

Upper Gastrointestinal Bleeding in Patients Taking Corticosteroids

Nielsen GL, Sorensen HT, Mellemkjoer L, et al. Risk of hospitalization resulting from upper gastrointestinal bleeding among patients taking corticosteroids: a register-based cohort study. *Am J Med* 2001;111:541-5.

Study Overview

Objective. To determine the association between use of corticosteroids and hospitalization for upper gastrointestinal (UGI) bleeding, taking into account concomitant use of drugs that increase bleeding risk.

Design. Retrospective cohort study.

Setting and participants. 52,104 patients taking corticosteroids during 1991 to 1995 were identified in North Jutland County, Denmark. Of these patients, 1287 were excluded because they were not permanent residents of the study area. An additional 4567 were excluded because they had a history of gastrointestinal bleeding or a medical condition predisposing them to bleeding.

Main outcome measures. Exposure to corticosteroids, aspirin, anticoagulants, and nonsteroidal anti-inflammatory drugs (NSAIDs) was measured by searching a database of prescription claims paid by Denmark's national health service. The authors assumed that the drug exposure for each corticosteroid prescription was 50 days, for each NSAID prescription was 30 days, and for each aspirin or anticoagulant prescription was 90 days. Hospitalization due to UGI bleeding was determined by searching the County Hospital Discharge Registry. Patient records from the 2 databases were matched using patients' personal identification number. The relative risk (RR) of UGI bleeding due to corticosteroids was estimated by dividing the UGI bleeding incidence in the corticosteroid cohort with the UGI bleeding incidence in a second cohort of unexposed patients from the same area.

Main results. The study cohort accumulated 18,379 person-years of current exposure to corticosteroids and 101,807 person-years of former exposure to corticosteroids. Current use of corticosteroids was associated with hospitalization for UGI bleeding with an estimated RR of 4.2 (95% confidence interval [CI], 3.4 to 5.0). Current corticosteroid users who did not use other drugs associated with risk of UGI bleeding had an estimated RR of 2.9 (95% CI, 2.2 to 3.7). Former use of corticosteroids also was associated with UGI bleeding with

an estimated RR of 1.9 (95% CI, 1.7 to 2.2). When corticosteroids were taken with NSAIDs or aspirin, the estimated RR rose to 9.8 (95% CI, 6.5 to 14) and 5.3 (95% CI, 2.9 to 8.8), respectively.

Conclusion. Corticosteroids are associated with a higher rate of hospitalization for UGI bleeding.

Commentary

The finding that corticosteroids are associated with hospitalization for UGI bleeding confirms previous epidemiologic studies describing this relationship. This study has several strengths. The outcome only included incident cases of UGI bleeding, while previous studies measured incident and recurrent episodes of bleeding. Drug exposure was measured using pharmacy records, which eliminates the possibility that prescriptions were unfiled. Finally, the study accounted for the impact of concurrent use of aspirin, NSAID, and anticoagulants. The high RR reported when using these other medications with corticosteroids is an important contribution to the field and has many safety implications.

Several study assumptions limit the generalizability of this study to other countries. The authors assumed the average corticosteroid prescription was for 50 days based on their clinical experience. Quicker corticosteroid tapers are widely used in the United States, which lower the cumulative drug exposure. Because there is no dose-response information in the article, it is unclear if the RR of bleeding would be maintained with less exposure to corticosteroids. Secondly, important confounders, such as concurrent smoking, alcohol use, *Helicobacter pylori* infection, and nonprescription medications use, could not be measured. Nevertheless, these limitations are unlikely to invalidate Nielsen et al's findings.

Applications for Clinical Practice

Because corticosteroids are associated with a higher rate of hospitalization for UGI bleeding, physicians should be particularly cautious when using corticosteroids with aspirin, NSAIDs, or anticoagulants.

—Review by Josh F. Peterson, MD