

Efficacy of local dexmedetomidine add-on for spermatic cord block anesthesia in patients undergoing intrascrotal surgeries: randomized controlled multicenter clinical trial

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Study objective: The objective of this study was to evaluate the effect of adding dexmedetomidine (DEX) to bupivacaine on the quality of spermatic cord block anesthesia and postoperative analgesia.

Design: This is a randomized, double-blind study.

Setting: This study was performed in an educational and research hospital.

Patients: One hundred twenty adult males were scheduled for intrascrotal surgeries.

Interventions: Patients were divided into two groups: group B received 10 mL of bupivacaine 0.25% for spermatic cord block and intravenous 50 µg of DEX and group BD received 10 mL of bupivacaine 0.25% added to 50 µg of DEX (9.5 mL bupivacaine 0.25% + 0.5 mL [50 µg] DEX) for spermatic cord block, and for masking purposes, the patients received isotonic saline intravenously.

Measurements: Time to first analgesic request, analgesic consumption, and visual analog scale (VAS) pain score in the first 24 hours postoperatively were assessed.

Main results: Time to first rescue analgesic was significantly delayed in group BD in comparison with group B, median (interquartile) range, 7 (6–12) hours versus 6 (5–7) hours, ($p=0.000$), the mean cumulative morphine consumption (mg) in the first postoperative 24 hours was significantly lower in group BD compared with group B, 8.13 ± 4.45 versus 12.7 ± 3.79 , with a mean difference (95% CI) of -4.57 (-6.06 to -3.07) ($p=0.000$); also, there was a significant reduction of VAS pain score in group BD in comparison with group B at all measured time points, VAS 2 hours (1.28 ± 0.9 vs 1.92 ± 0.8), VAS 6 hours (2.62 ± 1.5 vs 3.93 ± 1.2), VAS 12 hours (2.40 ± 1.1 vs 3.57 ± 0.65), VAS 24 hours (1.90 ± 0.68 vs 2.53 ± 0.62) ($p=0.000$)

Conclusion: The addition of 50 µg of DEX to bupivacaine 0.25% in spermatic cord block for intrascrotal surgeries resulted in delay of first analgesic supplementation, reduction of postoperative analgesic consumption as well as improvement of the success rate of the block.

Keywords: dexmedetomidine, spermatic cord, intrascrotal surgery

Introduction

Spermatic cord block has been done safely for many intrascrotal surgeries including operations on the testis, epididymis, and spermatic cord. It involves blocking of the genital branch of the genitofemoral nerve and the ilioinguinal nerve after their emergence from the external ring of the inguinal canal as well as the sympathetic plexuses of nerves around the cord.¹ Spermatic cord block anesthesia offers the advantages of avoiding the undesirable side effects of general and neuraxial anesthesia, along with increased dura-

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tion of postoperative pain relief,^{2,3} reduced hospital stay and decreased financial burden.⁴ The short duration of peripheral nerve blocks limits their role in the improvement of postoperative analgesia. Hence, several local anesthetic adjuvants have been used perineurally to improve the effect of local anesthetics such as opioids,^{5,6} clonidine,⁷ dexamethasone,⁸ magnesium,⁹ midazolam, and ketamine.¹⁰ Dexmedetomidine (DEX) is a potent and a highly selective α -2 adrenoceptor agonist that owes sympatholytic, sedative, and analgesic properties.^{11,12} Animal studies have shown that DEX fastens the onset of sensory and motor blockade along with increased duration of analgesia.^{13,14} In human studies, the addition of DEX to local anesthetics has shown to improve the quality of some regional blocks and prolong the duration of postoperative analgesia.^{15–17}

The aim of this study was to evaluate the effect of adding DEX to bupivacaine on the quality of spermatic cord block anesthesia and postoperative analgesia.

Methods

Ethical approval and registration

This study was approved by the ethical committee of the faculty of medicine and institutional review board of South Egypt Cancer Institute, Assiut University, and written informed consent was obtained from each patient. The study was performed at the Andrology Department, Assiut University Hospital and South Egypt Cancer Institute, Assiut University, Egypt. The trial was registered in www.pactr.org; the identification number for the registry is PACTR201506001158296.

Inclusion and exclusion criteria

One hundred and twenty adult males, scheduled for intrascrotal surgery were enrolled. Exclusion criteria included refusal of regional anesthesia, allergy to study drugs (bupivacaine, DEX, or morphine), bleeding disorders, infection in the inguino-scrotal region, history of drug or alcohol abuse, and patients suffering from chronic pain or treated with regular analgesics.

Randomization and blindness

Patients were randomly allocated using block randomization method to two groups, group B (n=60) received spermatic cord block with bupivacaine only and group BD (n=60) received spermatic cord block with a mixture of bupivacaine and DEX.

Coded study drug solutions were prepared by anesthesiologist assistant, and the solutions were handed over to the concerned anesthesiologist for administration. According to the randomization code for each patient, group B received 10 mL of bupivacaine 0.25% for spermatic cord block and

intravenous 50 μ g of DEX (Precedex[®], Hospira, Lake Forest, IL, USA) (diluted in 50 mL isotonic saline and delivered by syringe pump, programmed to give 1 mL per minute or group BD received 10 mL of bupivacaine 0.25% added to 50 μ g of DEX (9.5 mL bupivacaine 0.25% + 0.5 mL [50 μ g] DEX) for spermatic cord block, and for masking purposes, the patients received isotonic saline intravenously via 50 mL syringe pump, programmed to give 1 mL per minute.

The night before surgery, oral lorazepam 4 mg was given. Upon arrival at the operating room, a peripheral venous line was inserted. Monitoring probes (electrocardiography, noninvasive blood pressure, pulse oximeter) were attached.

Technique of the block

After sterilization of inguino-scrotal region, the spermatic cord is palpated at the neck of scrotum and under ultrasound (US) guidance (M-Turbo; SonoSite Inc., Bothell, WA, USA) using a linear transducer 10 MHz. The spermatic cord was identified as a half-circle structure containing the testicular artery identified by Doppler US and the vas deferent as a round non-compressible structure with no Doppler flow through it. The overlying skin was infiltrated with 2 mL of 1% lidocaine, 22 gauge block needle attached to extension tube was inserted toward the vas deferent under out-of-plane real-time US guidance, and just before touching the vas, 10 mL of prepared solution was injected around it.

In cases of insufficient block, according to the degree of patient's discomfort, the patient received either additional local anesthetic (from the same prepared solution), additional analgesics (fentanyl boluses, 50 μ g fentanyl), or conversion to general anesthesia, which entailed induction with propofol 2–3 mg/kg, maintenance with sevoflurane 2%–3% in 50% oxygen and air, and securing the airway with the insertion of suitable size laryngeal mask.

After the end of surgery, the patients were transferred to day care unit for 24 hours observation period. Our postoperative analgesic protocol was intravenous patient controlled analgesia (PCA) morphine, programmed to deliver 2 mg bolus with 5 minutes lock out interval and without background infusion.

Study outcomes

Our primary end point was the time to first analgesic demand and the secondary end points were 1) the success rate of the block (the block was considered unsuccessful if any additional intraoperative local anesthetic, analgesic, or sedative was used, and/or VAS score was >3 or conversion to general anesthesia), 2) 24 hours analgesic consumption, 3) the VAS score measured at 2, 6, 12, and 24 h postoperatively, and

4) the level of sedation assessed using Observer's Assessment of Alertness/Sedation Scale (OAA/S). Scores ≤ 3 were considered excessive sedation.

Statistical analysis

Based on a previous study,¹⁸ which reported a mean difference of 1.95 hours of postoperative analgesic duration and a standard deviation (SD) of 4.43 for the bupivacaine only group and 2.73 for the bupivacaine + DEX group, it was estimated that a minimum sample size of 57 patients in each study group would achieve a power of 80%, assuming a type I error of 0.05. We enrolled 120 patients to allow for dropouts. Statistical analysis was carried out on a personal computer using SPSS version 20 software. Normality of continuous data distribution was tested with the Anderson–Darling test prior to further statistical analysis. Categorical data were described as number and percent, where continuous data were described as mean \pm SD or 95% confidence interval (CI) where appropriate. Chi-square test was used for comparison between categorical variables, where continuous variables were compared using unpaired Student's *t*-test. Time to first analgesic request was not normally distributed, and data were described as median (interquartile range). General linear model was used for the analysis of repeated measures of VAS pain score over time to detect the overall effect of group, time, and group-by-time interaction, and subsequent multiple comparisons were achieved by post hoc tests and type 1 error was controlled with Bonferroni correction. Statistical significance was set at $p < 0.05$.

Results

There was no statistically significant difference between the two groups with respect to demographic data, type, and duration of surgery (Table 1).

The time to first rescue analgesic was significantly delayed in group BD in comparison with group B, median (interquartile) range, 7 (6–12) hours versus 6 (5–7) hours, respectively, $p = 0.000$ (Figure 1).

The mean cumulative morphine consumption (mg) in the first postoperative 8 hours was significantly lower in group BD compared with group B, 2.23 ± 2.21 versus 3.97 ± 2.28 , with an estimated mean difference (95% CI) of -1.73 (-2.55 to -0.92), also the mean cumulative morphine consumption (mg) in the first postoperative 16 hours was significantly lower in group BD compared with group B, 5.33 ± 3.41 versus 9.1 ± 3.05 , with an estimated mean difference (95% CI) of -3.77 (-4.93 to -2.6); moreover, the mean cumulative morphine consumption (mg) in the first postoperative 24 hours was significantly lower in group BD compared with group B, 8.13 ± 4.45 versus 12.7 ± 3.79 , with an estimated mean difference (95% CI) of -4.57 (-6.06 to -3.07) (Table 2).

The general linear model for repeated measures of VAS pain score over time revealed significant reduction of overall VAS pain score in group BD in comparison with group B, 2.05 versus 2.99 with an estimated mean difference (95% CI) of -0.94 (-1.18 to -0.69) ($p = 0.000$). Moreover, there was a significant reduction of VAS pain score in group BD in comparison with group B at all measured time points, VAS 2 hours (1.28 ± 0.9 vs 1.92 ± 0.8), VAS 6 hours (2.62 ± 1.5 vs 3.93 ± 1.2), VAS 12 hours (2.40 ± 1.1 vs 3.57 ± 0.65), VAS 24 hours (1.90 ± 0.68 vs 2.53 ± 0.62) ($p = 0.000$) (Figure 2).

The failure rate of the block was significantly higher in group B in comparison with group BD (11.67% vs 3.3%) ($p = 0.005$). The failure dynamics of the block were shown in (Table 3).

Regarding the perioperative hemodynamics, there were statistically significant reductions in the intraoperative mean heart rate and mean arterial blood pressure in the BD group at the following time points (15, 20, 25, and 30 minutes) (Figure 3).

Table 1 Demographic data

Variables	Group B (n=60)	Group BD (n=60)	p-value
Age (years)	36.9 (34.9–39.3)	37.8 (42.8–40.2)	0.936
BMI (kg/m ²)	28 (26.2–28.9)	27.7 (26.8–29.3)	0.532
ASA grade I/II/III	47/10/3	50/7/3	0.594
Type of operations			
Testicular biopsy	34	36	0.921
Orchidectomy	11	12	0.975
Epididymal cystectomy	8	5	0.521
Spermatocoelectomy	3	4	0.876
Epididymovasostomy	4	3	0.876
Duration of surgery (minutes)	37.1 (30.4–41.6)	36.7 (30.5–41)	0.832

Notes: Values are expressed as the mean (95% CI) or absolute numbers. B refers to bupivacaine group and BD to bupivacaine + DEX group.

Abbreviations: BMI, body mass index; ASA, American Society of Anesthesiologists; DEX, dexmedetomidine.

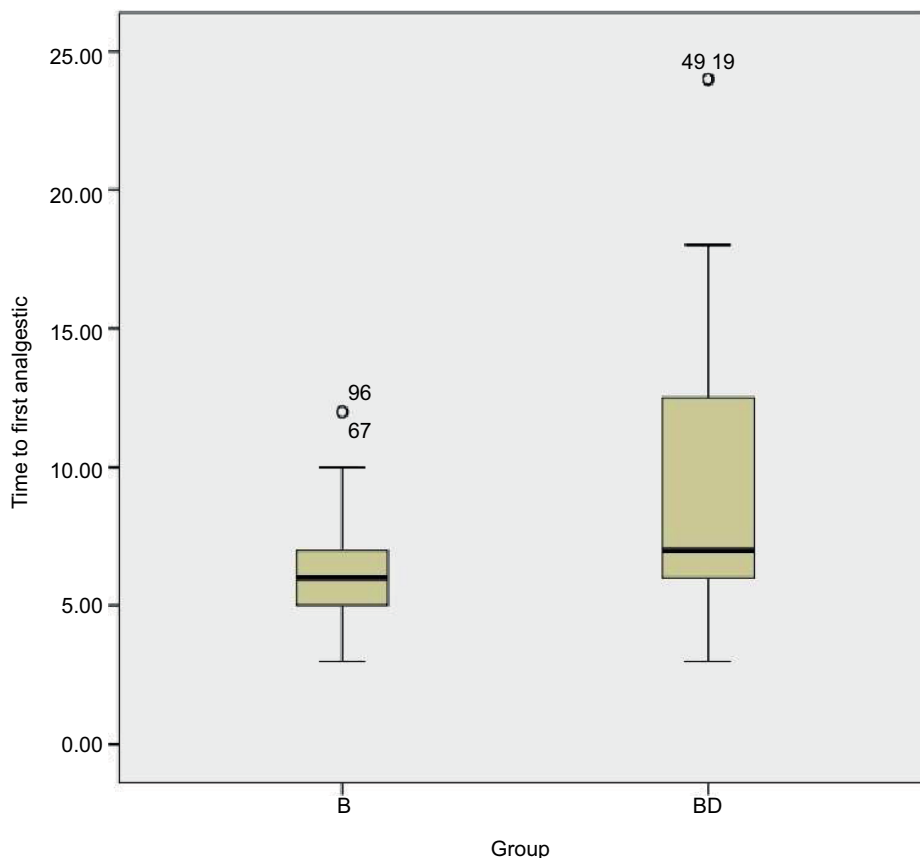


Figure 1 A box plot of postoperative time (hours) to rescue analgesic in each group. The middle line in each box represents the median value, the outer margins of the box represent the interquartile range, and the whiskers represent the 10th and 90th percentile. Circles represent the outliers. B refers to bupivacaine group and BD to bupivacaine + DEX group.

Abbreviation: DEX, dexmedetomidine.

Table 2 Cumulative postoperative 24 hours PCA morphine consumption and overall 24 hours VAS pain score

Morphine consumption (mg)	Group BD (N = 60)	Group B (N = 60)	Mean difference	95% CI (mean difference)
Cumulative 8 hours	2.23±2.21	3.97±2.28	-1.73 ^a	-2.55 to -0.92
Cumulative 16 hours	5.33±3.41	9.1±3.05	-3.77 ^a	-4.93 to -2.6
Cumulative 24 hours	8.13±4.45	12.7±3.79	-4.57 ^a	-6.06 to -3.07
Overall 24 hours VAS	2.05	2.99	0.94 ^a	-1.18 to -0.69 ^b

Notes: ^aThe mean difference is significant at the 0.05 level. ^bAdjustment for multiple comparisons: Bonferroni. B refers to bupivacaine group and BD to bupivacaine + DEX group.

Abbreviations: PCA, patient controlled analgesia; VAS, visual analog scale; DEX, dexmedetomidine.

Regarding DEX-related sedation, we did not report significant statistical differences between the two groups (Figure 4).

Discussion

In the present study, the addition of 50 µg of DEX to bupivacaine 0.25% for spermatic cord block for patients undergoing intrascrotal surgery resulted in significant delay of first analgesic demand, improved the success rate of the block, reduced postoperative analgesic consumption, and decreased pain intensity in the first postoperative 24 hours.

Kaye et al described the blind technique of the spermatic cord block, where they fixed the spermatic cord against the pubic tubercle and pierced it with a needle, inserted vertically to the pubic bone,¹⁹ 1 cm below and medial to the pubic tubercle, in addition to scrotal skin infiltration with local anesthetics. In the current study, we performed the spermatic cord block with the help of US guidance to avoid injury to testicular artery and vas deferent.¹

DEX is a selective α₂ adrenoceptor agonist with an eight-fold affinity compared to the α₂ adrenoceptor, clonidine.²⁰

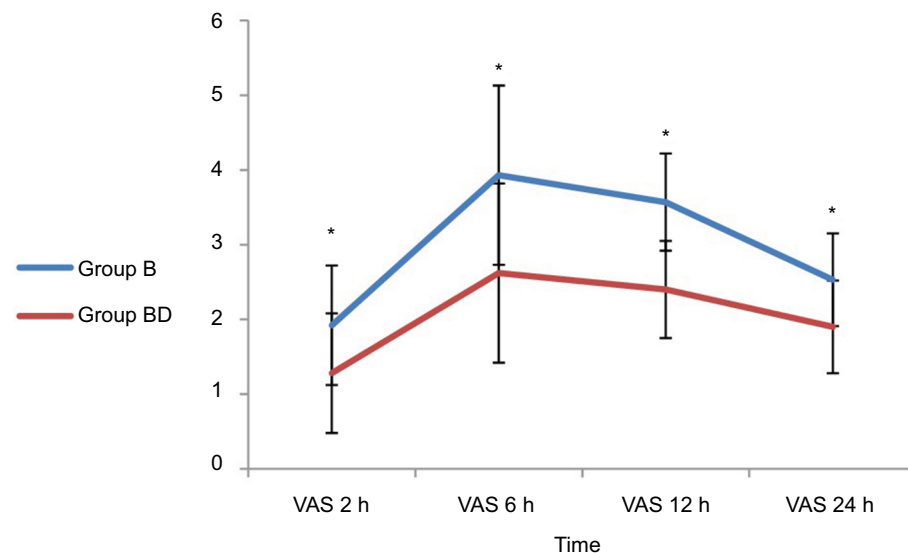


Figure 2 A line graph representing the postoperative VAS pain score in the two study groups. * $p < 0.05$ between the groups. B refers to bupivacaine group and BD to bupivacaine + DEX group.

Abbreviation: VAS, visual analog scale; DEX, dexmedetomidine.

Table 3 Failure dynamics of spermatic cord block anesthesia

Variables	Group B (n=60)	Group BD (n=60)	p-value
Failed block	7 (11.67%)	2 (3.3%) ^a	0.005
Additional analgesic (fentanyl)	3 (5%)	1 (1.67%) ^a	0.032
Additional local anesthetic	4 (6.6%)	1 (1.67%) ^a	0.021

Notes: Values are expressed as absolute numbers (%). ^a p -value < 0.05 . B refers to bupivacaine group and BD to bupivacaine + DEX group.

Abbreviation: DEX, dexmedetomidine.

It possesses a unique sedative, anxiolytic, and analgesic criteria.^{21,22}

The usage of DEX as a local anesthetic adjuvant is inspired from its prototype clonidine, which enhanced the activity-dependent hyperpolarization generated by the sodium-potassium pump and consequently blocked the conduction of pain impulses.²³

There is a great variability of DEX doses when it is used as a local anesthetic adjuvant,^{24–28} because the clinical studies are different in between in defining bradycardia and hypotension,^{28–30} which are the main drawbacks of DEX usage. As there were no previous reference dosage guidelines of DEX for spermatic cord block, the selection of the DEX dose (50 μ g) was based on our own anecdotal experience.

Our study showed that the success rate of the block was significantly improved in group BD (96.7%) compared with group B (88.4%), while it was 90%–95% for blindly injected spermatic cord blocks in previous studies.^{4,9,31} It deserves mentioning that these studies administered additional local anesthetics and systemic analgesics during surgery that was

considered failed blocks by our own study criteria for unsuccessful blocks. Moreover, we attempted diluted bupivacaine (0.25%) for surgical block to declare any beneficial effects of DEX adjuvant, specifically bupivacaine sparing effect, while these studies administered local anesthetics with higher concentration (bupivacaine 0.5% and lidocaine 2%).

Animal studies have declared that perineural DEX added to bupivacaine or ropivacaine prolongs the duration of sensory and motor block.^{13,14,32,33} Furthermore, human studies used DEX as local anesthetic adjuvants have been yielding prolonged block duration and decreased postoperative analgesic demand, but they are different in between regarding block characteristics.^{16,18,23,34,35} In this context, Fritsch et al reported that DEX added to ropivacaine extends the duration of interscalene brachial plexus blocks for elective shoulder surgery and minimized postoperative opioid supplementation.³⁴ Esmaoglu et al found that DEX enhanced the onset of brachial plexus block,¹⁸ whereas Gandhi et al showed a delay in sensory and motor block onset time.²⁴ In our study, we could not assess the block onset as the nerves anesthetized in spermatic cord block the supply of intrascrotal contents and the scrotal skin is supplied by sensory branches from pudendal nerve that is anesthetized by local infiltration. However, we detected a significant prolongation of postoperative analgesic duration in DEX group along with significant reduction in postoperative analgesic consumption.

The main limitations of DEX are dose-dependent bradycardia and hypotension.³⁶ In the present study, we observed a significant reduction in heart rate and mean blood pressure

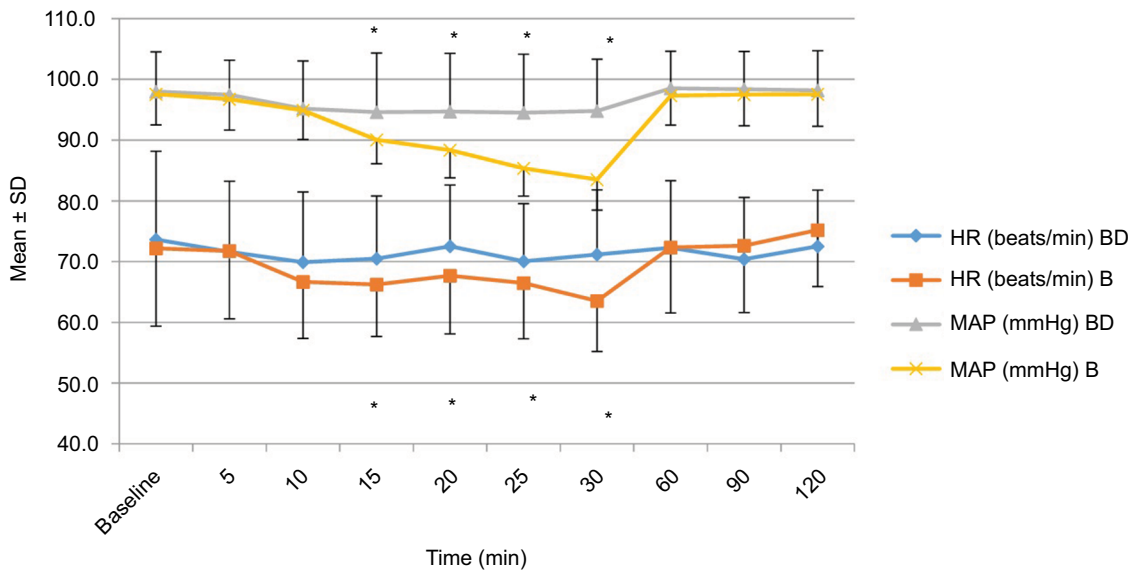


Figure 3 A line graph representing the perioperative HR and MAP in the two study groups. * $p < 0.05$ between the groups. B refers to bupivacaine group and BD bupivacaine + DEX group.

Abbreviations: HR, heart rate; MAP, mean arterial blood pressure; DEX, dexmedetomidine.

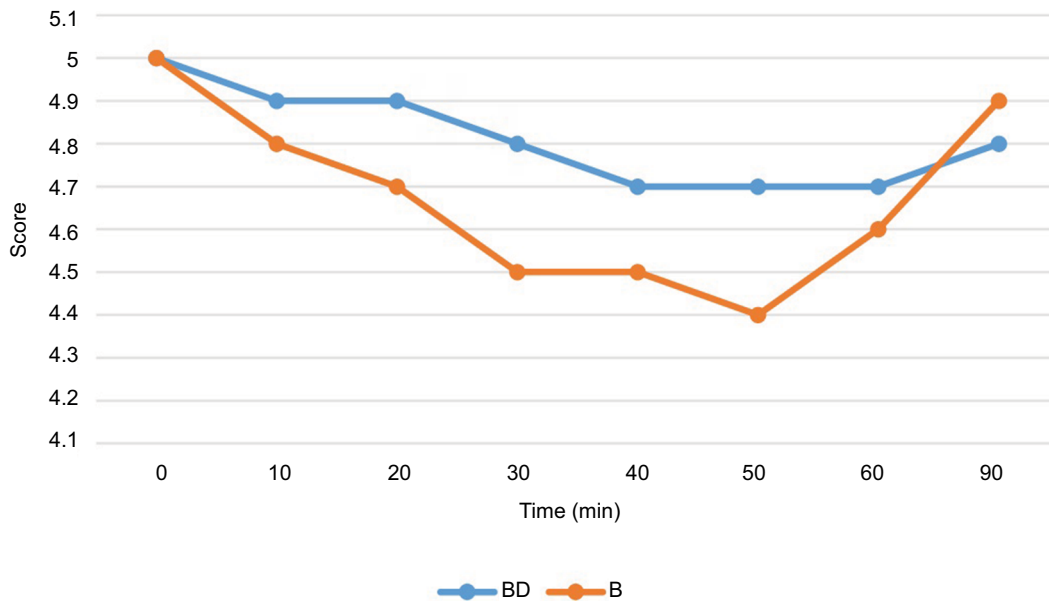


Figure 4 A line graph representing the OAA/S in the two study groups. B refers to bupivacaine group and BD to bupivacaine + DEX group.

Abbreviations: OAA/S, observer assessment of alertness and sedation score; DEX, dexmedetomidine.

intraoperatively, but they were in a safe limit and we did not report any cases of severe bradycardia or hypotension.

It is likely that the mechanisms by which DEX improved spermatic cord block are similar to the hypotheses suggested for perineural use of clonidine.³⁷⁻⁴¹ Brummett et al³³ suggested that the mechanism of perineural administration of DEX is by blocking the hyperpolarization-activated cation current, preventing the nerve from reaching the resting potential and capability of generation of subsequent action potential, thus

DEX decreases firing of pain impulse specifically from unmyelinated C-fibers. This is the most well-defined mechanism of perineural DEX.³³

There are a rising conflicts among researchers whether DEX as a local anesthetic adjuvant acts through a peripheral or central mechanism. To eliminate the concerns about a possible systemic analgesic mechanism of DEX due to systemic absorption of DEX from the pampiniform plexuses of veins around spermatic cord, we administered group B the same

dose of DEX (50 µg) used for group BD, but through intravenous routes. Abdallah et al reported a similar prolongation of an interscalene block whether DEX was administered perineurally or systemically in patients undergoing arthroscopic shoulder surgery,⁴² while Andersen et al concluded that DEX prolongs the duration of the saphenous nerve block by a peripheral mechanism when controlling for systemic effects, but not necessarily to a clinically relevant extent.⁴³

In conclusion, the addition of 50 µg of DEX to bupivacaine 0.25% in spermatic cord block for intrascrotal surgery resulted in significant improvement of the success rate of the block, delayed first demand for analgesic supplementation, and reduced postoperative analgesic consumption.

Disclosure

The authors report no conflicts of interest in this work.

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