

DO CORTICOSTEROIDS CAUSE PEPTIC ULCERS?

Conn & Blitzer 1976

Meta-analysis of 26 prospective, double blind, placebo-controlled studies from 1950-75.

Results: No significant difference in ulcers overall steroid v. placebo (1.4% v. 1.0%)

However, there was association between steroids and ulcer when dosage exceeded

1000mg equivalent of Prednisone, duration of steroids >30d, or history of PUD

See Editorial: "Steroids and peptic ulcer: a myth demolished?"

Messer et al. 1983

Meta-analysis of 71 trials, including ½ not blinded, many not controlled, some not randomized, and counted vague terms like "severe dyspepsia" and "gastritis" as equivalent to peptic ulcer (see critique by Conn & Poynard)

Results: RR 2.3 for "ulcer" and RR 1.5 for bleeding with steroids

"This study strongly suggests that corticosteroids do increase the risk of peptic ulcers and GI hemorrhage."

See Editorial: "Is the steroid ulcer a myth?"

Conn & Poynard 1984

A pointed critique detailing the flaws in the Messer meta-analysis

Estimates true NNH at ~1000

"From the clinical point of view, this controversy appears to be much ado about nothing."

Piper et al 1991

Nested case-control study of elderly Medicaid patients admitted to hospital for UGIB

Results: RR 1.1 steroids only; RR 4.4 steroids + NSAIDs

No increased risk of ulcer with steroids unless used in combination with NSAIDs

Conn & Poynard 1994

A new and improved meta-analysis, addressing the flaws noted in the Messer analysis

Results: Incidence of ulcer: 0.3% placebo v. 0.4% steroid (not statistically significant)

There *was* a statistically significant increase in dermatologic effects, diabetes, hypertension, and psychosis, supporting the soundness of this analysis

See Editorial: "Steroids and peptic ulcer: an end to the controversy?" An even-handed discussion of the discrepant meta-analyses.

See ACP Journal Club: "Corticosteroids do not cause peptic ulcer"

Hernandez-Diaz & Rodriguez 2001

Nested case-control from UK research database using computerized prescribing data

Cases: admitted to hospital or referred to specialist with diagnosis of UGIB or "clinical diagnosis of bleeding peptic ulcer"

Results: OR 1.8 steroids only; OR 4.0 NSAIDs only; OR 8.9 Steroids + NSAIDs

NSAID/steroid interaction similar to the case-control study of Piper, but this study differs in the finding of an effect from steroid use alone

What are the data regarding prophylaxis against PUD during steroid use?

Camarri et al 1980

Double blind, placebo controlled, cross-over study of 7 (count 'em, *seven*) patients

Results: Concurrent use of Cimetidine reduced GI symptoms

SUMMARY

When ACTH and corticosteroids were first used in the early 1950s, anecdotal case reports noted an association between these drugs and peptic ulcers. And steroids frequently do cause GI symptoms (i.e., dyspepsia, “gastritis”) that may reinforce this assumption that they cause ulcers. Subsequently, the notion that corticosteroids cause peptic ulcers has been taught to generations of house officers (including many faculty). The emergence of H-2 blockers and PPIs has led to a further presumption that such ulcers can be prevented by their prophylactic use. But, do the data support these beliefs?

In formal studies of the topic, the association between corticosteroid treatment and peptic ulcer has been variously described as a myth, associated with about a two-fold risk, or present only when steroids are used concomitantly with NSAIDs. There is notable variability in the methodological design of the different studies and analyses. And there is variability in defining the outcomes (e.g., diagnosis of ulcer by endoscopy or roentgenogram v. clinical diagnosis, inclusion of vague diagnoses like severe dyspepsia, inconsistent documentation of complications such as bleeding, perforation, etc.)

The strongest data appear to be those generated from the meta-analysis of double blind, placebo-controlled studies. The analysis by Conn & Poyard seems to be the most methodologically sound. In this analysis, no statistically significant difference was found between steroids and placebo and importantly, the *absolute difference* was extremely small: about 1 excess case of ulcer would be expected for every 1000 patients treated with corticosteroids. To place in perspective, about 200 excess cases of ulcer and 1 death from ulcer would be expected among a similar number of chronic NSAID users (Cochrane database). The use of steroids concurrently with NSAIDs does enhance the risk of ulcer and complications, likely via impaired healing of NSAID-induced ulcers.

There are no data regarding the efficacy of the prophylactic use of H-2 blockers or PPIs in preventing ulcers among patients treated with corticosteroids, although they might reduce GI symptoms. Given the extremely low incidence of ulcers with steroid use and the unknown efficacy of prophylaxis, routine prophylaxis is not warranted.

BOTTOM LINE

Corticosteroids frequently cause GI symptoms. Corticosteroids may rarely cause peptic ulcer and they enhance the ulcer-producing effect of NSAIDs. The risk of ulcer in patients receiving steroids is increased for patients concurrently taking NSAIDs, with the use of high dose steroids (>1000mg Prednisone-equivalent), and for patients with a prior history of ulcer. Routine prophylactic therapy is not warranted with short-term corticosteroid use (NNT ~1000, *assuming* that prophylaxis is 100% effective). Despite lack of data, prophylaxis may be considered for high-risk cases. The combined use of NSAIDs and corticosteroids should be avoided.