CLINICAL @LERT

Balsalazide led to greater remission rates and tolerance than mesalamine in acute ulcerative colitis

Green JR, Lobo AJ, Holdsworth CD, et al, and the ABACUS Investigator Group. **Balsalazide is more effective and better tolerated than mesalamine in the treatment of acute ulcerative colitis.** *Gastroenterology* 1998 Jan;114:15–22.

Question

In patients with acute ulcerative colitis, does balsalazide lead to greater remission rates and tolerance than mesalamine?

Design

12 week randomised, double blind, controlled trial.

Setting

19 clinical centres in the UK.

Patients

101 patients who were 18–80 years of age and had symptomatic (moderate or severe) grade 2 to 4 ulcerative colitis that extended ≥ 12 cm beyond the anal margin. Exclusion criteria were Crohn's disease, idiopathic proctitis, non-inflammatory bowel diseases, stool parasites, toxins, pathogens, use of steroids within the previous month, use of immunosuppressive agents in the previous 3 months, daily use of a rectal steroid to maintain remission, or use of mesalamine releasing compound releasing ≥ 1.2 g/day in the previous 14 days. Follow up was 98% (mean age 41 y, 63% men).

Intervention

Patients were allocated to balsalazide (Penn Pharmaceuticals, Tredegar, Gwent, UK), 2.25 g three times daily (n=50), or mesalamine, 0.8 g three times daily (n=49), for 4, 8, or 12 weeks as necessary. Patients were given a rectal steroid foam (hydrocortisone acetate [Colifoam]) for relief medication.

Main outcome measures

Complete remission (none or mild symptoms, no use of rectal steroid foam, and grade 0 or 1 ulcerative colitis on

sigmoidoscopy). Secondary outcome measures were symptom relief and adverse events.

Main results

By 12 weeks, more patients treated with balsalazide than with mesalamine had achieved complete remission (62% v 37%, $p=0.02$); this effect was evident by week 4. More patients in the balsalazide group than in the mesalamine group had achieved symptomatic remission (none or mild symptoms) by weeks 2 (64% v 43%, $p=0.04$), 8 (78% v 45%, $p<0.001$), and 12 (88% v 57%, $p<0.001$). After 2 weeks of treatment, patients in the balsalazide group rated their symptoms as being less severe than did those in the mesalamine group ($p<0.001$); this effect remained at weeks 4 ($p<0.05$), 8 ($p=0.001$), and 12 ($p=0.003$). The median time to complete relief of symptoms was shorter for patients in the balsalazide group than in the mesalamine group (10 v 25 days, $p=0.004$). Patients treated with balsalazide had more days without symptoms and use of relief medication than did those treated with mesalamine during the first 4 weeks of treatment (mean 24% v 14%, $p=0.008$). Fewer patients treated with balsalazide than with mesalamine reported adverse events (48% v 71%, $p=0.02$). Fewer patients in the balsalazide group than in the mesalamine group did not complete the study because of treatment failure (12% v 33%, $p=0.015$).

Conclusion

In patients with acute ulcerative colitis, balsalazide led to greater remission rates and tolerance than did mesalamine.

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Commentary

Green *et al* enrolled 101 (99 evaluable) patients with moderate to severe symptoms of ulcerative colitis (UC) into a randomised, double blind, double dummy trial comparing 6.75 g balsalazide (Colazide) and 2.4 g mesalamine (Asacol) over 12 weeks. The primary endpoint was complete remission defined as absent or mild symptoms with either a normal sigmoidoscopy or a sigmoidoscopy demonstrating erythema and loss of vascular pattern. 62% of balsalazide versus 37% of mesalamine treated patients achieved remission by 12 weeks. In addition, balsalazide treated patients had a shorter median time to complete relief, a higher percentage of symptom-free days, less treatment failures, and fewer serious adverse effects. The authors concluded that balsalazide was "more effective...with more favourable side effect profile".

This study suggests the clinical superiority of balsalazide over mesalamine in the formulations tested. The context, methodology and interpretations must, however, be viewed in perspective. This trial

compared equivalent amounts of 5-aminosalicylic acid (5-ASA) delivered from Colazide and Asacol at currently "approved" doses of Asacol (2.4 g/day in the USA). This is not an optimal dose; prior mesalamine studies have demonstrated a dose response up to 4.8 g/day. Furthermore, in prior comparative trials, balsalazide has been therapeutically similar to sulfasalazine. In one trial, for instance, 50% "remission" rates were shown in both groups. Similarly, in a second trial, treatment success was reported in 81% of patients treated with balsalazide compared with 61% with sulfasalazine; this was not a statistically significant difference. In addition, a prior trial of 154 patients with mild to moderate UC who received equal amounts of 5-ASA, 23% of patients receiving balsalazide versus 19% of patients on Asacol (NS) were in remission at the end of 8 weeks. Finally, a 4 week trial demonstrated no statistical difference between balsalazide and placebo for the endpoints of

stool frequency, blood in stool, sigmoidoscopic improvement, Physician's Global Assessment, or overall assessment.

Thus, although the current trial suggests superiority of balsalazide, the results must be interpreted with caution. In larger meta-analyses, it has not been possible to distinguish efficacy advantages between oral 5-ASA delivery systems. Compared with sulfasalazine, all of the non-sulfa aminosalicylates are better tolerated. In comparing aminosalicylate formulations in clinical trials, it is essential to consider study details including sample sizes, study populations of disease extent and severity, doses, endpoints, and duration of treatment.

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1 Anonymous. Colazide Monograph. UK: Biorex Laboratories Ltd, 1997.

2 Riley SA. What dose of 5-aminosalicylic acid (mesalazine) in ulcerative colitis? *Gut* 1998;42: 761–3.