

Evaluation of Presurgical Serum Cortisol Level in Patients Undergoing Major Maxillofacial Surgery

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Abstract

Background: Stress is an integral part of life. Anxiety levels may increase when it comes to being treated surgically due to road traffic accidents causing facial trauma, other pathologies or burns. The stress that is caused during a surgical procedure as well as during the treatment in debilitated patients or traumatic conditions is bound to cause disturbance in the metabolic and physiologic levels of cortisol. Therefore, a study was carried out to determine the cortisol levels just prior to surgery on the day of operation to quantify the stress levels and also aid in any preanesthetic medication changes for the patient undergoing maxillofacial surgery. **Aim:** To evaluate and compare pre-surgical serum cortisol levels in patients undergoing major maxillofacial surgery under general anaesthesia. **Objective:** To evaluate the serum cortisol level of patient 3 days prior to surgery, on the day of surgery and to compare and evaluate the difference seen in both the obtained values. **Methods:** A prospective, randomized, in-vivo study was carried out in the Department of Oral and Maxillofacial Surgery at a teaching dental hospital. A total of 32 patients were included in this study. Inclusion and Exclusion criteria was made along with pre-operative assessment of the patient, informed consent was obtained from all patients involved in the study. Patient blood sample, at 8 am three days prior to surgery and on the day of surgery and sent for laboratory investigations. **Result:** Participants in this clinical study underwent treatment of various ailments like facial trauma, and miscellaneous pathologies like Dentigerous Cyst, Oral submucosa fibrosis, Osteomyelitis, Benign Tumor and Orthognathic surgery. The anxiety of the patients were assessed by serum cortisol level preoperatively and on the day of operation. A total of 32 patients, 26 male and 06 female were included in the study. There was statistically highly significant difference seen between the mean values obtained three days prior to surgery and on the day of surgery. **Conclusion:** We have concluded from this study that the serum cortisol level shows significant increase on the day of surgery. A future study can focus on association between increased levels of serum cortisol and postoperative wound healing where patients can be divided into two groups one receiving pre-operative stress reduction protocol and other not receiving the same.

Keywords: Anxiety, cortisol responses, dental treatment, general anesthesia, pain, serum cortisol level, sex distribution, stress response

INTRODUCTION

Stress is an integral part of life. It can act as a double-edged sword, either by serving in useful purposes to motivate us to work more efficiently or causing poor performance. Anxiety levels in a person may increase when it comes to being treated surgically due to road traffic accidents causing facial trauma, other pathologies, or burns. The body secretes a hormone called cortisol during anxiety or stress.

The zona fasciculate of the adrenal cortex of the adrenal gland produces the glucocorticoid class of hormones called cortisols. It is secreted as a reaction to stress and decreased levels of glucose in the blood. It clamps down the immune

system and bolsters up the metabolism of primary classes of nutrients namely fat, protein, and carbohydrate to raise the levels of blood sugar through the path of glucose creation with noncarbohydrate substances while also affecting inflammatory

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response, regulating blood pressure and decreasing bone formation. In humans, cortisol controls health by affecting metabolic response and immune response. It also affects wound healing and electrolyte balance and acts on the stomach, kidneys, and memory.

The mere thought of a visit to the dentist may be a great source of dental anxiety and discomfort to the patient. One of the most rudimentary attributes of living organisms including human beings is that they are capable of responding to any noxious or stressful stimulus.^[1] Normally, cortisol is present in higher levels in the morning than at night.^[2] Hormonal and metabolic changes occurring during trauma is usually termed as stress response. This part of systemic reaction to injury encompasses a wide range of effects on the body.^[3] Stress secretion of cortisol into the blood stream is not the only reason for stress. It is also secreted in higher level during response to stress, and is responsible for several related changes in the body. Catecholamines and beta-adrenergic receptors enhance the production of cortisol.

In 1968, Vandam and Moore showed that glucogenic steroids antagonized the action of insulin. Variation of cortisol levels depends on the type of surgery.^[4] The stress that is caused during a surgical procedure as well as during treatment of debilitated patients or those who had undergone a traumatic condition is bound to cause disturbance at the metabolic and physiologic level. Moreover, stress has an impact during the initial inflammatory phase at the hormonal level and alters the genomic responses.^[5]

Atrophy of muscle, altered immune activity, failure of wound healing and organs, and demise of the patient are common complications of hypermetabolism.^[5] Free plasma 17-hydroxy-corticosteroid level increases promptly in response to major operations. In surgical trauma on animals, the adrenocortical response is dependent on the integrity of both hypothalamus and anterior pituitary lobe.^[5] Heart disease can occur due to high levels of cortisol in the body. Therefore, the degree of surgical stress is produced by cortisol. In 1969, Plumpton, Besser, and Cole had studied minor operations in which they observed increase in plasma cortisol.^[6] Dental anxiety or stress increases serum cortisol secretion as a result of increase in corticotropin-releasing hormone secretion and increases sympathetic tone, therefore cortisol plays a role in body response to stress.^[1] Much study has not been conducted on presurgical serum cortisol levels, particularly in oral and maxillofacial surgery. Our search showed that no studies are available in literature about the presurgical levels of serum cortisol in patients undergoing major maxillofacial surgery under general anesthesia. This has been checked preoperatively (at the day of admission) and on the day of surgery. Therefore, a study was carried out to determine the cortisol levels just prior to surgery on the day of operation. This would help quantify the stress levels and also aid if any changes are to be made in the preanesthetic medications for patients undergoing maxillofacial surgery.

MATERIALS AND METHODS

A prospective, randomized, *in vivo* study was carried out in the Department of Oral and Maxillofacial Surgery at a teaching dental institution. A total of 32 patients were included in this study.

Source of data

Any patients undergoing major maxillofacial surgery and treatment were considered in this study.

Sampling technique

Convenience sampling was used as the sampling technique.

Sample size derivation

Calculation of the sample was done as follows:

$$n = \left[\frac{(Z_{1-\alpha} - Z_{\beta})}{\delta} \right]^2$$

Where $Z_{1-\alpha} = 1.96$, $Z_{\beta} = 0.84$, $\sigma = 0.78$, and $\delta = 0.4$

Therefore, $n = 32$.

A total of 32 patients were taken up in this study.

Inclusion criteria

1. Patient with trauma, other pathologies, and orthognathic surgery
2. Patients willing to be a part of the study.

Exclusion criteria

1. Pediatric patients
2. Patients with a history of endocrine disorder
3. Patients who are unfit for surgery.

Preoperative assessment of the patient

A detailed and thorough history of the patient was recorded followed by a meticulous clinical examination. Valid written informed consent for the surgical procedure was obtained from each patient.

Investigations

The following investigations were carried out in patients who gave consent to become a part of the study.

- Hemogram
- Total leukocyte count and differential leukocyte count
- Bleeding time
- Clotting time
- Prothrombin time-international normalized ratio
- Blood grouping and matching
- Blood glucose levels (random)
- Urine analysis – routine and microscopic
- Liver function tests (serum bilirubin levels, serum glutamic oxaloacetic transaminase, serum glutamic pyruvic transaminase, and alkaline phosphatase)
- Renal function test (serum creatinine and blood urea level)
- HIV
- Hepatitis B surface antigen
- Serum cortisol test

- Chest radiograph
- Electrocardiogram
- Two-dimensional-echocardiography.

Medical fitness details of the patients were obtained from the physicians, and preanesthetic evaluation was done for all patients.

Armamentarium [Figure 1]

1. 5-ml syringe
2. Sterile rubber gloves
3. Tourniquet
4. Spirit
5. Sterile cotton swabs
6. Sterile blood bulbs with label.

Method of data collection

Patients fulfilling the selection criteria were selected in this study. Patients were admitted to the teaching dental institution for major surgery under oral and maxillofacial surgery. After recording a thorough history of the patient, a provisional diagnosis was made. Clinical evaluations were supported with blood reports. A valid written informed consent was obtained from all the patients involved in the study. Patients' blood was collected at 8 a.m., 3 days prior to surgery and on the day of surgery. All patients were subjected to standard hematological investigations. Evaluation of serum cortisol levels 3 days prior to surgery and on the day of surgery was performed. The procedure requires collection of 3-ml blood from the median cubital vein and was sent for laboratory investigations. The obtained values were tabulated and subjected for statistical evaluation.

OBSERVATIONS AND RESULTS

A clinical study was conducted at the teaching dental institution, from November 2016 to January 2018. The participants of the study underwent treatment for various ailments such as facial trauma and other pathologies such as dentigerous cyst, oral submucosa fibrosis, osteomyelitis,

benign tumor, and orthognathic surgery. The anxiety of the patients was assessed by serum cortisol level preoperatively and on the day of operation.

A total of 32 patients, 26 males and 6 females, were included in the study.

Total serum cortisol

Total serum cortisol level was evaluated for each patient 3 days prior to surgery and on the day of surgery. The readings were tabulated and evaluated.

Statistical analysis

Data obtained were compiled on the MS Office Excel Sheet (v 2010). Data were subjected to statistical analysis using the Statistical Package for Social Sciences (IBM Corp. Released 2013. IBM SPSS Solutions for Windows, Version 22.0 Armonk, NY : IBM Corp).

A group statistics of 32 patients was done, and standard deviation was achieved. Paired sample *t*-test was used to compare the difference in mean on the 3 days prior to surgery and on the day of surgery *t* variables was 3.93 of total serum cortisol level [Graph 1]. $P < 0.001$ was considered statistically significant. Keeping a mean difference of 3 days prior to surgery 5.64 and on the day of surgery were 3.17 in males and females [Graph 2].

Even gender distribution and percentage evaluated noted that males showed elevated levels (81.25%) than females (18.75%). In the category of surgery performed, trauma showed more elevated levels than any other surgery. So there was statistically highly significant difference seen between the means of 3 days of prior to surgery and on the day of surgery variable like serum cortisol, where overall for each variables it was the post means was higher than the pre ($P < 0.01$) [Graph 3].

DISCUSSION

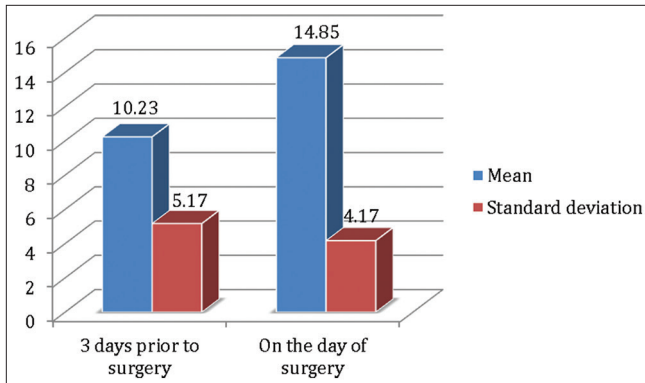
Fear and anxiety toward surgical procedure are common human emotions, and they are closely related to each other. The physical and chemical reaction that take place in the body, when threatened by immediate danger, is fear, whereas anxiety can be regarded as a possibility of danger and is perceived to be less immediate in nature. Hence, fear and anxiety may affect the possibility of the best treatment and care which could be provided to the patient and in turn affect the oral health parameters.^[4] This also increases the complexity of the procedure. Anxiety causes stimulation of the adrenal glands which are located above the excretory gland. The gland consists of an outer adrenal glandular tissue and inner medulla of nervous tissue. The cortex secretes fifty steroid hormones known as adrenocorticosteroids, which are divided into three groups, i.e., glucocorticoids, mineralocorticoid in humans, produced by zona fasciculata. The synthesis of cortisol takes place when cholesterol undergoes division to eliminate six carbon fragments to form pregnenolone. It is the most common precursor for the



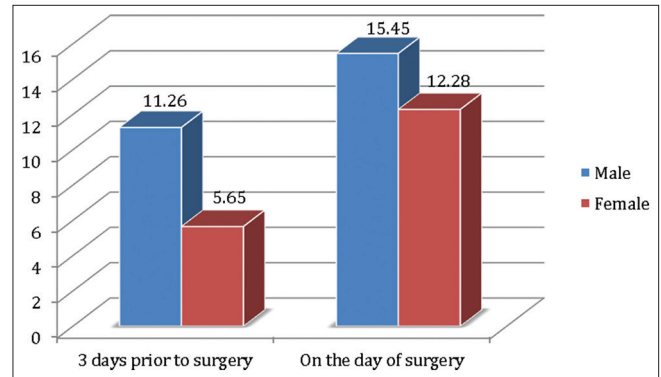
Figure 1: Armamentarium

synthesis of steroid hormones and is catalyzed by cytochrome P450 side-chain division enzyme. This reaction is aided by adrenocorticotrophic hormone. The enzyme hydroxylases,

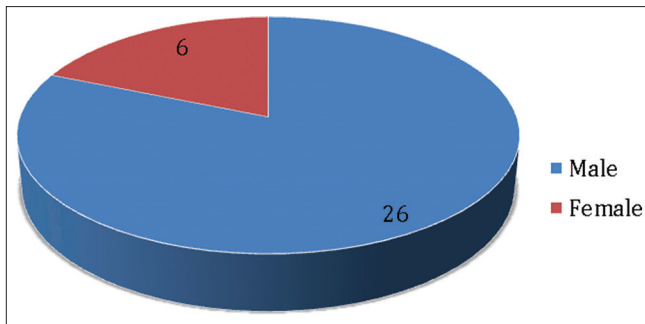
dehydrogenases associated with mitochondria and are responsible for synthesis of steroid hormones. Biosynthesis of major adrenocorticosteroids.^[7]



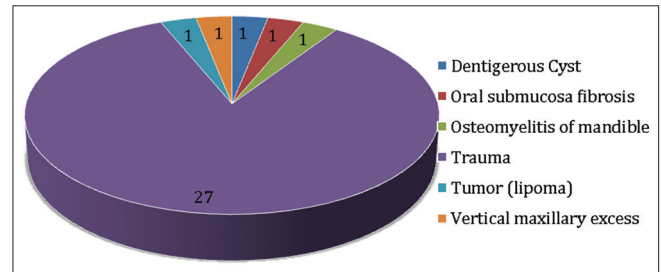
Graph 1: Serum cortisol level in the two groups



Graph 2: Serum cortisol level before and on the day of surgery according to gender



Graph 3: Distribution according to gender



Graph 4: Category of pathologies for which surgery was performed

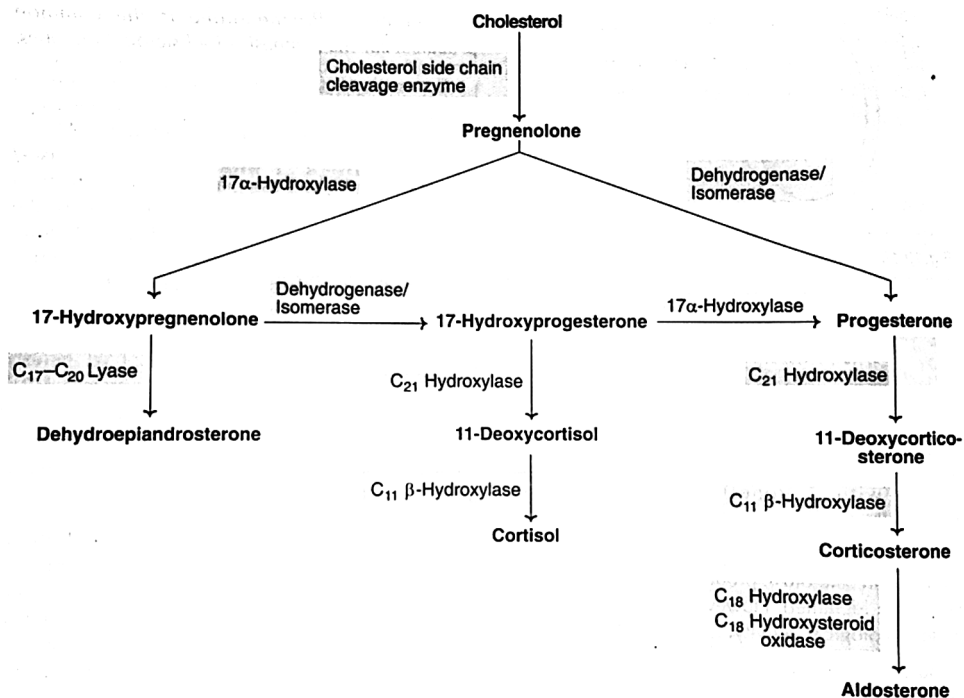


Figure 2: Biosynthesis of Adrenocorticotropic Hormone

A hypoadrenal shock is a life-threatening exacerbation of adrenal insufficiency (AI) when an increased hormone demand fails to increase the supply. AI is specifically a deficiency of adrenal gland hormone production in the cortex, and the common precipitants are surgery, infection, burns, sepsis, trauma, and metabolic or cardiovascular events [Figure 2].

Individuals with dental anxiety are treated with various modalities such as behavioral modification, systemic desensitization, hypnosis, and guided relaxation. For patients in whom these techniques fail, sedation and anti-anxiety premedication are required. Diazepam is considered as the prototypical benzodiazepine and the “grandfather” of the drug class, introduced around 1960 as an anti-anxiety sedative drug in dentistry for anxious patients. The depression of the central nervous system caused by benzodiazepine derivative, which are sedative hypnotic drugs (i.e., “drowsiness” or “hangover”). Drugs such as diazepam, lorazepam, alprazolam, and clonazepam can also be used to reduce anxiety.^[8]

The present study has been conducted for the evaluation of presurgical serum cortisol levels in patients undergoing major maxillofacial surgery under general anesthesia, with a sample size of 32 patients. The parameters considered were serum cortisol levels on the day of admission and on the day of surgery.

In literature, various scales are documented to measure the anxiety of dental patients, of which Corah’s Dental Anxiety Scale is the most often used. Other scales such as the Modified Corah Dental Scale, Charles Spielberger Psychologist Scale, KDFS, ISAR, Modified Dental Anxiety Scale,^[9] and Gatchel’s Anxiety Scale have also been used. In previous studies conducted by Gatchel’s^[10] Chanpong *et al.*^[11] it was found that Gatchel’s Anxiety Scale is easy to use and is a direct subjective measurement of anxiety on a numeric scale which is easy to understand by patients. In our study, blood sample was collected and sent for investigation. A literature search (PubMed/Google) failed to find out any study conducted for measuring the cortisol level in the blood stream on the admission and on the day of surgery.

Blood sample of each patient was collected and sent for investigation to the laboratory. In our study, the serum cortisol levels for each patient on the day of admission and on the day of surgery were evaluated. The mean presurgical level of 32 patients was 10.23% and the mean on the day of surgery was 14.85%. These results show a statistically significant increase in levels.

The reasons for elevated serum cortisol levels can be due to:

1. Hormonal and metabolic changes, followed by injury or trauma (stress response)
2. Anxiety of surgical operations, previous bad experiences.

A study done to see the severity of increase in blood sugar level was taken as a variable measuring anxiety response, which stated that the level varied according to the severity of surgery.^[3]

In our study of 32 patients, 27 had facial trauma (84.37%) and the remaining had miscellaneous pathology such as dentigerous

cyst, oral submucosal fibrosis, osteomyelitis, tumor, and orthognathic surgery, measuring 3.12% each [Graph 4].

A study was carried out on children during dental checkup, to evaluate the behavioral and physiological relation to dental anxiety, which showed that there was a significant change in systolic pressure and heart rate.^[1] Although the adrenocortical activity in human is controversial, some studies show that there is an increased baseline cortisol level in men, but no differences were found in other investigations.^[12] It has also been documented that in females, adrenocortical level is reduced during the follicular phase.^[11] A study was carried out to analyze the effect of surgery on melatonin production and compute the correlation between the melatonin and cortisol levels, which showed that the levels promptly increased and significantly on night and day on the procedure day.^[6] In our study of cortisol response, a total of 32 patients were taken, out of which 26 were male and 6 were female; the result of the study depicted that the change in cortisol level was higher in the male group when compared to the female group.

In our study, it has been found that there is an increase in the cortisol levels on admission, and it has subsequently increased on the day of surgery, indicating anxiety toward the procedure.

CONCLUSION

Stress is an integral part of our lives, and stress management plays a role like no other in today’s world. While there are professionals to help for stress during work or during sports training, stress due to a forthcoming surgery is natural and unavoidable. There can be plethora of health benefits due to reduction of serum cortisol levels such as decreased and increased uptake of insulin by peripheral skeletal muscles in diabetic patients and decreased bone resorption and improved bone healing in fractures. Another benefit of reducing cortisol is a decrease in protein catabolism, which will lead to better wound healing and healthier immune system. We have concluded from this study that the serum cortisol level shows a significant increase on the day of surgery. A future study can focus on the association between increased levels of serum cortisol and postoperative wound healing where patients can be divided into two groups, with one receiving preoperative stress reduction protocol and the other not receiving the same.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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