



Adrenal Insufficiency and the Dental Patient: A Review

KEYWORDS

Adrenal, dentist, corticoids

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ABSTRACT *Glucocorticoids and mineralcorticoids are "Life Saving" hormones secreted by the adrenal glands. They are steroidal in nature and have a wide range of effects on the metabolism of the body. Due to its anti-inflammatory and pain relieving properties, cortisol is widely exploited. It is used to treat diseases like arthritis and asthma. Deficiency as well as excess of this hormone can lead to serious disorders like Addison's Disease and Cushing Syndrome. A life threatening condition that can arise during dental surgery is "Adrenal Crisis" due to lack of cortisol. A dental practice serving 2000 adults can encounter 100 patients who use corticosteroids or have potential adrenal abnormalities. Hence, a dentist must take precautions to manage such medically compromised patients.*

Introduction

The adrenal glands are small endocrine glands located at the superior pole of the kidneys. Each gland has two parts- the adrenal cortex and the adrenal medulla. The adrenal cortex is further divided into three prominent zones: Zona Glomerulosa which majorly secretes aldosterone (mineralocorticoid), Zona Fasciculata which produces cortisol (glucocorticoid) and zona Reticularis which secretes androgens or sex hormone. Aldosterone controls homeostasis by regulating the levels of sodium and potassium in the blood. It acts on the distal tubules and the collecting ducts of the kidneys. Cortisol has an important effect on proteins and lipid mobilization, bone formation and has anti-inflammatory effects. Androgens are required for sexual maturation [1].

Functions of Cortisol

Cortisol (the main glucocorticoid of the body) greatly influences the body's metabolism. The most well known effect of cortisol is to increase gluconeogenesis. It stimulates a variety of enzymes in the hepatic cells that convert amino acids into glucose. Cortisol also stimulates the breakdown of amino acids and lipids in tissues (other than the liver) and increases their transport to the hepatic cells. There is also a decrease in the ability of the skeletal muscles to utilize glucose. Hence, while the stores of glycogen and protein in the liver increase, there is a decrease in other tissues. Cortisol acts as an insulin antagonist. It also activates osteoclasts and inhibits osteoblasts which have a direct effect on the alveolar part of the mandible [2, 3]

The other important function of cortisol is to "ready" the body for any sort of stress which can be physical like: trauma, infection, injury and surgery or emotional like anxiety. Cortisol has many anti-inflammatory and anti-allergic effects that are commercially exploited to treat diseases like rheumatoid arthritis, bronchial asthma and peptic ulcers [4]. Cortisol's weakening effect on the immunity can make people suffering from chronic stress vulnerable to infections [5].

Patients undergoing grafts, implants and organ transplants also use glucocorticoids on a long-term basis. In dental treatment, corticosteroids are used for reduction of pain, edema and trismus after oral surgery and endodon-

tic treatment [6] and the prevention of postoperative lingual and inferior alveolar nerve hypersensitivity following third molar extractions by using dexamethasone (synthetic cortisol) [2].

Regulation of Cortisol Secretion

The secretion of cortisol is finely regulated by the hypothalamus-pituitary axis (HPA). The hypothalamus releases a Corticotropin Releasing Factor (CRF), which via the hypothalamic portal system, in the median eminence of the hypothalamus, is transported to the anterior pituitary gland. CRF induces the pituitary to release ACTH (Adrenocorticotropic hormone), which acts on the adrenal cortex to cause the release of glucocorticoids (Fig. 1) [5]. Cortisol then acts on the body tissues. The normal secretion rate of cortisol is 20mg/day [1].

The major factors that control the release of cortisol are:

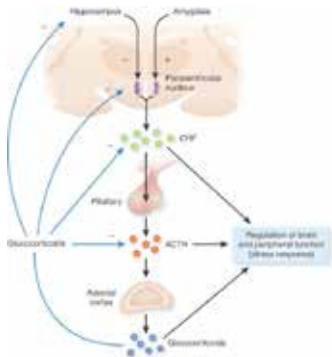
Stress: Any type of physical or mental stress can increase the production of cortisol up to 20 times. After any surgery, there is a spike in cortisol secretion to overcome the damaging effects of the invasive procedure. However, administering morphine like analgesics can relieve this [4].

Diurnal cycle: There is an increase in cortisol production in the day and fall during the night.

Cortisol: The circulating plasma level of cortisol inhibits the productions of ACTH and CTH, thus completing the negative feedback loop.

When ACTH is secreted by the anterior pituitary it also causes the secretion of several other hormones, which have similar chemical structure. This includes MSH or Melanocyte Stimulating Hormone, which causes skin darkening. Patients who suffer from Addison's disease, have high levels of ACTH, and present with bronzed skin and diffuse or focal brown macular hyper pigmentation of lips and oral mucosa [4].

Fig1: The Hypothalamus Pituitary Adrenal Axis



Medically Compromised Patients with Adrenal Insufficiency

Abnormality of the adrenal glands can lead to under or over secretion of adrenal hormones. There are two types of adrenal insufficiencies-

Primary Adrenal Insufficiency is caused due to destruction of adrenal cortex leading to severe deficiency of adrenocortical hormones.

Secondary Adrenal Insufficiency is more prevalent. This is caused to prolonged use of exogenous cortisol, which leads to the suppression of the HPA axis.

Hypoadrenalism- Addison's disease

When the adrenal glands are unable to produce sufficient adrenocortical hormones, it results in a condition called as Addison's disease. The cause could be: autoimmunity, tuberculous destruction, chronic infections like HIV and cancer [1].

In case a patient with adrenal insufficiency undergoes a surgical procedure, the dose of glucocorticoids must be increased up to 10 times or more, as the adrenal glands are unequipped to deal with a stressful condition and it may lead to an **Adrenal Crisis**. This is a severe medical emergency that can cause sweating, hypotension, nausea and circulatory collapse that can ultimately lead to death of the patient [1, 7].

Hyperadrenalism-Cushing's Syndrome

When the adrenal glands produce abnormally large amounts of adrenocortical hormones, it results in a condition called as Cushing's disease. The cause of this disease could be:

- Tumors of the anterior pituitary that secrete large amounts of ACTH, which in turn stimulates the adrenals to secrete more cortisol.

- High levels of CRH can also cause excess of ACTH release.
- Adenomas of the adrenal cortex
- In certain diseases like rheumatoid arthritis and asthma, cortisol is administered in high doses over a prolonged period of time. This can also lead to clinical manifestation of Cushing's syndrome. This is one of the most common causes of this disease [4].

Dental Management

Cortisol is extensively used in endodontic and oral surgery treatment. Steroids and antibiotic are used as capping agents on the pulp as they have anti-inflammatory and anti-allergic properties [8, 9]. Since, an adrenal crisis is a life threatening condition, a dental practitioner must take due care and carefully manage a patient suffering from adrenal insufficiency. The dentist must take into account the type of adrenal insufficiency (Primary or Secondary) the patient suffers from and the level of stress of the dental procedure and plan the treatment accordingly.

Studies have shown that patients with secondary adrenal insufficiency or controlled primary adrenal insufficiency can undergo routine dental procedures without the need for exogenous cortisol. However, patients with severe adrenal malfunction are at a risk of adrenal crisis during a dental surgery. The dentist should take a complete medical history and a thorough physical and biochemical examination of the patient. Severe infections, HIV infections, past trauma, injury, malignancy, discontinuation of treatment and removal of the gland should be given due importance. Biochemical testing (i.e., ACTH stimulation test) identifies patients suffering from primary adrenal insufficiency but it cannot pinpoint patients taking glucocorticoids. In primary adrenal insufficiency, a low ACTH stimulation test results (levels below 18 microgram/dL) indicate the need of exogenous glucocorticoids in case of a surgery [1].

Patients with hyperadrenalism and who are on corticosteroids for a prolonged period of time can develop hypertension, diabetes, delayed wound healing, decreased immunity and peptic ulcers [1].

Surgical procedures should be scheduled in the morning when the cortisol levels are the highest. Patients are recommended to take their usual steroid dosage 2 hours before the surgery. Local anesthesia does not require an increase in the dosage of cortisol but general anesthesia does. Pre-surgery anxiety does not require additional dosage of cortisol, however post surgery anxiety must be carefully managed (Table1). In case of hypotension and excessive blood loss, intravenous fluids and additional corticosteroids should be given. After the blood pressure has returned to normal, the usual dosage of corticosteroids should be resumed [1].

Table1: Surgical Procedure and Target Dose [1]

PROCEDURE	TARGET DOSE	
	Primary Adrenal Insufficiency	Secondary Adrenal Insufficiency
Routine Dentistry	None	None
Minor surgery	25mg hydrocortisone equivalent, pre operative on the day of surgery	Daily therapeutic dose
Moderate surgical stress	50-75mg on the day of surgery and up to 1 day after return to preoperative glucocorticoid dose on postoperative day 2	Daily therapeutic dose
Major Surgical stress	100-150mg per day of hydrocortisone equivalent given for 2-3 days. After preoperative dose, 50mg hydrocortisone IV every eight hours after initial dose for the first 48 to 72 hours after surgery	Daily therapeutic dose

Pain should be well controlled as extreme pain is a sign of stress and can elevate to an adrenal crisis. Narcotic analgesics, NSAIDs, corticosteroids are useful in controlling pain and swelling during third molar surgery.

The surgery should be no longer than an hour as longer surgeries are more stressful and require serious steroid supplements. Blood loss and fluid loss are to be reduced as this can lead to severe hypotension (Table 2). Patient should not take any anti-coagulant as this increases blood loss.

Table2: Dental Management of Patients with Possible Adrenal Insufficiency [1]

Potential Issues or Factors of Concern	
A	
Analgesics	Provide good postoperative pain control (eg Bupivacaine)
Anesthesia	Consider using long acting local anesthesia to account for pain control(eg. Bupivacaine). General anesthesia increases demand for glucocorticoids and renders an adrenal insufficient patient susceptible to adrenal crisis, therefore use cautiously.
Anxiety/Stress	Anxiety increases the chance of adrenal insufficiency, hence, anxiety should be controlled
B	
Bleeding	Minimize
Blood Pressure	The blood pressure should be monitored throughout the surgical procedure, as this is critical for recognition of adrenal crisis. During surgery, blood pressure should be evaluated at 5-minute intervals and before the patient leaves the hospital. Systolic blood pressure below 100mm of Hg and diastolic blood pressure below 60mm of Hg indicates hypotension. In case such a situation arises, corrective steps must be taken immediately. This could be in the form of proper patient positioning, fluid replacement and administration of vasopressors.
C	
Chair position	Supine position to avoid hypotension
D	
Devices	No issues
Drugs	Nitrous oxide-oxygen inhalation and benzodiazepine sedation are helpful in reducing anxiety and stress. Barbiturates should be prescribed cautiously as they increase the metabolism of cortisol and reduce the blood levels of cortisol. Inhibitors of corticosteroid production (e.g. ketoconazole metyrapone, aminoglutethimide) should be discontinued at least 24 hours before the surgery
E	
Equipment	Always keep emergency kit ready
F	
Follow up	Post surgery patients should be monitored for good fluid balance and adequate blood pressure during the first 24 hours. Communicate with the patient at the end of the appointment and within 4 hours postoperatively to determine whether features of weak pulse, hypotension, dyspnea, myalgias, arthralgia, ileus and fever are present. Signs and symptoms of an adrenal crisis require immediate transfer to emergency care.

Conclusion

A patient suffering from adrenal insufficiency needs extra care and attention as an adrenal crisis can be fatal. A dental practitioner must be well equipped to cater to these needs and must take the necessary precautions. Good pain, blood pressure and blood glucose control is the key to avoiding an adrenal crisis. After the surgery, follow up on wound healing is a must as there is an increased chance of infection.

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