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

Gastrointestinal and endocrinologic side effects

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Learning objectives
After completing this learning activity, participants should be able to describe important gastrointestinal and endocrinologic side effects of glucocorticoid use and devise strategies for preventing and diagnosing these complications in patients taking glucocorticoids.

Disclosures
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Part 2 of this 4-part continuing medical education series continues with a discussion of the prevention and management of gastrointestinal side effects associated with corticosteroid use, including peptic ulcer disease, gastrointestinal bleeding, and pancreatitis, followed by a review of corticosteroid-related endocrinologic side effects, such as diabetes, adrenal suppression, and Cushing syndrome. (J Am Acad Dermatol 2017;76:11-6.)

Key words: adrenal suppression; Cushing syndrome; diabetes; gastrointestinal bleeding; glucocorticoids; peptic ulcer disease; side effects; steroids.

GASTROINTESTINAL SIDE EFFECTS

Key points

- **Glucocorticoid therapy with concomitant nonsteroidal antiinflammatory drug use increases the risk of peptic ulcer disease and gastrointestinal bleeding**
- **Proton pump inhibitors are an effective means of gastrointestinal prophylaxis, but they are not without side effects**

Gastrointestinal (GI) side effects linked to glucocorticoid use include peptic ulcer disease (PUD), GI bleeding, and pancreatitis.

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Please note that infectious and other complications of steroid use will be discussed in the third and fourth installments of this Continuing Medical Education feature in the February 2017 issue of the *JAAD*.

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Peptic ulcer disease

There is conflicting evidence concerning the risk of PUD for patients who are taking glucocorticoid monotherapy. Two metaanalyses found no increased risk of PUD for patients who were taking glucocorticoids, while another found PUD to be a rare complication of corticosteroid therapy, occurring in <0.4% to 1.8% of patients.[1-3] In a nested case-control study of Medicaid patients, there was no increased risk of peptic ulcer disease at any dose or duration of glucocorticoid therapy.[4] Patients who are taking glucocorticoids may experience more symptoms of gastric irritation, yet in 2 separate studies these symptoms did not translate into an increased risk for PUD.[1,5] However, the combination of glucocorticoids with nonsteroidal antiinflammatory drugs clearly increases the risk for PUD. In the same case-control study cited above, there was a significantly increased risk of developing ulcers among patients taking this combination (relative risk, 4.4 [95% confidence interval {CI}, 2-9.7]).[4]

GI bleed

As with PUD, the concomitant use of glucocorticoids and nonsteroidal antiinflammatory drugs increases the risk of GI bleeding. In 1 study, patients who were taking low-dose aspirin plus high-dose corticosteroid therapy had a relative risk of 4.3 (95% CI, 2.10-9.34) for developing upper GI bleeding compared to those taking low-dose aspirin alone. Patients taking low-dose aspirin with low- or medium-dose corticosteroids, however, did not have increased risk.[6] It is not clear whether glucocorticoid use alone increases GI bleeding.[6-9] A metaanalysis of 71 controlled, randomized trials showed a low but independent risk of bleeding caused by steroids.[2] In the study cited above, patients who were taking high-dose glucocorticoids alone had a slight increased relative risk for developing GI bleed of 1.89 (95% CI, 1.05-3.38).[6] Finally, a metaanalysis comparing glucocorticoid use to placebo found an increased risk of bleeding or perforation limited to hospitalized patients only.[8]

Pancreatitis

The data linking pancreatitis to glucocorticoid use are similarly mixed. One case-control study found a nearly threefold increased risk of acute pancreatitis among current users of betamethasone, and a slightly lower but still significant risk among those taking prednisolone.[10] The risk reached its highest level in the first 4 to 14 days after the betamethasone was dispensed and 15 to 30 days after prednisolone, with the risk gradually decreasing thereafter.[10] In a randomized, placebo-controlled trial of steroids for optic neuritis that also evaluated corticosteroid side effects, there was only 1 case of acute pancreatitis among 457 patients.[5] A retrospective chart review of patients with systemic lupus determined that glucocorticoids were not the etiologic agent among those who developed pancreatitis.[11]

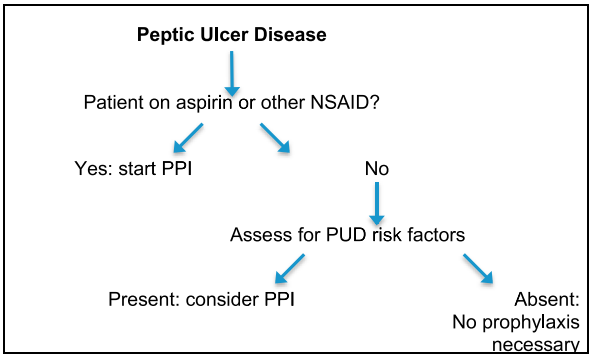

Fig 1. Approach to proton pump inhibitor prophylaxis for peptic ulcer disease. *NSAID*, Nonsteroidal antiinflammatory drug; *PPI*, proton pump inhibitor; *PUD*, peptic ulcer disease.

Management and prevention

Patients who must take a combination of glucocorticoids and nonsteroidal antiinflammatory drugs should be prescribed prophylaxis with a proton pump inhibitor (PPI). In patients with other risk factors for PUD, including those with previous peptic ulcer disease, heavy smokers, heavy alcohol users, patients >65 years of age, and patients taking other medications that may increase the risk of PUD, such as bisphosphonates, clinicians may choose to prescribe PPIs. For those taking glucocorticoids alone, without other risk factors, routine use of a PPI is not recommended (Fig 1). Patients should be counseled on the signs and symptoms of upper GI bleed, PUD, and, in the first 2 to 4 weeks of therapy, pancreatitis. These include black or tarry, melenic stools, fatigue, pallor, and severe abdominal pain, particularly if the pain is postprandial and radiating to the back or associated with nausea and vomiting.

PPIs

PPIs are an effective means of prophylaxis for PUD and GI bleeding. Esomeprazole 20 mg and 40 mg, pantoprazole 20 mg and 40 mg, lansoprazole 15 mg and 30 mg, omeprazole 20 mg and 40 mg, and rabeprazole 20 mg are all approved for prophylaxis. All are administered daily before breakfast, and, if needed, a second dose can be given before the evening meal. The choice of which PPI to prescribe comes down to cost, accessibility, and patient preference. However,