Br. J. clin. Pharmac. (1985), **20**, 511–513

Double-blind trial of flurbiprofen and phenylbutazone in acute gouty arthritis

R. C. BUTLER, D. H. GODDARD, C. S. HIGGENS, P. HOLLINGWORTH, C. T. PEASE, M. A. STODELL & J. T. SCOTT

Departments of Rheumatology, Charing Cross Hospital, Westminster Hospital, St Stephen's Hospital and Queen Mary's Hospital, London

Flurbiprofen has been compared with phenylbutazone in a double-blind study involving 33 patients with acute gout. Patients received either flurbiprofen 400 mg daily for 48 h followed by 200 mg daily, or phenylbutazone 800 mg daily for 48 h followed by 400 mg daily. The drugs were of comparable efficacy, while side-effects were uncommon and relatively mild. Flurbiprofen appears to be a satisfactory alternative to phenylbutazone in the management of acute gouty arthritis.

Keywords gout flurbiprofen phenylbutazone

Introduction

Three drugs have been widely used in the treatment of acute gout. Colchicine has been used for centuries but requires frequent administration and gastrointestinal side-effects often terminate treatment before resolution of the attack. Phenylbutazone is as effective as colchicine in the treatment of gout (Gutman, 1965), but is no longer licensed for this indication in the U.K. Indomethacin is as effective as phenylbutazone (Smyth & Percy, 1973), but unpleasant side-effects are not uncommon when it is used in the treatment of gout (Boardman & Hart, 1965). Other non-steroidal anti-inflammatory drugs have been used to treat acute gout, but few have been formally evaluated. Flurbiprofen is a potent inhibitor of prostaglandin synthetase with anti-inflammatory and analgesic properties (Adams & Buckler, 1979). It has been suggested that this agent may be of value in the management of acute gout (Camus *et al.*, 1983); the present study compares its efficacy with that of phenylbutazone.

Methods

This was a multi-centre double-blind parallel group study. Most patients selected for the study presented with acute gout; a few with recurrent acute attacks were given a supply of study medication with instructions to start treatment at the onset of an acute attack. The following exclusions were applied: a history of severe dyspepsia, gastrointestinal bleeding, concomitant administration of other non-steroidal anti-inflammatory drugs or of anti-coagulants.

Patients were randomly allocated to either flurbiprofen 400 mg daily for the first two days then 200 mg daily or phenylbutazone 800 mg daily for the first 2 days then 400 mg daily, in four equal divided doses for 10 days. The study drugs were supplied in identical unmarked capsules.

The diagnosis of acute gout was made on clinical grounds supported in 15 cases by the demonstration of urate crystals within synovial fluid from the affected joint. Forty patients were enrolled in the study but seven were subsequently withdrawn: two given phenylbutazone and five

Correspondence: Dr J. T. Scott, The Mathilda and Terence Kennedy Institute of Rheumatology, 6 Bute Gardens, London W6 7DW

given flurbiprofen. The reasons for withdrawal were: incorrect diagnosis 2 (pseudogout 1, cellulitis 1); request to be withdrawn from study because of continuing symptoms after 3 days on flurbiprofen 1; resolution of attack without treatment 1; prolonged interval (24 days) between onset of attack and initiation of treatment 1; and in two patients with recurrent gout who were given study medication but no subsequent acute gouty episode occurred.

Each patient was asked to judge the severity of pain in the affected joint on a five-point scale and 10 days after the commencement of study medication the patient was asked to assess the length of time between between the onset of treatment and resolution of symptoms to the extent that normal activities could be resumed. The patient was also asked whether any other analgesic medication had been taken during the study, and whether the study medication had had any adverse effects.

Results were analysed for statistical significance by the Wilcoxon rank sum tests.

Results

The two groups were of comparable age: mean 52.8 years (range 24–89) for phenylbutazone and 56.2 years (range 30–83) for flurbiprofen and had similar intervals between the onset of the attack and beginning of treatment (Table 1). The two groups were also similar in terms of mean time since first attack of gout, median number of previous gouty attacks, and mean serum urate. The subjective severity of pain at the onset of treatment as judged on a five-point scale was 4.2 for phenylbutazone and 3.9 for flurbiprofen.

There was no significant difference between the two groups in terms of duration of the attack after starting treatment: mean 4.3 days for phenylbutazone *vs* 5.2 days for flurbiprofen ($P > 0.10$ by Wilcoxon rank sum test; Table 2). An attack persisting for 8 days or more might be considered a treatment failure; two patients given phenylbutazone fell into this category as did four given flurbiprofen. These six patients all judged the severity of their symptoms on entry to the trial to be 'very severe'. One patient given phenylbutazone and three given flurbiprofen took additional medication during the study: either paracetamol or paracetamol/dextropropoxyphene.

Five patients given phenylbutazone and three given flurbiprofen experienced side-effects. These were rash, dyspepsia, constipation (two), sleepiness and irritability for phenylbutazone; and dry skin, diarrhoea and dyspepsia, and 'shaking of hand' for flurbiprofen.

Discussion

Few comparative studies of non-steroidal anti-inflammatory drugs have been undertaken in acute gout, but indomethacin (Smyth & Percy, 1973), naproxen (Sturge *et al.*, 1977) and feprazone (Reardon *et al.*, 1980) appear to be of similar efficacy to phenylbutazone, with a mean interval of approximately 4 days between the onset of treatment and resolution of the attack: an interval similar to that seen in the present study. Fenoprofen (Weiner *et al.*, 1979) and ketoprofen (Siegmeth & Placheta, 1976) were also considered to be of similar efficacy to phenylbutazone, but the data did not include the duration of attack following initiation treatment.

We accept that our failure to demonstrate a statistically significant difference in efficacy

Table 1 Time in days from onset of attack to beginning of treatment

	1 or less	*2*	*3*	*4*	*5*	*6*	*7 or more*
Phenylbutazone	10	3	0	0	0	1	2
Flurbiprofen	8	3	0	2	3	0	1

Table 2 Time in days from beginning of treatment to end of attack

	1 or less	*2*	*3*	*4*	*5*	*6*	*7*	*8 or more*
Phenylbutazone	0	4	6	2	0	0	2	2
Flurbiprofen	2	5	1	3	1	1	0	4

between the two drugs does not necessarily mean that they are of equal efficacy. Approximately 60 patients would be required in each group to detect a difference of two days in the mean intervals between onset of treatment and resolution of the attack at the 5% significance level with 90% power (Lachin, 1981), but it would be difficult to recruit such numbers within a reasonable period of time. Descriptions of acute gout before the advent of non-steroidal anti-inflammatory drugs (Bywaters, 1962) would suggest that it should be relatively easy to demonstrate the superiority of either phenylbutazone or flurbiprofen over placebo, but few informed patients would now agree to participate in such a study.

References

Adams, S. S. & Buckler, J. W. (1979). Ibuprofen and flurbiprofen. *Clinics in Rheumatic Diseases,* **5**, 359–379.

Boardman, P. L. & Hart, F. D. (1965). Indomethacin in the treatment of acute gout. *Practitioner,* **194**, 560–565.

Bywaters, E. G. L. (1962). Gout in the times and person of George IV: a case history. *Annals of the Rheumatic Diseases,* **21**, 325–338.

Camus, J-P., Prier, A., Mezler, C. & Koeger, A-C. (1983). Traitement de la goutte. *Revue du Practitien,* **33**, 2281–2294.

Gutman, A. B. (1965). The treatment of primary gout: the present status. *Arthritis and Rheumatism,* **8**, 911–920.

Lachin, J. M. (1981). Introduction to sample size determination and power analysis for clinical trials. *Controlled Clinical Trials,* **2**, 92–113.

Reardon, J. A., Stockman, A., Darlington, L. G. & Scott, J. T. (1980). Double-blind trial of feprazone and phenylbutazone in acute gout. *Curr. med. Res. Opin.,* **6**, 445–448.

Siegmeth, V. W. & Placheta, P. (1976). Doppelblindstudie: ketoprofen gegen Phenylbutazon bei akuter Gichtarthritis. *Wiener klin. Wochenschr.,* **88**, 535–537.

Smyth, C. J. & Percy, J. S. (1973). Comparison of indomethacin and phenylbutazone in acute gout. *Annals of the Rheumatic Diseases,* **32**, 351–353.

Sturge, R. A., Scott, J. T. & Hamilton, E. B. D. (1977). Multicentre trial of naproxen and phenylbutazone in acute gout. *Annals of the Rheumatic Diseases,* **36**, 80–82.

Weiner, G. I., White, S. R., Weitzner, R. I. & Rubinstein, H. M. (1979). Double-blind study of fenoprofen versus phenylbutazone in acute gouty arthritis. *Arthritis and Rheumatism,* **22**, 425–426.

(Received 7 May 1985, accepted 31 July 1985)