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Effect of Using Dexmedetomidine with Ultrasound Guided Transversus Abdominis Plane Block on Postoperative Stress Response in Abdominal and Pelvic Surgeries: Comparative Study

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Abstract

Background: Perioperative pain and stress of surgery induces changes in hormonal secretion. Tissue trauma that occurs as a result of surgical interventions is associated with both metabolic and endocrine responses. The present study was performed in abdominal and pelvic cancer surgeries, to compare the effect of bupivacaine versus bupivacaine with dexmedetomidine in ultrasound guided Transversus Abdominis Plane (TAP) block on post-operative heamodynamics and attenuation of endocrine response during surgery.

Patients and Methods: The study included seventy five patients who were randomly allocated into three groups: Bilateral ultrasound guided TAP block was done to all patients before recovery where group TAP (n=25) received bupivacaine (0.25%), group TAP + Dex (n=25) received dexmedetomidine with the bupivacaine and group TAP + IV-Dex (n=25) received bupivacaine in addition to intravenous dexmedetomidine. Blood samples were withdrawn before the block and at 8 hours and 24 hours post-operative.

Results: Heamodynamics did not show clinically significant difference in the three groups where only 3 patients had bradycardia that was treated with atropine. Serum cortisol and glucose levels were comparable in all study groups. Cortisol level was within normal range and showed decline at 8 and 24 hours postoperative which indicates attenuation of the surgical stress response.

Conclusion: The use of dexmedetomidine with TAP block blunted the stress response to surgery without affecting heamodynamics.

Key Words: *TAP block – Abdominal surgery – Dexmedetomidine – Cortisol – Stress response – Glucose level.*

Introduction

IN cases of trauma, burns, severe infection and exhausting exercise; a systemic reaction occurs in response to tissue injury that includes a wide range of effects on endocrinological, hematological and immunological systems, where the term "stress response" is the definition given to both the metabolic and hormonal changes that are evoked following surgery or trauma [1].

This stress response has been considered as the homeostatic defense mechanism that is important for the body to adapt and develop resistance to the noxious insults. Such exaggerated physiological changes in patients with coexisting diseases is always life threatening. Prolonged stress response causing continuous hyper-metabolic state may result in exhaustion of essential components of the body causing loss of weight, fatigue, decreased resistance, delayed ambulation and increased morbidity and mortality [2].

In the early post-operative period, the most important problems that should be avoided are stress and pain. Therefore, a vital goal of modern surgery is faster and better postoperative recovery. Factors that can affect stress response to surgery include pre-operative, intraoperative and post-operative factors. Effective post-operative analgesia can decrease the stress response to surgery and facilitate patient recovery [3].

General and regional anesthesia have been often compared regarding the ability of one to attenuate the stress response to surgery over the other. Considerable advantages are proposed by regional anesthesia including suppressing cortisol and catecholamine levels and reducing muscle breakdown post-operatively [4].

The purpose of this study was to evaluate the effect of using dexmedetomidine with ultrasound

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guided TAP block whether added to the local anesthetic or given intravenously regarding post-operative stress response and heamodynamics.

Material and Methods

After approval of the Institutional Ethics Committee at the National Cancer Institute (NCI), Cairo University, seventy patients were enrolled in the study with a written informed consent. The study was conducted in the period from May 2014 to April 2016. The patients scheduled for major abdominal or pelvic surgery, aged 18-65 years of both sexes and ASA (American Society of Anesthesiology) physical statuses I, II or III were included in this study. Patients were excluded in case of bradycardia or heart block, renal and hepatic impairment, low platelet count and coagulation defects, history of epilepsy, known allergy or hypersensitivity to the used drugs and local or systemic infection.

Premedication with intravenous midazolam (0.02mg/kg) was given to all patients in the holding area. Ranitidine (50mg IV) and metoclopramide (10mg IV) were given just prior to induction. In the operating room patients were continuously monitored with ECG, pulse oximetry and non-invasive automated arterial blood pressure. All patients received standardized anesthesia. Intravenous induction of anesthesia was achieved with propofol (2mg/kg), fentanyl (2ug/kg), and atracurium (0.5mg/kg) to facilitate endotracheal intubation, followed by volume controlled ventilation with FIO_2 50%. Upon skin closure, paracetamol at 15mg/kg IV was administered and continued every 6 hours in the Post Anesthesia Care Unit (PACU).

Patients were divided randomly into three equal groups of 25 patients each using permuted random blocks. At the end of the surgery, bilateral ultrasound (U/S) guided TAP block was performed in all the groups using ultrasound machine SonoSite M-Turbo. A linear multifrequency (6-13MHz) transducer was used for scanning. The block was done in the supine position sing a 20G spinal needle after obtaining sterile conditions and skin preparation where the transducer was placed in a transverse plane above the iliac crest in the region of midaxillary line. After verifying correct position by visualizing shaft of the needle in the correct plane and clear negative suction, 2ml normal saline were injected to widen the space then Group TAP: Received 30ml 0.25% bupivacaine (max. 3mg/kg) on each side, Group Tap + Dex: Received 30ml 0.25% bupivacaine with 0.5ug/kg dexmedetomidine on each side and Group TAP + IV-Dex received 30ml 0.25% bupivacaine on each side in addition to a loading dose of dexmeditomidine 1ug/kg i.v. over 20 minutes given during skin closure (approximately 30 minutes before performing the block) followed by an infusion of 0.5ug/kg/hr continued for 2 hours post-operative.

In PACU and Surgical Unit, hemodynamicsin the form of heart rate and blood pressure were recorded at 2, 4, 6, 12 and 24 hours post-operative. Blood samples were obtained from each patient to determine serum cortisol level and blood sugar to assess stress response. Samples were taken before performing the block, at 8 hours and at 24 hours post-operative. Data was analyzed using SPSS with statistical package Version 17. Quantitative data is expressed as mean and standard deviation or median and range as appropriate. Qualitative data is be expressed as frequency and percentage. Chi-square test or Fisher's exact test was used to examine the relation between qualitative variables. Comparison between quantitative data of the three groups was done using either parametric or non-parametric ANOVA test as appropriate. p-value less than 0.05 was considered to be significant.

Sample size estimation:

Based on the results obtained from a comparative study on the effect of dexmedetomidine added to bupivacaine intrathecal which found a difference in the VAS between the two groups (spinal anesthesia with or without dexmedetomidine) of 2.4 and a standard deviation of 2.2 [11], a sample of 23 cases in each group would be sufficient to elicit that difference at an alpha level of 0.05 and a power of the test of 95%.

Results

In this prospective, randomized clinical trial, the three groups were comparable regarding age, sex, and Body Mass Index (BMI) (Table 1). The patients had different types of surgery involving the abdomen and pelvis (Table 2). Hysterectomy was the most frequently performed surgery followed by radical cystectomy and colectomy.

In group TAP, Heart Rate (HR) decreased significantly after 2 and 4 hours relative to the baseline reading (p=0.011 and p<0.001, respectively). Then, HR increased to near the baseline reading (Table 3). In group TAP + Dex, HR was significantly lower than the baseline reading starting from 2 hours up to 12 hours post-operatively (p-value

<0.001 up to 6 hours and 0.011 after 12 hours). By 24 hours, HR increased to near the baseline reading. The same change of HR was observed in group TAP + IV-Dex with a p-value <0.001 for all readings up to 12 hours Fig. (1).

In group TAP, there was no significant change of Systolic Blood Pressure (SBP) throughout the 24 post-operative hours (p=0.118) (Table 4). In group TAP + Dex, SBP decreased significantly after 2 hours compared to the baseline reading (p= 0.014), then it increased to near the baseline reading. In group TAP + IV-Dex, SBP decreased significantly after 2 and 4 hours relative to the baseline reading (p<0.001 and p=0.001, respectively). Then SBP increased to near the baseline reading Fig. (2).

In group TAP, there was a significant decrease of Diastolic Blood Pressure (DBP) after 2 hours (p=0.001). Then DBP increased to near the baseline reading (Table 5). In group TAP + Dex, DBP was significantly lower than the baseline reading starting from 2 hours up to 12 hours post-operatively (p <0.001, p=0.001, p=0.019, and p=0.036, respectively). By 24 hours DBP increased to near the baseline reading. Similarly, in group TAP + IV-Dex, DBP was significantly lower than the baseline reading starting from 2 hours up to 12 hours post-operatively (<0.001, p<0.001, p=0.041, and p= 0.046, respectively). By 24 hours DBP increased to near the baseline reading Fig. (3).

There was no significant difference between the three groups in blood glucose and serum cortisol (Table 6) Figs. (4,5).

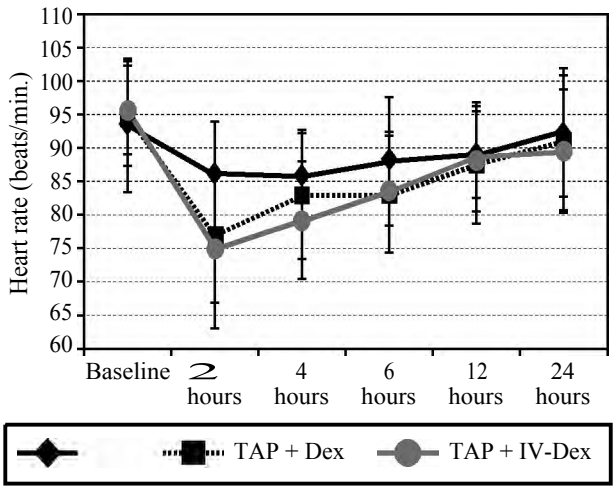

Fig. (1): Changes of heart rate during the first 24 post-operative hours in the three studied groups.

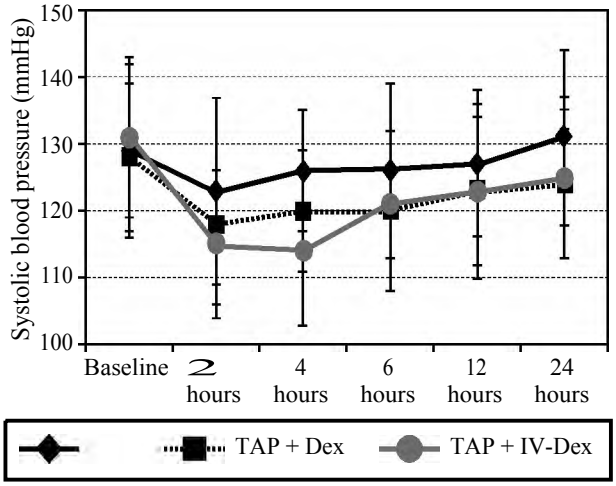

Fig. (2): Changes of systolic blood pressure during the first 24 post-operative hours in the three studied groups.

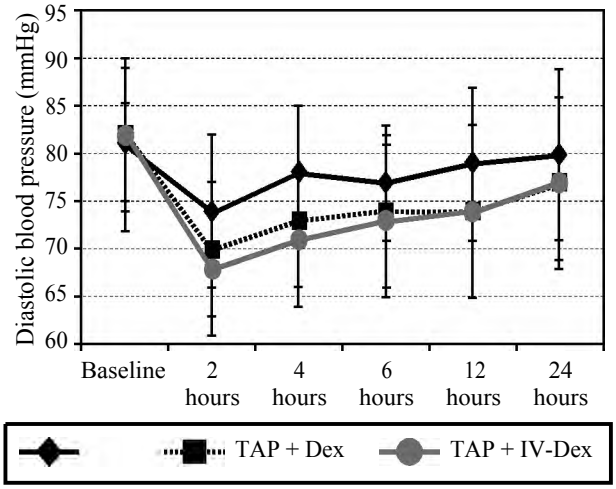

Fig. (3): Changes of diastolic blood pressure during the first 24 post-operative hours in the three studied groups.

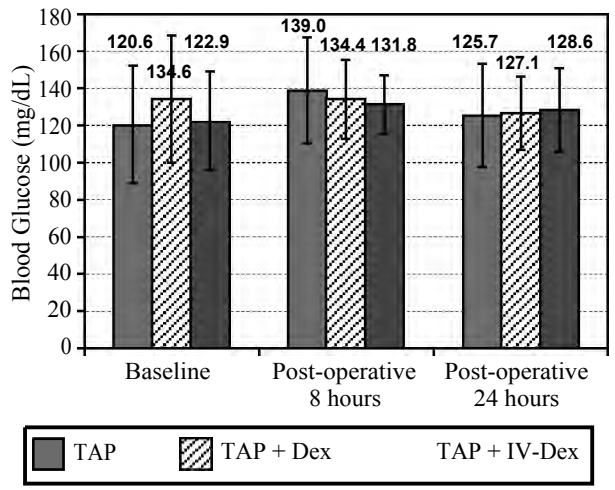

Fig. (4): Blood glucose levels during the first post-operative 24 hours in the three studied groups.

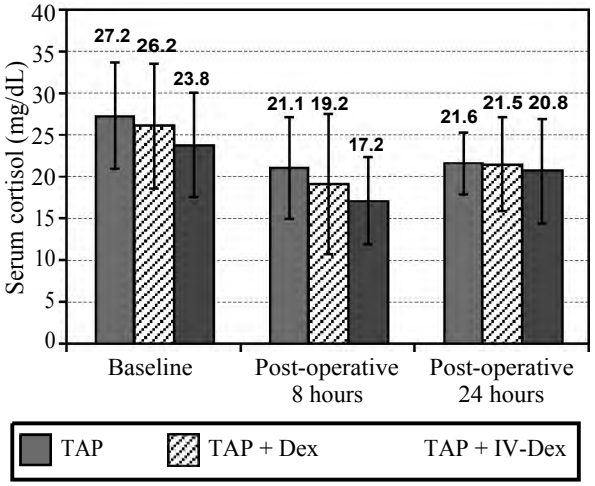

Fig. (5): Serum cortisol levels during the first post-operative 24 hours in the three studied groups.

Table (1): Baseline patients' characteristics of the three studied groups.

	TAP n=25	TAP + Dex n=25	TAP + IV-Dex n=25	*p*-value
• Age (years)	49.4±9.1	48.9±8.0	48.6±9.7	0.940
• Body mass index (kg/m^2)	30.7±3.1	31.0±2.8	30.5±3.0	0.811
• *Sex:*				
Male	9 (36.0%)	8 (32.0%)	10 (40.0%)	0.841
Female	16 (64.0%)	17 (68.0%)	15 (60.0%)	

Data are presented as mean ± SD, or number (%).

Table (2): Type of surgery performed in the three studied group.

	TAP n=25	TAP + Dex n=25	TAP + IV-Dex n=25
Hysterectomy	7 (28%)	5 (20%)	4 (16%)
Radical cystectomy	3 (12%)	4 (16%)	5 (20%)
Colectomy	4 (16%)	3 (12%)	3 (12%)
Ovariectomy	4 (16%)	4 (16%)	2 (8%)
Sigmoidetomy	2 (8%)	2 (8%)	3 (12%)
Trachilectomy	2 (8%)	2 (8%)	2 (8%)
Retroperitoneal mass	2 (8%)	1 (4%)	2 (8%)
Pelviabdominal mass	0 (0%)	2 (8%)	2 (8%)
Low anterior resection	1 (4%)	1 (4%)	1 (4%)
Pelvic abscess	0 (0%)	1 (4%)	0 (0%)
Staging laparotomy	0 (0%)	0 (0%)	1 (4%)

Table (3): Changes of heart rate during the first 24 post-operative hours in the three studied groups.

	TAP n=25	TAP + Dex n=25	TAP + IV-Dex n=25
Baseline	93±10	95±8	96±7
Post-operative 2 hours	86±8*	77±10*	75±12*
Post-operative 4 hours	86±7*	83±9*	79±9*
Post-operative 6 hours	88±10	83±9*	83±9*
Post-operative 12 hours	89±6	88±9*	89±8*
Post-operative 24 hours	92±10	91±10	90±9

Data are presented as mean ± SD.
*: Significant change relative to the baseline reading.

Table (4): Changes of systolic blood pressure during the first 24 post-operative hours in the three studied groups.

	TAP n=25	TAP + Dex n=25	TAP + IV-Dex n=25
Baseline	129±13	128±11	131±12
Post-operative 2 hours	123±14	118±12*	115±11*
Post-operative 4 hours	126±9	120±9	114±11*
Post-operative 6 hours	126±13	120±12	121±11
Post-operative 12 hours	127±11	123±13	123±11
Post-operative 24 hours	131±13	124±11	125±12

Data are presented as mean ± SD.
*: Significant change relative to the baseline reading.

Table (5): Changes of diastolic blood pressure during the first 24 post-operative hours in the three studied groups.

	TAP n=25	TAP + Dex n=25	TAP + IV-Dex n=25
Baseline	81±9	82±7	82±8
Post-operative 2 hours	74±8*	70±7*	68±7*
Post-operative 4 hours	78±7	73±7*	71±7*
Post-operative 6 hours	77±6	74±8*	73±8*
Post-operative 12 hours	79±8	74±9*	74±9*
Post-operative 24 hours	80±9	77±8	77±9

Data are presented as mean ± SD.
*: Significant change relative to the baseline reading.

Table (6): Blood glucose and serum cortisol during the first post-operative 24 hours in the three studied groups.

	TAP n=25	TAP + Dex n=25	TAP + IV-Dex n=25	*p*-value
Blood glucose (mg/dL):				
• Baseline	120.6±31.7	134.6±34.4	122.9±26.5	0.214
• Post-operative 8 hours	139.0±28.6	134.4±21.2	131.8±15.8	0.820
• Post-operative 24 hours	125.7±27.8	127.1±19.8	128.6±22.6	0.322
Serum cortisol (mg/dL):				
• Baseline	27.2±6.4	26.2±7.4	23.8±6.2	0.171
• Post-operative 8 hours	21.1±6.1	19.2±8.3	17.2±5.2	0.057
• Post-operative 24 hours	21.6±3.6	21.5±5.5	20.8±6.1	0.235

Data are presented as mean ± SD.

Discussion

This study focused on examining the effect of adding dexmedetomidine to TAP block, in cancer patients who underwent abdominal and pelvic surgeries, on postoperative heamodynamis and the stress response to surgery. Dexmedetomidine, being an α-2 receptor agonist, causes post-synaptic activation of α-2 receptors in the central nervous system which leads to decreased sympathetic activity leading to bradycardia and hypotension [5].

This effect can be decreased by slow infusion of the loading dose and is dose dependent regarding the maintenance dose. We administered the loading dose (1 μg/kg) in the IV Group slowly over 20 minutes and the used maintenance dose (0.5

µg/kg/hr) was relatively low where the recommended dose can go upto 1.4 µg/kg/hr. Therefore only 3 patients developed bradycardia and received atropine. Statistical analysis of the data we collected showed significant decrease in HR at 2 and 4 hours in all groups compared to baseline readings and remained lower up to 12 hours in the groups receiving dexmedetomidine but readings were not critically low. This can be explained by the nature of cancer patients and aggressive pre-operative preparation and dehydration resulting in relatively higher baseline readings.

A study on the efficacy of the addition of low dose dexmedetomidine as an adjuvant to lignocaine in Intravenous Regional Anesthesia (IVRA) showed improved postoperative analgesia without affecting hemodynamics. Both blood pressure and heart rate were comparable with the placebo control group which also comes in parallel with findings of our study [6].

On the other hand, studies comparing brachial plexus block with and without dexmedetomidine showed that although the incidence of hypotension was comparable in both study groups, the incidence of bradycardia was higher in patients recieving dexmedetomidine as a part of the brachial plexus block. The occurance of bradycardia was transient and easily reversed by atropine without affecting heamodynamics [7]. Helal et al., found that the addition of 100 µg dexmedetomidine to bupivacaine during combined femoral-sciatic nerve block for below knee surgery was associated with bradycardia and hypotension when compared to the control group [8].

Surgical stress is a variety of changes occurring throughout different systems in the body specifically the neuroendocrinal, metabolic, immunological and hematological systems. Elevated Adrenocorticotropic Hormone (ACTH) stimulates excessive release of cortisol and leads to insulin resistance which consequently raises blood glucose levels. It was found that regional anesthesia offers the advantage of dampening the stress response over general anesthesia [4].

The metabolic effects of cortisol are directed to overcome stressful conditions. Cortisol affects metabolism and consumption of glucose, amino acids and fatty acids in hepatic and extrahepatic tissues [9]. A prolonged stress response leads to a continuous hypermetabolic state and exhaustion of essential components of the body causing weight loss, fatigue, decreased immunity, delayed ambulation and increased morbidity and mortality [2].

Being an imidazole compound, similar to etomidate, dexmedetomidine has the ability to inhibit steroidogenesis perioperatively. ACTH-stimulated cortisol release was blunted by the administration of dexmedeomidine bolus (80 µg/kg) in dogs in a study done by Maze et al., [10]. In contrast to that, Venn et al., concluded that dexmedetomidine infusion does not inhibit adrenal steroidogenesis when used for short-term sedation after surgery [11].

Our study showed a blunted stress response with no significant difference between the groups as cortisol level remained within the normal range (reference range 5-25 µg/dL) in the tested postoperative period and even decreased when compared to baseline levels.

Bekker et al., found that intraoperative administration of dexmedetimidine to patients undergoing major spinal surgery significantly reduced cortisol levels in the PACU (15.25 ± 1.99mcg/dL vs 9.86 ± 2.15mcg/dL, p=0.031) [12].

On the contrary, Yacout et al., found that both cortisol and blood glucose levels increased after recovery and on the first day postoperative when dexmedetomidine infusion was used intraoperative in major abdominal surgeries but with significantly lower values in the dexmeditomidine than in the placebo group [13]. Their results support ours in the fact that cortisol level even when increased it remained within the normal range which indicates attenuation of the stress response. Uyar et al., also found that cortisol and blood glucose levels increased significantly after skull pin insertion during craniotomy but were higher in the placebo group than in the dexmedetomidine group [14].

Moreover, a study examining caudal dexmedetomidine in pediatric cardiac surgery concluded that dexmedetomidine attenuates neuroendocrinal stress response to surgery perioperatively. The authors found that both cortisol and glucose levels increased in dexmedetomidine group and control group but the increase was significantly lower in the dexmedetomine group [15].

Al-Medani et al., found that the mean value of cortisol and blood glucose at 6 and 24 hours postoperatively was significantly higher in patients on morphine infusion compared to dexmedetomidine infusion after open cardiac surgery [16].

On the other hand, Bulow et al., did not find a difference between the two studied groups regarding the elevation of cortisol and blood glucose level 24 hours postoperative when dexmedetomi-

dine infusion was added to conventional total intravenous anesthesia in cardiac surgery **[17]**.

Conclusion:

Dexmedetomidine showed attenuated stress response where serum cortisol and glucose levels were comparable and within the normal range in all groups. It is safe and can be used with no adverse effects as it did not affect heamodynamics; all groups were comparable and only 3 patient experienced clinically significant bradycardia.

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تآثير إستخدام عقار الدكسمديتوميدين مع التخدير الموضعى لجدار البطن على إستجابة الضغط النفسى بعد عمليات جراحية بالبطن والحوض؛ دراسة مقارن

الخلفية: إن آلام ما بعد الجراحة وإستجابة الضغط النفسى للجراحة تحدث تغيرات فى إفراز الهرمونات. إن إصابات الأنسجة التى تحدث بعد التدخلات الجراحية يصاحبها تغيرات فى ردود التمثيل الغذائى والغدد الصماء. تمت هذه الدراسة فى حالات جراحات البطن والحوض لأورام سرطانية لمقارنة تآثير إستخدام عقار البيوبيفاكين مقابل إستخدامه مع عقار الدكسمديتوميدين فى التخدير الموضعى للبطن بالموجات فوق الصوتية على ديناميكية الدم والتخفيف من إستجابة الغدد الصماء آثناء العمليات الجراحية.

الآساليب: شملت هذه الدراسة على خمس وسبعون مريضا مصابا بالسرطان مقررا لهم إجراء عمليات جراحية كبرى بالبطن والحوض، وقد تم تقسيمهم عشوائيا إلى ثلاث مجمو،عات وآجرى لجميع المرضى تخدير الموضعى للبطن بإستخدام الموجات فوق الصوتية حيث تلقت المجموعة (TAP) عقار البيوبيفاكين (٠.٢٥٪) وتلقت المجموعة (TAP + Dex) عقار البيوبيفاكين (٠.٢٥٪) مع إضافة الدكسمديتوميدين (0.5ug/kg) وتلقت المجموعة (TAP + Dex-IV) عقار البيوبيفاكين (٠.٢٥٪) مع إعطاء الد كسمديتوميدين (1ug/kg) عن طريق الوريد على مدى ٢٠ دقيقة فى آثناء خياطة الجلد (قبل التخدير الموضعى بحوالى ٣٠ دقيقة) يليه جرعة (0.5g/kg/hr) بإستخدام التنقيط الوريدى لمدة ساعتين بعد العملية. تم سحب عينات الدم قبل التخدير الموضعى وبعد الجراحة ب ٨ و٢٤ ساعة.

النتائج: لم يظهر فرق كلينيكى فى ديناميكية الدم فى المجموعات الثلاثة فى ما عدا ٣ حالات عانوا من هبوط فى ضربات القلب وتم علاجهم بعقار الآتروبين. إستجابة الضغط النفسى للمريض فى كل المجموعات كان ملطف حيث آن مستوى هورمون الكورتيزول ونسبة السكر فى الدم كانوا فى معدلاتهم الطبيعية.

الإستنتاج: إن إستخدام عقار الدكسمديتوميدين آثبت له القدرة على التخفيف من الإستجابة للضغط النفسى دون التآثير على ديناميكية الدم.