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The Effect of Fentanyl or Dexmedetomidine on the Ultrasound-Guided Paravertebral Block for Patients Undergoing Renal Surgeries: Randomized Controlled Trial

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Abstract

Objective: This study aimed to investigate the effect of the continuous paravertebral block using either fentanyl or dexmedetomidine as an additive to bupivacaine in patients undergoing renal surgeries.

Methods: Ninety adult patients presented for renal surgeries under general anesthesia and ultrasound-guided continuous paravertebral block were allocated in this study and randomly distributed into three groups. All the patients received a loading and a maintenance doses of local anesthetic mixtures composed of bupivacaine alone in Control group with addition of fentanyl or dexmedetomidine in Fentanyl and Dexmedetomidine groups. The measurements included the postoperative analgesic consumption, the time for the first request for rescue analgesia, postoperative pain scores, hemodynamic parameters, and incidence of complication.

Results: The addition of fentanyl or dexmedetomidine to plain bupivacaine in continuous paravertebral block significantly decreased the dose of postoperative morphine consumption from (11.33 ± 5.05 mg) to (7.33 ± 4.59 mg) (7.80 ± 4.15mg), significantly prolonged the time for first request of rescue analgesia from (6.87 ± 3.81 h) to (9.80 ± 4.50 h) (10.80 ± 5.22 h), and significantly decrease VAS score 2 h and 6 h postoperatively with insignificant difference between fentanyl and dexmedetomidine ($p>0.05$).

Conclusion: Fentanyl or dexmedetomidine can be helpful as an adjuvant to bupivacaine (0.25%) in the continuous paravertebral block as they decreased the postoperative analgesic consumption without increased incidence of complication.

Keywords: Fentanyl; Dexmedetomidine; Paravertebral block; Renal surgeries; Postoperative pain; Adjuvant; Rescue analgesia

Introduction

Patients presented for renal surgeries may suffer from an impaired renal function that limits the use of many analgesics. Therefore, regional anesthesia technique provides an excellent alternative especially with the use of adjuncts [1,2].

Paravertebral nerve block (PVB) which is performed by injection of local anesthetics alongside the vertebral column was first performed by Hugo Selheim in 1905 [3]. Since then, it had gained a high popularity as a postoperative analgesic technique for many surgical interventions such as thoracotomies, breast surgeries, and renal surgeries. Blind paravertebral block carries many technical difficulties especially in the location of the transverse process and introduction of a catheter. These difficulties may increase the failure rate and the incidence of complications [4]. The Sonographic guidance of the paravertebral block technique increased its success rate as it allows visualization of the transverse process and measurement of the distance from the skin to the paravertebral space and to the pleura. Also, it allows guidance of catheter [5].

The volume and concentration of local anesthetics used for PVB require the involvement of the desired level of block [6]. However, the use of higher volume or higher concentration of local anesthetics is associated with an increased risk of side effects and local anesthetic toxicity [7]. The use of local anesthetic adjuvant as fentanyl and clonidine may be useful in improving the paravertebral block criteria and improvement in the postoperative analgesia while minimizing the risk of local anesthetic toxicity [8,9].

Dexmedetomidine use as an adjunct in neuraxial and regional anesthesia had been increased based upon activation of many antinociceptive mechanisms through activation of α2 adrenoreceptor [10].

In this study, we suggested that the use of fentanyl or dexmedetomidine as an adjuvant to plain bupivacaine (0.25%) in the continuous paravertebral block may improve its postoperative analgesic properties. The purpose of the study was to evaluate the effect of the addition of either fentanyl or dexmedetomidine to plain bupivacaine (0.25%) in the continuous paravertebral block for patients presented for renal surgeries under general anesthesia considering the postoperative dose consumed of morphine as the primary outcome, and the quality of postoperative analgesia as the secondary outcome.

Patients and Methods

Dexmedetomidine is not accepted by the FDA for perineural injection until this moment. There is no available association in Egypt for permission of a new drug administration, so, the perineural administration of dexmedetomidine was explained to the Research Ethical Committee of the Tanta Faculty of Medicine to explain that administration of dexmedetomidine in a dose of 20-100 ug through the perineural route is safe based on the finding of the previous animal [11,12] and human studies [13-15]. The study was accepted by the local Research Ethical Committee (Tanta Faculty of Medicine Research Ethics Committee 30754/03/2017) and the study was registered on The Pan African Clinical Trial Registry and its unique identification number on the registry was (PACTR201703002140337).

This prospective, randomized controlled double-blinded study was carried out at Tanta University Hospitals for a duration of 12 months (from March 2017 until February 2018) starting after approval of the Ethical Committee. Patients included in this research work aged from 30- 60 years old, ASA class I or II, and scheduled for renal surgery under general anesthesia. Patients were excluded from the study if they refused to participate in the research, had suspected or diagnosed coagulopathy, with a localized skin infection, with suspected or known allergy to the used medications, or suffering from major cardiac disorders.

Adequate preoperative assessment of the patients was done through history taking, general and local examination, and revision of the patient investigations. Then, an adequate explanation of the purpose, technique, advantage, and potential hazards of the research to the patient was done, then, the patients were reassured. In case of approval of the patient to participate in the study, an informed written consent was obtained from the patient himself. All the collected data from the patients were used for this research work only and kept in a secret manner through private files.

On admission of the patients to the operating theatre, they were attached to a monitor in the form of oxygen saturation, noninvasive blood pressure measurement, and 3 leads electrocardiography. Then, an intravenous line was obtained through peripherally inserted 20 gauge cannula with starting of a fluid preload consisting of lactated ringer solution 7 ml/kg. The preparation of the resuscitation drugs and the ultrasound machine (SonoSite, Bothell, WA, USA) was done by the aid of expert assistant.

While the patients in a sitting position, the skin of the cervical and dorsal regions of the ipsilateral side were sterilized with covering of the probe of the ultrasound by sterile sheets. The 10th dorsal spine was scanned by the US probe (linear 6-13 MHz probe SonoSite HFL38x) by derangement from C7. The probe was placed over the spine of D10 then it was moved laterally till visualization of the transverse process and tilted till adequate visualization of the transverse process, the pleura, and the two layers of internal intercostal membrane. Then, injection of 3 ml of lidocaine 2% in the skin and the subcutaneous tissue 3 cm lateral to the 10th dorsal spine was performed.

A Tuohy epidural needle was used to puncture the skin 1 cm caudal to the US probe and guided slowly out of plane by the US until the tip of the needle appeared between the pleura and the internal intercostal membrane. Then, the catheter was introduced slowly in a cephalic direction until the tip of the catheter appeared in the paravertebral space opposite to the 8th dorsal spine. The needle was withdrawn with securing the catheter and the patients were turned to a supine position. After negative aspiration to exclude intrapleural, intravascular, or epidural placement, the test dose was injected slowly which was composed of 5 ml of lidocaine 2% with epinephrine 1:200000 [16].

Close monitoring of the heart rate and arterial blood pressure was then done every 3 minutes in the first 30 minutes for ruling out the intravascular or epidural injection. Any increase in the heart rate more than 30 % of the baseline or increase in the mean arterial pressure more than 30% of the baseline value suggested intravascular injection and the catheter was removed with the exclusion of the patient from the study. Moreover, the sensation of cold was tested in the ipsilateral dermatomes of D7, D8 and D9. A successful block was considered when there was a loss to the cold sensation at the level of tested dermatomes. The presence of sensation to cold at the corresponding dermatomes after more than 10 minutes from the injection of the test dose was considered as a failed block and the patient was excluded from the study.

Patients were randomly distributed into three studied groups using a computer-generated software. The local anesthetic mixtures were prepared in uniform syringes by an anesthesiologist who was blinded to the study and introduced them in closed envelopes to allow every patient to choose his own group.

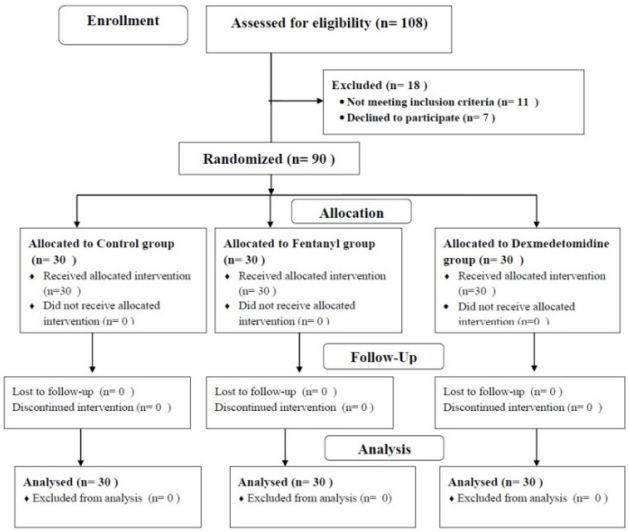

Figure 1: Consort flowchart showing the distribution of the patients of the study.

Control group (Group C) (30 Patients): Patients in this group had received a bolus dose of 0.2 mL/Kg of the loading solution (0.25% plain bupivacaine) injected slowly over 3 minutes and after 30 minutes a continuous infusion was started with 0.1 mL/Kg/h of the maintenance solution (0.125% plain bupivacaine) and continued throughout the time of surgery and for 24 h postoperatively.

Fentanyl group (Group F) (30 Patients): Patients in this group had received a bolus dose of 0.2 mL/Kg of the loading solution consisting of (0.25% plain bupivacaine and fentanyl 2 µg/ml) injected slowly over 3 minutes and after 30 minutes a continuous infusion was started with 0.1 mL/Kg/h of the maintenance solution consisting of (0.125% plain bupivacaine and fentanyl 2 µg/ml) and continued throughout the time of surgery and for 24 h postoperatively.

Dexmedetomidine group (Group D) (30 Patients): Patients in this group had received a bolus dose 0.2 mL/Kg of the loading solution (0.25% plain bupivacaine and dexmedetomidine 1 μg/kg) injected slowly over 3 minutes and after 30 minutes a continuous infusion of 0.1 mL/Kg/h of the maintenance solution (0.125% plain bupivacaine and dexmedetomidine 0.5 μg/kg) was started and continued throughout the time of surgery and for 24 h postoperatively.

Induction of general anesthesia was carried out following 3 minutes of preoxygenation through well-fitted face mask using 80% oxygen by fentanyl 1 μg/kg, propofol 1 mg/kg, and an intubating dose of cis-atracurium 0.15 mg/kg to facilitate tracheal intubation. The anesthesia was maintained by isoflurane inhalation 1.5% and incremental doses of cis-atracurium with adjustment of the parameters of mechanical ventilation to maintain the end-tidal Carbon Dioxide between 34-36 mmHg. The patient was turned laterally for surgical exposure with securing the patients adequately. During the intraoperative period, an increase in the heart rate or mean arterial pressure was managed by an additional dose of intravenous fentanyl 0.5 μg/kg. After termination of the surgery, the isoflurane was switched off with reversal of muscle relaxation and tracheal extubation, then, the patients were transported to PACU for adequate monitoring. An anesthesiologist who wasn't participating in this study and was blinded to it helped in the collection of the measured parameters.

The patient's and the surgical characteristics were recorded. The postoperative pain of the patients was assessed by the Visual Analogue Scale (0-10 scale where 0=no pain and 10=maximal pain) immediately postoperative, then every 2 hours till 6 hours, then, every 6 hours till 24 h. Any patients who had VAS score more than 3 had received rescue analgesia in the form of paracetamol 1000 mg i.v infusion and morphine 0.05 mg/kg i.v that may be repeated if required taking into consideration that total dose of morphine not exceeding 20 mg daily with calculation of the total dose of morphine consumption in the first 24 h (Primary outcome). The time interval from the recovery of anesthesia and the first request for rescue analgesia was calculated and recorded with considering the time in patients who didn't require rescue analgesia to be 24 h.

The hemodynamic parameters (Heart rate (b/min) and mean arterial pressure (mmHg)) were measured and recorded before induction of anesthesia, immediately after induction, and then every 10 min till 30 min, then every 30 min till the end of the surgery. Also, the hemodynamic parameters were measured in the postoperative period every 2 hours in the first 6 h, then every 6 h until 24 h. The incidence of any side effects including bradycardia, hypotension, postoperative nausea and vomiting, urinary retention, pneumothorax, intravascular injection, or sedation was recorded. Hypotension was considered when the mean arterial pressure decreased below 65 mmHg and it was managed by an intravenous fluid administration and 10 mg ephedrine i.v, while, bradycardia was diagnosed when the heart rate decreased below 50 b/min and was managed by atropine 0.3 mg intravenous that may be repeated.

Statistics

Twenty-eight patients at least were required in each group to detect a significant difference of the postoperative dose consumed of morphine of 2.5 mg at α value of 0.05 and 90% power of the study taking into consideration the results of a previous similar study [17]. The statistical analysis of the recorded data was done with the aid of (SPSS Inc., Chicago, IL, USA). Parametric data were evaluated by both One-way ANOVA test and post-hoc Turkey's HSD Test and then presented as mean values and standard deviation. Analysis of categorical data was carried out by Chi-square test and presented as number and frequencies (%). Whenever the P value was less than 0.05, the results were considered to be statistically significant.

Results

One hundred and eight patients were enrolled in this study, only 90 of them were randomly distributed into the three studied groups (Table 1).

		Control Group	Fentanyl Group	Dexmedetomidine Group	p value
Age (years)		52.30 ± 5.12	52.13 ± 4.82	52.37 ± 4.97	0.982
Gender	Male	19 (63.33%)	17 (56.67%)	18 (60%)	0.792
	Female	11 (36.67%)	13 (43.33%)	12 (40%)	
Body Weight (kg)		87.50 ±5.71	87.03 ± 4.79	86.90 ± 5.21	0.898
ASA Class	Class I	11 (36.67%)	10(33.33%)	12 (40%)	0.866
	Class II	19 (63.33%)	20 (66.67%)	18 (60%)	
Duration of surgery (min)		85.67 ± 10.32	86.33 ± 10.50	86.67 ± 8.84	0.924
Type of surgery	Pyeloplasty	13 (43.33%)	11 (36.67%)	12 (40%)	0.987
	Pyelolithotomy	12 (40%)	13 (43.33%)	12 (40%)	
	Nephrectomy	5 (16.67%)	6 (20%)	6 (20%)	

Table 1: Demographic data in the studied groups (Data were expressed as mean ± SD or patients number (%)).

Figure 1 the characteristics of the patients including age, gender, ASA class, or body weight were statistically insignificant between the studied groups (p=0.982, 0.792, 0.866 and 0.898 respectively). Also, the surgical characters including the duration and the type of the surgery were comparable among the three studied groups (p=0.924 and 0.987, respectively).

The total dose of morphine consumed by the patients was significantly lowered in the fentanyl and dexmedetomidine groups as compared to the control group (p=0.002 and 0.007 respectively) with an insignificant difference between fentanyl group and dexmedetomidine group (p=0.672).

Moreover, the time of the first request of the patients for postoperative rescue analgesia was significantly prolonged in fentanyl group and dexmedetomidine group in comparison to control group (p=0.009 and 0.002 respectively) with a statistically insignificant difference between fentanyl group and dexmedetomidine group (p=0.43) is shown in Table 2.

The mean values of VAS score were comparable between the three groups at the immediate postoperative period, 4 h, 12 h, 18 h, and 24 h postoperatively (p=0.744, 0.067, 0.141, 0.309, and 0.077 respectively).

	Control group	Fentanyl group	Dexmedetomidine group	P	P_1	P_2	P_3
Total dose of Morphine Consumption (mg)	11.33 ± 5.05	7.33 ± 4.59	7.80 ± 4.15	0.002*	0.002*	0.007 *	0.672
Time for the first request of rescue Analgesia (Hours)	6.87 ± 3.81	9.80 ± 4.50	10.80 ± 5.22	0.003*	0.009*	0.002*	0.43

Table 2: The need for postoperative analgesia.

Despite that, there was a significant decrease in VAS score in fentanyl and dexmedetomidine groups in comparison to the control group ($p<0.05$) at 2 h and 6 h postoperatively with an insignificant difference between the fentanyl group and dexmedetomidine group ($p>0.05$) (Fig 2).

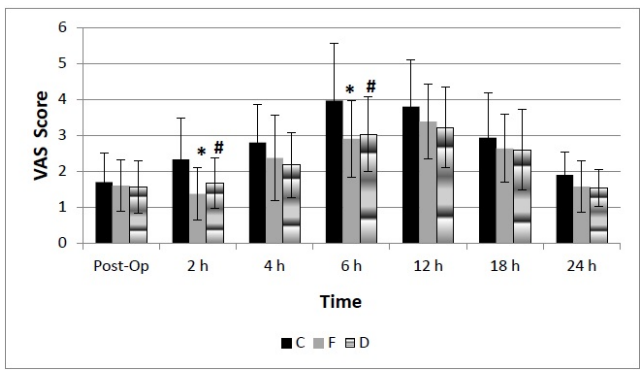

Figure 2: Postoperative Visual Analogue Score of the studied patients. Post-op, immediate postoperative. * indicates a statistically significant difference between control group and fentanyl group. # indicates a statistically significant difference between control group and dexmedetomidine group.

The hemodynamic parameters including heart rate and mean arterial pressure were statistically indifferent among the three studied groups during either the intraoperative or the postoperative period ($p>0.05$) is shown in Figure 3 and Figure 4.

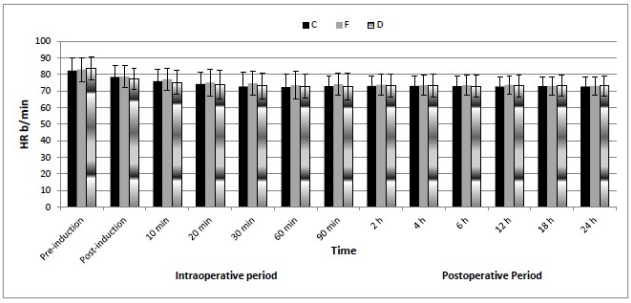

Figure 3: Changes in the mean values of heart rate.

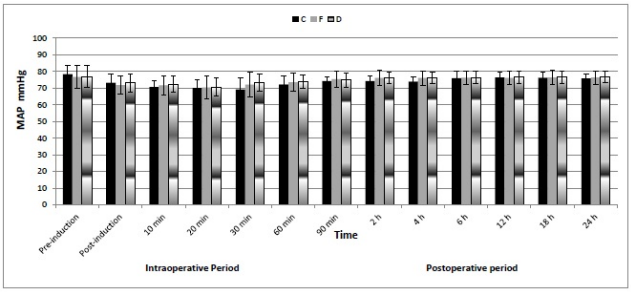

Figure 4: Changes in the mean values of Mean Arterial pressure charges.

The incidence of complications including bradycardia, hypotension, nausea, and vomiting, or sedation was comparable between the three groups ($p>0.05$). The use of either fentanyl or dexmedetomidine was not associated with significant increase in the patient's sedation in the

postoperative period (p>0.05). Moreover, there was no reported incidence of either pneumothorax or intravascular injection during the study (Table 3).

	Control Group	Fentanyl Group	Dexmedetomidine Group	p-value
Bradycardia	2 (6.67%)	3 (10%)	4 (13.33%)	0.691
Hypotension	2 (6.67%)	2 (6.67%)	3 (10%)	0.857
Nausea& Vomiting	3 (10%)	4 (13.33%)	3 (10%)	0.894
Intravascular injection	-	-	-	-
Pneumothorax	-	-	-	-
Urinary retention	1 (3.33%)	3 (10%)	2 (6.67%)	0.585
Sedation	-	2 (6.67%)	3 (10%)	0.227

Table 3: The incidence of Complications in the studied groups (Data were expressed as number of patients and %).

Discussion

The results of this study revealed that adding fentanyl (2 ug/ml) or dexmedetomidine (1 ug/kg) to plain bupivacaine (0.25%) in the continuous paravertebral block for patients presented for renal surgeries under general anesthesia was associated with significant reduction of the total dose consumption of rescue analgesia in the first 24 h postoperatively and significant prolongation of the duration for the first request of rescue analgesia. Also, their use was associated with significant decrease in the postoperative VAS score at 2 and 6 hours postoperatively without significant changes in hemodynamic parameters or incidence of complications. There was an insignificant difference between either fentanyl or dexmedetomidine usage.

The paravertebral block was first used to induce unilateral analgesia along the thorax and the abdomen without severe hemodynamic changes [18]. The paravertebral block acts mainly by the penetration of the local anesthetic mixture into the spinal nerves, sympathetic chain, and the dorsal ramus. The penetration of the local anesthetics into the spinal nerves is more sensitive as they are present in the form of small bundles without a fascial sheath [19]. Certain opinions suggested that epidural migration may explain its mechanism of action [20]. The analgesic effect of fentanyl administrated via paravertebral route is thought to be through stimulation of the opioid receptors in the dorsal root ganglia [21].

The mechanism of action of dexmedetomidine as an adjuvant in local and regional anesthesia isn't fully clear until now. It has both central and peripheral action [22]. Dexmedetomidine acts centrally at the dorsal root neuron through inhibition of the release of substance P at the nociceptive pathway; also, it stimulates the adrenergic alpha 2 receptors of the locus coeruleus [23]. Peripherally, it stimulates the peripheral adrenergic 2 receptors to decrease the release of norepinephrine and inhibition of nerve fiber action potentials [24].

Mohta et al. studied the analgesic effect of the continuous paravertebral block using either ropivacaine (0.375%) alone or ropivacaine (0.2%) added to fentanyl in the patients with multiple fractured ribs (3 or more) and revealed that 2 ug/ml of fentanyl added to ropivacaine 0.2% had the similar analgesic criteria to the higher concentration of ropivacaine without increase in the incidence of complications [25].

In spite of the few available studies evaluating the addition of dexmedetomidine to local anesthetics in the paravertebral block, Burlacu et al. conducted a randomized controlled study on 53 patients undergoing breast surgery under general anesthesia to compare the use of fentanyl, clonidine, or normal saline as an adjuvant to levobupivacaine in the paravertebral block versus no use of paravertebral block. They revealed that both fentanyl and clonidine improved the postoperative analgesia regarding its quality and duration. Despite that, their usage was associated with significant increase in the incidence of nausea and vomiting and hypotension [8].

Also, Dutta et al. evaluated the postoperative analgesic effect of the addition of dexmedetomidine to ropivacaine in the paravertebral block in patients presented to thoracotomy. They concluded that the use of dexmedetomidine was associated with significant improvement of the duration of postoperative analgesia and decreased rescue analgesia consumption without significant incidence of side effects or complications [17]. Moreover, Mohta et al. conducted a randomized double-blinded study on 45 female patients presented for breast cancer surgery under general anesthesia and a paravertebral block with plain bupivacaine 0.5% and either normal saline or dexmedetomidine 1 μg/kg. They revealed that the duration and the quality of postoperative analgesia were significantly improved with the use of dexmedetomidine. Also, the addition of dexmedetomidine didn't significantly alter the hemodynamic parameters or increased the incidence of side effects [26].

In addition, Sinha et al. concluded that the use of dexmedetomidine in a dose of 1 μg/kg as an adjuvant to ropivacaine in the paravertebral block in patients presented for renal surgeries led to significant improvement of the duration of postoperative analgesia and reduction of opioids consumption [27].

On the other hand, the systematic review of Kotzé, et al. included twenty-five trials and (763 patients) and aimed to detect the efficacy and safety of different paravertebral block regimens in patients after thoracotomy. They suggested that the addition of either clonidine or fentanyl to local anesthetics in the paravertebral block was not associated with significant improvement of the postoperative analgesia [28]. Also, Gupta et al. concluded that the use of either fentanyl or dexmedetomidine as an adjuvant to hyperbaric bupivacaine in intrathecal anesthesia did not alter the criteria of the postoperative analgesia [29].

Limitation of the Study

Despite being randomized double-blinded study, this clinical study was limited by the relatively low number of participating patients, Moreover; there are a relatively low number of available studies evaluating the use of fentanyl or dexmedetomidine as a local anesthetic adjuvant in the paravertebral block. Also, the use of a single concentration of plain bupivacaine limited the evaluation of the effect of fentanyl or dexmedetomidine on different concentrations of the local anesthetics.

Conclusion

In a conclusion, the use of fentanyl (2 μg/ml) or dexmedetomidine (1 μg/kg) as a local anesthetic adjuvant to plain bupivacaine (0.25%) in

the continuous paravertebral block for patients undergoing renal surgeries under general anesthesia was associated with significant decrease in the consumption of the postoperative analgesia and prolongation the time for request of analgesia with insignificant effect on the hemodynamic parameters or the incidence of complications. None of them appeared to be more favorable than the other.

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