine (H) 2.5ml + Inj. Fentanyl 25mcg (0.5ml) and 40 patients in Group II (Inj. 0.5% Bupivacaine (H) 2.5ml+ Inj. Nalbuphine 5mg (0.5ml). Age of patients ranged from 18-65 years of age and male:female ratio in the present study was 1: 0.5. Patients in both the above groups were comparable on age, gender, anthropometric variables, and baseline hemodynamic variables.

Results: In the study the mean age (36.30±14.10) of group II was comparatively more than the group I (33.88±9.42) while the mean weight (61.80±11.33) of group II was also comparatively more than group I mean weight (53.80±15.59). And the mean value of duration of surgery for the group I was (112.93±12.22) while it was (110.63±10.26) for group II. A significant difference was found in weight. The intergroup comparison of level of motor blockade where in group I the level of motor blockade was (65.0%) at 2 min (B/S-1) while in group II level of blockade (70.0%) at 2 min (B/S-1) after that from 8 min to 130 min it was (100%). The level of sensory blockade of group I (72.5%) at 2 min while it was (72.5%) at 6 min after that it was NA from 8 min to 130 min and in the group II level of sensory blockade (50.0%) at 2 min and (50.0%) at 8 min after that it was (100%) from 10 min to 130 min. During Intergroup Comparison of VAS significant differences was found at 30 min and 480 min.

Conclusion: Nalbuphine when compared to Fentanyl is almost safe and hemodynamically stable drug that can be used as an adjuvant in combined spinal epidural anesthesia with similar safety profile as for Fentanyl.

For pain relief opioids are commonly used as adjuvant to local anaesthetics [1]. Fentanyl is a narcotic analgesic with a potency of at least 80 times that of morphine, and its action is rapid during intrathecal administration. It has wider therapeutic index and duration of action of several hours as patients develop tolerance to opioids. It crosses the blood brain barrier easily due to lipid solubility as compared to morphine and it is fastly eliminated from cerebrospinal fluid [2]. Fentanyl causes dense blockade with complete intra- and postoperative analgesia without causing hemodynamic

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*Corresponding author.
E-mail address: msahmad4743@gmail.com

instability. It has very well tolerated by the patients and relatively least side effects.

Nalbuphine an agonist-antagonist opioid which is structurally similar to oxymorphone and naloxone it binds to μ-receptors as well as to κ- and δreceptors acting as antagonist at the μ-receptor and an agonist at the κ-receptor and used clinically primarily in postoperative pain therapy administered as a bolus, continuous infusion and patient-controlled analgesia [3]. Nalbuphine has been used intrathecally to enhance the postoperative analgesia and they did not show any evidence of neurotoxicity [4].

Many opioid come under Narcotics Act such as morphine, fentanyl, and other μ-opioids, so they are not easily available in many hospitals in India, while nalbuphine is available easily and devoid of side effects such as nausea, vomiting, pruritus, and respiratory depression. My aim of the study is to compare the efficacy of Fentanyl and Nalbuphine as an adjuvant to bupivacaine for spinal anesthesia in lower limb surgeries.

Methods

Institutional Ethical Committee and written informed consent was obtained for this prospective randomized double-blind study which was conducted at Department of Anesthesiology, Era's Lucknow Medical College, India, on 80 patients of American Society of Anesthesiologist (ASA) physical status I and II of both genders aged 18-65 years and male:female ratio 1: 0.5 scheduled for elective surgery of lower limbs under SAB. After institution of test dose (3ml inj. Lidocaine 0.2 & with adrenaline), two group were selected using computer generated randomization tool. Group-I: Inj. 0.5% Bupivacaine (H) 2.5ml + Inj. Fentanyl 25mcg (0.5ml) Group-II: Inj. 0.5% Bupivacaine (H) 2.5ml+ Inj. Nalbuphine 5mg (0.5ml) at baseline (T0) immediately after study drug is given (T1), every 5 minutes and then every 15 minutes thereafter till end of surgery hemodynamic parameters were recorded and postoperatively till demand of first rescue analgesic. After completion of surgery, the patients were shifted to post-operative ward, hemodynamic parameters and duration of analgesic was recorded in post-operative period at every 30-minute interval. Pain was assessed by using 10 pain Visual Scale (VAS) in which "No Pain" for "0" and Score of "10" "Worst Pain Imaginable". Duration of analgesic was recorded as first complain of pain (VAS>4) in the post-Operative period and rescue analgesic were administered. Rescue analgesic as 10 ml 0.25% Bupivacaine was administered at onset of pain (VAS>4) in Post-Operative period and at each incidence of complaint of pain (VAS>4) in next 24 hours. Hemodynamic parameters of systolic blood pressure (SBP) and Diastolic Blood Pressure and peripheral oxygen saturation (SpO 2) were recorded just after spinal injection, then at every 5 min till the end of surgery.

Results

Total 80 patients were considered for the study and the mean age (36.30±14.10) of group II was comparatively more than the group I (33.88±9.42) while the mean weight (61.80±11.33) of group II was also comparatively more than group I mean weight (53.80±15.59). And the mean value of duration of surgery for the group I was (112.93±12.22) while it was (110.63±10.26) for group II. A significant difference was found in weight (Table 1).

The mean of the pulse rate for Group I at 6 min was (75.90±4.66) which gradually decreased and reached a minimum mean value of (58.18±4.60) at 130 min and in the Group II the mean pulse rate was (74.90 ±8.21) at 6 min which after a little fluctuations reached to a minimum mean value (67.28±5.23) at 130 min (Figure 1). A highly significant difference was found after 85 min to 130 min.

Figure1- Intergroup Comparison of Pulse Rate

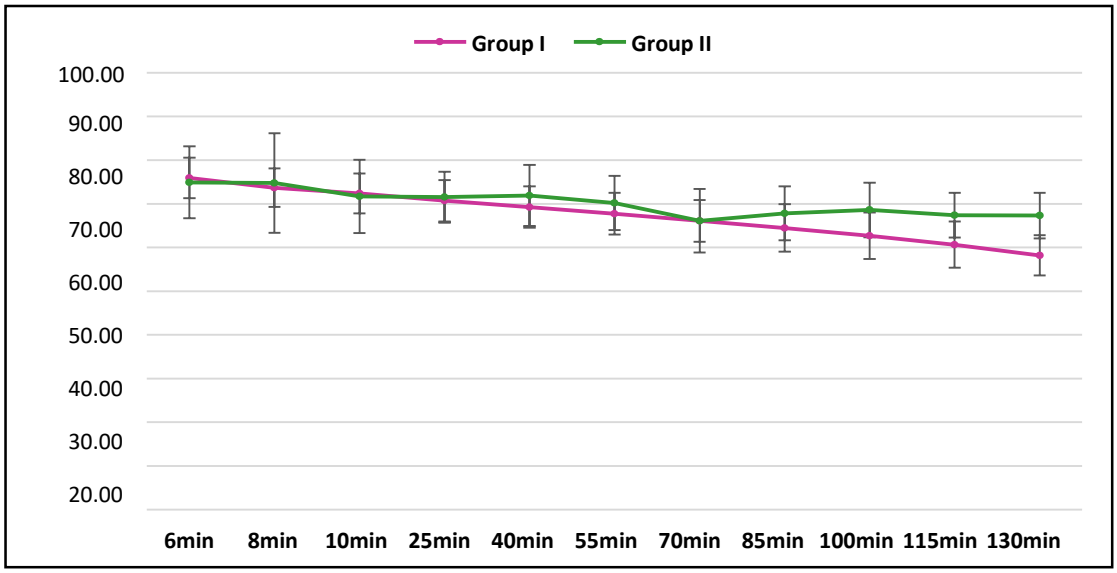
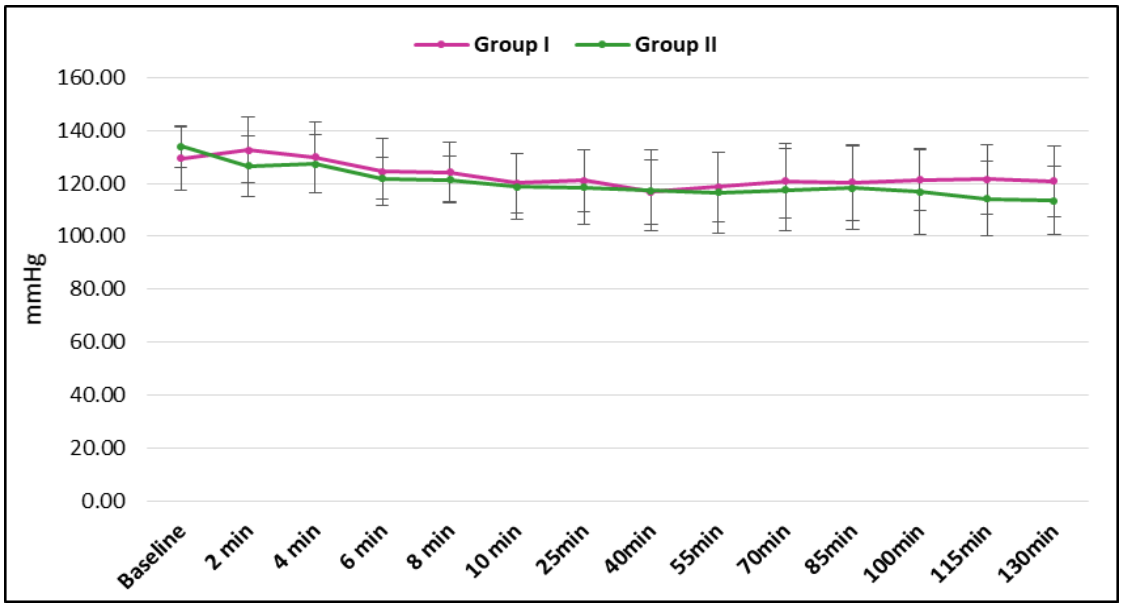


Table 1- Demographic parameter of patients

Group	Group I Mean	SD	Group II Mean	SD	T value	P value
Age	33.88	9.42	36.30	14.10	-0.90	0.369
Weight	53.80	15.59	61.80	11.33	-2.63	0.010
Duration of surgery(Min)	112.93	12.22	110.63	10.26	0.91	0.365

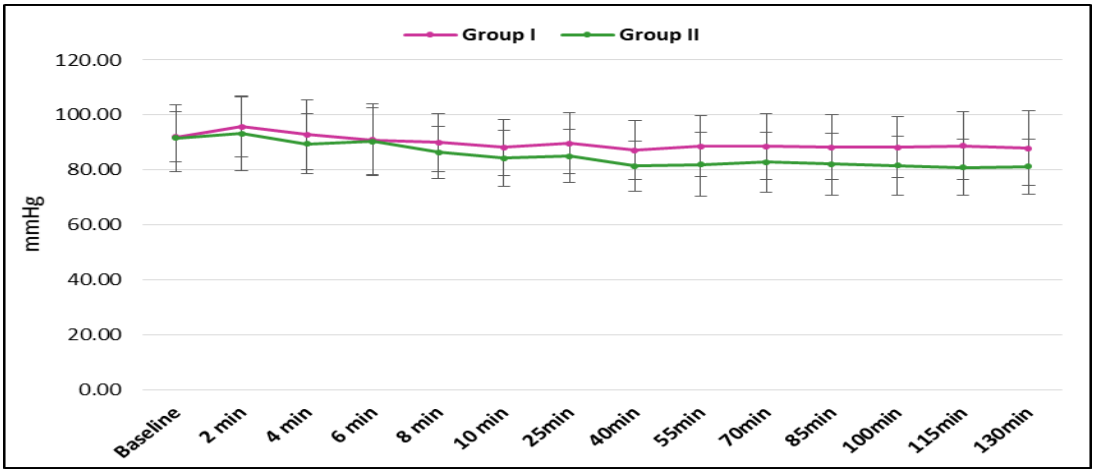
The mean value of Systolic Blood Pressure (SBP) in group I was found (129.4±11.87) at baseline while it was (132.63±12.55) at 2 min after that with fluctuations it reached (120.85±13.41) while in group II the mean value of SBP was (133.88±8.07) at baseline it decreased and reached (126.55±11.42) at 2 min and again it started to decrease and reached a minimum mean value (113.55±13.04) at 130 min. Significant differences was found after 115 min to 130 min.

Figure 2- Intergroup Comparison of Systolic Blood Pressure



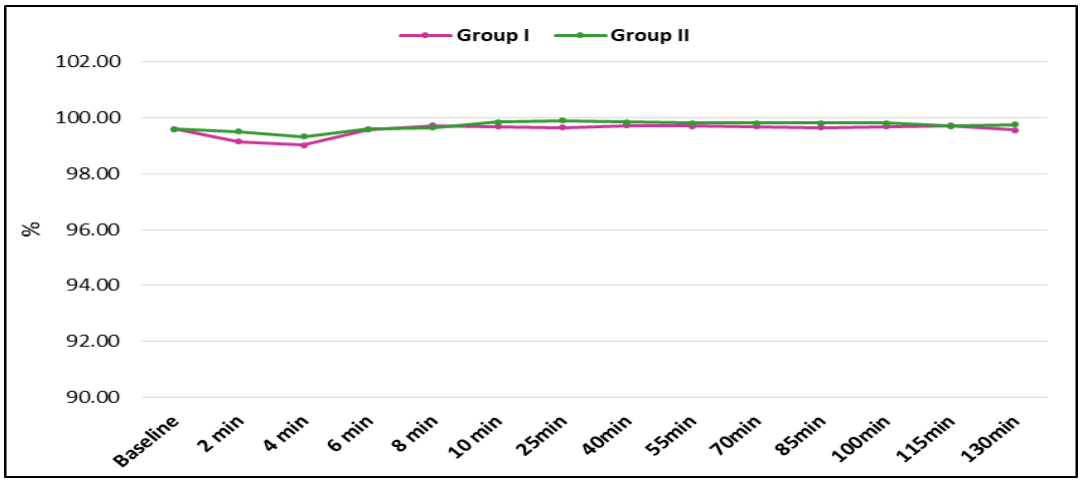
The mean value of group I of Diastolic Blood Pressure (DBP) (92.05±9.17) at baseline and it increased and reached (95.73±11.09) at 2 min and again it started decreasing and reached a minimum value (87.93±13.50) at 130 min and in group II the mean value of DBP (91.53±12.27) at baseline and after the fluctuations it reached to (81.18±10.10) at 130 min. Significant differences were found from 25 min to 130 min.

Figure 3- Intergroup Comparison of Diastolic Blood Pressure



The mean value of SPO2 (99.60±0.71) at baseline of group I and after minor fluctuations it reached a mean value (99.55±0.93) at 130 min and in the group II the mean value of SPO2 (99.60±0.74) at baseline and after fluctuation it also reached a mean value of (99.75±0.63) at 130 min (Figure 4). No significant difference was found at any point.

Figure 4- Mean value of SPO2 in group I and Group II



The level of sensory blockade of group I (72.5%) at 2 min while it was (72.5%) at 6 min and in the group II level of sensory blockade (50.0%) at 2 min and (50.0%) at 8 min after that it was (100%) from 10 min to 130 min (Table 2).

Table 2- shows the intergroup comparison of sensory blockade

Level of Sensory Blockade		Group I		Group II		chi sq	P value
		No.	%	No.	%		
2 min	T10	11	27.5%	20	50.0%	34.55	<0.001
	T12	0	0.0%	15	37.5%		
	T8	29	72.5%	5	12.5%		
4 min	T10	0	0.0%	15	37.5%	22.34	<0.001
	T12	0	0.0%	1	2.5%		
	T6	16	40.0%	5	12.5%		
	T8	24	60.0%	19	47.5%		
6 min	T4	11	27.5%	7	17.5%	20.02	<0.001
	T6	29	72.5%	17	42.5%		
	T8	0	0.0%	16	40.0%		
8 min	T4	40	100.0%	20	50.0%	26.67	<0.001
	T6	0	0.0%	20	50.0%		
10 min	T4	40	100.0%	40	100.0%	NA	NA
25 min	T4	40	100.0%	40	100.0%	NA	NA
40 min	T4	40	100.0%	40	100.0%	NA	NA
55 min	T4	40	100.0%	40	100.0%	NA	NA
70 min	T4	40	100.0%	40	100.0%	NA	NA
85 min	T4	40	100.0%	40	100.0%	NA	NA
100 min	T4	40	100.0%	40	100.0%	NA	NA
115 min	T4	40	100.0%	40	100.0%	NA	NA
130 min	T4	40	100.0%	40	100.0%	NA	NA

The intergroup comparison of level of motor blockade where in group I the level of motor blockade was (65.0%) at 2 min (B/S- 1) while in group II level of blockade (70.0%) at 2 min (B/S-1) after that from 8 min to 130 min it was (100%). No significant differences were found at any point (Table 3).

Table 3- intergroup comparison of level of motor blockade

Level of Motor Blockade		Group I		Group II		chi sq	P value
		No.	%	No.	%		
	B/S-0	14	35.0%	12	30.0%		
2 min	B/S-1	26	65.0%	28	70.0%	0.23	0.633
	B/S-1	14	35.0%	12	30.0%		
4 min	B/S-2	26	65.0%	28	70.0%	0.23	0.633
	B/S-2	14	35.0%	12	30.0%		
6 min	B/S-3	26	65.0%	28	70.0%	0.23	0.633
8 min	B/S-3	40	100.0%	40	100.0%	NA	NA
10 min	B/S-3	40	100.0%	40	100.0%	NA	NA
25min	B/S-3	40	100.0%	40	100.0%	NA	NA
40min	B/S-3	40	100.0%	40	100.0%	NA	NA
55min	B/S-3	40	100.0%	40	100.0%	NA	NA
70min	B/S-3	40	100.0%	40	100.0%	NA	NA
85min	B/S-3	40	100.0%	40	100.0%	NA	NA
100min	B/S-3	40	100.0%	40	100.0%	NA	NA
115min	B/S-3	40	100.0%	40	100.0%	NA	NA
130min	B/S-3	40	100.0%	40	100.0%	NA	NA

The duration of analgesia was (2.38±1.27) at 720 min in group I while in group II (2.45±1.52) at 720 min with statistically significant difference (P = 0.002) at 480 min.

Table 4- Intergroup Comparison of VAS

	Group I		Group II		Mann Whitney Test	
VAS	Mean	SD	Mean	SD	Z value	P value
0 min	1.00	0.00	1.00	0.00	0.00	1.000
30 min	1.10	0.31	1.00	0.00	-2.07	0.039
60 min	1.25	0.44	1.38	0.49	-1.20	0.231
90 min	1.85	0.43	1.83	0.38	-0.23	0.815
120 min	2.23	0.53	2.30	0.69	-0.33	0.739
240 min	2.68	0.86	2.73	0.88	-0.53	0.597
360 min	2.83	1.22	2.78	0.66	-0.41	0.679
480 min	2.38	1.21	3.10	0.93	-3.06	0.002
600 min	2.53	1.13	2.45	1.34	-0.47	0.639
720 min	2.38	1.27	2.45	1.52	-0.12	0.905

Discussion

Spinal analgesia with opiates as adjuvants are added to increase the duration of intraoperative and postoperative analgesia [5], but there is always a possibility of an increased incidence of urinary retention, purities, nausea, respiratory depression and vomiting. The likely cause of pruritus with spinal opioids is cephalad migration of opioids in CSF, and subsequent interaction of opioids receptors in trigeminal nucleus. Opioids release histamine from mast cells can be another reason of pruritus [6].

Our results established the well-known fact that intrathecal nalbuphine is an effective adjunct. In our study we used 3ml given intrathecal in both groups of fentanyl and nalbuphine i.e. Inj. 0.5%Bupivacaine (H) 2.5ml + Inj. Fentanyl 25mcg (0.5ml) and Inj. 0.5%Bupivacaine (H) 2.5ml+ Inj. Nalbuphine 5mg (0.5ml), which compatably with the studies of Prabhakaraiah et al. (2017) [7] on Comparison of Nalbuphine Hydrochloride and Fentanyl as an Adjuvant to Bupivacaine for Spinal Anesthesia in Lower Abdominal Surgeries with similar dosage.

In our study mean age of patients was (33.88+9.42) as compared to patients of both groups which was similar to the study by Bajwa et al. (2011) [8] reported the mean age of patients in their series 38.68 and 34.06 years respectively for the two study groups and the males proportion from group I & group II were (65.0%, 70.0% respectively) while females from group I & group II (35.0%, 30.0%) respectively with no significant p value, which was also evident in study by Kelly[9] who compared 90 patients age group 20-50 years of age with no significant difference found in gender ratio.

Patients were evaluated for haemodynamic changes, sensory and motor block, and early requirement of post-

operative analgesia. In present study, duration of surgery ranged from 110 to 120mins.The value of duration was 112.93±12.22 in group I and Group II was (110.63±10.26). Statistically, there was no significant difference between the two groups with respect to duration of surgery. The two groups were found to have haemodynamic differences in pulse and blood pressure recordings of both systolic and diastolic during the study except for SPO2.

The pulse rate of Group I at 6 min was (75.90±4.66) which gradually decreased and reached a minimum value of (58.18±4.60) at 130 min and in the Group II the mean pulse rate was (74.90 ±8.21) at 6 min which after a little fluctuations reached to a minimum value (67.28±5.23) at 130 min. A highly significant difference was found after 85 min to 130 min.

In present study, systolic blood pressure was found to be statistically significant between groups, except at 100 and 130 min follow-up intervals, the value was significantly lower in nalbuphine as compared to fentanyl group. During the study period, Nalbuphine group showed a reduction ranging from standard deviation (SD) of 11.42 (2min) to 15.93 (100min) whereas Fentanyl group showed a reduction in SD ranging from 12.55 (2min) to 11.74% (100min) significant differences were observed after 115 min to 130 min.

For diastolic blood pressure the difference between two groups was found to be significant from 25 min to 130 min. At most of the time intervals, the reduction in blood pressure did not exceed 20% cut-off levels soconsidered as hypotension in the present study. Hypotension or bradycardias have rarely been reported in different studies reviewed by us. Similar observations pertaining to hemodynamic changes is observed by Naaz S. et al (2017) [10]. None of the studies in this review reports of any hemodynamic side effect which might result into a hemodynamic emergency.

In this present study, both the groups have maximum block level of T6-T7. Time taken to achieve maximum block level was 8.23±1.43 min in fentanyl group and 7.53±1.85 min in nalbuphine group. Statistically, no significant difference was found in the study, similar findings are reported by Manuar MB et al (2014) [11] who compared intrathecal bupivacaine with either dexmedetomidnie or clonidine in 90 patients of age 20-50 years ASA grade 1 and II undergoing lower limb orthopaedic surgery, they found mean time for onset of sensory block at shin of tibia and onset of motor block were comparable. The study of efficacy in both the groups in this study and the results pertaining to time of surgery, duration of anaesthesia, post–operative analgesia are in accordance with Bindra TK [12] who studied on Postoperative Analgesia with Intrathecal Nalbuphine versus Intrathecal Fentanyl in Cesarean Section. Requirement of Rescue analgesics and Visual analogue scores (VAS) were significantly low in Nalbuphine than Fentanyl, similar to the study done by Tiwari and Tomar [13]. Similar findings were reported by Chatrath V et al. [14], wherein the duration of analgesia among those who received Nalbuphine was 380 minutes. Similarly, in another study done by Verma D et al [15], the duration of analgesia was longer with Nalbuphine, lasting for 378 minutes, similar to our study findings.

Conclusion

Nalbuphine is a potent alternative that can be used in place of fentanyl as an opioid with less incidences of respiratory depression, the side effects were minimum and hemodynamic stability was maintained for both adjuvants.

With other opioids comparative study is required and beta-2 adrenergic drugs are also recommended to find out the suitable drug-dose combination with a better and safe analgesic profile.

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