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ORIGINAL RESEARCH REGIONAL ANESTHESIA

A comparative study between the use of dexmedetomidine vs. dexamethasone as adjuvants to bupivacaine in ultrasound-guided transversus abdominis plane block for postoperative pain relief in patients undergoing lower abdominal surgeries

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Abstract

Background & objective: Transversus abdominis plane (TAP) block using local anesthetics is associated with relatively shorter duration of action, and thus additional analgesic drugs are required in the postoperative period. We compared the efficacy and duration of postoperative analgesia achieved with using dexmedetomidine or dexamethasone as adjuvants to bupivacaine in TAP block for lower abdominal surgeries.

Methodology: We enrolled 45 adult patients aged from 20-60 y, and randomly divided them into three equal groups. Group A received ultrasound guided TAP block with 0.25% bupivacaine 20 ml plus 4 mg dexamethasone on each side. Group B received 0.25% bupivacaine 20 ml plus dexmedetomidine 0.5 µg/kg on each side, and Group C (control group) patients received only 0.25% bupivacaine 20 ml on each side. Postoperative pain was assessed with VAS on arrival in post-anesthesia care unit (PACU), at 2 h, 6 h, 12 h, 18 h, and at 24 h postoperatively. Duration of analgesia was the time from drug injection to the time of first rescue of analgesia was recorded.

Results: Mean duration to first dose of rescue analgesia among patients of dexmedetomidine group (Group B) was significantly prolonged as compared to dexamethasone group and bupivacaine only group. Regarding postoperative pain scores there were no statistically significant difference between the three groups; except at 6 h between the A and B groups and the control group. Both dexamethasone group and dexmedetomidine group showed better pain control than bupivacaine only at 6 h interval.

Conclusion: Dexmedetomidine added to bupivacaine in ultrasound-guided transversus abdominis plane block for postoperative pain relief in patients undergoing lower abdominal surgeries prolongs the time to initial postoperative pain presented by time to first rescue analgesic demand than dexamethasone added to bupivacaine; the shortest time to first rescue analgesic was observed in bupivacaine alone group.

Abbreviations: TAP: Transversus abdominis plane block; LA: Local anesthetic; PACU: Post anesthesia care unit; VAS: Visual Analogue Scale; ASA: American Society of Anesthesiologists; SD: Standard deviation; IQR: Inter quartile range.

Key words: Ultrasound-guided transversus abdominis plane block; Dexmedetomidine; Dexamethasone; Lower abdominal surgeries; Pain, Postoperative

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1. Introduction

Ultrasound guided peripheral nerve blocks such as the transversus abdominis plane (TAP) block, have been used for improving analgesia after various lower abdominal surgeries.[1] TAP block is a peripheral nerve block used to anesthetize the nerves supplying the anterior abdominal wall (T6 −L1). The correct local anesthetic deposition is greatly enhanced by the use of ultrasound, thereby blocking the sensory nerves more efficiently and enhancing the quality of analgesia with fewer complicaions.[2]

Peripheral nerve blocks as part of a multimodal analgesic regimen, can decrease opioid requirement, achieving more satisfactory analgesia with fewer adverse effects.[3] However, using only local anesthetics in such blocks is associated with relatively short duration of analgesia and thus, early analgesic intervention is needed in the postoperative period. A number of adjuvants, such as dexmedetomidine and dexamethasone have been used to increase the duration of regional anesthesia.[4] Dexmedetomidine is a selective α2 adrenergic agonist with analgesic and sedative properties, used as an adjuvant to local anesthetics in the peripheral nerve blocks.[5] Corticosteroids such as dexamethasone have anti-inflammatory as well as analgesic properties. They suppress inflammation by inhibition of phospholipase A2 enzyme which in turn reduces synthesis of inflammatory mediated prostaglandins. Perineural injection of dexamethasone as an adjuvant to local anesthetics is reported to enhance the onset and duration of sensory and motor blockade.[6]

We compared the time to first rescue analgesia (starting from the block injection) in patients receiving bilateral ultrasound guided TAP block using dexmedetomidine or dexamethasone added to bupivacaine, or bupivacaine alone for bilateral TAP block for 24 h postoperatively. Secondary outcome was to compare pain scores using Visual Analogue Score (VAS) between the three groups for 24 h postoperatively.

2. Methodology

The study was a randomized controlled comparative study conducted at Ain Shams University Hospitals. A total of 45 adult patients, ASA I and II, 20–60 y old, body mass index 25–35 kg/m^2, scheduled for lower abdominal surgeries such as inguinal hernia repair and cesarean section under general anesthesia, were enrolled.

Exclusion criteria included patient refusal, infection at the site of injection, psychiatric or physical illness leading to inability to cooperate, speak or read, history or evidence of coagulopathy, known allergy to drugs used and preexisting neurological disorders.

Patients were randomized into 3 equal groups by a computer-generated random numbers table; each group consisted of 15 patients to receive bilateral TAP block as follows:

a) Group A: 20 ml 0.25% bupivacaine (Sunnypivacaine®) plus 4 mg dexamethasone diluted in 2 ml of normal saline.

b) Group B: 20 ml 0.25% bupivacaine (Sunnypivacaine®) plus 0.5 µg/kg of dexmedetomidine (Precedex® 100 µg/ml) diluted in 2 ml of normal saline.

c) Group C: 20 ml 0.25% bupivacaine (Sunnypivacaine®) plus 2 ml normal saline.

The primary outcome was to compare the duration of first rescue analgesia (starting from the completion of the block). The secondary outcome was assessment of postoperative pain using VAS score at arrival in PACU, at 2, 6, 12, 18 and 24 h.

Routine preoperative investigations were done to all patients. Age, weight, height and medical history were recorded. Patients were fasted for 8 h preoperatively.

The procedure was explained to the patients about general anesthesia and TAP block during the preanesthetic visit in detail. Patients were familiarized with the visual analogue scale (VAS) before surgery. Informed consent was signed by the patients for general anesthesia and TAP block.

Inside the operating room, intravenous access was obtained, standard monitors (pulse oximeter, noninvasive blood pressure, ECG, capnography) were connected and baseline noninvasive blood pressure (NIBP), heart rate (HR), electrocardiography (ECG) and pulse oximetry (SpO_2) were recorded. All patients received pantoprazole 40 mg and granisetron 1 mg, as premedication.

Anesthesia induction was similar in all groups; by propofol 1.5–2 mg/kg, fentanyl 1 µg/kg, and atracurium 0.5 mg/kg. Isoflurane inhalational anesthesia (1.2%) in oxygen/air mixture (FiO_2 60%) was used for maintenance and the patients were mechanically ventilated.

In all groups, ultrasound guided TAP block was performed on both sides before emergence of anesthesia.

Whilst the patient was in the supine position, a high frequency (8–13 µHz) linear probe was placed transverse to the abdominal wall between the costal margin and iliac crest at mid axillary line. The needle was introduced in plane of the ultrasound probe directly under the probe and advanced until it reached the plane between the internal oblique and transversus abdominis muscles. Upon reaching the plane and after negative aspiration test for blood, 2 ml of saline was injected to confirm correct needle position, after which the patients received the TAP block as per the group allocation.

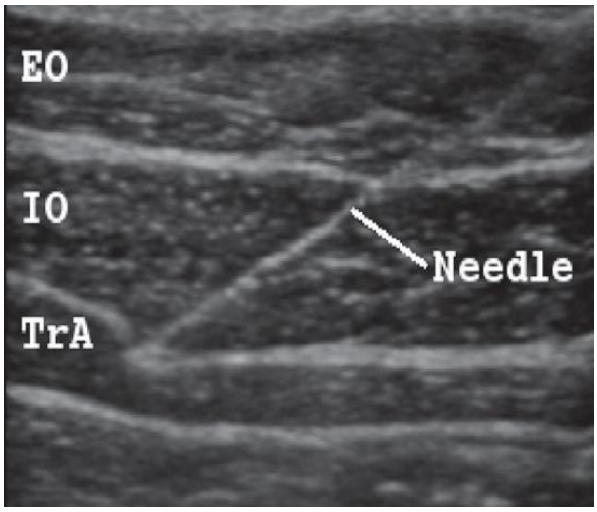

Figure 1: Ultrasound image showing the muscle layers of the lateral abdominal wall with the needle seen positioned above the transversus abdominis muscle. EO: external oblique, IO: internal oblique, TrA: transversus abdominis.

After the block, the anesthesia was terminated, residual effect of muscle relaxant reversed by using prostigmine 0.03–0.07 mg/kg plus atropine 0.03 mg/kg, extubation done and the patient shifted to post-anesthesia care unit (PACU).

Hemodynamic data, including heart rate (HR), systolic, diastolic and mean blood pressures were recorded on arrival in PACU, then at 2, 6, 12, 18, and 24th h postoperatively. Inj. paracetamol 1 gm was given every 6 h as analgesic protocol for all patients for 24 h.

Patients were observed for any complication, e.g., signs of local anesthetic toxicity and hematoma formation at the site of TAP block etc.

Quantitative relief of pain was assessed using VAS on arrival to PACU, then at 2, 6, 12, 18, and 24 h postoperatively. At score ≥ 4, inj. nalbuphine 5 mg IV was given as rescue analgesic.

Duration of analgesia, the time from the TAP block to the time of first rescue of analgesia, was recorded.

Statistical Analysis

Sample size was calculated using PASS® version 11 program, setting the type-1 α error at 0.05 and the power (1-β) at 80%.[9] In a one-way ANOVA study, sample size of 15 patients per group was obtained. A sample of 45 subjects achieved 99% power to detect differences among the means versus the alternative of equal means using an F test with a 0.005 significance level. The size of the variation in the means was represented by their standard deviation which was 0.47. The common standard deviation within a group was assumed to be 0.50.

Data were analyzed using Statistical Package for Social Sciences (SPSS) version 22.0. Quantitative data were expressed as mean ± standard deviation (SD) or interquartile range (IQR), as indicated. Qualitative data were expressed as frequency and percentage. Following tests were used: One-way analysis of variance (ANOVA) was used to test the difference between the means of several subgroups of a variable. Post-hoc test was used for pair-wise comparison of subgroups, when the ANOVA test was positive. Chi-square (X^2) test of significance was used to compare proportions between qualitative parameters. The Kruskal-Wallis test was used for several subgroup comparisons in non-parametric data. The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the $P < 0.05$ was considered significant, and $P < 0.001$ was considered as highly significant.

3. Results

Groups were comparable in demographic data (in terms of age, sex, BMI, duration of surgery and ASA status) and there was no statistically significant difference between groups ($P > 0.05$). (Table 1, 2).

Regarding time to first rescue analgesia, and was statistically significant differences between Group B and A, between Group C and B and between Group C and Group A ($P < 0.001$) (Table 2).

Groups were comparable regarding hemodynamic data all over the 24 hours as regard systolic arterial blood pressure (SABP), mean arterial blood pressure (MAP)

Table 1: Comparison between the studied groups as regard demographic data

Variable	Group A (n = 15)	Group B (n = 15)	Group C (n = 15)	Test	P
Age (y)	35.13 ± 11.08	32.6 ± 9.6	36 ± 10.35	F = 0.44	0.65
Sex					
Male	6 (40)	5 (33.3)	7 (46.7)	χ^2 = 0.556	0.757
Female	9 (60)	10 (66.7)	8 (53.3)		
ASA I	11 (73.3)	10 (66.7)	9 (60)	χ^2 = 0.600	0.741
ASA II	4 (26.7)	5 (33.3)	6 (40)		
Weight (kg)	79.97 ± 9.61	78.97 ± 8.6	75.33 ± 8.78	F = 1.099	0.343
Height (cm)	171.87 ± 7.15	169 ± 6.75	168 ± 6.93	F = 1.253	0.296
BMI (kg/m^2)	27.03 ± 2.36	27.65 ± 2.71	26.65 ± 2.26	F = 0.636	0.534

Data expressed as Mean ± SD or n (%). F: One-way ANOVA, χ2: Chi square test

Table 2: Comparison between the studied groups as regard duration of surgery

	Group A (n = 15)	Group B (n = 15)	Group C (n = 15)	Test	P
Duration of surgery(mins)		100.07 ± 12.63	96.2 ± 20.01	F = 1.582	0.218
Time to 1st rescue analgesia	350.0 ± 13.48	391.20 ± 13.02₱	308.40 ± 8.21€¥	F = 15.1	< 0.001*

*Data expressed as Mean ± SD. F: One-way ANOVA, Group A: Dexamethasone group, Group B: Dexmedetomidine group, Group C: control group. *: Statistically significant at P ≤ 0.05, ₱ = Tukey post hoc test significant between Group B and Group A, € = Tukey post hoc test significant between Group C and Group A, ¥ = Tukey post hoc test significant between Group C and Group B.*

Table 3: Comparison between the studied groups as regard systolic blood pressure

Systolic BP	Group A (n = 15)	Group B (n = 15)	Group C (n = 15)	Test F	P
At PACU	122.66 ± 8.21	117.67 ± 13.48	126.33 ± 13.02	2.04	0.143
2 h	117.33 ± 8.42	116.33 ± 8.33	117.67 ± 11.47	0.08	0.924
6 h	110.33 ± 6.51	108.33 ± 6.72	111 ± 10.21	0.5	0.613
12 h	108.33 ± 6.11	111.33 ± 6.39	106 ± 8.28	2.2	0.126
18 h	115.67 ± 6.78	113.67 ± 8.61	114 ± 8.70	0.4	0.662
24 h	121 ± 10.39	114.67 ± 8.96	116.67 ± 8.38	1.8	0.174

Data expressed as Mean ± SD; F: One-way ANOVA, Group A: Dexamethasone group, Group B: Dexmedetomidine group, Group C: control group.

and heart rate (HR) at regular intervals (PACU, after 2 h, 6 h, 12 h, 18 h and 24 h) there was no statistical difference between them throughout the 24 hours (Tables 3, 4, 5).

Groups were comparable for pain control all over the 24 h by visual analog scale (VAS) at regular intervals in PACU, after 2 h, 6 h, 12 h, 18 h and 24 h.

Table 4: Comparison between the studied groups as regard

Mean BP	Group A (n = 15)	Group B (n = 15)	Group C (n = 15)	Test	P
At PACU	86.66 ± 7.83	87.39 ± 7.29	85.84 ± 6.13	0.17	0.837
2 h	84.89 ± 7.9	86.56 ± 5.54	83.00 ± 7.46	0.96	0.392
6 h	82.00 ± 7.46	83.22 ± 6.76	79.44 ± 7.41	1.1	0.359
12 h	81.33 ± 6.73	84.22 ± 7.12	77.77 ± 7.47	3.1	0.056
18 h	83.66 ± 7.24	84.55 ± 7.43	80.44 ± 7.33	1.3	0.282
24 h	85.44 ± 7.13	84.22 ± 7.68	81.33.67± 7.07	1.25	0.296

Data expressed as Mean ± SD. F: One-way ANOVA, Group A: Dexamethasone group, Group B: Dexmedetomidine group, Group C: control group.

Table 5: Comparison of heart rates between the studied groups

Heart rate	Group A (n = 15)	Group B (n = 15)	Group C (n = 15)	Test (F)	P
At PACU	74.93± 7.55	74.13 ± 7.11	74.4 ± 4.21	0.06	0.942
2 h	73.53 ± 7.17	73.33 ± 7.18	71.6 ± 4.30	0.42	0.661
6 h	71.67 ± 7.45	71.2 ± 7.22	72.46 ± 3.44	0.15	0.857
12 h	70.4 ± 6.84	69.33 ± 7.29	72.4 ± 4.37	0.92	0.408
18 h	69.33 ± 7.41	69.13 ± 7.26	71.47 ± 4.36	0.59	0.556
24 h	70 ± 7.32	69.8 ± 7.47	71.87 ± 4.24	0.46	0.635

Data expressed as Mean ± SD; F: One-way ANOVA, Group A: Dexamethasone group, Group B: Dexmedetomidine group, Group C: control group

and there was no statistically significant difference between groups throughout the 24 hours except after 6 hours between Group C and A and between Group C and B (Table 6).

4. Discussion

TAP block has a great role in reducing postoperative pain and analgesic requirement resulting in early ambulation and discharge after lower abdominal

surgeries such as laparoscopic cholecystectomy, appendectomy, hysterectomy and cesarean section. Unfortunately, TAP block has a relative short duration of action related to the effect of the administered local anesthetics (LA). Several adjuvant drugs, such as dexmedetomidine and dexamethasone etc., have been added to LA with an aim to prolong the duration of analgesia of TAP block.[10]

Many studies have been done to determine the analgesic efficacy and safety of both as adjuvants to LA in peripheral nerve blocks. Analgesic effect of dexamethasone was mediated by its anti-inflammatory or immunosuppressive action. It potentiates the action of LA through modulation of the potassium channels.[11]

In our study, there were no statistically significant differences between the three groups regarding postoperative pain scores, except at 6 h between A and B groups and the control group. As both Group A (dexamethasone group) and Group B showed better pain control than Group C (bupivacaine only group) at 6 h interval.

Also, we found that addition of dexmedetomidine to bupivacaine 0.25% on each side (Group B) significantly prolonged the analgesia duration than bupivacaine plus dexamethasone (Group A).

Difference in mean time to the first dose of rescue analgesia among patients of dexamethasone Group was significantly earlier as compared to dexmedetomidine Group (350.0 ± 13.48 min vs. 391.20 ± 13.02 min; $P \leq 0.001$).

Possible mechanism explained by Yoshitomi et al., was that dexmedetomidine causes vasoconstriction mediated by its effect on α2 adrenoceptors around the site of injection, resulting in prolongation of the absorption of the local anesthetic. Also, it produces analgesia peripherally by reducing norepinephrine release and

Table 6: Comparison between the studied groups as regard VAS Score

VAS	Group A (n = 15)		Group B (n = 15)		Group C (n = 15)		Z	P value
	Median (Range)	IQR	Median (Range)	IQR	Median (Range)	IQR		
PACU	1 (0−2)	1−2	1 (0−2)	1−2	1 (0−2)	1−2	0.1	0.93
2 h	1 (1−2)	1−2	2 (1−2)	1−2	2 (1−2)	1−2	0.9	0.54
6 h	2 (1−3)	1−2	2 (1−3)	1−2	3 (1−3) €¥	2−3	9.6	0.005
12 h	3 (1−3)	2−3	3 (1−3)	1−3	3 (1−3)	2−3	0.1	0.95
18 h	2 (1−3)	2−3	2 (1−3)	2−3	3 (1−3)	2−3	1	0.55
24 h	2 (2−3)	2−3	2 (1−3)	2−3	2 (1−3)	2−3	0.3	0.85

Data expressed as Median (Range), and Interquartile range (IQR). Z = Kruskal-Wallis test, Group A: Dexamethasone group, Group B: Dexmedetomidine group, Group C: control group, € = Conover post hoc test significant between Group C and Group A, ¥ = Conover post hoc test significant between Group C and Group B

increasing the potassium conduction in C and A-delta neurons responsible for transmission of pain signals.[12]

Our results are in agreement to that of Swami et al. They found in their study on 60 patients undergoing supraclavicular brachial plexus block that addition of dexmedetomidine 1 µg/kg to bupivacaine 0.25% - clonidine 1µg/kg mixture significantly prolonged the duration of analgesia more than bupivacaine-clonidine mixture only.[13]

Similar findings have been reported in a study comparing dexamethasone (0.1 mg/kg) and dexmedetomidine (1 µg/kg) as adjuvants to bupivacaine (0.25%) in USG-guided TAP block in patients undergoing cesarean section under spinal anasthesia. The investigators concluded that addition of dexmedetomidine reduces postoperative pain, prolongs duration of analgesia and decreases demand for additional analgesic requirement as compared with dexamethasone added to bupivacaine.[14]

Also, Abdallah et al. in their meta-analysis, mentioned that the addition of dexmedetomidine to the LA for brachial plexus block at the axillary, supraclavicular, or infraclavicular levels, may prolong the duration of sensory and motor blocks by a relative increase of 76% and 87% respectively compared with LA alone, and increase time to first analgesia request by a relative increase of 70% compared with LA alone.[15]

On the other hand, Ozalp et al. compared dexmedetomidine 1 µg/kg + ropivacaine 0.2% mixture to ropivacaine 0.2% alone in 40 patients undergoing upper extremity surgery under controlled interscalene nerve block guided by nerve stimulator before general anesthesia and they reported similar pain scores in both groups without any advantage of dexmedetomidine and without any major side effects.[16]

Liu et al. demonstrated that perineural dexamethasone (1, 2 and 4 mg) significantly prolongs analgesia and motor block duration with 0.25% bupivacaine in ultrasound guided supraclavicular brachial plexus block. However, this study did not show statistically significant differences among different doses of dexamethasone on analgesia duration and motor block prolongation.[17] Another researcher observed significant prolongation of duration of analgesia with the use of dexamethasone (8 mg) as an adjuvant to bupivacaine 0.5% compared to clonidine (1 µg/kg) as an additive to bupivacaine 0.5% in their study on 90 patients receiving ultrasound guided brachial plexus block in their study.[18]

In the study created by Zhang et al., they showed that addition of both dexamethasone 10 mg and dexmedetomidine 1 µg/kg to ropivacaine 0.5% in intercostal nerves block was a safe and effective strategy increasing postoperative analgesia duration more than the use of only one of them or the use of local anesthetic only in adult patients undergoing thoracoscopic surgeries.[19]

Similarly, the addition of dexamethasone to 0.5% ropivacaine for postoperative analgesia in USG guided TAP block for inguinal hernia repair significantly prolonged the duration of postoperative analgesia.[20]

Regarding hemodynamic parameters the results were not significantly different between the three groups. This result was in line with the results of other researchers, who found that addition of dexmedetomidine to ropivacaine 0.75% in supraclavicular brachial nerve block can significantly prolong the duration of postoperative analgesia without any serious adverse effects.[21,22]

Dexmedetomidine might be associated with some side-effect such as hypotension, bradycardia and sedation,

particularly at higher doses, probably related to the post-synaptic activation of central α2 adrenoceptors.[23,24]

In the present study, none of our patients developed bradycardia or hypotension. This may be because a smaller dose of dexmedetomidine was used by us.

There were no recorded complications related to the block techniques or to the drugs.

5. Conclusion

Dexmedetomidine added to bupivacaine in ultrasound-guided transversus abdominis plane block for postoperative pain relief in patients undergoing lower abdominal surgeries prolongs the time to initial postoperative pain presented by time to first rescue analgesic consumption than dexamethasone added to bupivacaine and more than bupivacaine alone.

6. Limitations

Inability to assess dexmedetomidine plasma concentration among study patients to determine whether its action was related to systemic absorption or pure local effect. This was considered as a limitation to our study.

7. Future scope

We recommend to use dexmedetomidine as an adjuvant to bupivacaine to improve postoperative analgesia in patients undergoing lower abdominal operations. Also, both dexamethasone and dexmedetomidine are safe and effective additives in prolongation of postoperative analgesia with more better pain control than using the local anesthetic only.

8. Ethics approval and consent to participants

This study was approved by the research ethics committee at the faculty of medicine, Ain Shams University (ID: FMASU M D 184/2020) and registered on Clinical Trial Registry, identifier: NCT05323565. Written informed consent was obtained from all patients.

9. Availability of data

The datasets used and/or analyzed during the current study are available from the corresponding author on a reasonable request.

10. Competing interests

The authors declare that there were no conflicts of interest.

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