Supplemental corticosteroids for dental patients with adrenal insufficiency

Reconsideration of the problem

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ABSTRACT

Background. Dental patients with primary or secondary adrenal insufficiency, or AI, may be at risk of experiencing adrenal crisis during or after invasive procedures. Since the mid-1950s, supplemental steroids in rather large doses have been recommended for patients with AI to prevent adrenal crisis.

Methods. To evaluate the need for supplemental steroids in these patients, the authors searched the literature from 1966 to 2000 using MEDLINE and textbooks for information that addressed AI and adrenal crisis in dentistry. Reference lists of relevant publications and review articles also were examined for information about the topic.

Results. The review identified only four reports of purported adrenal crisis in dentistry. Factors associated with the risk of adrenal crisis included the magnitude of surgery, the use of general anesthetics, the health status and stability of the patient, and the degree of pain control.

Conclusions. The limited number of reported cases strongly suggests that adrenal crisis is a rare event in dentistry, especially for patients with secondary AI, and most routine dental procedures can be performed without glucocorticoid supplementation.

Clinical Implications. The authors identify risk conditions for adrenal crisis and suggest new guidelines to prevent this problem in dental patients with AI.

For more than 50 years, medicine and dentistry have appreciated the importance of the adrenal glands in maintaining physiological integrity. This appreciation grew from studies[1,2] in the 1930s that demonstrated that adrenocortical insufficiency was associated with electrolyte disturbances, and a decade later[3] that cortisol prevented hypovolemia and circulatory collapse associated with adrenalectomy. During the 1940s, organic chemists isolated and elucidated the structures of 28 steroids from the adrenal cortex.[4] It was against this background that Hench and colleagues[5,6] reported the beneficial effects of cortisone in the treatment of diseases other than adrenocortical insufficiency (for example, rheumatoid arthritis). These findings ushered in the era of glucocorticoid therapy for patients with primary adrenal insufficiency, or AI, and inflammatory connective-tissue disease.

Adrenal crisis is a rare event in dentistry, and most routine dental procedures can be performed without glucocorticoid supplementation.

The concept of secondary AI evolved in the early 1950s from reports of patients experiencing refractory hypotension at the end of routine surgical procedures and dying hours later as a consequence of glucocorticoid therapy withdrawal and resultant AI.[7,8] These outcomes resulted in a list of recommendations for perioperative glucocorticoid supplementation that became the standard of care for many years.[8]

Although these recommendations have served as important guidelines, knowledge of the adrenal cortical response to physical stressors has been refined during the past 30 years.[9-11] Based on these more recent findings, reconsideration of the guidelines for perioperative glucocorticoid supplementation in dentistry appears needed. We consider gluco-

corticoid supplementation in dentistry by addressing AI, current medical recommendations, adrenal crisis and identification of risk in dentistry, and prescribing guidelines for perioperative coverage.

ADRENAL INSUFFICIENCY

The adrenal cortex produces mineralocorticoids and glucocorticoids that are important in maintaining fluid volume. Cortisol, the principal glucocorticoid, maintains extracellular fluid, whereas aldosterone, the principal mineralocorticoid, regulates salt and water balance.[12] Insufficient production of these hormones can result from primary or secondary adrenal disease. Primary adrenocortical insufficiency, also known as Addison's disease, is uncommon, occurring in about eight people per million population per year, with a prevalence of about 40 to 100 per million.[13-15]

It is caused by a progressive destruction of the adrenal cortex, usually of an idiopathic nature (most commonly autoimmune), but also results from hemorrhage, sepsis, infectious diseases (such as tuberculosis, human immunodeficiency virus, cytomegalovirus and fungal infection), malignancy, adrenalectomy, amyloidosis or drugs.[16] Clinical evidence of the deficiency generally arises only after 90 percent of the adrenal cortices have been destroyed.[17] Affected patients have high levels of adrenocorticotropic hormone, or ACTH, in blood, and a very low to undetectable level of aldosterone and cortisol in blood. Cortisol levels during this disease do not increase in response to stress and ACTH.

Secondary adrenocortical insufficiency results from hypothalamic or pituitary disease, or from the administration of exogenous corticosteroids. Although classified together, these two entities have different physiological effects. In the absence of hypothalamic or pituitary function, the adrenal cortex undergoes irreversible atrophy.[18] In contrast, long-term administration of corticosteroids blunts adrenal cortical function, with variable and reversible effects.[19] Cases of hypothalamic-pituitary disease are less common than those induced by use of corticosteroids. Researchers estimate that 5 percent of adults in the United States regularly use corticosteroids[20] and are at risk of developing secondary adrenocortical insufficiency.

Depending on the inflammatory condition, corticosteroids in medicine generally are administered at a target equal to, or less than, the normal daily output of cortisol (that is, 20 to 30 milligrams per day).[18] For example, hydrocortisone, which has the equivalent anti-inflammatory potency of cortisol, usually is administered at 20 mg/day; prednisone and prednisolone, which have four times the anti-inflammatory potency of cortisol, usually are administered at 5 mg/day; and dexamethasone, which has 25 times the anti-inflammatory potency of cortisol, is administered at 0.75 mg/day.

Such regimens, when administered as a morning dose, are less suppressive because of the diurnal rhythm of cortisol secretion, resulting in highest levels in the morning. Higher and divided daily doses are more suppressive, and often begin producing clinical manifestations of glucocorticoid excess (that is, Cushing's syndrome) after three weeks of use.[20] Although the level of cortisol production in patients with secondary AI due to hypothalamic or pituitary disease can be low because of its dependence on the level of circulating ACTH, the administration of corticosteroids alone does not determine which patients secrete sufficient levels of cortisol in response to stress. For example, the average cortisol production rate in patients with Cushing's syndrome has been reported to be 36 mg/day.[21]

The table presents the signs and symptoms associated with AI and corticosteroid treatment. The manifestations of primary AI (Addison's disease) relate to a deficiency of aldosterone and cortisol. The most common complaints are weakness, fatigue and nausea. The most common sign is melanin hyperpigmentation of the skin and mucous membranes. Hypotension, anorexia, fever and weight loss are common findings.

In secondary AI, the severity of symptoms is often less marked, and normal mineralocorticoid function is preserved. The preservation of mineralocorticoid function makes it less likely for patients with secondary AI to experience adrenal crisis than it is for patients with primary AI. Cushing's syndrome, which is due to chronic glucocorticoid excess, produces several features recognizable to the dentist, including plethora (red face), moon face, hirsutism, acne, capillary fragility and bruising, hypertension, osteoporosis and muscle weakness.

ADRENAL CRISIS

The most significant acute adverse outcome of AI

TABLE

FEATURES OF ADRENAL INSUFFICIENCY.

VARIABLE	PRIMARY ADRENAL INSUFFICIENCY	SECONDARY ADRENAL INSUFFICIENCY	CUSHING'S SYNDROME	ADRENAL CRISIS
Underlying Problem	Glucocorticoid and mineralocorticoid deficiency due to destruction or atrophy of adrenal gland	Glucocorticoid deficiency due to hypothalamic or pituitary disease	Potential glucocorticoid insufficiency due to long-term administration of corticosteroid for inflammatory condition or organ transplantation	Severe glucocorticoid deficiency with or without mineralocorticoid deficiency due to stress (for example, surgery, infection) and inability of adrenal cortex to meet demand
Clinical Features	Weakness, fatigability, weight loss, hypotension (may be orthostatic), hyperpigmentation of skin, mucous membranes and creases; less common are anorexia, nausea, vomiting, abdominal pain, salt craving, myalgia, personality changes, diarrhea, malaise; body hair loss in women; history of HIV* or TB† infection	Similar to primary adrenal insufficiency except less dramatic, no hyperpigmentation and patients tend not to be salt-depleted or extracellular volume–depleted	Cushingoid features: weight gain, moon face, thin skin, buffalo hump (that is, fat pad on neck), central obesity, acne, bruisability, hypertension	Major categories: - Gastrointestinal (nausea, vomiting, diarrhea, stomach cramps) - Hypotension, weak pulse, profuse sweating, weakness, fatigue - Headache, sunken eyes, cyanosis - Fever, dehydration, dyspnea progressing to hypothermia - Myalgias, arthralgia
Laboratory Features	Hyponatremia, hyperkalemia, elevated BUN,‡ occasionally hypercalcemia, low serum glucose level with sensitivity to fasting, mild anemia, eosinophilia	Fluid and electrolyte disturbances are less common than in primary disease except mild hyponatremia, hypoglycemia, mild anemia and eosinophilia	Can be normal or abnormal based on underlying condition	Hyponatremia and eosinophilia, hypoglycemia, azotemia
Therapy	Glucocorticoid and mineralocorticoid	Glucocorticoid	Addition of steroid-sparing drugs (azathioprine, methotrexate can reduce the adverse effects of steroids)	Intravenous bolus of 100 milligrams of hydrocortisone, fluid and electrolyte replacement

* HIV: Human immunodeficiency virus.
† TB: Tuberculosis.
‡ BUN: Blood urea nitrogen.

is adrenal crisis. This event can occur when a patient with AI, most commonly in the form of Addison's disease, is challenged by stress (for example, illness, infection or surgery), and, in response, is unable to synthesize adequate amounts of cortisol and aldosterone. This potentially life-threatening emergency usually evolves slowly during a few hours and then is manifested by severe exacerbation of the condition, including profuse sweating, hypotension, weak pulse, cyanosis, nausea, vomiting, weakness, headache, dehydration, fever, sunken eyes, dyspnea, myalgias, arthralgia, hyponatremia and eosinophilia. If not treated rapidly, the patient may develop hypothermia, severe hypotension, hypoglycemia, confusion and circulatory collapse that can culminate in death.[22]

Adrenal crisis is rare in patients with secondary AI, because the majority of these patients have normal aldosterone levels.[17] Since the manifestations usually are limited to those of glucocorticoid deficiency, the features of rapid hypotension, dehydration and shock seldom are encountered in patients with secondary AI.[12]

Features more commonly involve hypoglycemia, weakness, gastrointestinal complaints and a slowly evolving hypotension.

Adrenal crisis requires immediate intravenous administration of a glucocorticoid—usually a 100-mg hydrocortisone bolus—and intravenous fluid and electrolyte replacement to restore the blood pressure. Intramuscular injection of glucocorticoid is less desirable for emergency treatment because it results in slow absorption. After the initial treatment, 100 mg of hydrocortisone is administered slowly intravenously every six to eight hours during the first 24 hours, along with fluid replacement, vasopressors and correction of hypoglycemia, if needed. Resolution of the event or condition that precipitated the crisis also is required.

MEDICAL RECOMMENDATIONS

Since the mid-1950s, supplemental steroids have been recommended before and during surgery to prevent adrenal crisis in patients who receive steroid therapy.[7,8] The consensus among the medical community has been to provide "stress coverage" of 200 mg of hydrocortisone or its equivalent in the morning and 100 mg in the evening during periods of acute stress (such as surgery), trauma or illness.[16,17] This regimen is based on clinical inferences from case reports that the cortisol secretion rate increases during acute stress and can reach levels in the range of 100 to 300 mg per day.[17,23-25] However, cortisol secretion in the first 24 hours after surgery rarely exceeds 200 mg,[10,26] and the plasma cortisol level required to maintain homeostasis following stress has not been defined precisely.

The recommendations described above recently have undergone revision,[9,26] with emphasis placed on reducing the dose of supplemental steroid based on factors that influence cortisol demand. We review some of these factors below.

Surgery. Surgery is known to cause increased plasma corticosteroid levels during and after operations, with plasma cortisol levels reaching their peak (twofold to 10-fold above baseline) between four and 10 hours after surgery.[27,28] The level of response is based on the magnitude of the surgery[10,29] and whether general anesthetic is used.[28,30] Postoperative pain also is contributory, as is evident from the fact that urine levels of 17-hydroxycorticosteroids remain increased during the recuperative phase (three to six days after surgery),[28] and the plasma cortisol levels decline after postoperative administration of an analgesic.[29]

General anesthesia. General anesthesia in corticosteroid-treated patients significantly depresses the plasma cortisol response to surgery compared with that in patients who have not received corticosteroid drugs.[31,32] This may be an effect of steroid-induced AI or the use of barbiturate anesthetic drugs that can lower cortisol production.[30,33]

Although the role of these factors has not been fully determined, several prospective studies have shown that the vast majority of patients who regularly take the daily equivalent dose of steroid or less (that is, mean dose, 5 to 10 mg of prednisone daily) for renal transplantation or rheumatoid arthritis maintain adrenal function and do not require supplementation for minor surgical procedures.[31,34,35] Furthermore, for minor surgery, the risk of adrenal crisis appears to be low. A significant proportion of patients receiving prednisone therapy (5 to 50 mg daily) for between six days and 10 years who stopped therapy before surgery produced plasma cortisol levels similar to those of healthy subjects for up to seven days after minor or major surgery, and followed a normal postoperative course.[29,32,34]

Salem and colleagues[26] suggested that clinicians replace glucocorticoids only in an amount equivalent to the normal physiological response to surgical stress, and that the risk of an adverse outcome depends on the duration and severity of the surgery, the preoperative glucocorticoid dose and the overall health of the patient. Kehlet and Binder[10] and Hume and colleagues[24] estimated that an average adult secretes 75 to 150 mg a day in response to major surgery, and 50 mg a day during minor procedures. Based on these findings, Salem and colleagues[26] made the following general surgery and general anesthesia recommendations.

Minor surgical stress. For minor surgical stress, the glucocorticoid target is about 25 mg of hydrocortisone equivalent on the day of surgery. For example, an asthmatic patient who takes 5 mg of prednisone every other day should receive 5 mg of prednisone before surgery.

Moderate surgical stress. For moderate surgical stress, the glucocorticoid target is about 50 to 75 mg per day of hydrocortisone equivalent for up to one to two days. For example, a patient with systemic lupus erythematosus who takes 10 mg of prednisone daily should receive 10 mg of prednisone (or parenteral equivalent) before surgery and 50 mg of hydrocortisone intravenously during

surgery. On the first postoperative day, 20 mg of hydrocortisone is administered intravenously every eight hours (that is, 60 mg per day). The patient returns to his or her preoperative glucocorticoid dosage on postoperative day 2.

Major surgical stress. For major surgical stress, the glucocorticoid target is 100 to 150 mg per day of hydrocortisone equivalent for two to three days. For example, a patient with Crohn's disease who has taken 40 mg of prednisone daily for several years should receive his or her usual 40 mg of prednisone (or the parenteral equivalent) before surgery (within two hours) and 50 mg of hydrocortisone intravenously every eight hours after the initial dose for the first 48 to 72 hours after surgery. In comparison, a patient who takes 5 mg of prednisone daily and is undergoing a similar major operation should receive 5 mg of prednisone (or the parenteral equivalent) as a preoperative dose, with 25 mg of hydrocortisone administered intraoperatively and 25 mg administered within the first eight hours after surgery. The clinician should prescribe hydrocortisone (25 mg) every eight hours for the next 48 hours.

The above protocol accounts for individual differences in glucocorticoid coverage based on the patient's current daily steroid regimen and the severity of surgery or other stresses, and recommends that the preoperative steroid dose be taken within two hours of surgery (to afford high plasma levels during and after surgery). The protocol also recommends advising the surgeon, anesthetist and nurses of the potential for complications. If the postoperative course is uneventful, the patient receives his or her usual glucocorticoid dosage on completion of the regimen.

Factors that can complicate the postoperative course and exacerbate AI include liver dysfunction, sepsis and certain drugs.[36] Drugs that can lower plasma cortisol levels include aminoglutethimide (an adrenolytic), etomidate (an anesthetic agent), ketoconazole and inducers of hepatic cytochrome P-450 oxygenases (that is, phentyoin, barbiturates or rifampin) that accelerate degradation of cortisol. In contrast, the action of oral anticoagulants can be potentiated by intravenous high-dose methylprednisolone,[37] which can contribute to increased bleeding and the potential for hypovolemia.

ADRENAL CRISIS AND IDENTIFICATION OF RISK IN DENTISTRY

The above discussion leads one to ask, "Who is at risk of experiencing adrenal crisis during dental procedures?" This question, unfortunately, has not been addressed fully despite the presence of several excellent review articles in the dental literature.[38-41] These reports have provided recommendations for preventing adrenal crisis in dentistry based, in large part, on medical reports; however, few people have analyzed the risks associated with dental procedures.

To this end, we searched the medical literature using MEDLINE from 1966 through 2000 for reports in English that addressed adrenal crisis in dentistry. In MEDLINE, we searched the key words adrenal, adrenal crisis and dentistry alone and in combination. Reference lists of relevant publications and review articles were examined to identify further studies. We analyzed the information in these reports on the basis of the reported features, quality of documentation and response to therapy.

The significance of each report was based on evidence that the clinical or laboratory features or both were consistent with adrenal crisis,[17,41] as shown in the table; the condition responded to glucocorticoid therapy; and factors such as hypotension, hypovolemia and hypoglycemia were reasonably dispelled. These criteria were important since hypotension, fever and nausea are nonspecific signs of disorders (such as unrecognized blood loss, septicemia, myocardial infarction and the effects of general anesthesia) that could be confused with the clinical picture of adrenal crisis.

Our analysis resulted in the identification of only four reports[42-45] published in peer-reviewed journals that purported that an adrenal crisis related to dental treatment had occurred. This limited number of reported cases (four in 35 years) indicates that this medical emergency is seldom encountered in dentistry. Features common in three of the four reports included AI in patients who were at least 40 years of age and who had multiple extractions performed with administration of general anesthetic, or in whom an oral infection was present. The authors reported a significant drop in blood pressure in the postoperative phase of each case, a feature suggestive of adrenal crisis. However, these three reports had one or more of the following:

- clinical features of the "crisis" were poorly documented;
- other disorders (that is, hypovolemia, bleeding, infection or hypoglycemia) were not ruled out

adequately;
- inadequate evidence was provided that patients would have responded to fluids, glucose and/or vasopressors alone.

These inadequacies call into question the validity of these three reports. The fourth report appears to document a hypotensive-hypoglycemic event—a common finding in primary AI—because there was evidence of undiagnosed AI that responded to dextrose, fluids and vasopressors, but did not require corticosteroids for resolution.[44]

Although all four reports lacked adequate documentation, it is possible that these cases, individually or as a group, truly represented adrenal crises. Either way, a significant hypotensive event occurred that required emergency treatment. We analyzed the overlapping features of these cases to identify risk factors potentially contributing to the purported crisis. The overlapping features identified were primary or secondary AI, use of a general anesthetic, extraction of multiple teeth, low blood pressure at the end of the appointment, a crisis developing 1½ to five hours after surgery and an uncertainty about whether postoperative analgesia was obtained.

We identified the following additional factors that could have increased the patients' risk of developing hypotension and features of adrenal crisis:
- the stress of multiple extractions and the presence of oral infection;
- hypovolemia resulting from recent diarrhea or bleeding from the surgical site;
- inadequate circulating plasma cortisol (or glucose) levels as a result of AI, a fasting state, use of a barbiturate-containing general anesthetic that can metabolize circulating cortisol,[46] or inadequate or inappropriate dosing of hydrocortisone before and during the procedure.

GUIDELINES FOR PERIOPERATIVE COVERAGE IN DENTISTRY

Because no carefully controlled, randomized trials have been conducted in patients who have AI to definitively establish that corticosteroids are required for dental procedures, guidelines rely on evidence from the above-mentioned studies and the few purported adrenal crisis cases associated with dentistry.[42-45] From these studies, four factors appear to contribute to the risk of adrenal crisis during the perioperative period of oral surgery. These include the magnitude of surgery, use of general anesthetic, overall health of the patient (for example, stable vs. ongoing infection) and the degree of pain control.

Based on these data, we suggest guidelines for risk stratification of patients who have AI (Box, "Dental Procedures and Recommended Corticosteroid Supplementation in Patients With Adrenal Insufficiency"). Three categories are introduced, primarily on the basis of the type and magnitude of the procedure performed and the risk of adrenal crisis. However, the clinician also should realize that risk is influenced by drugs administered, health of the patient and degree of pain control. We realize that these recommendations are a departure from current common approaches. However, available evidence no longer supports routine recommendations for corticosteroid supplementation for all dental procedures

DENTAL PROCEDURES AND RECOMMENDED CORTICOSTEROID SUPPLEMENTATION IN PATIENTS WITH ADRENAL INSUFFICIENCY.*

NEGLIGIBLE RISK CATEGORY

- Nonsurgical dental procedures
  Regimen: No supplementation required

MILD RISK CATEGORY

- Minor oral surgery: A few simple extractions, biopsy
- Minor periodontal surgery
  Regimen: The glucocorticoid target is about 25 milligrams of hydrocortisone equivalent (5 mg of prednisone) the day of surgery

MODERATE-TO-MAJOR RISK CATEGORY

- Major oral surgery: Multiple extractions, quadrant periodontal surgery, extraction of bony impactions, osseous surgery, osteotomy, bone resections, cancer surgery, surgical procedures involving general anesthesia, procedures lasting more than one hour, procedures associated with significant blood loss
  Regimen: The glucocorticoid target is about 50 to 100 mg per day of hydrocortisone equivalent the day of surgery and for at least one postoperative day

* General anesthesia, infection and pain can increase the risk of adrenal crisis in susceptible patients.

for patients who potentially have AI or who are currently receiving or have recently stopped receiving steroid therapy.[47]

NEGLIGIBLE RISK: NONSURGICAL DENTAL PROCEDURES

Available evidence[11,34,35,48] indicates that the vast majority of patients with AI can undergo routine, nonsurgical dental treatment without the need for supplemental glucocorticoids. This conclusion is supported by the fact that routine, nonsurgical dental procedures do not stimulate cortisol production at levels comparable to those of oral surgery,[49] and local anesthetic blocks neural stress pathways required for ACTH secretion.[50,51]

In presenting this guideline, however, we do not advocate the performance of dental treatment in patients whose AI is uncontrolled or undiagnosed (see Table for clinical features). However, patients with AI who are in stable condition, and those with a history of steroid use who have had their glucocorticoid therapy discontinued before surgery have withstood general surgical procedures without experiencing adrenal crisis.[10,29,34]

MILD RISK: MINOR ORAL SURGERY

Patients at risk of experiencing adrenal crisis are those who undergo stressful surgical procedures and have no, or extremely low, adrenal function as a result of primary or secondary AI. Evidence[10,14,26] indicates that the risk of adrenal crisis is greater for primary AI than for secondary AI due to hypothalamic or pituitary disease or destruction. This secondary AI carries a risk equal to or greater than that for secondary AI associated with steroid administration (30 mg/day or more of cortisol equivalent) and recent failure to take the medication, which in turn presents a greater risk than that for secondary AI associated with current steroid administration. Patients who receive less than 30 mg/day of cortisol equivalent, or who receive topical or inhaled steroid therapy rarely have adrenal suppression unless the topical agents cover large inflamed areas with occlusive dressings[52] or the inhalation doses exceed 1.5 mg of beclomethasone equivalent per day.[53]

Studies[27,29,48,54] that have investigated the stress response to minor general and oral surgical procedures have concluded that significant cortisol increases generally are not seen before or during the operation, but occur in the postoperative period, approximately one to five hours after the start of the procedure. The postoperative increase in plasma cortisol levels likely is a response to pain, since postoperative increases in cortisol levels correlate with the loss of local anesthesia[54] and are blunted by the use of analgesics.[27]

Clinicians can reduce the risk of adrenal crisis by requesting that the patient take his or her usual steroid dose before coming to the dental office, scheduling the appointment in the morning when cortisol levels are highest, and providing stress reduction measures with appropriate postoperative analgesia. Consistent with this, Ziccardi and colleagues reported[41,55] that supplementation is not required for patients who receive corticosteroid therapy when uncomplicated minor surgical procedures of the orofacial complex are performed with local anesthesia, with or without conscious sedation (V. Ziccardi, D.D.S., oral communication, November 2000).

Controversy surrounds the need for supplemental steroid therapy in patients who are undergoing oral surgery and have recently discontinued steroid therapy. A conservative approach is to wait two weeks for the normal adrenal function to return[56-59] before performing elective oral surgical procedures. However, this conservative waiting period appears to be unneeded for patients who are receiving 30 mg of hydrocortisone (that is, 5 mg of prednisone) or less per day.[48] Alternatively, biochemical testing (that is, ACTH stimulation test, the insulin hypoglycemia test or the corticotropin-releasing hormone test)[19,20] can be performed if surgical procedures are required within the two-week window, with the need for supplemental steroid therapy determined on the basis of low adrenal response. However, the clinical response is not always well-correlated with test results.[19]

MILD RISK REGIMEN

For minor oral and periodontal surgery (for example, a few simple extractions, soft-tissue surgery), evidence suggests that AI is prevented when circulating levels of glucocorticoids are about 25 mg of hydrocortisone equivalent per day.[26] This is equivalent to a dose of about 5 mg of prednisone. The clinician should confirm that the patient has taken the recommended dose of steroid within two hours of the surgical procedure, and should schedule the surgery in the morning when normal cortisol levels are highest.

Stress reduction measures should be implemented. Benefits can be gained from use of the following:

- oral, inhalation or intravenous sedation that provides stress reduction;
- intravenous fluids (that is, 5 percent dextrose) that can prevent hypovolemia and hypoglycemia;
- long-acting local anesthetics;
- adequate postoperative analgesics.

MODERATE-TO-MAJOR RISK: MAJOR ORAL SURGERY

Patients who have AI and are undergoing major oral surgery are at increased risk of experiencing adrenal crisis compared with the risk associated with minor surgery. Major surgical procedures are more stressful than minor surgical procedures.[26] They increase the demand for cortisol because of postoperative pain. Also, blood loss is greater, thus increasing the risk of developing hypovolemia and hypotension.

MODERATE-TO-MAJOR RISK REGIMEN

For major oral surgical stress (for example, multiple extractions, quadrant periodontal surgery, extraction of bony impactions, osseous surgery, osteotomy, bone resections, oral cancer surgery), surgical procedures involving the use of general anesthetic, procedures lasting more than one hour, or procedures associated with significant blood loss, the glucocorticoid target is about 50 to 100 mg per day of hydrocortisone equivalent for the day of surgery and for at least one postoperative day. For reasons of simplicity, our guideline represents a merger of the moderate and major surgical stress categories proposed by Salem and colleagues.[26] Higher doses may be needed if excessive bleeding or complications are encountered. Patients should take their usual steroid dose before the procedure, and supplemental intravenous hydrocortisone should be administered during surgery to achieve a total glucocorticoid level of 100 mg. Clinicians should consider hospitalizing these patients since blood pressure can be more closely monitored after surgery in this setting.[48] Hydrocortisone (25 mg) usually is prescribed every eight hours after surgery for 24 to 48 hours, depending on the procedure and the

DENTAL MANAGEMENT GUIDELINES FOR PATIENTS WITH ADRENAL INSUFFICIENCY.

- Define the risk of adrenal insufficiency through medical history and clinical examination. An increased risk of adrenal insufficiency exists when there is a history of tuberculosis or human immunodeficiency virus infection, since opportunistic infectious agents can attack the adrenal glands.[20,60]
- Ensure that patients with adrenal insufficiency take their usual glucocorticoid dose before a stressful surgical procedure.
- Schedule surgery in the morning, when cortisol levels usually are highest.
- Provide proper stress reduction, since anxiety can increase cortisol demand.
- Minor surgeries require minimal steroid coverage. The patient's usual daily dose typically is sufficient.
- Major surgeries and those lasting more than one hour or involving general anesthesia should be performed in a hospital with steroid supplementation.
- Use of nitrous oxide-oxygen or intravenous or oral benzodiazepine sedation[61] is helpful, since plasma cortisol levels are not reduced by these agents.[28]
- Avoid general anesthesia for outpatient procedures, since it increases glucocorticoid demand.[61,62] Avoid the use of barbiturates, since these drugs increase the metabolism of cortisol and reduce blood levels of cortisol.[30]
- Discontinue drug therapy that decreases cortisol levels (for example, ketoconazole) at least 24 hours before surgery, with the consent of the patient's physician.
- Provide adequate pain control during the operative and postoperative phases of care. Clinicians should ensure good postoperative pain control by administering long-acting local anesthetics (for example, bupivicaine) at the end of the procedure, as well as regular analgesic dosing.
- Blood and other fluid volume loss, as well as the use of anticoagulants can exacerbate hypotension and increase the risk of adrenal insufficiency-like symptoms. Thus, methods to reduce blood loss should be used.
- Monitor blood pressure throughout the procedure and before the patient leaves the dental office. Patients whose blood pressure is at or below 100/60 millimeters of mercury should receive fluid replacement (5 percent dextrose), vasopressors or, if needed, glucocorticoids.
- Recognize the signs of hypotension, hypoglycemia and hypovolemia and take corrective action quickly.

anticipated level of postoperative pain.

The box ("Dental Management Guidelines for Patients With Adrenal Insufficiency," page 1577)[60-62] provides further recommendations for reducing the risk of adrenal crisis associated with surgical stress in patients with AI.

CONCLUSION

Our analysis of the literature suggests that adrenal crisis is rare in dentistry, specific risk factors increase the risk of an adverse event developing in patients who have AI, and perioperative glucocorticoid supplementation can be prescribed in a more rationale manner than is currently the case. As new evidence becomes available, the suggested recommendations for perioperative glucocorticoid supplementation in dentistry may need to be modified. ■

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