SULPHASALAZINE IN RHEUMATOID ARTHRITIS

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SYPNOSIS

30 patients with rheumatoid arthritis were treated with sulphasalazine. Evualation after 12 weeks treatment showed reduction of inflammatory activity in 18 patients. The adverse effects of the drug were mild, the commonest being gastrointestinal. The results suggest that sulphasalazine is a potentially effective and safe second-line drug in the treatment of rheumatoid arthritis.

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INTRODUCTION

Sulphasalazine has been successfully and widely used for treating inflammatory bowel diseases. Recent studies have suggested that sulphasalazine could be used as a second-line anti-rheumatic drug in the treatment of rheumatoid arthritis(1). The purpose of our study was to investigate the effects of the drug and to examine the acetylator phenotype of our patients.

MATERIALS AND METHODS

30 patients fulfilling the American Rheumatism Association(2) criteria for definite or classical rheumatoid arthritis were studied. There were 25 female and 5 male patients with a duration of illness ranging from 1 to 17 years - Table 1A.

9 patients stopped sulphasalazine within a month of commencement of therapy. The remainder 21 patients continued with the drug for between 3 to 12 months. The patients had a mean age of 45 years (range 23-75) and a mean duration of disease of 6.1 years (range 1-17 years). 21 (70%) patients were sero-positive with latex agglutination titers of 1:132 or greater. 12 patients had previous use of oral corticosteroids and 5 (16%) had previously been treated with other disease-modifying agents - Table 1B.

Enteric-coated sulphasalazine was started at an initial dose of 0.5g daily, increasing by 0.5g increments at weekly intervals to a maximum of 2-3g per day (that is, the highest tolerated dose). The dosage was not allowed to fall below 1.5g per day. A patient was deemed to have inadequate clinical response when there is no clinical improvement after receiving 3 months of the drug.

Subjective clinical state, duration of morning stiffness, number of joints involved and the erythrocyte sedimentation rate were recorded at each visit. Full blood counts, urinalysis, liver function tests were performed regularly at monthly intervals. The acetylator phenotype was assayed in 15 patients. 11 were fast acetylators.

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RESULTS

18 patients showed good response to the drug. The mean ESR fell at 6 weeks of therapy and plateau below 40mm in the first hour at 6 months. The duration of morning stiffness dramatically decreased to below 10 mins at 6 months - Figs 1 and 2. The main reasons for termination of therapy were adverse effects (5 patients) and failure to respond (3 patients). The commonest side-effects were nausea, rash and giddiness - Table 3. One patient with severe nausea had toxic levels of sulphapyridine 166.9 ug/ml (normal 10-40 ug/ml). She was a slow acetylator and was prescribed sulphasalazine 3g per day. The dosage was promptly reduced to 1g per day and the symptoms resolved. No patient developed serious side-effect of neutropenia.

DISCUSSION

The results showed clinical improvement in 18 patients who had more than 12 weeks treatment of sulphasalazine. This improvement was sustained in 10 patients. However, the small number of patients in this study preclude any definitive conclusions regarding long term benefit of the drug.

The mode of action of sulphasalazine in rheumatoid arthritis is not exactly known. Sulphasalazine and 5-aminosalicylic acid (5- ASA) are respectively weak and very weak inhibitors of both cyclo-oxygenase and lipoxygenase pathways(3). 5-ASA is poorly absorbed from the gut lumen and this mechanism of inhibition of prostaglandin synthesis in the bowel wall is unlikely. Local action of an antimicrobial nature on the digestive tract has been suggested but not confirmed(4).

It appears that the acetylator phenotype does not affect the efficacy of sulphasalazine in rheumatoid arthritis. However one would expect that slow acetylators would have higher gastro- intestinal symptoms and therefore are more likely to stop therapy. The routine assessment of acetylator phenotype before commencement of sulphasalazine does not appear to have much practical value(5).

As with other second-line anti-rheumatic drugs, toxicity is a limiting factor in the use of sulphasalazine. Most of the toxic events were gastrointestinal and trivial. Worrying side-effects of leucopenia and megaloblastic anaemia have been reported(6). Regular blood counts are therefore recommended.

This study shows that sulphasalazine does benefit some patients with rheumatoid arthritis. The addition of this drug to the limited armamentarium of second-line anti-rheumatic drugs is noteworthy in view of its safety profile. Whether sulphasalazine compares well with gold salts or penicillamine remains to be determined.

TABLE 1A
PATIENT CHARACTERISTICS

No. of patients	30
Sex ratio (Female:Male)	25:5
Mean age	45 years (range 23–75years)
Mean duration of illness	6.1years (range 1–17years)

TABLE 1B
PATIENT CHARACTERISTICS

Rheumatoid factor +ve	19 (79%)
Functinal class (1:11:111)	24:3:3
Previous use of oral steriods	12 (40%)
Previous use of disease–modifying drugs	5 (16%)

FIG. 1 — CHANGE IN ESR FOLLOWING THERAPY

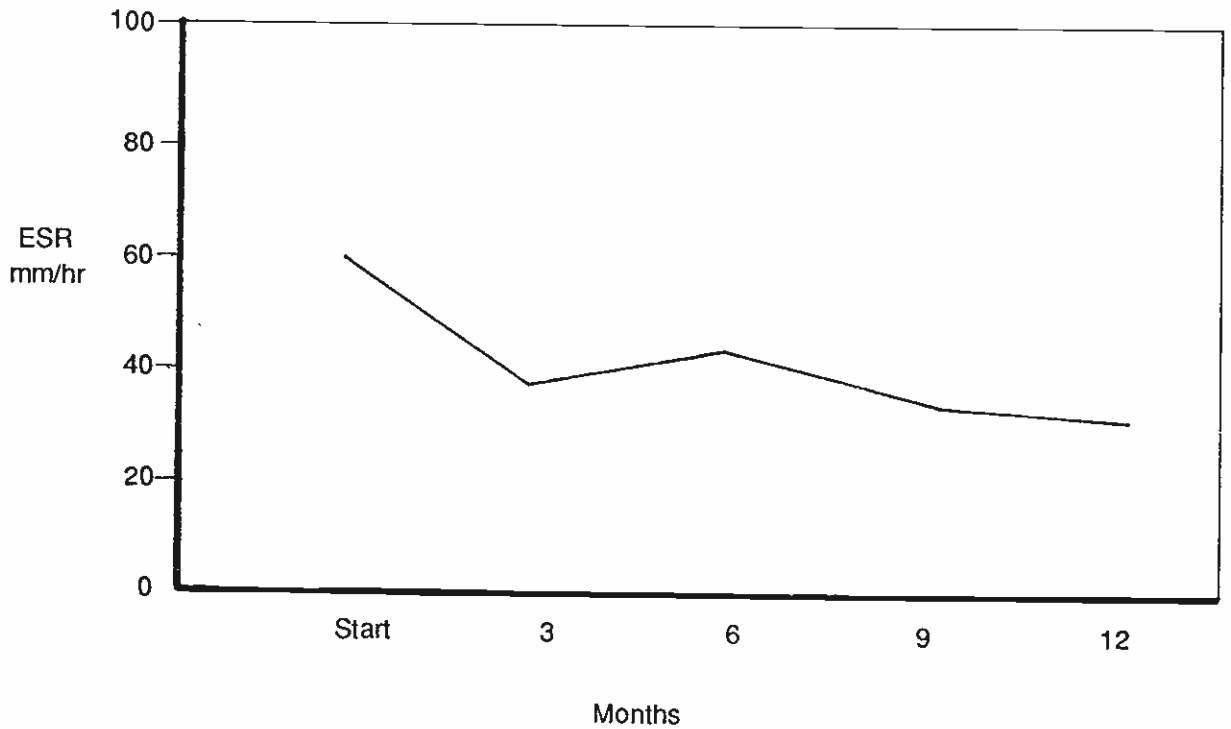
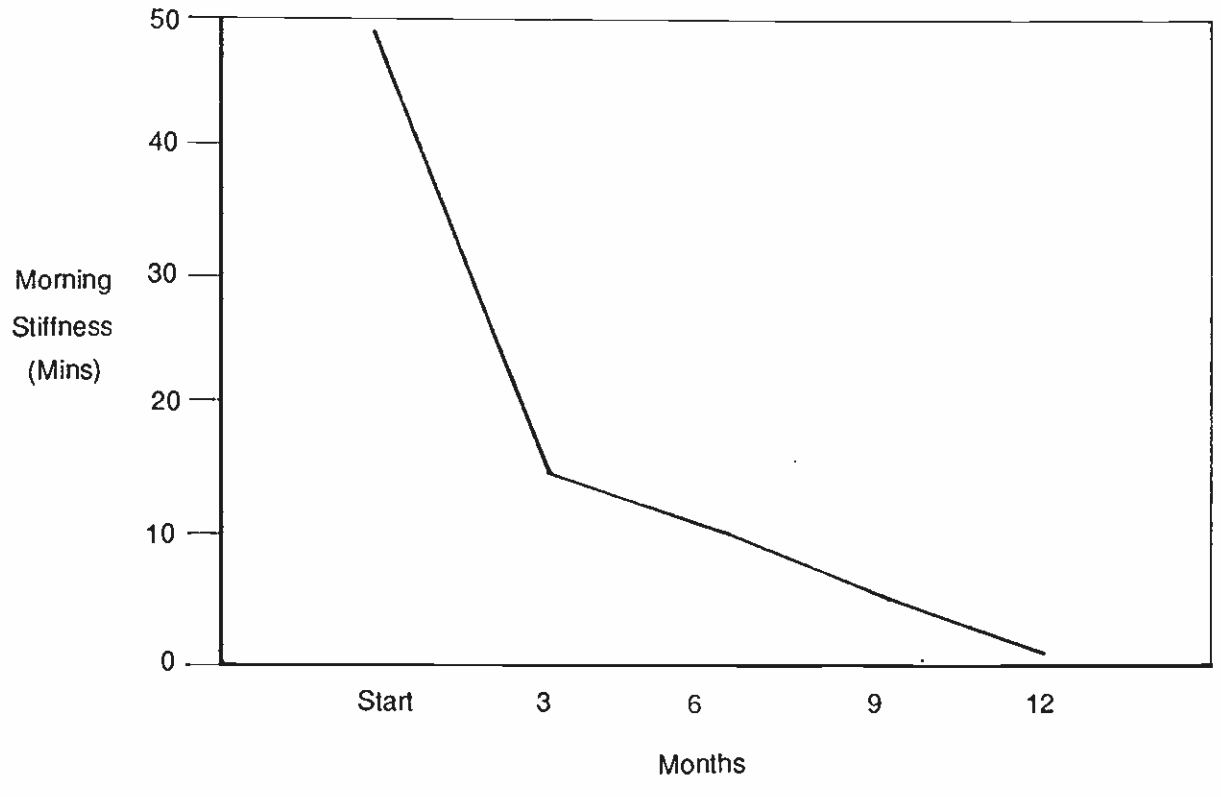


TABLE 2
RESULT OF STUDY

Responders	18
Non-responders	3
Defaulters	2
Non-compliance	2
Side-effects :	5
Nausea	3
Rash	1
Giddiness	1

FIG 2 — CHANGE IN MORNING STIFFNESS FOLLOWING THERAPY



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BOOK REVIEW

ANATOMY — REGIONAL, FUNCTIONAL AND CLINICAL

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This is a book on gross anatomy which includes brief accounts of histology, embryology and neuroanatomy. It is intended for both the undergraduate student and the postgraduate candidate preparing for the Primary FRCS examination. It consists of about 600 pages of text and 287 Figures, of which 32 are radiographs of both normal adult and child and fractures. Though not exhaustive, which is not the intention of the authors, these radiographs serve to introduce the students to radiographic anatomy and show them the differences between the child and the adult, and between the normal and the pathological.

The style of writing is simple, flowing and concise with appropriate headings which make referencing easy. More important, the student is not overburdened with unnecessary details which are eminently provided for in the larger textbooks. The "Objectives" at the end of each Chapter gives the student a sense of direction in his study. But there is a glaring absence of such "objectives" in "Head and Neck II". The omission appears to be intentional although the reason is not clear. There are many important topics in this Section which would warrant the inclusion of the "Objectives".

Perhaps the student should also be made aware of the new trends in the teaching and learning of anatomy. In this respect, certain areas of anatomy need no longer be emphasized. For example, in many institutions in Europe and U.S.A., questions have been raised regarding the usefulness of burdening the student with details of muscle attachments and classification of the layers of muscles in the sole of the foot and the postvertebral muscles.

However, as the price is affordable, the size of the book reasonable, the contents factually accurate and many other useful features which are invaluable aids to the student in their learning of anatomy, the book would find favour.

Dr Tan Choon Kim