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A comparison of the postoperative analgesic effects of intravenous dexmedetomidine with a combination of dexmedetomidine and bupivacaine wound infiltration for lower segment cesarean section: a prospective, randomized study

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Background and aim
This study was designed to compare the postoperative analgesic effect of dexmedetomidine administered intravenously or in wound infiltration with bupivacaine in patients undergoing cesarean section.

Patients and methods
Ninety female patients scheduled for cesarean section were randomly allocated into three equal groups: group I received 100 ml normal saline infusion over 10 min before closure plus wound infiltration with 25 ml of 0.25% bupivacaine at the end of surgery; group II received 1 μg/kg of dexmedetomidine in 100 ml normal saline infusion over 10 min before closure plus wound infiltration with 25 ml of 0.25% bupivacaine at the end of surgery; and group III received 100 ml normal saline infusion over 10 min before closure plus wound infiltration with 1 μg/kg of dexmedetomidine added to 25 ml of 0.25% bupivacaine at the end of surgery. The number of patients requiring rescue analgesia, total morphine consumption during the first 24 h after the operation, and the level of sedation were recorded.

Results
Morphine consumption was significantly less in patients receiving dexmedetomidine by either route. All patients in group I required supplemental morphine, whereas 14 patients in group II and 16 patients in the wound infiltration group required supplemental morphine. Patients in group II had more hypotension and sedation compared with other groups.

Conclusion
Dexmedetomidine provided effective postoperative analgesia and reduced morphine consumption when administered intravenously or in wound infiltration with bupivacaine. The incidence of complications was less with wound infiltration.

Keywords:
dexmedetomidine, elective caesarean section, postoperative analgesia, wound infiltration

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Introduction

Cesarean sections differ from other major laparotomies because women are expected to recover quickly and care for their newborns within a few hours following surgery. Therefore, women after cesarean delivery are reluctant to feel drowsy, sleepy, or attached to intravenous lines that does not allow them to freely attend to their babies. An ideal postcesarean analgesic regimen must be cost-effective, simple to implement, with minimal impact on staff workload, and with no adverse effects on the newborn [1]. Dexmedetomidine, a highly selective α2-adrenergic receptor agonist with a relatively high ratio of α2/α1-activity (1620: 1), has been the focus of interest for its sedative, analgesic, perioperative sympatholytic, anesthetic-sparing, hemodynamic-stabilizing properties, but lacks respiratory depression, making it a useful and safe adjunct in many clinical applications [2]. Its opiate-sparing effect has important implications in the management of acute postoperative pain [3]. The peripheral analgesic effects of dexmedetomidine that potentiate local anesthetics are mediated by α2-adrenergic receptor binding [4] and have been utilized to enhance postoperative analgesia after direct infiltration of dexmedetomidine at a dose of 1 μg/kg as an adjunct to local anesthetics [5]. This study aimed to determine the analgesic efficacy of dexmedetomidine

in wound infiltration with bupivacaine and to compare it with intravenous administration for postoperative analgesic requirement and side effects in patients undergoing cesarean section.

Patients and methods

After local ethical committee approval and patient's informed written consent, this prospective, randomized, controlled, double-blind clinical trial was conducted on 90 female patients of ASA grade I and II between 19 and 38 years of age posted for cesarean section. This study was carried out from March 2011 to November 2013 from Monday to Wednesday every week in Benha University Hospitals. Patients with difficult airway, morbid obesity, Reynaud's disease, hepatic or renal insufficiency, hypertension, preeclampsia, and patients receiving any drugs that may interfere with the action of the study drugs were excluded. All patients underwent a preoperative assessment on the day before surgery. They were premedicated with ondansetron 0.1 mg/kg intravenous, ranitidine 50 mg intravenous, and glycopyrrolate 0.01 mg/kg 1 h before the operation.

Patients were randomly allocated using a computer-generated random number table into three equal groups:

(1) Group I patients received 100 ml normal saline infusion over 10 min before wound closure plus wound infiltration with 25 ml of 0.25% bupivacaine at the end of surgery.
(2) Group II patients received 1 μg/kg of dexmedetomidine in 100 ml normal saline infusion over 10 min before wound closure plus wound infiltration with 25 ml of 0.25% bupivacaine at the end of surgery.
(3) Group III patients received 100 ml normal saline infusion over 10 min before wound closure plus wound infiltration with 1 μg/kg of dexmedetomidine added to 25 ml of 0.25% bupivacaine at the end of surgery.

After adequate preoxygenation for 3 min, anesthesia was induced with sodium thiopental 3–5 mg/kg, and cricoid pressure was applied until tracheal intubation was facilitated with succinylcholine 1–1.5 mg/kg. Anesthesia was maintained with isoflurane 1.5% in 100% oxygen and *cis*-atracurium 0.1–0.2 mg/kg. Fentanyl 2 μg/kg, intravenous, was given after delivery of the fetus. Intraoperative monitoring included electrocardiogram, noninvasive arterial pressure (at 5 min intervals), oxygen saturation, and end-tidal carbon dioxide. Intermittent positive pressure ventilation with a tidal volume of 6–8 ml/kg and respiratory rate of 10–12/min was used.

Heart rate and mean arterial pressure were maintained within 20% of the preoperative value. At the end of surgery, residual neuromuscular block was reversed with 0.04–0.08 mg/kg of neostigmine and 0.01–0.02 mg/kg of atropine. Tracheal extubation was performed on meeting the standard criteria for extubation.

Patients were observed for 24 h after operation in the postanesthesia care unit. Rescue analgesia was given with morphine 3 mg, intravenous, boluses on demand, or whenever visual analogue scale (VAS) pain score was 4 or greater.

The parameters recorded included the demographic characteristics of patients (age, weight, and ASA physical status), duration of surgery (the time from the start of insertion of the endotracheal tube until skin closure), number of patients requiring rescue analgesia, and total morphine consumption during the first 24 h after operation.

Level of sedation was assessed using the four-point sedation score described by Chernik *et al.* [6] (0 = awake, 1 = sleeping comfortably and responding to vocal commands, 2 = somnolence, deep sleep but responding to vocal commands, and 3 = not arousable, deep sleep).

Adverse effects if any were noted, including nausea and/or vomiting, were treated with ondansetron 0.1 mg/kg, intravenous. Hypotension (mean arterial pressure<20% of baseline or <60 mmHg) was treated with an infusion of normal saline and if necessary an intravenous injection of ephedrine 5–10 mg incremental doses was administrated. Bradycardia (heart rate <60 beats/min) was treated with intravenous atropine 0.01–0.02 mg/kg bolus. Dry mouth, dizziness, and diplopia were also recorded.

Statistical analysis

Analysis of data was performed by using SPSS (version 16; SPSS Inc., Chicago, Illinois, USA). Quantitative data were presented as mean and SD and were analyzed using one way analysis of variance test. Qualitative data were presented as numbers and percentages and were analyzed using the χ^2 and Fisher exact tests. A *P*-value less than 0.05 was considered significant, whereas a *P*-value less than 0.01 was considered highly significant. The sample size was calculated according to the reduction of morphine consumption on the basis of pilot study from the first 10 patients at 95% significance level and 80% power. Assuming 30% reduction in morphine consumption, 30 patients were required for each group.

Results

A total of 97 patients were screened during the study period. Four patients did not match the inclusion criteria and one patient refused to participate. A total of 92 patients were included in the study, but two more patients were excluded shortly thereafter: one because of difficult intubation (n = 1) and the other because of significant hypotension (n = 1). Thus, 90 patients completed the study protocol (Fig. 1).

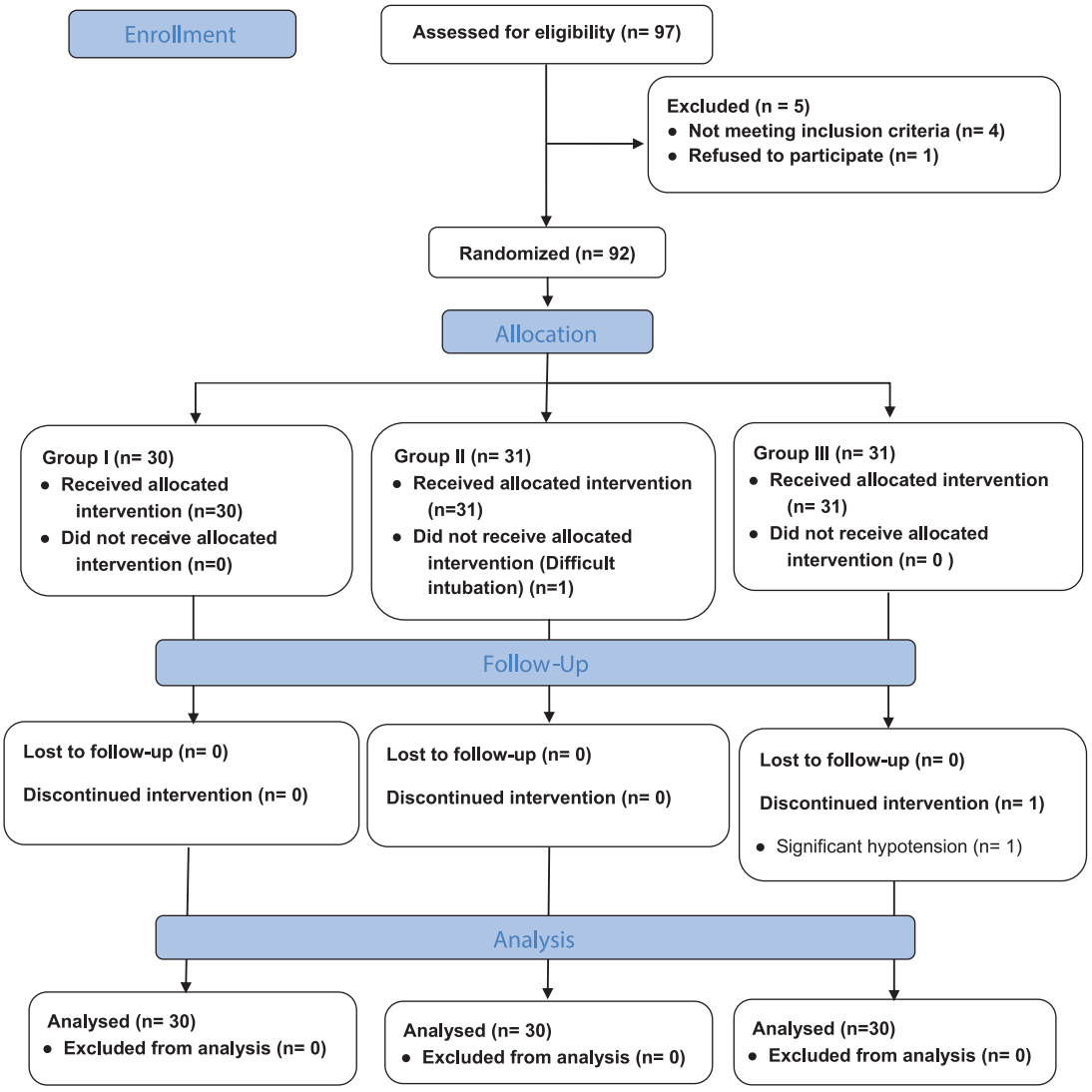
All groups were similar with respect to patient demographic characteristics, ASA physical status, and duration of surgery (Table 1).

Morphine consumption during the first 24 h was less in both dexmedetomidine groups in comparison with the control group (Table 2). All patients in group I required supplemental morphine, whereas only 14 (46.6%) patients in group II and 16 (53.3%) patients in group III required supplemental morphine (Table 2). The difference in morphine consumption was not statistically significant between the two dexmedetomidine groups.

As regards the level of sedation, most of the patients (27 patients) in group I had score 0, 21 patients in group III had score one, and five patients had score 2. Group II showed the highest level of sedation (score 1 = 17 patients, score 2 = 12 patients, and score 3 = one patient) (Table 3).

The number of patients who developed postoperative hypotension was also high in group II when compared with the other two groups. Six patients developed hypotension in group II compared with one patient in the control group and two patients in group III. One patient in each group had nausea or vomiting and required intravenous ondansetron. Only one patient

Figure 1



Consort flow diagram.

Table 1 Demographic characteristics and time of surgery

Item	Group 1	Group 2	Group 3	Test	*P*
Age (years)	27.46 ± 5.09	27.5 ± 5.44	27.133 ± 5.22	$F = 0.44$	0.95
Weight (kg)	73.1 ± 11.72	73.26 ± 11.64	73.8 ± 13.7	$F = 0.29$	0.97
ASA (I : II)	23 : 7	24 : 6	21 : 9	$\chi^2 = 0.84$	0.65
Duration of surgery (min)	41.3 ± 6.42	42 ± 4.67	42.3 ± 4.79	$F = 0.24$	0.77

Data are expressed as mean and SD except ASA, which are expressed as numbers; value of analysis of variance test.

Table 2 Total morphine consumption and number of patients requiring analgesia

Item	Group 1	Group 2	Group 3	Test	*P*-value
Total morphine consumption (mg)	9.3 ± 1.6	2.2 ± 1.09	3.9 ± 1.4	$F = 212.9$	<0.01**
Number of patients requiring analgesia	30 (100%)	14 (46.6%)	16 (53.3%)	$\chi^2 = 22.8$	0.00**

F value of analysis of variance test; **Highly significant.

Table 3 The level of sedation using four-point sedation score

Scores	Group 1	Group 2	Group 3	χ^2	*P*-value
0	27 (90)	0	4 (13.3)	67.7	<0.01**
1	3 (10)	17 (56.7)	21 (70)		
2	0	12 (40)	5 (16.7)		
3	0	1 (3.3)	0		

Data are expressed as *n* (%) of patients; **Highly significant.

in group II developed hypotension and required intravenous ephedrine. No other side effect was recorded.

Discussion

Childbirth is an emotional experience for a woman and her family. Our aim is to facilitate bonding between the mother and the newborn baby as early as possible. This helps in not only promoting breastfeeding but also contracting the uterus and accelerating the process of uterine involution during the postpartum period [7]. Postoperative pain control after cesarean section should be considered as one of the most important tasks in our clinical practice that helps us to achieve our aim. Infiltration of wound with local anesthetic agents is a safe and effective method for postoperative pain control [8]. The duration of action can be prolonged by adding various agents, such as dexmedetomidine, to the local anesthetic [9]. The results of the present study are in agreement with those of Patel *et al*. [10], who found that intraoperative infusion of dexmedetomidine combined with inhalation anesthetics provided satisfactory intraoperative conditions for tonsillectomy and adenoidectomy without adverse hemodynamic effects. Postoperative opioid requirements were significantly reduced, and the incidence and duration of severe emergence agitation was lower with fewer patients having desaturation episodes. Surgical wound administration of dexmedetomidine may be useful to avoid the adverse hemodynamic effects of intravenous administration while still providing postoperative analgesia. Kang [11] found that a combination of dexmedetomidine and ropivacaine infiltration reduced the pain significantly with no adverse effects during the postoperative period after inguinal herniorrhaphy. Esmaoglu *et al* [12], on adding dexmedetomidine to levobupivacaine for axillary brachial plexus blockade, found that it shortens the onset and prolongs the duration of the block and the duration of postoperative analgesia. However, dexmedetomidine also may lead to bradycardia. Olutoye *et al*. [13] used intraoperative dexmedetomidine for postoperative analgesia and sedation in pediatric patients undergoing tonsillectomy and adenoidectomy, and found that the total postoperative rescue opioid requirements were similar in tonsillectomy patients receiving intraoperative dexmedetomidine or morphine. However, the use of dexmedetomidine 1 μg/kg and morphine 100 μg/kg had the advantages of an increased time to first analgesic request and a reduced need for additional rescue analgesia doses, without increasing discharge times. Sitilci *et al* [14] studied the effect of perioperative infusion of dexmedetomidine on postoperative remifentanil consumption. Additional analgesic requirement, total demand for patient controlled analgesia (PCA), total amount of PCA consumption, and mean VAS were higher in the control group, which did not receive dexmedetomidine. First demand time for PCA was longer in the study group in mastoidectomy operations. Cheung *et al*. [15] studied the analgesic effects of locally applied dexmedetomidine in third molar surgery under general anesthesia. Dexmedetomidine seems to have an antihyperalgesic effect when administered locally after bilateral third molar surgery. There is no delay in psychomotor recovery or increase in postoperative clinically significant adverse events. As regards the level of sedation, the present study found that the intravenous dexmedetomidine group showed the highest level of sedation in comparison with the two other groups. This is in agreement with

the findings of Paris and Tonner [16], who studied the usefulness of dexmedetomidine in anesthesia practice and concluded that intravenous dexmedetomidine provided dose-dependent sedation, analgesia, sympatholysis, and anxiolysis without relevant side effects.

Conclusion

Dexmedetomidine when administered in wound infiltration with bupivacaine provides effective postoperative analgesia as on intravenous administration but had fewer side effects.

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Conflicts of interest

There are no conflicts of interest.

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