

Olsalazine was not better than placebo in maintaining remission in inactive Crohn disease

Mahmud N, Kamm MA, Dupas JL, et al. Olsalazine is not superior to placebo in maintaining remission of inactive Crohn's colitis and ileocolitis: a double blind, parallel, randomised, multicentre study. *Gut*. 2001 Oct;49:552-6.

QUESTION

In patients with Crohn colitis or ileocolitis, is olsalazine more effective than placebo in maintaining remission?

DESIGN

Randomized (unclear allocation concealment*), blinded (unclear),* placebo-controlled trial with 52-week follow-up.

SETTING

25 hospitals in 3 countries.

PATIENTS

328 patients who were ≥ 18 years of age and had Crohn colitis or ileocolitis in complete remission (Crohn disease activity index [CDAI] ≤ 150) for ≥ 1 month before randomization. Exclusion criteria were receipt of steroid, azathioprine, or other immunosuppressive therapy within 8 weeks of the start of treatment; antibiotic therapy ≥ 1 month; potential for pregnancy or lactation; clinically important hepatic or renal insufficiency; strictures causing obstruction; fistulae; oral or symptomatic anal Crohn disease; stoma or small-bowel disease other than terminal ileal disease; or hypersensitivity to sal-

icylates. 327 patients (99.7%) (mean age 39 y, 54% women) received the study drugs and had follow-up data.

INTERVENTION

Patients were allocated to olsalazine, 2 g daily ($n = 167$), or placebo ($n = 161$) for 52 weeks.

MAIN OUTCOME MEASURES

The primary outcome was relapse (CDAI score > 150). Adverse events were also assessed.

MAIN RESULTS

The groups did not differ for relapse ($P = 0.49$)† (Table). The study was powered to detect a difference in relapse rate of 15%. The failure rate (patients not completing the study) was higher in the olsalazine group

than in the placebo group ($P = 0.038$) (Table). Adverse events were mild to moderate in severity, but occurred in more olsalazine than placebo recipients ($P = 0.035$) (Table).

CONCLUSION

In patients with Crohn colitis or ileocolitis, olsalazine was not better than placebo in maintaining remission.

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For correspondence: Dr. N. Mahmud, Trinity College Dublin, Dublin, Ireland. E-mail nmahmud@tcd.ie. ■

*See Glossary.

† P value calculated from data in article.

Olsalazine vs placebo for Crohn colitis or ileocolitis at 52 weeks‡

Outcomes	Olsalazine	Placebo	RRI (95% CI)	NNH (CI)
Relapse	48.5%	45.0%	8.5% (-37 to 14)	Not significant
Failure to complete study	66%	53%	23% (3.1 to 48)	9 (5 to 55)
≥ 1 adverse event	39%	28%	42% (3.7 to 95)	9 (5 to 84)

‡Abbreviations defined in Glossary; RRI, NNH, and CI calculated from data in article.

COMMENTARY

Inflammatory bowel disease, particularly Crohn disease, provides a daunting therapeutic challenge for clinicians, despite recent advances in the use of such rationally developed biological agents as infliximab. Although treatment can successfully suppress active disease, it is problematic to maintain remission in these patients, unlike in their counterparts with ulcerative colitis who do well on such 5-acetylsalicylic acid (ASA) preparations as mesalamine. However, some data suggest a modest reduction in the relapse rate of symptomatic Crohn disease with mesalamine (1, 2). Olsalazine, another drug in the ASA class, consists of two 5-ASA molecules bound together with an azo bond. It has not been previously rigorously evaluated for its efficacy in maintaining remission in Crohn disease.

The results of the study by Mahmud and colleagues are disappointing: Not only was there no effect of the active drug on relapse rates (approximately 50% at 1 y), but indeed, overall failure was higher in patients receiving olsalazine. This finding probably resulted from the high incidence of diarrhea, a factor in the disease activity index used to monitor relapse in this study. Olsalazine can cause diarrhea in 10% to 20% of patients, probably because it stimulates chloride and fluid secretion in the small bowel.

This study highlights the difficult task of finding a prophylaxis that prevents Crohn disease reactivation, and it effectively rules out the use of olsalazine for this purpose. In the absence of safer and proven alternatives, however, prescribing mesalamine for such patients is still reasonable. Although its effects are weak overall, mesalamine can be of value particularly in postoperative patients, those with ileitis, and those with long-standing disease (3).

Gurinder Luthra, MD
P. Jay Pasricha, MD
University of Texas Medical Branch
Galveston, Texas, USA

References

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