

Managing Complications of Chronic Systemic Corticosteroid Use

While the prescription of long-term corticosteroids is often warranted, there are ways to mitigate and manage potential metabolic, immunologic and other complications.

By Bob Geng, MD



CORTICOSTEROIDS ARE produced in the adrenal glands of the human body. They are important hormones that serve significant physiologic purposes in the regulation of the metabolic and immunologic systems. Their natural levels fluctuate throughout the day, and their production and release are highly regulated by the hypothalamus and pituitary glands.

Cortisol is the main corticosteroid naturally produced in humans. Due to important function of cortisol in regulating the metabolic and immunologic systems, many different synthetic corticosteroids have been created that mimic its function. Some of the most commonly used synthetic corticosteroids include prednisone, prednisolone, dexamethasone, betamethasone, hydrocortisone, methylprednisolone and triamcinolone. These can have very potent effects when used

at high doses to treat a variety of immunologic and inflammatory disorders, and they have been widely used for a long period of time.

The efficacy of corticosteroids is often quite remarkable, but equally remarkable are the deleterious effects they may have on many organ systems — particularly associated with prolonged use. The purpose of this article is to highlight some of the commonly known and recognized complications of chronic systemic corticosteroid use and discuss ways to mitigate use and manage complications.

Adverse Complications of Chronic Corticosteroid Use

The complications of exogenous corticosteroid use can be grouped into several main categories, including metabolic

changes, immunologic problems, ocular disease, skin health and behavioral changes.

From a metabolic standpoint, one of the biggest concerns is hyperglycemia secondary to impaired glucose tolerance and insulin resistance. This can lead to diabetes, or worsening of glycemic control in existing diabetic patients. Significant caution needs to be taken when prescribing high doses for diabetic patients. In addition to hyperglycemia, exogenous chronic corticosteroid use can lead to an increase in truncal obesity and body mass index. This is because corticosteroid use leads to appetite stimulation contributing to weight gain. Weight gain can have a further negative impact on glycemic control. Both hyperglycemia and obesity lead to the development of the metabolic syndrome, which will result in a negative impact on the cardiovascular system associated with hypertension, cardiovascular and cerebrovascular complications. In addition, corticosteroids can have a direct negative impact on the cardiovascular system by mimicking the effects of aldosterone to increase fluid retention.

Another aspect of metabolic disruption secondary to long-term corticosteroid use is growth and hormonal dysregulation. Chronic systemic corticosteroid use has been linked to linear growth retardation and menstrual cycle abnormalities. In addition, its use can have detrimental effects on bone health, leading to osteopenia and osteoporosis.

Beyond weight gain, chronic corticosteroid use is associated with an overall distortion of body appearance. A shift in distribution of body fat toward the face leads to the appearance of “moon face” (very rotund appearance of the face) and toward the posterior neck leads to the formation of a “buffalo hump.” Weight also increases in the abdominal region leading to the appearance of truncal obesity, and weight will often shift away from the extremities in both fat and muscle (atrophy of muscle). Overall, these body appearance changes can be termed as “Cushingoid features.” Fortunately, all of these tend to resolve upon discontinuation of corticosteroid use.

Chronic administration of exogenous corticosteroids will lead to adrenal suppression of endogenous production of cortisol. This means if exogenous corticosteroids are withdrawn abruptly or without tapering, patients may develop symptoms of adrenal insufficiency due to an insufficient level of endogenous cortisol.

The immunologic complication of exogenous corticosteroid use is mainly in immunosuppression. This is also the main purpose of therapeutic corticosteroid use since it is often administered to counteract an overactive inflammatory reaction.

Indeed, corticosteroids can have a tremendous impact in suppression of both the innate and adaptive immune systems, potentially leading to a secondary immunodeficiency. Initial exogenous corticosteroid use can lead to a seemingly higher peripheral blood leukocyte count (white blood cell count) because it prevents the transit of these immune cells out of the bloodstream. However, long-term use of corticosteroids can lead to a decrease in T cell, B cell and neutrophil number and function due to the significant effects of suppressing the immune system. Chronic corticosteroid use has also been linked to low immunoglobulin counts and, in some instances, the need for immune globulin replacement therapy. The degree of immunosuppression may lead to a state of immunodeficiency that makes patients susceptible to a myriad of opportunistic infections (pathogens that would not normally be able to infect a healthy individual with normal immune function), as well as more severe manifestations of common infections.

Beyond metabolic and immunologic adverse complications, chronic systemic corticosteroid use has been associated with ocular disease such as cataracts and glaucoma. Special caution is needed for patients with those baseline conditions, and consultation with ophthalmology may be warranted. Skin health such as the development of significant thinning of the skin is also adversely affected by chronic corticosteroid use. Lastly, behavioral changes may be observed with corticosteroid use. Patients can demonstrate an increase in irritability and excitability. If corticosteroids are administered at night, they can interfere with sleep. In some instances, they have been associated with the development of “steroid psychosis” with frank hallucinations.

Managing Complications of Chronic Corticosteroid Use

Due to the myriad adverse complications associated with chronic corticosteroid use, all attempts are usually made by physicians to limit their use to the lowest possible dose for the shortest possible duration. During times of severe acute inflammation, it may not be possible to avoid the use of systemic corticosteroids, but the goal is short-term use. For patients who may need long-term immunosuppression due to persistent autoimmunity or inflammation, steroid-sparing agents are often used to mitigate the need for chronic systemic corticosteroid administration. Steroid-sparing agents are often other immunosuppressive medications that act through different pathways and mechanisms to achieve a similar targeted

clinical outcome as corticosteroids. Some steroid-sparing agents have the ability to decrease inflammation by blocking pathways that are not immunosuppressive.

Another method of decreasing the use of chronic systemic corticosteroid use has been targeted localized corticosteroid application. These topical local administrations can take many different forms. For lower-respiratory diseases like asthma and chronic obstructive pulmonary disease, inhaled corticosteroids will deliver the medication directly into the airways, decreasing the amount of systemic absorption. For upper-airway diseases like chronic rhinosinusitis, intranasal steroids can deliver the medication directly into the nasal cavity in a concentrated fashion with minimal systemic absorption. For inflammatory ocular disorders, steroid eye drops can be given (although baseline intraocular pressures should still be checked prior to administration). For chronic inflammatory skin disorders such as atopic dermatitis and psoriasis, topical corticosteroid creams and ointments may be used to target the skin directly with less systemic absorption. For arthritis, corticosteroids can be directly injected into the joint space to concentrate the medication in the affected area while minimizing the systemic impact of adverse effects.

From an immunologic perspective, being vigilant about infections is crucial.

Unfortunately, localized administration of corticosteroids help to reduce long-term complications, but they do not eliminate them. Excessive use of high-potency topical steroids on the skin over a long period of time can still lead to skin thinning and atrophy. Long-term use of inhaled corticosteroids has been linked to linear growth suppression in children. Fortunately, additional steroid-sparing agents have been developed to also limit the use of localized corticosteroid administration.

Overall, close communication with patients' healthcare providers is key when chronic systemic corticosteroid therapy is used. Potential metabolic complications can be monitored with routine lab work such as a comprehensive metabolic

panel (which checks the blood glucose and liver enzymes that may be affected), the hemoglobin A1c (to screen for diabetes and prediabetes) and cholesterol testing. Routine physician follow-up is helpful to track blood pressure and weight since both are adversely affected by systemic corticosteroid therapy. For postmenopausal women, routine evaluation of bone density scans is helpful to screen for development of osteopenia and osteoporosis.

From an immunologic perspective, being vigilant about infections is crucial. If an opportunistic infection such as thrush or yeast infection arises, topical antifungal agents can be prescribed. There should be a low threshold to seek medical attention for any unusual, severe or prolonged infections since chronic corticosteroid use can lead to a degree of being immunocompromised. Routine complete blood counts and other immune surveillance labs such as quantitative immunoglobulin counts and lymphocyte subset flow cytometry may also be helpful to monitor and screen for any potential development of immunodeficiency secondary to chronic corticosteroid use.

Useful and Effective, But Caution Is Warranted

Corticosteroids are very potent and effective medications. However, due to their impact on so many organ systems, their long-term use can have significant detrimental consequences. Therefore, every effort should be made to limit their use to the lowest effective dose for the shortest duration possible. Sometimes, due to lack of alternative treatments and the ready availability of corticosteroids, high-dose administration for a short period of time is necessary to overcome overwhelming inflammation. However, every attempt should be made to decrease and gradually taper the use of systemic corticosteroids to minimize their negative impact. Localized administration, topical administration and use of safer alternative steroid-sparing agents should always be considered for all disease states. If there are no other good options besides the use of chronic systemic corticosteroids, then all attempts should be made to closely monitor patients metabolically and immunologically to ensure early detection of any potential adverse complications. ■

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