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Comparative Study of Dexmedetomidine versus Fentanyl as Adjuvant to Bupivacaine Spinal Anesthesia in Cesarean Section

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ORIGINAL ARTICLE

Comparative Study Of Dexmedetomidine Versus Fentanyl As Adjuvants To Bupivacaine Spinal Anesthesia In A Cesarean Section

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Abstract

Background: **Spinal anesthesia is considered the first choice for cesarean sections owing to its deep sensory block as well as fewer side effects on the mother and the fetus. Despite many benefits of this method, it has a short duration and cannot provide sufficient postoperative analgesia.**

Objective: **The aim was to compare the efficacy of dexmedetomidine versus fentanyl as adjuvant to pubivacaine spinal anesthesia in a cesarean section.**

Patients and methods: **The current study was conducted on a total of 90 females who had undergone cesarean sections. They were further subdivided into three groups ($n = 30$). Group B comprised 30 patients where bupivacaine alone was injected. Group BF included patients who were injected by fentanyl with bupivacaine and group BD included patients who were injected with dexmedetomidine with bupivacaine.**

Results: **No significant differences were recorded among the three studied groups concerning sociodemographic features as well as anthropometric measurements. Time to reach T10 and time to reach peak sensory block as well as time to reach peak motor block demonstrated insignificant differences among the three studied groups.**

Conclusion: **The use of dexmedtomidine as an adjuvant to bupivacaine in cesarean surgeries was demonstrated to be associated with better intraoperative and postoperative analgesia with minimal analgesic requirements without having significant side effects or hemodynamic alterations.**

Keywords: Bupivacaine, Cesarean section, Dexmedetomidine, Fentanyl

1. Introduction

Spinal anesthesia is commonly used in a cesarean section surgery. Apart from being economical and easy to administer, spinal anesthesia provides both analgesia and muscular relaxation with rapid onset of action.[1]

However, the administration of local anesthetics alone has a short duration of effect, and is insufficient for preventing visceral pain and nausea especially at an earlier stage.[2]

Visceral pain is common during spinal anesthesia with mini doses of local anesthetics. It is especially uncomfortable in a cesarean surgery as the surgeons need to lift the uterus and suture the peritoneal cavity during surgery. Moreover, there remains a lack of long-lasting postoperative analgesia. To overcome the defects of local anesthetics, joint administration of adjuvant drugs has become a widely accepted practice in clinical work.[3]

Adjuvant drugs added to the intrathecal bupivacaine can decrease the dose of local anesthetics and guarantee sensory and motor block. Intrathecal adjuvants include fentanyl and dexmedetomidine as receptor agonists, which have sedative, analgesic, perioperative sympatholytic, anesthetic-sparing, and hemodynamic-stabilizing properties.[4]

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Dexmedetomidine is a highly selective alpha-2-adrenergic agonist, which has been used as a premedication and as an adjuvant to general anesthesia. Dexmedetomidine has several beneficial actions during the perioperative period. It reduces opioids and inhalational anesthetic requirement and has been widely used for ICU sedation with hemodynamic stability.[5]

Fentanyl is a synthetic opioid with central action, which is used widely for pain control. Intrathecal fentanyl is usually added to other local anesthetics to increase anesthesia and analgesia. It has improved spinal anesthesia and reduced the anesthetic drug-related side effects including pruritus, nausea, and vomiting.[6]

Dexmedetomidine and fentanyl have been used as adjuvants to local anesthetics in different surgeries to provide superior analgesia and to improve the duration of the block.[7]

2. Objective

To compare the efficacy of dexmedetomidine versus fentanyl as adjuvants to bupivacaine spinal anesthesia in a cesarean section. The primary outcome was to assess the postoperative analgesia. Our secondary outcome was to assess hemodynamic changes.

2.1. Patients and methods

Study design: this was a prospective comparative study conducted on a total of 90 patients, who had undergone a cesarean section at the Anesthesiology and Intensive Care Department, Al-Azhar University Hospital.

Inclusion criteria: age: at the child-bearing period of about 18–40 years and women undergoing an elective cesarean section.

Sample size calculation was based on the mean duration of motor block in the B-D and B-F group retrieved from a previous research.[8] Using G*power, version 3.0.10 to calculate the sample size based on an effect side of 1.11, two-tailed test, α error = 0.05 and power 90.0% and then the total sample size will be 20 cases at least in each group.

Exclusion criteria: long history of opioid analgesic use or NSAIDs, psychiatric disorders, preoperative heart rate of less than 50 bpm with cardiac conduction or rhythm abnormalities and neuromuscular and endocrine diseases or allergic reactions to α2-adrenergic agonist.

A total of 90 patients were divided randomly into three groups: group BF: 30 patients who were injected with fentanyl 20 μg (0.4 ml) added to 0.5% bupivacaine heavy 2.4 ml.[9] Group BD: 30 patients who were coadministered dexmedetomidine (3 μg) with bupivacaine 2.4 ml.[10] Group B: 30 patients who were injected with 0.5% bupivacaine heavy 2.4 ml alone.[9]

Patient consent: our study was conducted according to the ethics committee, and informed written consent was obtained from all patients after full explanation of the procedures as well as its comorbidities.

Procedures: intravenous cannula was inserted into a peripheral vein. Standard intraoperative monitoring was used, consisting of ECG, pulse oximetry, and noninvasive arterial blood pressure; an intravenous infusion of lactated Ringer's solution 500 ml was administered. The spinal injection was performed with a 25-G pencil point needle, sensory block was evaluated every 5 min with a pinprick test, and the motor block was evaluated with the Bromage scale (0 = no motor loss, 1 = inability to flex the hip, 2 = inability to flex the knee, and 3 = inability to flex the ankle).

The following parameters were observed immediately after the administration of spinal block: maximum sensory level, time to maximum sensory level, duration of motor block (two lower limbs bromage score return to 0), patients NRS 6, 12 h after surgery, first rescue analgesia drug time when the patient start complaining of pain and signs of pain appear, for example, tachycardia and increase in respiratory rate, which were treated using analgesics such as paracetamol 1 g/6 h or pethidine 50 mg intramusclar, then 0.7 mg/kg every 6 h and the first anal aerofluxus time (the first anal aerofluxus time and anus exhausting time. It reflected the recovery time of gastrointestinal function recovery) and side effects include shivering, nausea and vomiting, hypotension, pruritus, etc.

2.2. Statistical analysis

Data were fed to the computer and analyzed using IBM SPSS Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. (IBM Corp., Armonk, New York, USA). Qualitative data were described using number and percent. Quantitative data were described using median (minimum and maximum) for nonparametric data and mean, SD for parametric data after testing normality using the Kolmogrov–Smirnov test. Significance of the obtained results was judged at the (0.05) level.

2.3. Data analysis

Qualitative data: χ^2 test for comparison of two or more groups.

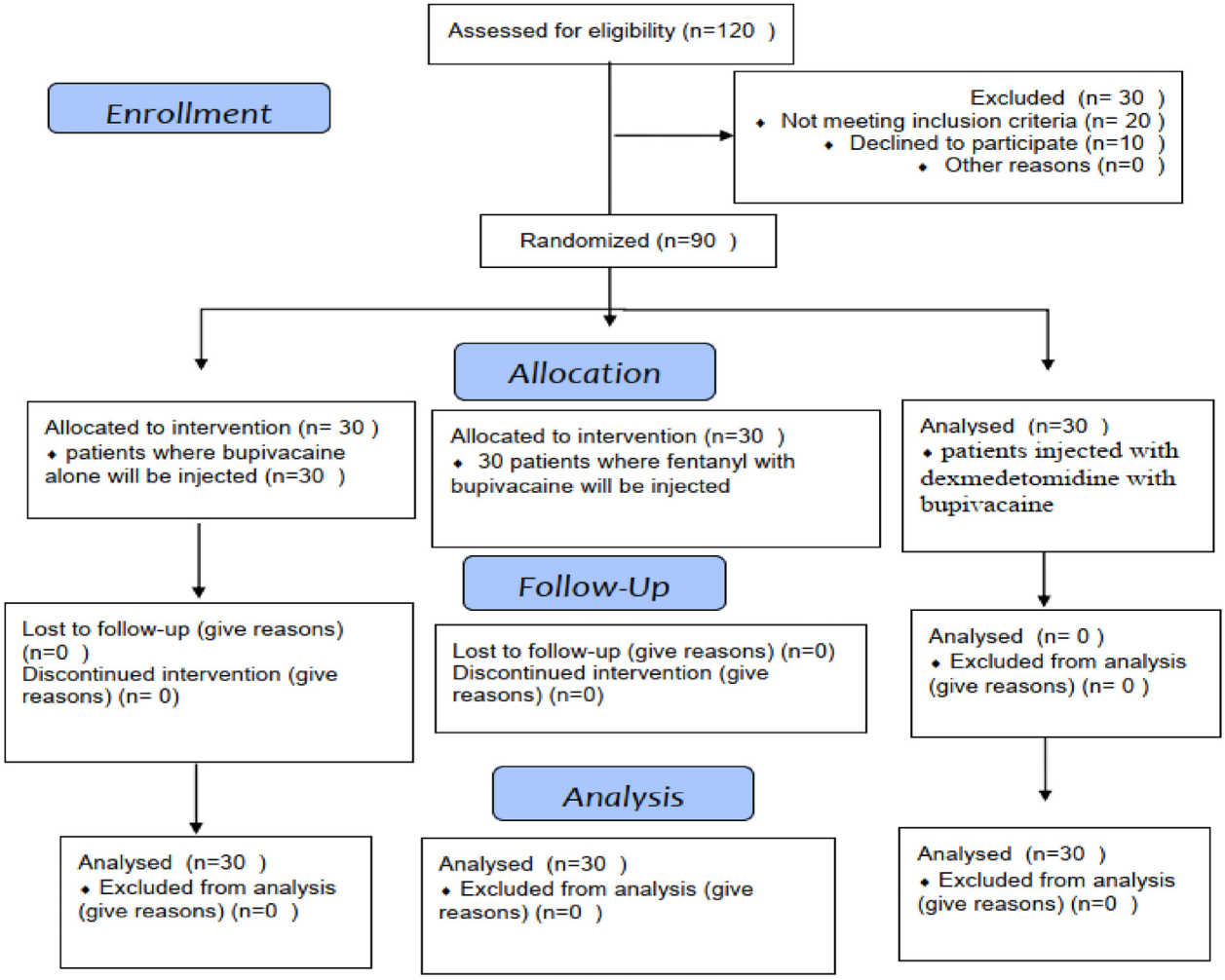

Fig. 1. Consort flow chart showing the study design.

Quantitative data between groups: parametric tests: one-way analysis of variance test was used to compare more than two independent groups with post-hoc Tukey test to detect pairwise comparison and nonparametric tests: Kruskal–Wallis test was used to compare more than two independent groups with Mann–Whitney *U* test to detect pairwise comparison.

3. Results

The current study was conducted on a total of 90 females who had undergone a cesarean section. They were further subdivided into three groups ($n = 30$). Group B comprised 30 patients where bupivacaine alone was injected; group BF in which patients were injected by fentanyl with bupivacaine;

Table 1. Comparison of age and body mass index between the studied groups.

	Group B	Group BF	Group BD	Test of significance	Within-group significance
Age (years) (mean ± SD)	30.97 ± 5.41	30.87 ± 5.65	29.77 ± 5.08	$F = 0.458$ $P = 0.634$	$P1 = 0.943$ $P2 = 0.391$ $P3 = 0.431$
BMI (kg/m^2) (mean ± SD)	30.58 ± 4.22	29.1 ± 3.67	31.14 ± 4.89	$F = 1.82$ $P = 0.1668$	$P1 = 0.184$ $P2 = 0.613$ $P3 = 0.07$

F, one-way analysis of variance test.
*P*1: difference between group B and group BF.
*P*2: difference between group B and BD.
*P*3: difference between group BF and BD.

Table 2. Characteristics of spinal block in the studied groups.

	Group B	Group BF	Group BD	Test of significance	Within group significance
Time to reach T 10 (min) (mean ± SD)	5.08 ± 0.31	5.02 ± 0.38	4.92 ± 0.26	$F = 1.86$ $P = 0.162$	$P1 = 0.491$ $P2 = 0.06$ $P3 = 0.229$
Time to reach peak sensory block (min) (mean ± SD)	9.84 ± 0.39	10.02 ± 0.38	9.96 ± 0.28	$F = 2.14$ $P = 0.124$	$P1 = 0.06$ $P2 = 0.189$ $P3 = 0.477$
Time to reach peak motor block (min) (mean ± SD)	9.39 ± 0.31	9.06 ± 0.77	9.17 ± 0.73	$F = 2.05$ $P = 0.135$	$P1 = 0.06$ $P2 = 0.185$ $P3 = 0.520$
Time to sensory regression to S1 segment (mean ± SD)	143.34 ± 5.66	188.54 ± 3.65	293.66 ± 4.09	$F = 8618.37$ $P < 0.001$[a]	$P1<0.001$[a] $P2<0.001$[a] $P3<0.001$[a]
Time to motor block regression (Bromage 0) (min) (mean ± SD)	113.74 ± 5.39	158.05 ± 3.57	255.27 ± 11.48	$F = 2717.78$ $P < 0.001$[a]	$P1<0.001$[a] $P2<0.001$[a] $P3<0.001$[a]

F, one-way analysis of variance test.
*P*1: difference between group B and group BF.
*P*2: difference between group B and BD.
*P*3: difference between group BF and BD.
[a] Statistically significant if *P* value less than 0.05.

Table 3. NRS and postoperative analgesic requirement in the first 24 h among the studied groups.

NRS	Group B	Group BF	Group BD	Test of significance	Within group significance
Preoperative	5.10 ± 0.61	5.02 ± 0.42	4.90 ± 0.48	$F = 1.18$ $P = 0.310$	$P1 = 0.811$ $P2 = 0.154$ $P3 = 0.234$
1 h	1.07 ± 0.57	1.0 ± 0.53	0.70 ± 0.65	$F = 3.48$ $P = 0.03$[a]	$P1 = 0.613$ $P2 = 0.014$[a] $P3 = 0.05$[a]
4 h	4.07 ± 1.04	3.43 ± 0.85	2.06 ± 1.23	$F = 28.08$ $P < 0.001$[a]	$P1 = 0.023$[a] $P2<0.001$[a] $P3<0.001$[a]
8 h	4.90 ± 0.84	4.36 ± 0.93	4.20 ± 0.85	$F = 5.25$ $P = 0.007$[a]	$P1 = 0.02$[a] $P2 = 0.003$[a] $P3 = 0.462$
12 h	4.57 ± 0.73	5.2 ± 0.71	4.23 ± 0.63	$F = 15.15$ $P < 0.001$[a]	$P1 = 0.001$[a] $P2 = 0.065$ $P3<0.001$[a]

F, one-way analysis of variance test.
*P*1: difference between group B and group BF.
*P*2: difference between group B and BD.
*P*3: difference between group BF and BD.
[a] Statistically significant if *P* value less than 0.05.

and group BD in which patients were injected with dexmedetomidine with bupivacaine as shown in Fig. 1, Tables 1–8.

4. Discussion

Spinal anesthesia is still the first choice for a cesarean section due to its deep sensory block as well as fewer side effects on the mother and the fetus. But it is of short duration and insufficient postoperative analgesia.[6]

Fentanyl is the most common short-acting opioid that is used intrathecally in combination with local anesthetics. It has synergistic effects with local anesthetics and improves the status of intraoperative and postoperative analgesia.[11]

Table 4. Paracetamol and pethidine dosage among the three studied groups.

NRS	Group B	Group BF	Group BD	Test of significance	Within group significance
Paracetamol (g)	3.87 ± 1.11	3.5 ± 0.97	3.1 ± 0.40	$F = 5.67$ $P = 0.005$[a]	$P1 = 0.082$ $P2 = 0.001$[a] $P3 = 0.111$
Pethidine (mg)	26.77 ± 1.76	22.27 ± 3.93	11.73 ± 2.26	$F = 226.80$ $P < 0.001$[a]	$P1<0.001$[a] $P2<0.001$[a] $P3<0.001$[a]

F, one-way analysis of variance test.
*P*1: difference between group B and group BF.
*P*2: difference between group B and BD.
*P*3: difference between group BF and BD.
[a] Statistically significant if *P* value less than 0.05.

Table 5. Basal and post-operative respiratory rate and temperature among the studied groups.

	Group B	Group BF	Group BD	Test of significance	Within group significance
Respiratory rate Mean ± SD	12.0 ± 0.37	12.0 ± 0.05	12.4 ± 0.14	F = 4.5 P = 0.158	P1 = 0.45 P2 = 0.15 P3 = 0.25
Temperature	37.48 ± 2.5	37.89 ± 4.1	37.17 ± 5.8	F = 8.7 P = 1.25	P1 = 0.14 P2 = 0.08 P3 = 0.24

Table 6. Basal and postoperative heart rate among the studied groups.

Heart rate	Group B	Group BF	Group BD	Test of significance	
Basal	76.6 ± 5.6	76.35 ± 5.9	76.7 ± 5.2	$P = 0.95$	$P1 = 0.842$ $P2 = 0.936$ $P3 = 0.780$
Induction	77.1 ± 5.7	76.9 ± 5.8	77.1 ± 5.1	$P = 0.98$	$P1 = 0.841$ $P2 = 0.984$ $P3 = 0.856$
15 min	77.5 ± 5.6	77.2 ± 5.7	78.1 ± 4.8	$P = 0.72$	$P1 = 0.772$ $P2 = 0.605$ $P3 = 0.421$
30 min	77.6 ± 5.6	77.15 ± 5.7	76.8 ± 5.3	$P = 0.80$	$P1 = 0.717$ $P2 = 0.763$ $P3 = 0.507$
1 h	77.3 ± 5.6	76.1 ± 5.6	75.8 ± 5.1	$P = 0.43$	$P1 = 0.325$ $P2 = 0.219$ $P3 = 0.805$
2 h	76.7 ± 5.6	75.3 ± 5.5	75.4 ± 5.3	$P = 0.45$	$P1 = 0.255$ $P2 = 0.299$ $P3 = 0.919$

Dexmedetomidine, a new selective α2-agonist, is being introduced as an adjuvant to local anesthetics with significant analgesic, sympatholytic, and sedative properties.[12,13]

Many reports have indicated that intrathecal administration of dexmedetomidine can prolong analgesia and reduce the side effects associated with the administration of opioids.[12,14]

However, some studies have reported that intrathecal injection of dexmedetomidine is frequently associated with some side effects, such as a decrease in heart rate and blood pressure.[11,15]

Therefore, the aim of the current study was to compare the effect of adding dexmedetomidine versus fentanyl as an adjuvant to bupivacaine spinal anesthesia in women who had undergone a cesarean section. The primary outcome was to assess the postoperative analgesia. Our secondary outcome was to assess hemodynamic changes.

Concerning demographic data and anthropometric measurements the current study demonstrated that both age and BMI demonstrated insignificant differences among the three studied groups ($P > 0.05$).

Table 7. Basal and postoperative MAP among the studied groups.

MAP	Group B	Group BF	Group BD	Test of significance	
Basal	92.50 ± 5.8	92.48 ± 6.9	95.9 ± 6.95	$P = 0.87$	$P1 = 0.986$ $P2 = 0.876$ $P3 = 0.684$
Induction	87.68 ± 7.07	89.78 ± 8.18	88.98 ± 8.18	$P = 0.09$	$P1 = 0.08$ $P2 = 0.15$ $P3 = 0.35$
15 min	85.73 ± 7.88	86.11 ± 9.38	85.05 ± 8.28	$P = 0.15$	$P1 = 0.14$ $P2 = 0.2$ $P3 = 0.31$
30 min	85.45 ± 6.48	84.15 ± 7.21	85.43 ± 6.32	$P = 0.74$	$P1 = 0.384$ $P2 = 0.458$ $P3 = 0.574$
1 h	84.35 ± 5.82	86.55 ± 6.92	85.15 ± 7.29	$P = 0.09$	$P1 = 0.08$ $P2 = 0.74$ $P3 = 0.15$
2 h	85.20 ± 5.73	86.38 ± 6.78	85.23 ± 7.18	$P = 0.25$	$P1 = 0.147$ $P2 = 0.987$ $P3 = 0.151$

Table 8. Basal and postoperative respiratory rate and temperature among the studied groups.

	Group B	Group BF	Group BD	Test of significance	Within group significance
Respiratory rate (mean ± SD)	12.0 ± 0.37	12.0 ± 0.05	12.04 ± 0.14	$F = 4.5$ $P = 0.158$	$P1 = 0.45$ $P2 = 0.15$ $P3 = 0.25$
Temperature	37.48 ± 2.5	37.89 ± 4.1	37.17 ± 5.8	$F = 8.7$ $P = 1.25$	$P1 = 0.14$ $P2 = 0.08$ $P3 = 0.24$

With regard to the characteristics of the spinal block in the studied groups, the current study has demonstrated that there were no statistically significant differences among the three studied groups in terms of time to reach T10, time to reach peak sensory block, and time to reach peak motor block ($P > 0.05$). However, there were highly statistically significant differences as regards time to sensory regression to S1 segment (being significantly reduced in group BF followed by BD then B) as well as time to motor block regression (being significantly increased in group BD followed by BF then B) among the three studied groups as well as among each other ($P < 0.001$).

Noor El-Din et al.[16] conducted a study on a total of 40 adults full-term pregnant female submitted for elective cesarean section who were randomly classified into two equal groups of 20 patients each: group D: patients received intrathecally bupivacaine and dexmedetomidine. Group F: patients received intrathecally bupivacaine and fentanyl.[16]

They have demonstrated that sensory and motor block onset times were shorter in group D than in group F. The regression of the sensory block to S1 dermatome and Bromage 0 were longer in group D than in group F. The two-dermatome regression time was longer in group D than in group F.[16]

These results were consistent with Gupta in which intrathecal (5 μg) dexmedetomidine was compared with fentanyl (25 μg) as adjuvants to 12.5 mg hyperbaric bupivacaine in patients organized for surgery of the lower abdomen and concluded that intrathecal dexmedetomidine was associated with sustained motor and sensory blockade and reduced demand for rescue analgesics in 24 h relative to fentanyl.[1]

In addition, Bajwa compared dexmedetomidine with fentanyl in epidural analgesia in orthopedics and reported comparable results. The sensory and motor blockade started earlier and lasts longer with a reduction of the postoperative need for analgesia. Dexmedetomidine also had a higher safety profile.[17]

Also, Al-Ghanem and his colleagues investigated the effect of the addition of dexmedetomidine to bupivacaine for the spinal block for gynecological surgeries and reported that plain bupivacaine (10 mg) with 5 μg dexmedetomidine was associated with significantly long motor and sensory blockade when compared with 25 μg fentanyl.[18]

In addition, Khosravi et al.[8] have demonstrated that there was no significant difference between the

two groups (B-D and B–F) in the sensory block level, which was consistent with the findings of other studies.[14,19]

Sun et al.[14] have displayed that regression time to T10 was significantly longer in the B-D group; sensory block was also prolonged in the B-D group without any difference in the duration of motor block.[14]

Concerning NRS as well as postoperative analgesic requirement in the first 24 h among the studied groups, the current study revealed that there were no statistically significant differences among the three studied groups before operation ($P > 0.05$). However, there were statistically significant differences among the three studied groups at all times following the operations (1, 4, 8, 12, 16, 20, and 24 h) being significantly decreased in group BD followed by BF and then B ($P < 0.05$).

Furthermore it has been demonstrated that the use of dexmedetomidine especially at a dose of 3 μg as an adjuvant to bupivacaine in a cesarean surgery provides better intraoperative somato-visceral sensory block characteristics and postoperative analgesia compared with bupivacaine (10 mg) alone, with no influence on Apgar scores, side effects, and stress response.[10]

On the contrary, Kamali et al. conducted their study on 84 pregnant women candidates for caesarian who were randomly divided into fentanyl and dexmedetomidine groups. In the first group, 25 Î¼g fentanyl was added to lidocaine 5% while in the second group, 0.5 Î¼g per kilogram dexmedetomidine was added to lidocaine 5%. They have demonstrated that fentanyl results in a longer period of postoperative analgesia and less consumption of drugs after the operation. Fentanyl is recommended in cesarian sections.[20]

Regarding analgesic requirement, the current study demonstrated that there were statistically significant reductions in paracetamol and pethidine requirements among the three studied groups being significantly decreased in group BD followed by BF and then B ($P < 0.05$).

Similarly, Noor El-Din have demonstrated that hemodynamic parameters (SBP, DBP, MAP, HR, and SpO_2) in two groups were comparable at different time periods, and the findings revealed that there was no significant statistical difference between them ($P > 0.05$). Moreover, following hypotension, the mean dose of ephedrine in the B-D and B–F groups were 5.36 ± 7.07 and 6.82 ± 5.25 mg, respectively. In this regard, the Mann–Whitney test showed that there was no significant difference between the two groups ($P = 0.955$). With respect to bradycardia, the mean dose of atropine in the B-D and B–F groups were 0.10 ± 0.26 and 0.05 ± 0.17 mg, respectively. According to the Mann–Whitney test, in this regard, no significant difference was seen between the two groups ($P = 0.350$).[8]

4.1. Conclusion

The use of dexmedtomidine as an adjuvant to bupivacaine in cesarean surgeries was demonstrated to be associated with better intraoperative and postoperative analgesia with minimal analgesic requirements without having significant side effects or hemodynamic alterations.

Conflicts of interest

Authors declare that there is no conflict of interest, no financial issues to be declared.

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