CHAPTER **45**

PODIATRIC USES OF ORAL CORTICOSTEROIDS

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Since their introduction in the late 1940s, corticosteroids have proven to be invaluable pharmacologic agents in the treatment of many disease states and inflammatory conditions. The use of injectable corticosteroid is widespread among podiatric physicians, yet the prescribing of oral preparations is minimal, largely supplanted by the nonsteroidal anti-inflammatory drugs (NSAIDs). The undesirable effects of corticosteroids are as numerous and significant as their benefits. However, when used in proper doses over limited periods, these drugs can be valuable additions to the pharmacologic regimen.

PHARMACOLOGY

Corticosteroids are hormones secreted by the adrenal cortex. They are typically divided into the glucocorticoids and mineralocorticoids, but these classifications are not absolute. The mineralocorticoids primarily regulate electrolytes and fluids by their actions on the kidneys. They have little or no anti-inflammatory activity. The large group of both natural and synthetic corticosteroids which are used therapeutically for their anti-inflammatory effects are the glucocorticoids. Hydrocortisone (cortisol) and cortisone are naturally occurring hormones.

Corticosteroid production is regulated via the hypothalamic-pituitary-adrenal axis (HPA). The hypothalamus secretes corticotropin releasing factor, which prompts the pituitary to release adrenocorticotropin hormone (ACTH). Circulating ACTH stimulates the adrenal cortex to release corticosteroid. Both ACTH and cortisol secretion are related to the wake-sleep cycle. By 4:00 A.M., ACTH levels are at their highest, so that by 8:00 A.M., maximal cortisol levels are obtained. High cortisol levels directly feedback to the pituitary, ending ACTH production. By midnight, serum cortisol levels are barely detectable. The adrenal cortex secretes an average of 20 mg of cortisol daily, and any increase above this amount will suppress the HPA axis.

The exact mechanism of glucocorticoid anti-inflammatory action is not known. It is believed that the following effects are generated by the stabilization of lysosomal membranes: 1. decreasing vascular permeability (thereby reducing edema and white blood cell migration), 2. decreasing production of prostaglandin, 3. inhibiting macrophage accumulation, 4. decreasing complement component, 5. inhibiting the release of histamine and kinin, and 6. decreasing fibroblastic proliferation and collagen deposition. They are also immunosuppressive which plays a role in its anti-inflammatory actions.

ADVERSE REACTIONS

There are many well-documented, harmful effects of glucocorticoids. Fortunately, these side effects are associated largely with long-term therapy.

One long-term effect is adrenal insufficiency. The degree of adrenal suppression is determined by the type of steroid, dosage, and method and length of administration. Adrenal suppression requires the tapering of the dosage until the adrenal cortex is again responsive. Various formulas are used to taper the dosage including: reduction of the dosage by 10% to 25% per week regardless of the starting dose, and reduction of dosage based on measurement of plasma cortisol levels. Corticoid withdrawal syndrome is characterized by weakness, fatigue, anorexia, low-grade fever and a drop in blood pressure. It is important to note that adrenal suppression is unlikely to occur with less than a one-month course of therapy. Therefore, dosage tapering in this time frame is unnecessary.

The musculoskeletal effects from long-term glucocorticoid use are osteoporosis and aseptic necrosis of bone. Glucocorticoids are catabolic and subsequently result in muscle weakness, pain and wasting.

Suppression of the immune system may also occur. They should not be administered in patients with systemic fungal infections. In large doses, corticosteroids may inhibit the signs and symptoms

of infection, as well as increase one's susceptibility to bacterial, viral and fungal infections.

An increase in gluconeogenesis may also precipitate diabetes in the "latent" individual. They also result in centripetal redistribution of fat. Corticosteroids should be used cautiously in know diabetics.

Gastric ulceration and hemorrhage, manifestation of psychotic disorders, opthalmic, cardiovascular and renal disorders are additional potential complications that can result from long-term therapy.

Although these various complications can manifest during long-term therapy, treatment periods of less than four weeks are well-tolerated by the patient. The side-effects of short-term therapy include gastro-intestinal intolerance (generally of less intensity than that associated with NSAID use), anxiety and agitation (generally seen in females).

DOSAGE AND INDICATIONS

In the podiatric practice, oral corticosteroids are reserved for situations where potent anti-inflammatory action is needed, but cannot be provided by other means. These situations include inflammatory skin disorders (acute tinea pedis, poison ivy, contact dermatitis), soft tissue inflammation (plantar fascitis, achilles tendinitis), and acute arthropathies.

The oral medication is well-absorbed and well-tolerated. The medication should be administered in the morning to prevent adrenal suppression. Although the dosages may be discontinued abruptly if treatment periods do not exceed one month, they are generally tapered-off to prevent reactivation of the inflammatory condition. Various dosage schedules should be utilized based on clinical conditions. Most inflammatory conditions requiring the use of oral corticosteroids should begin with a minimum of 30 mg to 40 mg of prednisone, or its equivalent (Table 1). Some examples of dosages are shown in Table 2.

Dosepacks, particularly methylprednisolone (Medrol) are commonly employed. The initial daily dose is equivalent to 30 mg of prednisone, and rapidly tapers to 5 mg by the end of one week. Although the initial dose is fairly potent, the author believes the dosage diminishes too quickly to be effective for most podiatric conditions. Dosepacks appear to be most effective for short-term inflammatory conditions such as acute dermatitis (poison ivy) or acute gout.

Oral corticosteroids should not be used in patients with active peptic ulcer disease or active infection. Allergic reactions are uncommon and usually result from food colorings or sulfites used as preservatives. Short-term use in children is well tolerated. Corticosteroids should not be used during pregnancy, as they are transferred to maternal milk in lactating women.

Table 1

CORTICOSTEROID EQUIVALENT DOSAGES

DRUG	EQUIVALENT DOSE
cortisone	25 mg
hydrocortisone	20 mg
prednisone	5 mg
methylprednisolone	4 mg
triamcinolone	4 mg
dexamethasone	0.75 mg
betamethasone	0.6 mg

Table 2

SUGGESTED DOSE SCHEDULES FOR PREDNISONE

1. 60 mg x 5 days, then 40 mg x 5 days, then 20 mg x 5 days
2. 40 mg x 7 days, then 20 mg x 7 days
3. 8O mg, 60 mg, 40 mg, 20 mg, 10 mg daily
4. 60 mg, 50 mg, 40 mg, 30 mg, 20 mg, 10 mg daily

DRUG INTERACTIONS

As with the use of any drug, interactions occur with the use of corticosteroids. However, in short-term use, there are few significant reactions. Potassium wasting effects of diuretics will be increased. Serum levels of Dilantin may increase. Women on estrogen may see a potentiation of the glucocorticoid. Due to the suppression of the immune system, toxoids and vaccines should not be administered concomitantly with corticosteroids.

Aside from the important ulcerogenic potential, there does not appear to be any adverse reaction between corticosteroids and NSAIDs. Both these medications reduce inflammation through different mechanisms, therefore their simultaneous use may prove beneficial. In conditions requiring long-term therapy, (plantar fascitis), the author will implement therapy of both prednisone and NSAID. The prednisone is used for its immediate and profound effects. When the use of the prednisone is terminated, the anti-inflammatory effects of the NSAID will be in effect, and can be continued.

CONCLUSION

Although numerous side effects are attributed to the long-term use of glucocorticoids, their safety and efficacy in the short-term can not be ignored. Corticosteroids should be a part of the physician's pharmacologic armamentarium.

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