ORIGINAL ARTICLE

The effect of anesthesia type on stress hormone response: Comparison of general versus epidural anesthesia

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Abstract

Aim: The aim of this study was to investigate the effect of different types of anesthesia on stress hormones.

Materials and Methods: The study was included 60 ASAI-II cases scheduled for major lower extremity surgery. The cases were randomized into 2 groups: The EA group was administered epidural anesthesia and the GA group was administered standard general anesthesia. In order to evaluate the surgical trauma - related stress response, CRP, TSH, cortisol, and fasting blood sugar(FBS) levels were measured preoperatively, 30 min after surgical incision, and 24 h post surgery.

Results: Between-group comparisons; Preoperative values were not significantly different between the groups.($P > 0,05$) Pulse rate and cortisol values significantly higher in general group at 30 min. ($P < 0,05$), and the FBS values were significantly higher in the epidural group at 24 h.($P < 0,05$) There were not found differences for other parameters at evaluation times.

Conclusion: No differences were observed between the two anesthesia methods, in terms of minimizing the stress response due to surgical trauma during major low extremity surgery.

Key words: Epidural anesthesia, general anesthesia, stress hormones

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Introduction

The stress response to surgery is an unconscious response to tissue injury and refers to sympathetic nervous system activation, endocrine stress response, immunological and hematological changes that follow injury or trauma.[1]

Adams *et al*.[2] reported that the most important factors determining the level of stress response were the patient, and the type of anesthesia and surgery, and that anesthesia might modify the stress response via afferent blockage (local anesthesia), central modulation (general anesthesia), and peripheral interaction with the endocrine system (etomidate).

Administration of intravenous or volatile agents in normal "low" doses has no major effect on endocrine-metabolic parameters. In contrast, "high-dose" opiate anesthesia or

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administration of volatile agents at high minimum alveolar concentration (MAC) values suppress the intraoperative endocrine-metabolic response to surgery but without a persistent effect on postoperative responses or on nitrogen balance.[3,4] Regional anesthesia prevents a predominant part of the endocrine- metabolic response to surgery. This inhibitory effect of neurogenic blockade on the surgically induced endocrine-metabolic changes is most consistent during lower abdominal surgery and operations on the lower extremities.[3,4]

However, in recent years, response to stress tried to be evaluated by surgical stress index. One of these studies found that regional anesthesia group has higher surgical stress index than general anesthesia group.[5]

As such, the present study aimed to investigate the effect of different types of anesthesia on the stress response to surgery.

Materials and Methods

The study was approved by the local institutional ethic committee, and written informed consent was obtained from all patients. We enrolled 60 patients, ASA status I or II, aged between 27 and 75 years, scheduled for elective lower extremity surgery by the orthopedic clinics under anesthesia. Exclusion criteria were known neurological disorders, any medication affecting the central nervous system or heart rate, major cardiac problems, uncontrolled hypertension, history of alcohol or drug abuse, and body mass index over 30 kg m^{-2}, drug and alcohol dependency, allergy to local anesthetic agents, and any pathology preventing the administration of epidural anesthesia.

Patients were randomly allocated to two groups according to a computer-generated list of random numbers that were placed in opaque, sealed envelopes. EA group (n = 30) received epidural anesthesia; GA group (n = 30) received standard general anesthesia.

None of the patients received premedication. Each patient was taken to the surgical suite as the day's first case between 08 am and 10 am. Then, an 18- gauge intravenous catheter was inserted from the dorsum of the left hand. Patients underwent prehydration with 10 ml/kg of lactated ringer's solution. When patient were taken to the operation room, ECG, non-invasive arterial blood pressure, and peripheric oxygen saturation (SpO_2) were monitored, and mean arterial pressure (MAP), heart rate (HR), and SpO_2 were measured and recorded as control values.

Patients in the EA were placed in the left lateral position. The region was disinfected with 10% povidone-iodine complex and covered with sterile compress. For local anesthesia, 2% lidocaine was administered. A Tuohy needle 18-G disposable kit (Braun Perifix®) was used, and the epidural area was entered between L4 and L5 using loss of resistance. After aspiration to ensure that blood or CSF was not leaking, the catheter was advanced 3-4 cm in epidural space and fixed to the skin. A bacteria filter was attached to the end of the catheter and fixed to the supraclavicular fossa.

The insertion site was closed under sterile conditions, and the patients were then placed in the supine position. Patients were administered 2-3 L min^1 of nasal oxygen using a face mask. Then, 15 ml 0.5% bupivacaine (1 mg kg^{-1}) was completed to 20 mL with serum physiologic and administered from the catheter. After 5 min, the level of sensation block was checked using the pinprick test at 1-min intervals. We planned to achieve the highest level of Sensation block between T8 and T10. The degree of motor block was determined according to the Bromage score.[6] After Sensation block developed in the surgical region, surgery was initiated in the EA group patients.

In the GA group, anesthesia induction was carried out using fentanyl (2 μg kg^{-1}) and thiopental (5 mg kg^{-1}); afterwards, endotracheal intubation was performed with administering 0.5 mg kg^{-1} of atracurium. Anesthesia was maintained with a mixture of 50% O_2 and 50% N_2O, and 1.5%-3% sevoflurane. When mean arterial blood pressure and heart rate increased to more than 25% of the baseline value, 1 μg kg^{-1} of i.v. fentanyl was added, and when maintenance of muscle relaxation was required, atracurium was administered.

Hemodynamic data and blood samples were obtained from all the patients as follows: Upon arrival in the surgical theater (preoperative); t0, 30 min after incision (perioperative); t1, 24 h post-surgery (postoperative); t2.

The blood specimens were centrifuged at 3500 ×g for at least 10 minutes and then serum samples eluted. C-reactive protein (CRP), cortisol, TSH, fasting blood sugar (FBS) levels were measured.

Serum Cortisol and TSH levels were measured using a competitive immunoassay; the direct chemiluminesan immunassay (Architect, Abbott Diagnostics device). The CRP test was performed by nephelometric assay (Image 800, Beckman Coulter Diagnostics device). The fasting blood sugar levels were measured by glucokinase enzyme assay by Roche Modular P800, Roche Diagnostics device.

Statistical analyses were conducted with SPSS 12 for Windows. The results were expressed as mean and SD and number of patients. The sample size was calculated based on the assumption that a 20% difference in cortisol rate was significant. In accordance with the power calculation method, 30 patients per group were required to demonstrate a 20% difference in cortisol value at a = 0.05 and power of 70%. The statistical comparisons between groups were

analyzed with Mann- Whitney U, *t* test, whereas intragroup comparisons were evaluated by Wilcoxon signed-rank test. $P < 0.05$ was recognized as statistically significant in all the analyses.

Results

Among the 60 patients included in the study, 33 (55%) were males and 27 (45%) were females. There weren't any significant differences between the groups with regard to age, weight, or duration of surgery [Table 1].

Compared between the groups, preoperative values did not differ significantly between groups [Table 2]. Pulse rate and cortisol values were significantly higher in general group at 30 min [Table 3]. FBS values were significantly higher in the epidural group at 24 h [Table 4]. There were not found differences for other parameters at evaluation times.

In the epidural group evaluation, preoperative FBS values were significantly lower, (t0 *vs.* t1, t0 *vs.* t2; $P < 0.05$). Preoperative TSH values were significantly higher, (t0 *vs.* t1, t0 *vs.* t2; $P < 0.05$). Cortisol values were significantly higher at 24 h measure (t0 *vs.* t2, t1 *vs.* t2; $P < 0.05$). Preoperative CRP values were significantly lower than 30 min and 24 h values, and 30 min values were lower than 24 h values (t0 *vs.* t1, t0 *vs.* t2, t1 *vs.* t2; $P < 0.05$).

Table 1: Patients' demographic data and duration of surgery

Variable	EA group	GA group
Male/Female	17/13	16/14
Age (years)	60.55±14.66	56.50±14.39
Weight (kg)	64.90±14.84	67.60±10.35
Duration of surgery (min)	93.50±33.47	110.50±35.08

Values are mean±SD or numbers of patients (*n*). SD=Standard deviation; EA=Epidural anesthesia; GA=General anesthesia

Table 2: Between-group comparisons; preoperative values were not difference between groups

Variable	EA group (*n*=30)	GA group (*n*=30)	*P*
t0 SBP	135.8±18.5	136.4±19.1	0.95
t0 DBP	85.5±10.1	85.5±10.7	0.983
t0 eart rate	80.1±10.0	79.5±11.9	0.835
t0 SpO2	95.1±1.9	95.6±1.3	0.4
t0 FBS	97.4±15.7	95.2±14.5	0.95
t0 TSH	2.2±0.8	2.0±0.9	0.678
t0 Cortisol	12.2±5.2	12.6±6.1	0.885
t0 CRP	7.6±5.7	11.2±6.0	0.074

Values are mean±SD. SD=Standard deviation; EA=Epidural anesthesia; GA=General anesthesia; SBP=Systolic blood pressure; DBP=Diastolic blood pressure; FBS=Fasting blood sugar; TSH=Thyroid-stimulating hormone; CRP=C-reactive protein

In the general group evaluation, preoperative FBS values were significantly lower (t0 *vs.* t1, t0 *vs.* t2; $P < 0.05$), preoperative TSH values were significantly higher (t0 *vs.* t1, t0 *vs.* t2; $P < 0.05$); preoperative cortisol values were significantly lower (t0 *vs.* t1, t0 *vs.* t2; $P < 0.05$), preoperative CRP values were significantly lower than 30 min and 24 h values. (t0 *vs.* t1, t0 *vs.* t2; $P < 0.05$).

Discussion

It is known that in anesthetized patients, stress due to anesthesia and surgical incision leads to an increase in plasma levels of stress hormones, such as ACTH, cortisol, TSH.[7] As in trauma, metabolic and endocrine events occur during surgical interventions as well. As serum levels of catabolic hormones increase, the levels of anabolic hormones decrease. This response is correlated with the severity of surgical trauma.[8] Various studies reported that even under anesthesia of sufficient depth, surgical stimulation leads to hormonal and metabolic changes, triggering the release of pituitary anterior lobe hormones.[8] The present study investigated the stress hormones cortisol and TSH. The levels of these hormones were measured as soon as the patients arrived in the surgical theater, 30 min after incision, and 24 h post-surgery, and these values

Table 3: Between-group comparisons; patient values 30 min after incision

Variable	EA group (*n*=30)	GA group (*n*=30)	*P*
t1 SBP	128.6±15.1	130.6±13.6	0.934
t1 DBP	80.5±9.5	82.3±7.9	0.573
t1 Heart rate	73.5±6.3	80.3±9.9	0.039
t1 SpO2	96.2±1.5	97.1±1.2	0.076
t1 FBS	108±22.4	106.7±14.1	0.835
t1 TSH	1.7±0.8	1.6±0.8	0.819
t1 Cortisol	14.3±5.6	23.6±13.2	0.031
t1 CRP	19.3±17.6	34.0±32.7	0.141

Values are mean±SD. SD=Standard deviation; EA=Epidural anesthesia; GA=General anesthesia; SBP=Systolic blood pressure; DBP=Diastolic blood pressure; TSH=Thyroid-stimulating hormone; CRP= C-reactive protein

Table 4: Between-group comparisons; 24 h post-surgery (postoperative)

Variable	EA Group (*n*=30)	GA Group (*n*=30)	*P*
t2 SBP	133.6±14.2	134.7±12.6	0.787
t2 DBP	85.3±8.9	86.3±10.5	0.708
t2 Heart rate	76.5±6.9	78.7±11.0	0.603
t2 FBS	113.9±15.3	102.0±13.1	0.042
t2 TSH	1.6±0.7	1.5±0.7	0.493
t2 Cortisol	24.7±10.6	23.2±12.7	0.494
t2 CRP	62.1±31.2	64.1±38.4	0.917

Values are mean±SD. SD=Standard deviation; EA=Epidural anesthesia; GA=General anesthesia; SBP=Systolic blood pressure; DBP=Diastolic blood pressure; FBS=Fasting blood sugar; TSH=Thyroid-stimulating hormone; CRP=C-reactive protein

were compared. Perioperative TSH was lower as compared to control levels, and there was no difference between the groups in this study. Our finding is compatible with knowledge. TSH concentrations decrease during the first 2 h and then return to preoperative level.[9]

Cortisol secretion from the adrenal cortex increases rapidly following the start of surgery as a result of stimulation by ACTH.[10] The cortisol response can be modified by anesthetic intervention. Usually, a feedback mechanism operates so that increased concentrations of circulating cortisol inhibit further secretion of ACTH. This control mechanism appears to be ineffective after surgery so that concentrations of both hormones remain high.

Cortisol did not change significantly perioperatively 30 min in our EA group, whereas it increased 24 h post-surgery. In the GA group, it increased significantly perioperatively 30 min and 24 h post-surgery, and there was difference between the groups at 30 min intraoperativly. Venkata *et al*.[11] reported that cortisol decreased significantly in the EA group 15 and 60 min after incision, whereas it increased in the GA group; however, 2 h post-surgery, there was no difference between the groups.

The net effect of the endocrine response to surgery is an increased secretion of catabolic hormones. Blood glucose concentrations increase after surgery begins. Cortisol and catecholamines facilitate glucose production as a result of increased hepatic glycogenolysis and gluconeo-genesis. In addition, peripheral use of glucose is decreased.[9]

Blood glucose concentrations are related to the intensity of the surgical injury; the changes follow closely the increases in catecholamines. The usual mechanisms that maintain glucose homeostasis are ineffective in the perioperative period. Hyperglycemia persists because catabolic hormones promote glucose production and there is a relative lack of insulin together with peripheral insulin resistance. The risks of prolonged perioperative hyperglycemia are less well established, although potential risks include wound infection and impaired wound healing.[9] In the present study, FBS levels were lower preoperatively than other measures in the both groups. However, FBS levels were higher in group EA than in group GA at 24 h.

When the stress response is triggered by trauma, catabolism occurs in protein metabolism. It has been reported that trauma due to accidents or surgical interventions is followed by local inflammation, which is followed by systemic acute-phase response.[12] According to the dimensions of stress, protein breakdown may increase 2-fold. Proteins whose synthesis increases in metabolic response to stress are acute phase proteins, which generally have specific structures, i.e. CRP, synthesized by the mediation of interleukin-1 in the liver and leucocytes, alpha acid glycoprotein, haptoglobin, alpha 1 antitrypsin, ceruloplasmin, and fibrinogen. In the present study, acute-phase response triggered by the stress response was evaluated based on CRP levels in venous blood samples. CRP was significantly higher than the control values perioperatively and 24 h post-surgery in both groups.

In present study, preoperative CRP levels were lower as compared to other levels and there was no difference between the groups. Büyükkoçak *et al*.[13] divided 40 pregnant patients into 4 groups and administered GA, spinal anesthesia, and EA to 3 groups scheduled for cesarean delivery, and EA to the group scheduled for vaginal delivery. They reported that the anesthesia techniques did not influence acute-phase response based on CRP and albumin levels at admission, at delivery, and 24 h after cesarean delivery. Their finding indicates that there were not any significant differences in acute-phase response between GA and EA like of the present study.

The limitation of this study is the hormonal measurements were not evaluated together surgical stress index.

Conclusion

We did not observe any difference between EA and GA in terms of the stress response related to surgical trauma during major lower extremity surgery. Surgical trauma is an injury model in which tissue repair occurs. This tissue repair is a process involving neuroendocrine and immuno-inflammatory activity at the local and systemic level. This process results in the least harm when the most appropriate type of anesthesia is administered. In recent years, surgical stress response is assessed by surgical stress index. We think these studies should be evaluated with objective hormonal values.

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