



# Prevention and management of glucocorticoid-induced side effects: A comprehensive review

## Ocular, cardiovascular, muscular, and psychiatric side effects and issues unique to pediatric patients

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### Learning objectives

After completing this learning activity, participants should be able to describe the ocular, cardiovascular, muscular, and psychiatric side effects of glucocorticoid use and devise strategies to prevent complications in adult and pediatric patients taking glucocorticoids.

### Disclosures

#### Editors

The editors involved with this CME activity and all content validation/peer reviewers of the journal-based CME activity have reported no relevant financial relationships with commercial interest(s).

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The final article in this 4-part continuing medical education series reviews the ocular, cardiovascular, muscular, and psychiatric side effects of glucocorticoids and discusses side effects unique to pediatric patients. (J Am Acad Dermatol 2017;76:201-7.)

**Key words:** cataracts; glucocorticoids; glaucoma; growth suppression; side effects; steroid myopathy; steroid psychosis; steroids.

## OCULAR ADVERSE EVENTS

### Key points

- **The risk for developing glaucoma and cataracts while taking glucocorticoid therapy appears to be dose-dependent**
- **When long-term glucocorticoid therapy is planned, clinicians should ask about the history of glaucoma and cataracts and consider referral for ophthalmologic examination**

Glucocorticoid use increases the risk of glaucoma and cataracts.<sup>1</sup> The risk appears to be both duration and dose-dependent. In 1 study, glaucoma risk increased with doses >7.5 mg of prednisone per day taken for ≥6 months.<sup>2</sup> A separate case-control study found an increased risk for glaucoma among patients who had taken glucocorticoids within 2 weeks, but not for those who had previously taken glucocorticoids.<sup>1</sup> The risk for glaucoma increased over time and for all doses of

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Please note that bone health and gastrointestinal and endocrinologic side effects of glucocorticoid were discussed in the first two installments of this Continuing Medical Education feature in the January 2017 issue of the JAAD.

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glucocorticoids; however, doses of hydrocortisone >40 mg per day (prednisone 10 mg equivalent) were associated with an almost 2-fold increased risk for glaucoma.<sup>1</sup>

Importantly, patients may not be aware of early visual loss. The increase in intraocular pressure is painless, but it can lead to permanent optic nerve damage. Discontinuation of glucocorticoid therapy leads to reversal of intraocular hypertension within 2 weeks, at which time pressures appear to normalize.<sup>1</sup>

Increased risk for posterior subcapsular cataracts can also be associated with long-term glucocorticoid use.<sup>3</sup> In 1 study, 39% of patients with rheumatoid arthritis developed cataracts, but only at prednisone doses of >10 mg per day for  $\geq 1$  year.<sup>4</sup> In a study of 230 patients with systemic lupus who were taking prednisone for 5 years, only 6 developed cataracts at doses ranging from 8 to 30 mg prednisone per day.<sup>5</sup> Another study of lupus patients found that cumulative prednisone dose was significantly associated with increased risk for cataracts at a reference dose of 10 mg per day for 10 years.<sup>6</sup> This side effect is more likely to occur at higher glucocorticoid doses, but as with other steroid-related complications, even doses  $\leq 5$  mg prednisone per day have been linked to cataract formation.<sup>2</sup> Therefore, there may be no safe dose at which clinicians can disregard this complication completely.<sup>3,7</sup> Other side effects, such as exophthalmos and chorioretinopathy, rarely occur.

**Management.** Clinicians should inquire about personal and family history of glaucoma or cataracts before starting glucocorticoid therapy. All patients for whom long-term glucocorticoid therapy at any dose is planned should have a baseline ophthalmology evaluation, with additional management and regular follow-up based on findings at the initial visit, the underlying disease, comorbidities, and anticipated steroid course (Table I). In the event an ophthalmologic examination cannot be performed in a timely fashion before beginning glucocorticoid therapy, patients can be referred after therapy has started. Given the risk of diabetic retinopathy with poor glucose control and the association of glucocorticoid use with diabetes, adequate diabetes management is also important to mitigate ocular complications of corticosteroids.

## CARDIOVASCULAR/HYPERTENSION/ LIPIDS

### Key point

- **Glucocorticoid therapy may increase the risk of cardiovascular disease, as may the patient's underlying inflammatory condition**

**Table I.** Ocular side effects

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Ask about history of cataracts and glaucoma
Consider referral for baseline ophthalmology examination
Follow-up ophthalmologic examination as needed (check intraocular pressure after about 3 months of systemic steroids)

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### Cardiovascular

Glucocorticoids may increase the risk of cardiovascular disease. One large case-control study found a dose-response relationship between daily glucocorticoid dose and the risk of heart failure among current users of glucocorticoids, including patients with rheumatoid arthritis, chronic obstructive pulmonary disease, and other conditions. The risk of ischemic heart disease was also increased, but there was not an association with cerebrovascular disease.<sup>8</sup> In a large, population-based study, patients taking  $\geq 7.5$  mg of prednisone per day or the equivalent had a significantly higher composite risk of myocardial infarction, angina, coronary revascularization, hospitalization for heart failure, transient ischemic attack, and stroke.<sup>9</sup> Patients taking glucocorticoids within the preceding 6 months were at increased risk. Continuous use ( $\leq 180$  days between prescriptions) was also associated with higher risk compared to intermittent use.<sup>9</sup> Patients with iatrogenic Cushing syndrome have a higher hazard ratio of developing a cardiovascular event and a higher risk of coronary heart disease and cardiac insufficiency.<sup>10</sup>

The association between cardiovascular disease and glucocorticoid use is confounded by the underlying inflammatory condition, which may increase the incidence of cardiovascular disease because of chronic inflammation and the need for higher doses of glucocorticoids. For example, increased mortality from heart disease has been noted among patients with inflammatory arthritis; however, many patients have been treated with high-dose steroids.<sup>9</sup>

Pulse glucocorticoids, defined as high-dose glucocorticoids delivered over a short period of time, are used to treat severe inflammatory disorders and are also associated with cardiovascular disease. Sudden death caused by pulse dose glucocorticoids has been reported, usually if given over <2 hours, but this tends to occur in patients with underlying cardiac disease or in patients receiving steroids for nondermatologic conditions.<sup>11</sup> Continuous cardiac monitoring should be considered in patients with severe cardiac or kidney disease who are receiving pulse dose glucocorticoids.<sup>11</sup> Patients treated for

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