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Conference report

Salazopyrin EN in rheumatoid arthritis

A meeting on the effects of Salazopyrin EN in rheumatoid arthritis was held at St Thomas's Hospital on 11 December 1986.

Dr I Bjarnason (Northwick Park Hospital) presented evidence to suggest that non-steroidal anti-inflammatory drugs (NSAIDs) increase intestinal permeability through a mechanism of reduced mucosal prostaglandin production. Salazopyrin (SASP) was found to reduce drastically the NSAID induced small intestinal inflammation, whereas other second line drugs did not. The beneficial effect of SASP on the joints themselves thus appeared to be independent of the intestinal action of the drug. This suggested that previous speculation about the importance of the intestine in the aetiology of rheumatoid arthritis (RA) was incorrect.

Dr J R Hoult (King's College, London) discussed the pharmacological actions of SASP. He pointed out that there were many unanswered questions concerning diseases in which SASP was used, which hampered analysis of the mode of action. In particular, the unknown aetiology of ulcerative colitis and RA, the lack of simple models of the diseases, and the fact that SASP was a unique drug whose target cell(s) or molecule(s) were unknown and which had two potential active moieties—sulphapyridine and *S*-aminosalicylic acid. He described work suggesting direct effects on human leucocytes, which suggests that SASP is not merely an 'aspirin-like' drug.

Professor B Amor (France) presented the results of his recently published work using SASP as an adjunctive treatment with NSAIDs in patients with axial ankylosing spondylitis.[1] In this six month, double blind, placebo controlled study there was a significant trend in favour of the active drug, the effect becoming apparent after three months. Discussion drew attention to the fact that when SASP was effective in RA it often happened early, after four to six weeks of therapy. As Professor Amor had only performed assessments at one and three months he could not say whether the effect of SASP had begun nearer one or three months. When asked whether this trial suggested a use for SASP in patients refractory to NSAIDs and physiotherapy he emphasised that he had not selected for such patients and could not, therefore, make any judgment. Nevertheless, the trial certainly encouraged further study of SASP in axial arthritis, and toxicity was minimal.

Dr B McConkey (Birmingham) gave a comprehensive review of the history of SASP in RA from Svartz' original work in 1948.[2] He showed that long term analysis of gold and SASP showed very comparable drop out rates for termination of treatment. When analysed from the two angles of lack of effect and toxicity, clear differences were observed. Terminations due to toxicity were more likely with gold and D-penicillamine. With termination due to lack of efficacy, however, the situation was reversed, with gold showing a clear advantage over the other two drugs, which were otherwise comparable. Although SASP seemed to be less effective overall than other second line agents such as gold or penicillamine, when remissions were obtained they were good. Dr McConkey made the depressing observation that overall there was only a 1:5 chance of a given second line agent being continued effectively for five years, with a 1:4 chance of an adverse effect over the same period.

Dr H Capell (Glasgow) described her two year radiological follow up of patients responding to SASP. She emphasised the difficulty of providing adequate controls for such assessments, particularly as it was now almost impossible to treat patients with placebo for two years. Comparison of her SASP responders with retrospective controls (patients who had consistently refused second line agents for two years) showed a trend in favour of SASP for the slowing of erosive progression.

Dr H Englert (London) briefly presented a small study of five patients with rheumatoid nodules who were part of a larger SASP study. While receiving SASP four of the five showed regression of nodules suggesting a possible disease modifying effect for SASP.

Dr R Amos (Sheffield) reviewed the data on the long term toxicity of SASP in 774 patients, which he analysed with workers from Glasgow and Birmingham.[3] The overall impression was the relative safety of SASP compared with other second line drugs—such toxicity as did occur was rarely danger-

ous even if it did require cessation of therapy. Toxicity also mostly occurred within three months of starting the drug. There were differences between centres in the incidence of leucopenia, but it was possible that such differences were unrelated to the drug therapy. Even so, it was rarely severe, with only one of 32 patients having to stop SASP permanently. These differences between centres had resulted in different recommendations for monitoring. The value of SASP densensitisation in allowing reintroduction of the drug after adverse cutaneous reactions was also mentioned.

Dr Amos outlined a case of resistant inflammatory Achilles tendinitis in which SASP had been given with subsequent improvement. A further four out of five such patients with symptoms for more than six months also improved after SASP.

Rheumatology Unit,
St Thomas's Hospital,
London

RONALD A ASHERSON
MARTIN RIDLEY

References

1 Dougados M, Boumier P, Amor B. Sulphasalazine in ankylosing spondylitis: a double blind controlled study in 60 patients. *Br Med J* 1986; **293:** 911–4.
2 Svartz N. The treatment of rheumatic polyarthritis with acid azo compounds. *Rheumatism* 1948; **4:** 180–5.
3 Amos R S, Pullar T, Bax D F, Situnayake D, Capell H A, McConkey B. Sulphasalazine for rheumatoid arthritis: toxicity in 774 patients monitored for one to 11 years. *Br Med J* 1986; **293:** 420–3.