# Four New Anti-Inflammatory Drugs

# Responses and Variations

*by* *E. C. Huskisson,*
**MD, MRCP**
Senior Lecturer

*D. L. Woolf,*
**MRCS, LRCP, D.Phys. Med**
Consultant Rheumatologist
Department of Rheumatology, Wanstead Hospital

*and* *H. W. Balme*
**SRN, SCM**
Measurement Technician

*Jane Scott*
**MCSP**
Measurement Technician

*Sue Franklyn*
**MD, FRCP**
Consultant Physician
Department of Rheumatology,
St Bartholomew's Hospital

**Summary**

90 PATIENTS with rheumatoid arthritis completed a double-blind crossover trial comparing fenoprofen, ibuprofen, ketoprofen and naproxen. Fenoprofen and naproxen were slightly more effective than the other two drugs but there were striking individual variations in response. It was possible to identify groups of patients who preferred each one of the four drugs.

The commonest side effects were those related to the upper gastro-intestinal tract. Such side effects also showed individual variation and seldom occurred with more than one or two of the drugs. Side effects were least common in patients receiving ibuprofen and naproxen.

Since naproxen combined greater effectiveness and a lower incidence of side effects, it must be regarded as the first choice of drugs in this group. The individual variation suggests that it may be necessary to try several before finding the right drug for a particular patient.

If aspirin is no longer the first line treatment of rheumatoid arthritis (Huskisson, 1974; Huskisson et al, 1974; Lee et al, 1974) its place must surely have been taken by one of the propionic acid derivatives. But by which one? The four currently available compounds claim analgesic potency comparable to that of aspirin but with a very much lower incidence of side effects. In this study their effectiveness and tolerability have been compared.

## Methods

105 out-patients with definite or classical rheumatoid arthritis by the ARA criteria were admitted to the study. They were treated for two weeks with each of four drugs, fenoprofen 2.4 G daily, ibuprofen, 1.2 G daily, ketoprofen 150 mg daily and naproxen 500 mg daily. The order of treatment was randomised and balanced in a latin square design. Patients who dropped out of the study for reasons unrelated to the treatment were replaced to ensure that at least three complete balanced blocks of 24 patients were achieved. The doses used were those recommended by the manufacturers at the time of the study. To avoid recognition of tablets which patients might already have received, each treatment was supplied by its manufacturer in a formulation different from the marketed form – fenoprofen was supplied in 300 mg white capsules, ibuprofen in 300 mg white tablets, ketoprofen in 25 mg white capsules and naproxen in 125 mg yellow capsules. Data confirming their bioavailability was available in all cases. Simple analgesics were allowed during the study and in 10 patients who were taking small doses of corticosteroids, these were continued. No other anti-rheumatic therapy was allowed during the study.

At the end of each fortnight, measurements were made of pain using a visual analogue scale, the duration of morning stiffness and proximal interphalangeal joint circumference. A preference was sought for each pair of treatments and after the third and fourth treatment periods, a rank order of preference was noted. The patients were asked a standard question at the end of each treatment period: "Has the treatment upset you in any way?" Any side effects elicited were recorded as either slight, moderate or severe. Returned tablets were counted. Measurement of a particular patient was

**Table 1 Means of measurements made after 2 weeks treatment with each drug**

| | Pain | Duration of morning stiffness (mins) | Joint size (mm) | Number of first choices * | Preference (sum of ranks) |
|---|---|---|---|---|---|
| Fenoprofen | 10.6 | 63.0 | 568.0 | 29 | 210.5 |
| Ibuprofen | 11.6 | 98.2 | 568.5 | 13 | 245.0 |
| Ketoprofen | 11.4 | 89.0 | 569.2 | 12 | 241.0 |
| Naproxen | 10.3 | 70.3 | 568.3 | 34 | 203.5 |

| | Total side effect score | Gastric side effect score | Returned tablets (number of days supply) |
|---|---|---|---|
| Fenoprofen | 171 | 119 | 1.6 |
| Ibuprofen | 67 | 36 | 1.1 |
| Ketoprofen | 114 | 87 | 1.8 |
| Naproxen | 62 | 43 | 0.4 |

* Two additional patients divided their first choice between two drugs.


## Acknowledgements

The authors are indebted for assistance with this project to Mrs R Cromack, Miss M Leighton, Miss E Thornton, other members of the staff of the Departments of Rheumatology at Wanstead and St Bartholomew's Hospitals, and the pharmaceutical companies who supplied their particular products.


## References


Beck, EF and Hayes-Allen, MC (1974) British Medical Journal 1,572.

Hart, FD and Matts, SGF (1974) British Medical Journal 2,51.

Huskisson, EC (1974) Reports on rheumatic diseases No 54. Arthritis and Rheumatism Council.

Huskisson, EC, Wojtulewski, JA, Berry, H, Scott, J, Hart, FD and Balme, HW (1974) British Medical Journal, 1,176.

Lee, P, Ahola, SJ, Grennan, D, Brooks, P and Buchanan WW (1974) British Medical Journal, 1,424.

Reynolds, PMG and Whorwell, PJ (1974) Current Medical Research and Opinion, 2, 461.