Motor and sensory blocking effect of intrathecal fentanyl versus dexmedetomidine as adjuvants to bupivacaine for cesarean section

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Background Intrathecal α_2 agonists prolong the duration of action of local anesthetics and reduce the required dose. Dexmedetomidine is an α_2 receptor agonist, and its α_2/α_1 selectivity is eight times higher than that of clonidine.

Aim The aim of this study was to determine the effect of adding dexmedetomidine and fentanyl to intrathecal bupivacaine on the onset time and duration and intensity of motor and sensory blocks for cesarean section.

Patients and methods The study was carried out on 40 adult female patients who were randomly classified using closed envelope method into two equal groups, with 20 patients in each: group D patients received intrathecally 2.5 ml volume of 10 mg (2 ml) 0.5% hyperbaric bupivacaine and 10 μg dexmedetomidine in 0.5 ml (prepared by diluting 1 ml dexmedetomidine in 5 ml of normal saline), and group F patients received intrathecally 2.5 ml volume of 10 mg (2 ml) 0.5% hyperbaric bupivacaine and 20 μg fentanyl in 0.5 ml (prepared by diluting 2 ml fentanyl in 2.5 ml of normal saline). The aim was to evaluate motor and sensory block.
Sensory block assessment: the onset and duration of sensory block was assessed by ice cube method, and time taken from intrathecal injection to the highest level of sensory block and sensory regression to the L_1 dermatome were recorded. On achieving T7 sensory blockade level, surgery was allowed.
Motor block assessment: onset and degree of motor block was assessed by Bromage scale: 0, no paralysis; 1, inability to raise extended leg; 2, inability to flex the knee; and 3, inability to flex the ankle (complete motor block).

Results 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 group F. The two-dermatome regression time was longer in group D than group F. There was a statistically significant decrease in group F regarding systolic, diastolic, and mean arterial blood pressures and heart rate than group D. There was no statistically significant difference among the two groups regarding arterial oxygen saturation and respiratory rate. Neonatal outcome was normal in all groups.

Conclusion Intrathecal dexmedetomidine addition to bupivacaine for spinal anesthesia synergistically increases block duration and shortens sensory and motor block onset time without any significant adverse effects.
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Introduction

Spinal anesthesia is the most commonly used technique for elective cesarean deliveries. However, postoperative pain control is a major problem because spinal anesthesia using only local anesthetics is associated with relatively short duration of action, and thus early analgesic intervention is needed in the postoperative period. A number of adjuvants, such as clonidine, midazolam, and others, have been studied to prolong the effect of spinal anesthesia [1].

The present prospective, randomized, double-blind study was aimed to determine the effect of adding dexmedetomidine and fentanyl to intrathecal bupivacaine on the onset time and duration of motor and sensory blocks for cesarean section.

Patients and methods

The study was carried out after local ethics committee approval, and written informed consent was taken from 40 adult female patients, aged from 21 to 35 years old, admitted to Al-Azhar University Hospitals scheduled for elective or emergency cesarean deliveries. Patients were selected according to American Society of Anaesthiologist physical status class I–II. The study began in May 2016 to June 2017.

Exclusion criteria were more than American Society of Anaesthiologist status II, BMI more than 30%, patients have allergy to the study medication, and any absolute contraindication for spinal anesthesia.

Patients were randomly classified using computer-generated closed envelope method into two equal groups, with 20 patients each:

Group D: patients received intrathecally 2.5 ml volume of 10 mg (2 ml) 0.5% hyperbaric bupivacaine and 10 μg dexmedetomidine in 0.5 ml (prepared by diluting 1 ml dexmedetomidine in 5 ml of normal saline).
Group F: patients received intrathecally 2.5 ml volume of 10 mg (2 ml) 0.5% hyperbaric bupivacaine and 20 μg fentanyl in 0.5 ml (prepared by diluting 2 ml fentanyl in 2.5 ml of normal saline).

Primary outcome

The primary evaluation included motor and sensory onset and intensity and duration of block.

Every patient was subjected to careful preanesthesia assessment including the following: history taking regarding current medical illness, drug therapy, and previous experience with general or regional anesthesia if any, and thorough clinical examination and laboratory investigations including complete blood picture, serum creatinine, prothrombin time, international normalized ratio, fasting blood sugar, serum glutamic oxaloacetic transaminase, and serum glutamic-pyruvic transaminase.

In the operating room, an intravenous cannula (18 G) was inserted, and patients received intravenous prehydration with 15 ml/kg Ringer's lactate solution within 20 min.

All patients received preanesthesia ranitidine 50 mg and metoclopramide 10 mg intravenously.

Standard monitoring was instituted including noninvasive blood pressure, lead II ECG, and peripheral pulse oximetry SpO_2 using (A Nihon Kohden monitor; Nihon kohden Europe GmbH, Rosbach, German).

The drug solutions were prepared by a junior anesthetist who was not involved in the study or care of the patient. Both the patients and the anesthetist performing the block were blinded to the study drug.

Baseline pulse rate, blood pressure, and respiratory rate were recorded before spinal anesthesia.

Under all aseptic precautions, lumbar puncture was carried out with a 25-G Quincke's needle in the L4–L5 or L3–L4 space in sitting position, and intrathecal injection was given over ~10–15 s. After noting the time of injection, the patient was placed in supine position with 15° lateral tilt (right hip uppermost) and low flow oxygen (4 l/min) was administered via oxygen mask.

The onset and duration of sensory block was assessed by ice cube method every minute until level stabilized for two consecutive tests, then every 10 min for an hour, and every 30 min till recovery. Time taken from intrathecal injection to the highest level of sensory block and sensory regression to the L_1 dermatome were recorded. On achieving T7 sensory blockade level, surgery was allowed.

Degree of motor block was assessed by Bromage scale [2]: 0, no paralysis; 1, inability to raise extended leg; 2, inability to flex the knee; and 3, inability to flex the ankle (complete motor block).

The regression time for sensory and motor block was recorded. All durations were calculated considering the time of spinal injection as time zero. Patients were discharged from the PACU after sensory regression to S1 dermatome and Bromage 0 (group D 6.5 h, group F 4.5 h).

Secondary outcome

Sedation was recorded by Ramsay sedation score [3] intraoperatively every 5 min. The scale, from 1 to 6, describes a patient as follows (Table 1):

Postoperatively, the pain score was recorded by using visual analog pain scale [4] between 0 and 10 (0, no pain and 10, most severe pain), initially every 1 h for 2 h, then every 2 h for the next 6 h, and then after every 4 h till 24 h.

All patients received (30 mg) intravenous ketorolac at the end of surgery and every 6 h for 24 h for postoperative analgesia. Meperidine 20 mg was given intravenously as rescue analgesia when visual analog scale (VAS) is at least 4 after 2 h of administered dose of intravenous ketorolac.

Statistical analysis

Data entry and statistical analyses were performed using statistical package of social sciences (SPSS)

Table 1 Ramsey sedation score [3]

Score	Response	Score	Response
Ramsey 1	Anxious, agitated, and restless	Ramsey 4	Brisk response to light glabellar tap or loud noise
Ramsey 2	Cooperative, oriented, and tranquil	Ramsey 5	Sluggish response to light glabellar tap or loud noise
Ramsey 3	Responds to commands only	Ramsey 6	No response to light glabellar tap or loud noise

version 21 (SPSS Inc., Chicago, Illinois, USA) [5]. Continuous normally distributed data were expressed in mean and SD. The quantitative data were examined by Kolmogrov–Smirnov test for normality of data. Independent sample *t*-test (Student's *t*-test) was used for continuous normally distributed data. Analysis of variance test was used for multivariate continuous normally distributed data. Statistical significance was considered when *P* value was less than or equal to 0.05.

Results

Demographic data

There was no significant difference between both the groups regarding age, weight, and height ($P>0.05$) as shown in Table 2.

Sensory characteristics of spinal block

The onset of sensory block was significantly faster in group D than group F. The mean time to two-segment regression of sensory block was significantly longer in group D than group F, and the mean time to full sensory recovery was significantly longer in group D than group F as shown in Table 3.

Motor characteristics of spinal block

The mean time to achieve Bromage scale 3 motor block was significantly faster in group D than group F, and the time to complete motor recovery was significantly longer in group D than group F as shown in Table 4.

Sedation score

There was no significant difference between both groups regarding Ramsey sedation score, as shown in Table 5.

Visual analog scale

There was a significant difference between both groups by VAS at 2 and 4 h postoperatively as shown in Table 6 and Fig. 1.

Total rescue analgesic dose

The total dose of meperidine (mg) received by patients in group D was significantly less than group F as shown in Table 7.

Discussion

Spinal anesthesia is the most commonly used technique for elective cesarean deliveries. However, postoperative pain control is a major problem because spinal anesthesia using only local anesthetics is associated with relatively short duration of action, and thus early analgesic intervention is needed in the

Table 2 Comparison between the two studied groups regarding age (years), weight (kg), and height (cm)

	Group D	Group F	*P* value
Age (years)			
Minimum	21	19	0.649
Maximum	32	35	
Mean	26	26.5	
SD	3.03	4.4	
Weight (kg)			
Minimum	93	74	0.888
Maximum	92	93	
Mean	81.4	81.2	
SD	4.6	4.2	
Height (cm)			
Minimum	153	153	0.663
Maximum	168	169	
Mean	159.9	160	
SD	4.3	4.3	

Table 3 Comparison between the two studied groups regarding onset of sensory block, two-segment regression of sensory block, and full sensory recovery

	Group D	Group F	*P* value
Onset of sensory block (min)			
Minimum	1.5	2	0.0001**
Maximum	2.5	3.5	
Mean	1.8	2.4	
SD	0.3	0.4	
Two-segment regression sensory block (min)			
Minimum	119	74	0.0001**
Maximum	144	98	
Mean	129.7	83.9	
SD	6.3	8.3	
Full sensory recovery time (min)			
Minimum	315	243	0.0001**
Maximum	395	278	
Mean	347.9	263	
SD	25.6	9.8	

**$P>0.0001$, highly significant.

Table 4 Comparison between the two studied groups regarding onset to reach Bromage 3 and regression to Bromage 0

	Group D	Group F	*P* value
Onset to reach Bromage 3 (min)			
Minimum	3.5	4	0.0001**
Maximum	4.5	7.5	
Mean	3.8	5.2	
SD	0.3	0.9	
Regression to Bromage 0 (min)			
Minimum	295	220	0.001*
Maximum	390	259	
Mean	336.5	242.6	
SD	25.4	10.5	

**$P>0.0001$, very highly significant. *$P>0.001$, highly significant.

Table 5 Comparison between the two studied groups regarding Ramsey sedation score intraoperatively

Time intraoperative (min)	5	10	15	20	25	30	35	40	45	50	55	60
Group D												
Minimum	2	2	2	2	2	2	2	2	2	2	2	2
Maximum	2	2	3	3	3	3	3	3	3	3	2	2
Mean	2	2	2.05	2.1	2.2	2.2	2.2	2.1	2.1	2.1	2	2
SD	–	–	0.22	0.36	4.1	4.1	4.1	0.36	0.31	0.31		
Group F												
Minimum	2	2	2	2	2	2	2	2	2	2	2	2
Maximum	2	2	3	3	3	3	3	3	3	3	2	2
Mean	2	2	2.05	2.1	2.2	2.2	2.2	2.1	2.1	2.1	2	2
SD	–	–	0.22	0.36	4.1	4.1	4.1	0.36	0.31	0.22		
P	–	–	1	0.64	1	1	1	1	1	0.65	–	–

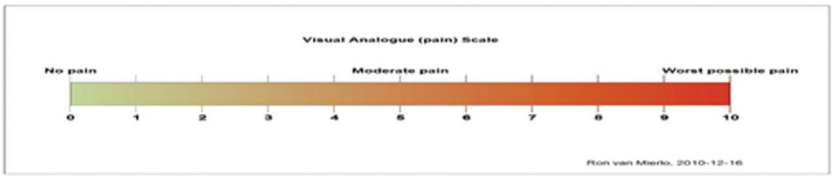
P comparison between two groups.

Table 6 Comparison between the two studied groups regarding visual analog scale

Time postoperative (h)	1	2	4	6	8	12	16	20	24
Group D									
Minimum	0	0	0	0	0	0	1	0	0
Maximum	0	2	4	4	4	4	4	4	5
Mean	0	0.9	1.5	2.2	1.4	2.1	2.3	1.5	2.1
SD	–	0.8	0.8	1	1	1.2	1.2	1.1	1.4
Group F									
Minimum	0	0	0	0	0	0	0	0	0
Maximum	0	3	5	5	5	4	5	5	5
Mean	0	1.6	3	2.7	2.6	2.1	2.3	2.2	2.2
SD	–	1	1.4	1.3	1.8	1.4	1.7	1.4	1.3
P	–	0.02*	0.001*	0.15	0.67	0.99	0.99	0.11	0.91

P comparison between two groups. *Indicates significance.

Figure 1



Visual analog scale [6].

postoperative period. A number of adjuvants, such as clonidine, midazolam, and others have, been studied to prolong the effect of spinal anesthesia [1].

The present study revealed that intrathecal 10 mg heavy bupivacaine supplemented with 10 μg dexmedetomidine significantly affects spinal block characteristics evident by shortened onset time of both sensory and motor block, compared with intrathecal 20 μg fentanyl and heavy bupivacaine in patients undergoing elective or emergency cesarean deliveries.

Moreover, addition of 10-μg dexmedetomidine significantly prolonged duration of block with prolonged analgesic effects of spinal hyperbaric bupivacaine evident by decreased postoperative pain scores (VAS), total analgesic consumption, and prolongation of time to first request analgesia.

Table 7 Total analgesic dose of meperidine in the two studied groups (mg)

	Group D	Group F	*P* value
Total analgesia dose			
Minimum	0	20	0.0001**
Maximum	40	80	
Mean	24	50	
SD	12.3	20	

***P*>0.0001, very highly significant.

These results were consistent with Gupta *et al.* [1] who compared intrathecal (5 μg) dexmedetomidine with fentanyl (25 μg) as adjuvants to 12.5 mg hyperbaric bupivacaine in patients scheduled for lower abdominal surgeries and concluded that intrathecal dexmedetomidine is associated with prolonged motor and sensory block and reduced demand for rescue analgesics in 24 h compared with fentanyl.

In a comparative evaluation of dexmedetomidine and fentanyl for epidural analgesia in lower limb orthopedic surgeries, Bajwa *et al.* [2] reported that onset of sensory and establishment of complete motor blockade were significantly earlier in the dexmedetomidine group, as well as prolonged postoperative analgesia with lower consumption of postoperative analgesia, and they concluded that dexmedetomidine seems to be a better alternative to fentanyl as an epidural adjuvant.

Moreover, Al-Ghanem *et al.* [7] studied the effect of adding dexmedetomidine or fentanyl to intrathecal bupivacaine on spinal block characteristics in gynecological procedures and demonstrated that, in women undergoing vaginal reconstructive surgery under spinal anesthesia, 10 mg plain bupivacaine supplemented with 5 μg dexmedetomidine produces prolonged motor and sensory block compared with 25 μg fentanyl as well as reduced postoperative pain scores and a longer analgesic duration.

The present results were in agreement with that obtained by Khalifa [8] who studied the effects of adding either dexmedetomidine (5 μg) or sufentanil (5 μg) to heavy bupivacaine (0.5% 10 mg) for postoperative analgesia in patients undergoing inguinal hernia repair and reported that addition of dexmedetomidine prolonged time to two-segment regression, sensory and motor resolution, and time to first rescue analgesic.

Regarding mean sedation score by Ramsay sedation score in the present study, the patients showed no significant difference in the two groups at all study times.

These results were comparable with Al-Mustafa *et al.* [9] who stated that usage of 5 and 10 μg of dexmedetomidine added to spinal bupivacaine in urological procedures did not affect the level of consciousness, and all patients in the two groups had a Ramsay sedation score of 2 (patient cooperative and oriented). They concluded that increasing dose of dexmedetomidine did not increase level of sedation.

In contrast with the results of the present study, Chavda *et al.* [10] and Motiani *et al.* [11] concluded that addition of 25 μg fentanyl to hyperbaric bupivacaine causes mild sedation.

In the present study, pain intensity measured by VAS was significantly less in group D than group F in the most of the studied times with significant increase of total rescue analgesic consumptiom of mepiridine hydrochloride in group F than group D.

These results might be explained by increasing the analgesic action of α-2 adrenergic receptor agonists in pregnant versus nonpregnent or by supressing phosphorylation of the *N*-methyl-d-aspartate receptor in spinal dorsal horn neurons. This comes in agreement with Gupta *et al.* [1] and Al-Ghanem *et al.* [7].

Conclusion

Intrathecal dexmedetomidine addition to bupivacaine for spinal anesthesia shortens sensory and motor block onset time and prolongs block duration.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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