Effect of Adding Dexmedetomidine as Adjuvant to Different Regional Anesthetic Techniques after Inguinal Herniorrhaphy

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ABSTRACT

Background: Inguinal herniorrhaphy is one of the most commonly performed surgeries, often performed on a fast-track basis. However, inguinal herniorrhaphy is frequently associated with persistent postoperative discomfort and pain, which can lead to patient distress, delayed discharge, and subsequent complication.

Objective: Aim of this work is to compare TAP block technique versus local infiltration with or without dexmedetomidine regarding analgesic effect and endogenous stress response.

Patients and Methods: This randomized prospective study included 120 patients of both genders scheduled for non-complicated inguinal hernioplasty. Their age ranged between 18 and 60 years, with ASA physical status I and II, and body mass index ≤ 35 kg /m². The study was approved by the medical ethics committee of Al-Azhar University Hospital in Assiut and a written informed consent is obtained from all patients.

Results: The major finding in this study was that the pain scores were statistically significantly lower when we added dexmedetomidine than when we did not add it and in the surgical site infiltration groups than TAP block groups at postoperative 2nd, 6th, and12th hours. 1st request for analgesia in this study among all groups was similar. Frequency of analgesic doses was statistically significant among all groups, and group T used the most frequent doses. In this study, local wound infiltration and TAP block with dexmedetomidine showed decrease number of analgesic doses and attenuated the stress response indicators (norepinephrine and glucose levels) without side effects.

Conclusion: Dexmedetomidine added to bupivacaine in both local infiltration and TAP block had better visual analogue scale, decreased number of analgesic doses and attenuated postoperative stress response indicators. Norepinephrine is the most accurate stress response indicator while blood glucose is accurate and the cheapest one.

Keywords: Dexmedetomidine, Regional anesthetic techniques, Inguinal herniorrhaphy

INTRODUCTION

Post-herniorrhaphy pain is conventionally treated with non-steroidal anti-inflammatory drugs (NSAIDS) or opioids. However, these drugs can induce certain side effects, such as gastrointestinal adverse events, postoperative bleeding, vomiting, respiratory depression and sedation [(1)].

They eventually lead to delayed discharge from hospital, thus attenuating the advantage of fast-track basis surgery for which early postoperative pain relief is imperative. Therefore, a continuous search is underway to reduce the use of post-operative analgesics, such as ilioinguinal nerve blockade [(2)], caudal blockade [(3)], systemic administration or infiltration of local anesthetics (LA) directly into the wound [(4)], and transversus abdominis plane block (TAP) [(5)].

Local and/or regional analgesia techniques are critical components of an optimal multimodal analgesia techniques, as they have been shown to improve pain relief, as well as reduce opioid requirement. Surgical site local anesthetic infiltration has been shown to provide excellent analgesia and is recommended, when appropriate. Transversus abdominis plane blocks have been increasingly used in patient undergoing lower abdominal surgical procedures because of improved pain relief and reduced opioid requirement [(6)].

Dexmedetomidine is a newly developed selective alpha 2-adrenoceptor (AR) agonist used as a sedative or adjuvant anesthetic. The results of a recent study demonstrated that synergistic interactions exist between dexmedetomidine and LA.

Systemic administration of dexmedetomidine enhanced spinal and epidural anesthesia [(7)], intravenous regional anesthesia [(8)], and its addition to LA prolonged the duration of blockade and enhanced the analgesic and anesthetic property in a caudal and sciatic nerve block [(9)].

Various animal studies have been conducted using intrathecal dexmedetomidine at a dose range of 2.5 to 100 μg without any neurological complications [(10)]. Antinociceptive effect of dexmedetomidine, a highly selective alpha 2 adrenergic agonist was evaluated in animal studies. Dexmedetomidine was used to enhance the analgesic property of local anesthetics like lidocaine, bupivacaine and ropivacaine. In vivo and in vitro studies indicated that these local anesthetics had significant neurotoxicity [(11)]. Dexmedetomidine showed protective or growth promoting properties in tissues, including nerve cells from cortex and has a neuroprotective effect similar to methylprednisolone in spinal cord injury when used intrathecally [(12)].

AIM OF THE WORK

To compare local infiltration versus transversus abdominal plane block (TAP) with or

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without adding dexmedetomidine as regard the analgesic effect and endogenous stress response.

PATIENTS AND METHODS

Ethical approval:

This randomized prospective clinical trial was approved by the medical ethics committee of Al-Azhar University Hospital in Assiut. Written informed consent is obtained from all patients.

This study included 120 patients of both genders scheduled for non-complicated inguinal hernioplasty, age ranged between 18 and 60 years, with ASA physical status I and II, and body mass index ≤ 35 kg /m².

Exclusion criteria:

- Patients with sensitivity to local anesthetics,
- Uncontrolled systemic disease: hepatic, renal, coronary artery disease,
- Endocrine diseases and diabetes mellitus,
- Patients on corticosteroid therapy,
- bleeding tendency,
- emergent or complicated hernia,
- Inability to obtain written informed consent (patient refusal or psychological diseases).

Group Allocation:

Patients who fulfilled the inclusion criteria were allocated randomly using computer generated random table into four equal groups each of 30 patients.

- **Group LD**: underwent local infiltration at the end of surgery by bupivacaine with dexmedetomidine,
- **Group L**: underwent local infiltration at the end of surgery by bupivacaine without dexmedetomidine,
- **Group TD**: underwent TAP at the end of surgery by bupivacaine with dexmedetomidine
- **Group T**: underwent TAP at the end of surgery by bupivacaine without dexmedetomidine.

Preoperatively, patients were taught in how to evaluate their own pain intensity using the visual analogue scale (VAS), scored from 0-10 (where 0= no pain and 10=worst pain imaginable). Preoperative sedation was avoided and plasma levels of epinephrine and norepinephrine, serum level of cortisol and blood level of glucose were measured.

Anesthetic technique (for all groups):

The anesthetic technique was standardized in all groups. Anesthesia was induced with fentanyl 1µg/kg, 2mg/kg of propofol IV and 0.1mg/kg of cisatracurium IV. The trachea was intubated and ventilation was controlled at a tidal volume of 6-7ml/kg and at a respiratory rate of 12 breaths/min. Anesthesia was maintained using 1.2% isoflurane in 3 l/min O2 and 0.25mg/kg of cisatracurium every 30 min.. During surgery, patients received an IV infusion of Ringer's solution at a rate of 3–6ml /kg/h. No additional analgesics were injected during the surgery. Heart rate, pulse oximetry and systolic, diastolic and mean blood pressure were monitored all the time of operation.

Group LD and L (local wound infiltration groups).

After repair of muscle and before closure of wound, all layers of the surgical incision were infiltrated with a 22-gauge, 40-mm needle in a controlled and systemic manner under direct visualization in fanlike fashion on each side of incision. In group LD, **20 ml** of **0.25%** isobaric bupivacaine added by **0.5 µg/ kg** of dexmedetomidine was used. In group L, **20 ml** of **0.25%**isobaric bupivacaine was used.

Group TD and T (TAP block groups).

Ultrasound guided TAP block technique:

The TAP block was performed with the use of ultrasound under complete aseptic technique. Images were obtained using a Sonosite M-Turbow ultrasound machine (Sonosite Inc., Bothell, WA, USA) with a10-5 MHz 38 mm broadband linear array probe. The ultrasound probe was placed transversely to the abdomen (horizontal plane) in the midaxillary line midway between the costal margin and the iliac crest. Three muscle layers are clearly seen in the image. The needle (Sono Plex Stim cannula (PAJUNK) 22G×80mm, GERMANY) was inserted in a sagittal plane approximately 3-4 cm medial to the ultrasound probe. For optimal imaging of the needle it should be held parallel to the long the needle tip was directed into the plane below the internal oblique and above the transversus abdominis muscle. For confirmation of proper needle placement, a small volume of normal saline (2ml) was seen to open the plane between the two muscles and was followed by insertion of the full dose of local anesthetic. If the 2ml dose appears to be within muscles rather than between them, needle adjustment was required. In group TD, **20** ml of **0.25%** isobaric bupivacaine **a**dded by **0.5 µ*g/kg*** of dexmedetomidine was injected. In group T, **20** ml of **0.25%** isobaric bupivacaine was injected. The local anesthetic injectate appeared hypoechoic (black compared to the muscle layers) on ultrasound image.

Then reversal of muscle relaxant by neostigmine (0.05 mg/kg) and atropine (0.01mg/kg) and extubation was performed when the patient met the following criteria: hemodynamic stability, adequate muscle strength, full consciousness, and adequate ventilation (respiratory rate: 10 to 30 breath/min, SpO2: 94% or more). All patients were transmitted to recovery room until become fully recovered.

Postoperatively, all patients were admitted to post anesthesia care unit (PACU). The patient's heart rate and non-invasive arterial blood pressure were monitored for the first 24 hour postoperatively and the values were recorded at 2nd, 4th, 6th, 12th, and 24th hours. The severity of pain, nausea, vomiting, and respiratory depression were assessed postoperatively. Plasma levels of epinephrine and norepinephrine, serum level of cortisol and blood level of glucose were measured as indicator of endogenous stress response at 2nd and 6th

hours postoperatively. The severity of pain was assessed using a 10-cm visual analogue scale (0 = no pain and 10 = worst imaginable pain). Rescue analgesia was given for visual analogue scale (VAS) ≥ 3 by IV infusion of 15 mg/kg paracetamol. Time to the first rescue analgesia and the frequency of the given drug in the first 24 hours, and also nausea and vomiting were recorded. Rescue antiemetic (10 mg metocloperamide) was given for any patient who complained of vomiting. Signs of side effects was recorded: hypotension (defined as mean arterial blood pressure ≤ 60 mmHg) and this was managed by IV fluids infusion and intravenous boluses of ephedrine 0.1 mg/kg, bradycardia (defined as heart rate ≤ 55 beats/min) was managed by IV atropine 0.01 mg/kg and respiratory depression (arterial O2 saturation ≤ 94%) and this will be managed by supplementary O2 delivered by face mask. For assessment of sedation we used Ramsay scale. In the 1st 3 degrees of the scale we considered patient not sedated while in the last 3 degrees of the scale we considered patient sedated.

Data collection:

- Preoperative patient's data including age, weight and gender was collected.
- Systolic, diastolic and mean arterial blood pressure and heart rate were recorded before surgery,
- Plasma level of epinephrine and norepinephrine, serum level of cortisone and blood level of glucose were measured night before surgery.
- VAS scores were collected at 2nd, 6th, 12thand 24th hours postoperatively.
- Time to the first rescue analgesia and its frequency were recorded.
- Systolic, diastolic and mean arterial blood pressure and heart rate were recorded at 2nd, 4th, 6th, 12th, and 24th hours postoperatively.
- Venous sample was withdrawn at 2nd and 6th hours postoperatively for detection of plasma level of epinephrine and norepinephrine, serum level of cortisone and blood level of glucose.
- Side effects as hypotension, bradycardia, respiratory depression, sedation and vomiting were recorded.

Statistical analysis

Data were verified, coded by the researcher and analysed using the Statistical Package for Social Sciences (IBM-SPSS ver. 21).

Descriptive statistics: Means, standard errors, medians and percentages were calculated. Test of significances: Chi square test was used to compare the difference in distribution of frequencies among different groups. For continuous variables with more than two categories; ANOVA test was calculated to test the mean differences of the data that follow normal distribution, post-hoc test was calculated to calculate pairwise differences using Bonferroni corrections. Repeated Measure ANOVA test was used to compare the differences in mean values over the study time. A p-value equal to or less than 0.05 was considered statistically significant.

RESULTS

During 14 months from January 2017 to March 2018, this randomized controlled study included one hundred and twenty patients scheduled for elective inguinal hernioplasty surgery. The study aimed at comparing the effect of adding dexmedetomedine to TAP block and local infiltration versus not adding dexmedetomedine to TAP block and local infiltration on VAS, hemodynamics, and the inflammatory stress response.

For this purpose patients were randomly allocated into four groups: local infiltration with dexmedetomedine (group LD) (n=30), local infiltration without dexmedetomedine (group L) (n=30), TAP block with dexmedetomedine (group TD) (n=30), TAP block without dexmedetomedine (group T) (n=30).

General patient characteristics (table 1):

Patients' general characteristics were summarized in table (1). All groups were comparable to each other as regard age, gender, and weight.

Table (1): Comparison between the different groups regarding to general characteristics.

	G LD (n=30)	G L (n=30)	G TD (n=30)	G T (n=30)	P-value
Age/years • **Mean ± SD**	37.87 ± 2.4	36.60 ± 2.2	35.37 ± 2.1	36.47 ± 2.2	= 0.836*
Gender n (%)					= 0.232***
• **Female**	7 (23.3%)	2 (6.7%)	4 (13.3%)	3 (10.0%)	
• **Male**	23 (76.7%)	28 (93.3%)	26 (86.7%)	27 (90.0%)	
Weight/kg • **Mean ± SD**	71.30 ± 13.1	70.03 ± 10.7	69.10 ± 12.1	72.53 ± 8.8	= 0.675*

*ANOVA test was used to compare the means among groups
**Post-hoc analysis with Bonferroni corrections. ***Chi-square analysis was used to compare the proportions between groups

Postoperative VAS (Table 2)

There was significant difference among all groups from 2nd hour postoperatively until 12th hour postoperatively. P-value for VAS at 2nd hour was 0.014 while it was 0.045 for VAS at 6th hour and it was <0.001 for VAS at 12th hour. Patients in group LD showed the lowest VAS value at 2nd, 6th and 12th hours postoperatively. At 24th hour, there was no significant difference among all groups with P-value= 0.359.

Table (2): Comparison of the VAS among the different groups

	G LD (n=30)	**G L (n=30)**	**G TD (n=30)**	**G T (n=30)**	**P-value**
VAS after 2 hours					**= 0.014***
Mean ± SD	0.47 ± 0.1	0.83 ± 0.1	0.70 ± 0.1	1.17 ± 0.3	
P-value**	**LD vs L =0.011** **LD vs TD =0.034**	L vs TD =0.186 **L vs T =0.006**	**TD vs T =0.002**	**LD vs T <0.001**	
VAS after 6 hours					**= 0.045***
Mean ± SD	1.53 ± 0.2	1.93 ± 0.3	1.60 ± 0.2	2.37 ± 0.3	
P-value**	**LD vs L =0.033** LD vs TD =0.117	L vs TD =0.060 L vs T =0.069	**TD vs T =0.016**	**LD vs T =0.011**	
VAS after 12 hours					**< 0.001***
Mean ± SD	2.90 ± 0.2	3.47 ± 0.3	3.07 ± 0.5	3.90 ± 0.5	
P-value**	**LD vs L =0.011** **LD vs TD =0.021**	L vs TD =0.137 L vs T = 0.087	**TD vs T =0.042**	**LD vs T =0.004**	
VAS after 24 hours					= 0.359*
Mean ± SD	2.20 ± 0.4	2.67 ± 0.6	2.43 ± 0.5	2.90 ± 0.7	
P-value**	**LD vs L =0.042** LD vs TD =0.075	L vs TD =0.214 L vs T =0.158	TD vs T =0.398	**LD vs T =0.013**	

*ANOVA test was used to compare the means among groups
**Post-hoc analysis with Bonferroni corrections
***Repeated Measure ANOVA test was used to compare the means over study time

1st analgesic request Time and Number of Analgesic Doses (Table 3)

The time for 1st analgesic request had no statistically significant differences among all groups with P-value > 0.05.

Although there was no statistically significant difference between group LD and group L or group TD, there was statistically significant difference between group LD and group T.

There was significant difference among four groups in total analgesic dose with P- value < 0.05.

Table (3): Comparison of 1st Dose timing and number of analgesic doses among the studied groups

	G LD (n=30)	**G L (n=30)**	**G TD (n=30)**	**G T (n=30)**	**P-value**
1st Analgesia Time					=
Mean ± SD	7.60 ± 0.7	7.30 ± 0.3	6.80 ± 0.5	5.87 ± 0.3	0.079*
P-value**	LD vs L =0.671	L vs TD =0.479	TD vs T =0.188	**LD vs T =0.015**	
	LD vs TD =0.259	**L vs T =0.044**			
No. of Doses					=
Mean ± SD	1.77 ± 0.2	2.07 ± 0.1	1.80 ± 0.1	2.33 ± 0.1	**0.004***
P-value**	LD vs L =0.087	L vs TD =0.128	**TD vs T =0.003**	**LD vs T =0.001**	
	LD vs TD =0.848	L vs T =0.128			

*ANOVA test was used to compare the means among groups
**Post-hoc analysis with Bonferroni corrections

Laboratory data:

A. Norepinephrine level (Table 4)

Baseline values in all groups were comparable to each other.

There was significant difference at norepinephrine level at preoperative, 2nd and 6th hours among all groups with P- value < 0.05.

Table (4): Comparison of nor-epinephrine level among the groups

	G LD (n=30)	G L (n=30)	G TD (n=30)	G T (n=30)	P-value*
NE Level at Baseline					**= 0.037**
Mean ± SD	103.50 ± 20.6	271.20 ± 48.3	130.30 ± 27.6	174.30 ± 8.2	
P-value**	**LD vs L =0.007**	**L vs TD =0.022**	TD vs T =0.459	LD vs T =0.236	
	LD vs TD =0.651	L vs T =0.108			
NE Level after 2 hours					**= 0.007**
Mean ± SD	93.50 ± 13.8	231.80 ± 32.4	123.20 ± 24.3	187.60 ± 12.7	
P-value**	**LD vs L =0.002**	**L vs TD =0.011**	TD vs T =0.119	**LD vs T =0.025**	
	LD vs TD =0.466	L vs T =0.280			
NE Level after 6 hours					**= 0.001**
Mean ± SD	90.50 ± 3.6	244.30 ± 34.4	119.90 ± 4.1	178.80 ± 8.2	
P-value**	**LD vs L <0.001**	**L vs TD =0.002**	TD vs T =0.121	**LD vs T =0.023**	
	LD vs TD =0.433	L vs T =0.085			
P-value***	= 0.323	= 0.555	= 0.486	= 0.807	

*ANOVA test was used to compare the means among groups

**Post-hoc analysis with Bonferroni corrections

***Repeated Measure ANOVA test was used to compare the means over study time

B. Serum epinephrine level (Table 5)

There were no significant differences in serum epinephrine level among all groups preoperatively or postoperatively with P-value > 0.05.

Table (5): Comparison of epinephrine level among the studied groups

	G LD (n=30)	G L (n=30)	G TD (n=30)	G T (n=30)	P-value*
EP Level at Baseline					= 0.910
• **Mean ± SD**	53.20 ± 10.3	64.20 ± 9.1	59.20 ± 11.3	59.90 ± 13.6	
• **P-value****	LD vs L =0.492	L vs TD =0.754	TD vs T =0.836	LD vs T =0.866	
	LD vs TD =0.707	L vs T =0.603			
EP Level after 2 hours					= 0.511
• **Mean ± SD**	48.50 ± 8.1	68.00 ± 10.4	58.60 ± 8.3	63.90 ± 9.7	
• **P-value****	LD vs L =0.156	L vs TD =0.490	TD vs T =0.696	LD vs T =0.260	
	LD vs TD =0.458	L vs T =0.763			
EP Level after 6 hours					= 0.152
• **Mean ± SD**	49.20 ± 8.6	98.30 ± 17.5	57.90 ± 9.1	67.80 ± 8.2	
• **P-value****	**LD vs L =0.033**	L vs TD =0.067	TD vs T =0.657	LD vs T =0.406	
	L vs TD =0.696	L vs T =0.176			
P-value***	= 0.494	= 0.353	= 0.860	= 0.356	

*ANOVA test was used to compare the means among groups

**Post-hoc analysis with Bonferroni corrections

***Repeated Measure ANOVA test was used to compare the means over study time

C. Serum cortisol level (table 6)

- There was no significant difference in preoperative level among all groups with P-value > 0.05.
- There was no significant difference in postoperative level at 2 and 6 hours among all groups with P-value > 0.05.
- There was no significant difference among preoperative and postoperative level among all groups with P-value > 0.05.

Table (6): Comparison of serum cortisol level among the different groups

	G LD (n=30)	G L (n=30)	G TD (n=30)	G T (n=30)	P-value*
Cortisol Level at Baseline					= 0.110
• **Mean ± SD**	278.30 ± 52.9	274.90 ± 9.8	429.50 ± 53.9	201.40 ± 48.7	
• **P-value****	LD vs L =0.893	L vs TD =0.101	**TD vs T =0.018**	LD vs T =0.356	
	LD vs TD =0.130	L vs T =0.492			
Cortisol Level after 2 hours					= 0.993
• **Mean ± SD**	228.50 ± 57.7	232.60 ± 49.3	248.70 ± 41.1	244.60 ± 69.2	
• **P-value****	LD vs L =0.958	L vs TD =0.838	TD vs T =0.958	LD vs T =0.838	
	LD vs L =0.789	TD vs T =0.879			
Cortisol Level after 6 hours					= 0.981
• **Mean ± SD**	253.00 ± 62.7	235.40 ± 51.5	232.60 ± 45.8	263.50 ± 57.9	
• **P-value****	LD vs L =0.837	L vs TD =0.974	TD vs T =0.718	LD vs T =0.912	
	LD vs TD =0.812	L vs T =0.748			
P-value***	= 0.347	= 0.393	**= 0.007**	= 0.159	

*ANOVA test was used to compare the means among groups
**Post-hoc analysis with Bonferroni corrections
***Repeated Measure ANOVA test was used to compare the means over study time

D. Blood glucose level (Table 7)

- There was no significant difference in preoperative level among all groups with P- value > 0.05.
- At 2nd hour and 6th hours postoperative, there was significant difference among all groups with P-value < 0.05.
- At 2nd hour there was significant difference between group LD and groups L and T.
- At 6th hour there was significant difference between group LD and groups L and T.

Table (7): Comparison of blood glucose level among the studied groups

	G LD (n=30)	G L (n=30)	G TD (n=30)	G T (n=30)	P-value*
Glucose Level at Baseline					= 0.890
• **Mean ± SD**	131.60 ± 11.8	131.20 ± 5.7	123.50 ± 12.1	133.70 ± 8.1	
• **P-value****	LD vs L =0.977	L vs TD =0.582	TD vs T =0.466	LD vs T =0.880	
	LD vs TD =0.562	L vs T =0.858			
lucose Level after 2 hours					**= 0.008**
• **Mean ± SD**	109.90 ± 7.3	133.70 ± 5.3	123.20 ± 5.5	136.80 ± 4.1	
• **P-value****	**LD vs L =0.005**	L vs TD =0.199	TD vs T =0.099	**LD vs T =0.002**	
	LD vs TD =0.106	L vs T =0.702			
lucose Level after 6 hours					**= 0.026**
• **Mean ± SD**	117.60 ± 8.5	148.80 ± 7.3	135.60 ± 5.1	138.70 ± 6.6	
• **P-value****	**LD vs L =0.003**	L vs TD =0.190	TD vs T =0.756	**LD vs T =0.040**	
	LD vs TD =0.077	L vs T =0.314			
P-value***	= 0.248	**= 0.046**	= 0.240	= 0.702	

*ANOVA test was used to compare the means among groups, **Post-hoc analysis with Bonferroni corrections
***Repeated Measure ANOVA test was used to compare the means over study time

Incidence of complications (table 8):

Patients of all groups were followed up post-operatively for incidence of complications. There was no significant difference between all groups as regard vomiting, hypotension and bradycardia with P-value > 0.05. Incidence of vomiting was comparable in both groups. Hypotension is defined as decrease of more than 20% of baseline value occurred only in 2 cases in group TD. Bradycardia defined as decreased heart rate less than 50 beats/min. of baseline was recorded in 3 patients in group LD and only 2 patients in group TD. Sedation has significant difference between groups with P-value < 0.05. There were 4 cases in group LD and 5 cases in group TD.

Table (8): Distribution of the study group according to incidence of complications

	G LD (n=30)	G L (n=30)	G TD (n=30)	G T (n=30)	P-value*
Vomiting n (%)					
• **No**	26 (86.7%)	25 (83.3%)	27 (90.0%)	29 (96.7%)	= 0.150
• **Yes**	4 (13.3%)	5 (16.7%)	3 (10.0%)	1 (3.3%)	
Sedation n (%)					
• **No**	26 (86.7%)	30 (100%)	25 (83.3%)	30 (100%)	**= 0.019**
• **Yes**	4 (13.3%)	0 (0%)	5 (16.7%)	0 (0%)	
Hypotension n (%)					
• **No**	30 (100%)	30 (100%)	28 (93.3%)	30 (100%)	= 0.107
• **Yes**	0 (0%)	0 (0%)	2 (6.7%)	0 (0%)	
Bradycardia n (%)					
• **No**	27 (90.0%)	30 (100%)	28 (93.3%)	30 (100%)	= 0.131
• **Yes**	3 (10.0%)	0 (0%)	2 (6.7%)	0 (0%)	

*Chi-square test was used to compare the proportions among groups
**Post-hoc analysis with Bonferroni corrections

DISCUSSION

In this study, 120 patients of both genders scheduled for non-complicated inguinal hernioplasty. They were divided into four groups: group LD; local infiltration with dexmedetomidine, group L; local infiltration without dexmedetomidine, group TD; TAP with dexmedetomidine, group T; TAP without dexmedetomidine.

The major finding in this study was that the pain scores were statistically significantly lower when we added dexmedetomidine than when we did not add it and in the surgical site infiltration groups than TAP block groups' at postoperative 2nd, 6th, and12th hours.

1st request for analgesia in this study among all groups was similar. Frequency of analgesic doses was statistically significant among all groups, and group T used the most frequent doses.

Our observations can be explained by the fact that in spite of the performance of the TAP blocks with real-time ultrasound, the spread of local anesthetic may not be uniformly consistent because of the presence of anatomical variations [(13)]. In addition, nerves located between the inguinal ligament and the costal margin in the anterior axillary line have variable segmental origin from T9-L1, which may influence the efficacy of TAP blocks [(14)].

Our results are consistent with previous published reports comparing local wound infiltration and TAP block.

Three studies reported that meticulous local infiltration of all layers of anterior abdominal wall result in better analgesia than ultrasound guided TAP block [(15)].

In one study by **Irina *et al.*** [(6)] comparing the analgesic efficacy of surgical site infiltration with liposomal bupivacaine and bilateral TAP block with 0.5% bupivacaine in open abdominal hysterectomy. The pain scores at rest and with coughing were significantly lower in the surgical site infiltration group at all postoperative time points (p< 0.0001). The opioid requirements between 24 and 48 hours were significantly lower in infiltration group (p= 0.009). The nausea scores, occurrence of vomiting, and need for rescue analgesia were similar.

In another study by **Petersen *et al.*** [(16)] comparing the analgesic of local wound infiltration, TAP and placebo in inguinal hernia repair, VAS pain score during coughing which was the primary objective was higher in TAP block group than local infiltration group and placebo.

On the other hand, in a systematic review performed by **Yu *et al.*** [(17)], they compared Transversus abdominis-plane block versus local anesthetic wound infiltration in lower abdominal surgery. They concluded that TAP block and LAI provide comparable short-term postoperative analgesia, but TAP block has better long-lasting effect [(17)]. This difference in his results from our results may due to change in type of operation.

Dexmedetomidine gave better pain scores in local wound infiltration and TAP block groups (group LD, group TD)

In a meta-analysis by **Yu *et al.*** [(17)], they concluded that wound infiltration and TAP block with local anesthetic alone provided short-term postoperative analgesia in lower abdominal surgery.

In this study, local wound infiltration and TAP block with dexmedetomidine showed decrease number of analgesic doses and attenuated the stress response indicators (norepinephrine and glucose levels) without side effects.

Our findings regarding the analgesic efficacy of dexmedetomidine were in accordance with **Ulgey *et al.*** [(18)] where they found that dexmedetomidine reduced rescue analgesic consumption and provided a better

pain relief when added to local anesthetic solution infiltrated to the surgical wound.

Luan *et al.* [19] reported that adding 1.0 μg/kg dexmedetomidine to 0.3% ropivacaine for wound infiltration prompted the analgesic properties of ropivacaine, reduced sufentanil consumption, and had no effect on wound healing.

In addition, **Kang** [20] found that a combination of dexmedetomidine and ropivacaine infiltration reduced postoperative pain significantly with no adverse effects after inguinal herniorrhaphy.

In another study by **Singh and Prasad** [21] concluded that wound infiltration of bupivacaine with dexmedetomidine 1.0 μg/kg provides superior pain relief and decrease in total opioid consumption compared to wound infiltration with bupivacaine alone.

Eldegwy and Alfke [22] reported in their study that using dexmedetomidine as an additive to levobupivacaine in ultrasound-guided TAP block for herniorrhaphy provides prolonged duration of postoperative analgesia, and lowered VAS pain scores. Also, local anesthetic infiltration can give accepted postoperative analgesia but with shorter duration than TAP block.

Performing two different block technique or addition of dexmedetomidine was found to insignificantly affect the investigated hemodynamics. We found insignificant differences in the patients' hemodynamics before and after the block at all investigated period.

Serum norepinephrine level in current study was significantly decreased in addition of dexmedetomidine at postoperative 2nd and 6th hours while epinephrine level show minor decrease which represent insignificant difference. Although serum cortisol level shows insignificant differences among groups, blood glucose level showed significant decrease when adding dexmedetomidine.

It is expected for stress response to surgery to be attenuated by sympatholytic effects of central α2-adrenergic receptor activation, leading to reductions in anti-inflammatory effects. Dexmedetomidine activates receptors in the medullary vasomotor center, reducing norepinephrine turnover, reducing its neuron-associated activity, and decreasing central sympathetic outflow through the medullo-spinal noradrenergic pathway, resulting in alterations in sympathetic function [23]. In addition, it was found that dexmedetomidine inhibited the hyperglycemic response to surgery significantly more than placebo, and this may reflect attenuation of sympathoadrenal response [24].

Studies investigating both regional and systemic use of dexmedetomidine have confirmed its surgical stress-suppressing effects; **Nasr and Abdelhamid** [25] reported that caudal dexmedetomidine attenuated stress response to surgical trauma and provided better postoperative analgesia.

Abd El-Moneim *et al.* [26] proved that dexmedetomidine alleviated stress response in patients undergoing cancer surgeries, but it was associated with higher sedation.

Khalil *et al.* [27] also in accordance with our results, found that cortisol and prolactin levels fell during the first postoperative hour in children between 18 months and 10 years old, given 1 mL/kg 0.25% bupivacaine by caudal block.

Local stress-attenuating effects of dexmedetomidine can be referred to its chemical nature, being an imidazole, which may lead to inhibition of cortisol synthesis; this may participate to its stress-attenuating effects when administered by all routes [28].

However, we believe that stress response attenuation in dexmedetomidine group is principally the result of its local analgesic effects, as pain and stress are mutually interactive. The local site of administration of dexmedetomidine is the main reason for the absence of side effects associated with its systemic use.

Mohamed *et al.* [29] found in their study that Local wound infiltration with ketamine or dexmedetomidine added to bupivacaine decreased the total dose of morphine consumption, delayed first request of rescue analgesia, and attenuated postoperative stress response, especially with ketamine in patients underwent total abdominal hysterectomy.

Performance of either local infiltration or TAP block technique resulted in no complication related to technique. The use of dexmedetomidine as adjuvant to local anesthetic has insignificant effect on hemodynamics, respiration, and nausea and vomiting. Dexmedetomidine caused sedation in nine cases of total sixty cases in our study.

Mandal *et al.* [30] found no dizziness, drowsiness or other side effects, in local wound infiltration with dexmedetomidine.

Mohta *et al.* [31] also reported that dexmedetomidine added to bupivacaine for paravertebral block decreased the incidence of post-operative nausea and vomiting (PONV) in patients who underwent major breast cancer surgery.

Conclusion:

Dexmedetomidine added to bupivacaine in both local infiltration and TAP block had better visual analogue scale, decreased number of analgesic doses and attenuated postoperative stress response indicators.

Local wound infiltration performed under direct visualization, is a simple and quick technique and it is more effective; on the other hand, ultrasound-guided TAP block is operator-dependent, time-consuming, and less effective; thus, future researches are required to demonstrate the time requirements and cost efficiency of these two methods.

Norepinephrine is the most accurate stress response indicator while blood glucose is accurate and the cheapest one.

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