Review: Budesonide is better than mesalazine but not conventional corticosteroids for inducing remission in active Crohn disease

Papi C, Luchetti R, Gili L, et al. **Budesonide in the treatment of Crohn's disease: a meta-analysis.** Aliment Pharmacol Ther. 2000 Nov;14:1419-28.

QUESTION

In patients with Crohn disease (CD), how effective and safe is budesonide in inducing remission and in preventing relapse in those with medically or surgically induced remission?

DATA SOURCES

Randomized controlled trials were identified by searching MEDLINE with the terms budesonide and Crohn or inflammatory bowel disease. Bibliographies of studies and lists of gastrointestinal meeting proceedings (1993 to 1999) were also reviewed.

STUDY SELECTION

Studies were selected if they were randomized, double-blind, controlled trials of oral budesonide therapy in patients > 18 years of age and if they fully reported results on inducing remission, preventing clinical relapse, preventing endoscopic or clinical recurrence after surgery, or evaluating corticosteroid-related adverse effects in CD.

DATA EXTRACTION

Data were extracted on patient demographics, study design, control treatment, outcomes, and end points, including the drug's ability to induce remission and prevent relapse.

MAIN RESULTS

12 trials met the selection criteria. 6 trials addressed active CD, 4 addressed prevention of clinical relapse, and 2 addressed prevention of endoscopic and clinical recurrence after curative resection. Study results were recorded using an intention-to-treat analysis. Budesonide, 9 mg/d for 16 weeks, had a higher rate of remission than did mesalazine, 4 g/d (Table). Budesonide (3, 9, and 15 mg/d for 8 weeks; treatment groups combined) was better than placebo (Table). Budesonide, 9 mg/d for 8 weeks, did not have a higher rate of remission than did conventional corticosteroids (Table). Budesonide, 3 to 6 mg/d for 1 year, was not more effective than was placebo for preventing clinical relapse ($P = 0.4$), endoscopic recurrence ($P = 0.3$), and clinical recurrence ($P = 0.3$).

CONCLUSIONS

Budesonide is better than melasazine and placebo but not better than conventional corticosteroids for inducing remission in patients with active Crohn disease. Budesonide is not better than placebo for preventing relapse.

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Budesonide (Bud) vs mesalazine, placebo, and conventional corticosteroids to induce remission of active Crohn disease (at 8 or 16 wk)*

Comparison	Number of studies	Event rates	RBI (95% CI)	NNT (CI)
Bud vs mesalazine	1†	62% vs 36%	70% (24 to 139)	4 (3 to 10)
Bud vs placebo	1‡	42% vs 20%	114% (32 to 264)	5 (3 to 11)
		Weighted event rates	RBR (CI)	NNH (CI)
Bud vs corticosteroids	4	52% vs 60%	14% (1 to 25)	12 (7 to 141)

*RBR = relative benefit reduction. Other abbreviations defined in Glossary; RBI, RBR, NNT, NNH, and CI calculated from data in articles as noted.
†**Thomsen OO, Cortot A, Jewell D, et al.** N Engl J Med. 1998;339:370-4.
‡**Greenberg GR, Feagan BG, Martin F, et al.** N Engl J Med. 1994;331:836-41.

COMMENTARY

Budesonide, a glucocorticoid with high first-pass metabolism, is more effective than placebo for inducing remission in active CD. Budesonide is available in Europe and Canada and will probably be available in the United States within the year. The potential advantage of the drug is lower incidence of Cushing syndrome. Papi and colleagues provide important data on the efficacy and safety of budesonide: On average, it is 8% less effective for inducing clinical remission than are conventional glucocorticoids, and the incidence of glucocorticoid-related side effects is reduced by approximately 22%. No benefit for maintenance of remission was identified.

The review raises several important issues. First, does the improved tolerability of budesonide warrant first-line use for inducing remission in appropriate patients, given its higher cost and probably slightly lower effectiveness than conventional glucocorticoids? The authors conclude that such use is unjustified. They suggest that use be restricted to high-risk patients with contraindications to prednisone or prednisolone because budesonide might increase the proportion of patients in whom treatment ultimately fails or who become dependent on glucocorticoids. This conclusion is not based on good data: No randomized controlled trials have specifically addressed this question. My own experience is that many patients in whom budesonide induction therapy fails subsequently respond to treatment with conventional glucocorticoids.

Second, is the decreased risk for such minor glucocorticoid-related side effects as acne, moon facies, or edema clinically relevant? Patients generally prefer budesonide because of its superior tolerability. No data indicate that more serious adverse effects, such as aseptic necrosis, osteoporosis, and cataract formation, are less common. Additional studies of safety, economic modeling, and patient preference are required to determine whether budesonide has a better value than does conventional therapy.

Finally, the authors have combined data from 2 formulations of budesonide. Budesonide controlled–ileal-release capsules have been designed to release the drug in the ileum and proximal colon, whereas the pH-modified formulation has different dissolution properties. At least 1 study has suggested that the latter formulation may be active in patients with more distal disease (1).

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Reference

1. **Bar-Meir S, Chowers Y, Lavy A, et al.** Gastroenterology. 1998;115:835-40.

