THERAPY UPDATE

Which 5-ASA?

S P L Travis

When Asacol commands 65% of the UK market, can so many British gastroenterologists be wrong? Possibly. The market leader in France is Pentasa (72%) and is Salofalk in Germany (57%). In Canada it is Asacol (46%). Nevertheless, a Cochrane review of 11 trials involving 1598 patients showed that sulphasalazine was more effective than other 5-aminosalicylic acid (5-ASA) drugs for maintaining remission in ulcerative colitis (odds ratio (OR) 1.29, confidence interval (CI) 1.06–1.57). Diagnosis, disease location, activity, side effect profile, efficacy, and cost all affect the choice of 5-ASA.

As far as disease location is concerned, the key to treatment is a high concentration of 5-ASA at the site of inflammation. Suppositories are often appropriate for proctitis because >90% liquid 5-ASA enemas bypass the rectum. For active proctitis, a 1 g Pentasa suppository is more rapidly effective than two 500 mg Claversal (similar to Asacol) suppositories and also maintains remission.

For distal or left sided disease, suppositories can be used. Asacol foam is better tolerated than liquid 5-ASA, while expensive Salofalk enemas provide double the necessary dose. The optimum dose for topical treatment is 1 g.

The main role for 5-ASA remains maintenance of remission in ulcerative colitis. Individual 5-ASA derivatives all show comparable efficacy to sulphasalazine but the therapeutic advantage of the parent compound should be noted. Azo bonded compounds may be better for distal disease, which predominates in ulcerative colitis, and olsalazine was better than Asacol in one of the very few direct comparisons between 5-ASA derivatives. The advantage of balsalazide over Asacol however, welcomed as an azo bonded compound with few side effects, has been disappointing. In any case, the theoretical advantage of azo bonded compounds for distal disease can be overcome simply by increasing the dose of mesalazine.

The principal advantage of 5-ASA derivatives over sulphasalazine is that they are better tolerated. In the Cochrane review of maintenance therapy however, sulphasalazine and 5-ASA had similar adverse event profiles (OR 1.16 (CI 0.62–2.16), and 1.31 (CI 0.86–1.99), respectively). The numbers needed to harm also favoured sulphasalazine, being 171 and 78, respectively. Even so, some side effects can be used to therapeutic advantage. Olsalazine induced diarrhoea may help patients with distal disease and proximal constipation. Sulphasalazine may be better for patients with colitis associated arthropathy. Maintenance therapy with all 5-ASA drugs probably reduces the risk of colorectal cancer by 75% (OR 0.25, CI 0.13–0.48), which supports long term treatment in those with extensive colitis.

Cost is a final consideration and as a clinical director in the UK, sulphasalazine (tolerated by 80% at 2 g/day, costing the NHS £110 pa) still deserves serious consideration. The alternatives, all tolerated by about 90%, are 3–5-fold more expensive, which mounts up over the decades. An average primary care trust serving 170 000 people would save in the region of £10 000 pa if most patients with ulcerative colitis were prescribed the least expensive mesalazine. If general practitioners can be persuaded to contribute this saving to the salary of an inflammatory bowel disease nurse specialist, then so much the better!

And if I had one choice for a desert island? Pentasa wins on dose flexibility, different preparations, and low systemic absorption, but in practice I use all 5-ASA derivatives. The patient often declares a preference and that is the key to compliance.

Conflict of interest. Dr Travis has cheerfully enjoyed hospitality from all manufacturers of 5-ASA derivatives and has done advisory work for Ferring Pharmaceuticals, Pharmacia, and SmithKline Beecham.

REFERENCES


Key points

- Diagnosis, disease location, activity, side effect profile, efficacy, and cost all affect the choice of 5-ASA.
- Sulphasalazine has a small but significant benefit over 5-ASA derivatives for maintaining remission in ulcerative colitis and may harm fewer patients.
- Mesalazine dose is more important than the delivery system.
- Pentasa suppositories are best for proctitis.
- Combine suppositories and enemas for distal disease.

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