Budesonide increased remission rates more than mesalamine in active Crohn disease


Question
In patients with active Crohn disease affecting the ileum, ascending colon, or both, what is the efficacy and safety of controlled ileal-release budesonide compared with slow-release mesalamine?

Design
Randomized, double-blind, placebo-controlled trial with follow-up at 16 weeks.

Setting
25 study centers in Denmark, France, the United Kingdom, Norway, Italy, Spain, Portugal, Greece, South Africa, Austria, Australia, and Ireland.

Patients
182 patients (age range 18 to 74 y, 68% women) who had Crohn disease confined to the distal ileum, the ileocecal; women) who had Crohn disease confined to the distal ileum, the ileocecal; women) who had Crohn disease confined to the distal ileum, the ileocecal valve, ileostomy, or colostomy; resection of > 100 cm of the ileum; need for immediate surgery; diabetes mellitus; active peptic ulcer disease; clinically important renal, hepatic, or cardiovascular disease or asthma; pregnancy or lactation; or allergy to glucocorticoids or mesalamine.

Intervention
Randomization was done at each study center in permuted blocks of four. 93 patients were allocated to budesonide, 9 mg once daily; 89 patients were allocated to mesalamine, 2 g twice daily.

Main outcome measures
Main outcome was clinical remission (defined as Crohn’s Disease Activity Index score ≤ 150). Secondary outcomes included length of time to remission and adverse events.

Main results
Analysis was by intention to treat, although 8 patients were not included in the analysis of remission because of missing data. 77 patients (83%) in the budesonide group and 50 patients (56%) in the mesalamine group (P < 0.001) were able to complete 16 weeks of treatment. At 16 weeks, the budesonide group had a higher remission rate than the mesalamine group (P < 0.001) (Table) and a shorter median time to remission (28 vs 84 d, P = 0.04). Fewer patients in the budesonide group had severe adverse events (defined as incapacitating events that led to inability to work or participate in normal activities) (12 vs 22, P = 0.04).

Conclusions
In patients with active Crohn disease affecting the ileum, ascending colon, or both, controlled-release budesonide led to a higher remission rate and shorter time to remission than slow-release mesalamine. Patients who received budesonide had fewer severe adverse effects.

Source of funding: Astra Draco.

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Abstract and Commentary also published in ACP Journal Club. 1999;130:35.

Budesonide vs mesalamine for active Crohn disease at 16 weeks*

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Budesonide</th>
<th>Mesalamine</th>
<th>RBI (95% CI)</th>
<th>NNT (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remission</td>
<td>62%</td>
<td>36%</td>
<td>70% (24 to 139)</td>
<td>4 (3 to 10)</td>
</tr>
</tbody>
</table>

*Abbreviations defined in Glossary; RBI, NNT, and CI calculated from data in article.

Commentary
In this study by Thomsen and colleagues, which compared budesonide and mesalamine, patients who were likely to respond had done so by 8 weeks. Subgroups with ileal or milder disease seemed to benefit more, although the study lacked the power for such comparisons. 30% of the enrolled patients did not complete 16 weeks of treatment because they were in remission or because the treatment was not efficacious. Of the patients who withdrew, more patients receiving budesonide had adrenal suppression by corticotropin stimulation (10% vs 0%). The clinical importance of this difference is unclear.

Budesonide should be considered before conventional steroids for patients with diabetes or osteopenia (1, 2). Patient concerns about adverse effects of conventional steroids and willingness to pay by third-party payers may also play a role in treatment selection.

2 studies that addressed the role of budesonide in similar patients for maintenance therapy showed that median time to relapse was considerably prolonged by budesonide, 6 mg/d, compared with placebo (158 vs 39 d and 258 vs 92 d), but no statistical difference existed in 1-year relapse rates (3, 4).

Future studies should address which patient subgroups benefit most, whether combining budesonide with mesalamine or antibiotics has any role, and whether higher doses or other formulations are needed for more extensive disease or reduction of relapse.

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References