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- 1 Rijk MCM, van Schaik A, van Tongeren JHM. Deposition of mesalazine from mesalazine-delivering drugs in patients with inflammatory bowel disease, with and without diarrhoea. *Scand J Gastroenterol* 1992; 27: 863-8.
- 2 De Vos M, Verdievel H, Schroonjans R, Praet M, Bozeart M, Barbier F. Concentrations of 5-ASA and Ac-5-ASA in human ileocolonic biopsy homogenates after oral 5-ASA preparations. *Gut* 1992; 33: 1338-42.
- 3 Sninsky C, Hanauer S, Powers B, et al. Sensitive markers of renal dysfunction are elevated in chronic ulcerative colitis. 10th World Congress of Gastroenterology 1994; Los Angeles, CA: 1778.
- 4 Calder JC, Funder CC, Green CR, Ham KN, Tange JD. Nephrotoxic lesions from 5-aminosalicylic acid. *BMJ* 1972; 1: 152-4.

New salicylates as maintenance treatment in ulcerative colitis

EDITOR,—I read with interest the paper by Järnerot (*Gut* 1994; 35: 1155-8) in which he reviewed the oral use of the new aminosalicylates in the maintenance treatment of ulcerative colitis. Firstly, I disagree with the author's suggestion that 5-ASA containing compounds should be relegated to solely maintenance treatment. We, and others, have clearly shown efficacy of 5-ASA preparations in mildly to moderately active ulcerative colitis.^{1,2} However, we agree it should not be used as sole treatment for severe disease activity. Secondly, the article attempts to provide a synopsis of available sulpha-free aminosalicylic acid preparations with a guideline for the preferred use of specific 5-ASA preparations. I question the author's statements regarding the comparison of Asacol *v* olsalazine and his conclusions on the risk of renal lesions associated with the use of pH dependent formulations of 5-ASA.

In his review, Järnerot presents the results from a study by Courtney *et al*,³ which compared the efficacy and tolerability of olsalazine and mesalazine in maintenance treatment of ulcerative colitis. Two separate letters to the editor of *Lancet* have criticised this study and suggested that 'there is good reason to suspect the difference found may be due to chance or some methodologic flaw'.⁴⁻⁵ Hopefully, well controlled studies in the future will directly tackle this issue.

With respect to renal safety, Järnerot's statements about potential risks of nephrotoxicity associated mainly with pH dependent 5-ASA preparations are at best speculative. The mechanism by which 5-ASA causes nephrotoxicity is still undefined and the mechanism, be it hypersensitivity or dose related toxicity, continues to be investigated. Consequently, the potential of 5-ASA to cause nephrotoxicity should be considered a class effect common to all formulations that release 5-ASA or are converted to 5-ASA, as is the case with olsalazine. This position is reflected in the labelling for all 'new aminosalicylates' available in the US, including Asacol, Dipentum, Pentasa, and Rowasa. In a poster presentation at the 10th Congress of Gastroenterology,⁶ we showed that sensitive markers of renal function (alanine aminopeptidase and *N*-acetyl- β -D-glucosaminidase) are increased in the absence of clinically significant renal dysfunction in a substantial

subgroup of patients maintained with mesalamine containing formulations (including sulphasalazine) and patients receiving placebo for six months. Further research should clarify whether these changes are: (a) drug effects of mesalamine, (b) clinically relevant, or (c) result from intrinsic renal processes in patients with ulcerative colitis. At present, published works support our recommendation that 5-ASA preparations be used for mildly to moderately active ulcerative colitis and for maintenance of remission. Furthermore, the 5-ASA preparation of choice should be the least expensive, best tolerated preparation with a reported safety profile. We suggest avoiding speculation of toxicity until claims can be substantiated with scientific evidence.

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- 1 Sninsky CA, Cort DH, Shannahan F, Powers FJ, Sessions JT, Pruitt RE, et al. Oral mesalamine (Asacol) for mildly to moderately active ulcerative colitis. *Ann Intern Med* 1991; 115: 350-5.
- 2 Sutherland LR, May GR, Shaffer EA. Sulfasalazine revisited: a meta-analysis of 5-aminosalicylic acid in the treatment of ulcerative colitis. *Ann Intern Med* 1993; 118: 540-9.
- 3 Courtney MG, Nunes DP, Bergin CF, O'Driscoll M, Trimble V, Keeling PWN, et al. Randomized comparison of olsalazine and mesalazine in prevention of relapses in ulcerative colitis. *Lancet* 1992; 339: 1279-81.
- 4 Gait JE, Simerl NA. Comparison of olsalazine and mesalazine in prevention of relapses in ulcerative colitis. *Lancet* 1992; 340: 486-7.
- 5 Record CO, MaCrae K. Mesalazine versus olsalazine for prophylaxis of ulcerative colitis. *Lancet* 1992; 340: 1468.
- 6 Sninsky C, Hanauer S, Powers B, Robinson M, Mayle J, Elson C, et al. Sensitive markers of renal dysfunction are elevated in chronic ulcerative colitis. 10th Congress of Gastroenterology, October 2-7, 1994. Los Angeles, CA: 1778.

Reply

EDITOR,—My leading article was on new salicylates as maintenance treatment in ulcerative colitis and thus I did not discuss the treatment of mildly to moderately active ulcerative colitis with 5-ASA based formulations. I am aware of the fact that they can be used for that condition. What I pointed out was that they are not as effective as corticosteroids. In my opinion it is important to treat active ulcerative colitis aggressively to reduce the risk of developing a state of chronic continuous or refractory disease.

With regard to the study by Courtney *et al* comparing olsalazine and Asacol, I also remarked that this study was only observer blind. Future studies are needed to discover if the results were caused by chance.

I refer to my reply to Drs Rhodes and Coles with regard to the question of nephrotoxicity.

GUNNAR JÄRNEROT

- 1 Courtney MG, Nunes DP, Bergin CF, O'Driscoll M, Trimble V, Keeling PWN, et al. Randomized comparison of olsalazine and mesalazine in prevention of relapses in ulcerative colitis. *Lancet* 1992; 332: 1279-81.

NOTES

Coloproctology

The annual scientific meeting of the Association of Coloproctology of Great Britain and Ireland will take place at University College Cork on 2-4 July 1995. Enquiries to Professor W O Kirwan, Department of Surgery, Cork University Hospital, Cork, Ireland. Tel: 010 353 21546400 ext 2385.

Liver disease

The XXth International Update on Liver Disease will be held at the Royal Free Hospital School of Medicine, London on 6 to 8 July 1995. Further information from: Professor Neil McIntyre, University Department of Medicine, Royal Free Hospital, Pond Street, London NW3 2QG. Tel: 0171 794 0500 ext 3969; fax: 0171 794 4688.

Liver studies

The 30th annual meeting of the European Association for the Study of the Liver will be held in Copenhagen, Denmark on 21-23 August 1995. Further information from: Local secretary, Helmer Ring-Larsen, Rigshospitalet, DK-2100 Copenhagen, Denmark. Tel: 45 3545 2451; fax: 45 3545 2913.

Digestive endoscopy

The European Postgraduate Gastro-Surgical School is organising a course on digestive endoscopy in Amsterdam, the Netherlands on 7/8 September 1995. Further information from: Helma Stockmann, Managing Director European Postgraduate Gastro-Surgical School, Room G4-109.3, Academic Medical Center, Meibergdreef 9, 1105 AZ Amsterdam, the Netherlands. Tel: 31 20 5663926; fax: 31 20 6914858.

Pancreatic Society Travelling Fellowship

The Pancreatic Society awards a fellowship annually to allow a young researcher to travel to obtain experience and visit centres of excellence abroad. The award is made on the basis of applicants' *curricula vitae* and proposed itinerary, and applications are requested in the autumn of each year. An award of £3000 will be made in November 1995, for travel during 1996. Potential applicants should contact the Secretary: Mr C D Johnson, University Surgical Unit, F Level, Centre Block, Southampton General Hospital, Tremona Road, Southampton, SO16 6YD. Tel: 0703 706146; fax: 0703 794020.

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ETHICS Ethical aspects will be considered in the assessment of papers (see the Medical Research Council's publications on the ethics of human experimentation, and the World Medical Association's code of ethics, known as the Declaration of Helsinki (see *BMJ* 1964; ii: 177)).

SI UNITS All measurements except blood pressure are expressed in SI units. In tables and illustrations values

are given in SI units. For general guidance on the International System of Units and some useful conversion factors, see *The SI for Health Professions* (WHO, 1977). **NB: Such conversion is the responsibility of the author.**

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