

# Systemic Steroids in Podiatric Medicine

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## INTRODUCTION

Steroids, also known as corticosteroids, glucocorticoids, or cortisones were developed in the 1950s when clinicians noticed that pregnant women with rheumatoid arthritis had improvement in their rheumatoid symptoms during pregnancy. Researchers theorized that a natural occurring anti-inflammatory hormone was responsible for this observation and this led to the discovery of steroids.

Systemic steroids are synthetic derivatives of the natural steroid, cortisol, which is produced by the adrenal glands. Natural cortisol regulates protein, carbohydrate, lipid, and nucleic acid metabolism. Cortisol also regulates inflammation and immune response, and the distribution and excretion of water and solutes throughout the body. Natural cortisol also regulates the secretion of adrenocorticotrophic hormone (ACTH) from the pituitary and corticotropin-releasing hormone (CRH) from the hypothalamus.

Systemic steroids are given orally, intravenously, or intramuscularly. Injectable steroids, inhaled steroids or topical steroids are not considered systemic, but all may have some systemic effects, especially side effects. Systemic steroids include, but are not limited to, cortisone, hydrocortisone, prednisone, prednisolone, methylprednisolone, dexamethasone, betamethasone, and triamcinolone. Prednisone is probably the most widely used systemic corticosteroid today and will be the main focus of this article.

Each systemic steroid has unique pharmacodynamic and pharmacokinetic properties. Cortisone is used as the standard when comparing these properties. They can be compared in equivalent dose, mineralocorticoid potency, half-life, and the dose required to suppress the hypothalamic-pituitary-adrenal (HPA) axis as demonstrated in Table 1.

## USES

Systemic steroids are widely used in medicine. Some of the many indications include: asthma, chronic obstructive pulmonary disease, rheumatic diseases, ulcerative colitis, Crohn's, multiple sclerosis, lupus, Meniere's disease, organ transplant, leukemia, lymphomas, multiple myeloma, muscular dystrophy, sarcoidosis, and heart failure.

Systemic steroids are predominantly used in podiatric medicine for their anti-inflammatory effects. As with nonsteroidal antiinflammatory drugs (NSAIDs), steroids

work by blocking the production of prostaglandins. Prostaglandins are mediators of the inflammatory cascade. Conditions of the lower extremity caused by, or producing, inflammation may be treated with systemic steroids. These conditions may include inflammatory joint disorders, tendonitis, gout, plantar fasciitis, inflammatory dermatologic conditions, and, as an adjunct in the management of pain secondary to inflammatory conditions.

The increased risks associated with NSAIDs have narrowed the patient population in which prescribers can safely use these medications. From the well-known renal and gastrointestinal potential adverse effects, to the more recently elucidated cardiovascular adverse effects, physicians must thoroughly question patients, review their medical history, and medication lists, before prescribing any prescription NSAID or recommending an over-the-counter NSAID. Before a prescription for a NSAID is written, the prescribing physician should ask the patient if they have any kidney disease, current or past gastrointestinal conditions, and/or current or past cardiovascular risk factors, including hypertension.

Because short-term use of systemic steroids does not carry many of these potential adverse effects associated with NSAIDs, they can be used more confidently and safely in a broader range of patients. Treatment with a systemic steroid less than 1 month is considered short-term management. Treatment with a systemic steroid for more than 3 months is considered long-term management. Our profession rarely would manage a condition long-term with systemic steroids as this would be better managed by rheumatology. The beneficial effects and the side effects are also proportional to the dose given. Low dose systemic steroids are considered to be less than 10mg/day of prednisone, or equivalent dose of another steroid. Medium dose is considered to be 10-20

**Table 1. Comparison of Systemic Steroids**

Drug	C	HC	Pred	MP	Dex
Equivalent dose	25	20	5	4	0.75
MC potency	2+	2+	1+	0-0.5+	0
Half-life	8-12	8-12	24-36	24-36	36-54
HPA axis suppression dose	25-30	20-30	7.5	7.5	1-1.5

C= cortisone; HC= hydrocortisone; Pred= prednisone; MP= methylprednisolone; Dex= dexamethasone; MC= mineralocorticoid.

mg/day of prednisone, and high dose is considered to be more than 20 mg/day of prednisone or equivalent. In the treatment of inflammatory conditions of the foot and leg, a typical course of an oral steroid would be in the high dose range initially, tapering down to a low dose range over a short period of time, usually less than 2 weeks.

## SIDE EFFECTS

Side effects from a short course of systemic steroids are rarely serious and mainly represent a nuisance for the patient. The most common side effects from a short course of treatment include sleep disturbance, increased appetite, weight gain, psychological effects (depression or anxiety), increased or decreased energy level, increased blood sugar, and fluid retention. Rare side effects from a short steroid course may include: mania, psychosis, delirium, depression, suicidal tendencies, heart failure, peptic ulceration, diabetes, and aseptic necrosis.

Side effects from long-term management with systemic steroids are much more potentially serious and more frequent. Those potential adverse effects of the skin with long-term steroid use include: increased risk of infection, skin thinning, striae, acne, hypertrichosis, alopecia, and subcutaneous fat atrophy with injectable forms of steroid. Adverse effects associated with body fat include: moon face, buffalo hump, truncal obesity, and weight gain secondary to increased appetite and increased food intake. Glaucoma, cataracts, and exophthalmos can be seen in the eye with long-term use. The risk of atherosclerosis, ischemic heart disease, cerebrovascular accident, and transient ischemic attack can increase with long-term therapy of systemic steroids.

Side effects of the nervous system include psychological changes (mood alterations, energy changes), psychiatric changes (psychosis, delirium, memory loss, depression), insomnia, tremors, and headaches. Gastritis, peptic ulcer, and hepatic steatosis are possible. Sodium and fluid retention, leg swelling, weight gain, increased blood pressure, and potassium loss are also possible due to changes in fluid balance with long-term use. Reproductive system side effects include irregular menstruation and lowered fertility. Musculoskeletal effects may include osteoporosis, osteonecrosis, myopathy, and higher incidence of vertebral fracture, even without osteoporosis. Because of the effects on T-cells, B-cells, phagocytes and cytokines, long-term use of systemic steroids can increase the risk of infections (bacterial, fungal, and viral) and decrease the efficacy of vaccines.

## OTHER CONSIDERATIONS

Prednisone is the most commonly used systemic corticosteroid. Prednisone is transported in the blood after administration to the liver where it is metabolized to its

active form, prednisolone. Prednisolone, after circulating throughout the body, is then metabolized by the liver to inactive metabolites. These metabolites are filtered by the kidneys and excreted in the urine. The onset of action is 1-2 hours. It will take 18 to 36 hours for complete clearance from the body for prednisone.

Drug interactions with other medications to consider include phenobarbital, phenytoin, and rifampin, which may increase the clearance of prednisone. Ketoconazole, due to its enzyme inhibition, may increase the therapeutic and toxic effects of prednisone. Estrogen and hormone replacement therapies may also increase the therapeutic and toxic effects. Diuretics can increase the clearance of prednisone. Moxifloxacin, levofloxacin, and ciprofloxacin can increase the risk of tendonitis and/or tendon rupture when taken concurrently with systemic steroids.

Because of the immunosuppression properties of steroids, they should not be prescribed in active infections or with systemic fungal infections. Prednisone should not be prescribed in patients receiving adalimumab injections (Humira) or etanercept (Enbrel) injections, due to the increased risk of infections.

Prednisone can be used safely in elderly patients but with caution if they are immunocompromised, due to the decreased immune response to potential viral and bacterial infections. The psychological side effects can be exaggerated in the elderly also. Prednisone is classified as a pregnancy B category drug. It has not been studied in humans but has shown no harmful effects to the fetus in animal studies. Some have reported the possible increased incidence of cleft palate and clubfoot in an infant exposed to corticosteroids during pregnancy. Prednisone is passed to the breast-feeding infant but poses minimal risk in low doses of breast milk. Nursing mothers requiring prednisone should be advised to nurse 3 hours after taking the steroid.

In conclusion, systemic steroids offer the practitioner a potentially more potent therapeutic option, and often a safer option, for the short-term use in inflammatory conditions. These can be used in patients with renal disease, past gastrointestinal problems, and those at risk for cardiovascular disease, more safely than NSAIDs. The side effects in short-term use are rarely serious. These side effects are more of a nuisance for the patient and diminish as the dose decreases and resolves quickly after completion of the therapy.

With short-term use in low doses, (less than 1 week), tapering is usually not needed. The author's preference is a high dose initially tapering to a low dose over time. For dermatological conditions, I find that a 6-7 day therapy course is sufficient. For musculoskeletal inflammatory conditions, I prefer a 12-14 day course. Prednisone is available in 5 mg and 10 mg dose packs for both 6-day

and 12-day dosing. These dose packs will allow high dose therapy initially tapering to a low dose of prednisone. These prepackaged doses of prednisone make it easy for the prescribing physician and more convenient for the patient to take and adhere to the prescribing regimen.

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