Diclofenac and Ibuprofen in Rheumatoid Arthritis and Osteoarthritis

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Forty patients with arthritis (26 rheumatoid and 14 osteoarthrosis) entered a five-week double-blind crossover trial of diclofenac and ibuprofen. Four patients failed to complete the 10-week trial. There was no statistically significant difference in parameters of disease activity for the rheumatoid arthritis patients, but patients with osteoarthrosis fared significantly better on diclofenac. There was a low incidence of side effects on both regimens.

Diclofenac Sodium (Voltaren) is a non-steroidal non-pyrazole compound with anti-inflammatory, antipyretic and analgesic activity in laboratory animals.[1] It has been shown to be well tolerated and effective in short-term therapy of degenerative joint disease[2] and rheumatoid arthritis. To assess the place of diclofenac in clinical practice, we studied the effectiveness of this drug against ibuprofen in patients with rheumatoid arthritis and osteoarthrosis.

METHODS

A five-week double-blind crossover design was used, each patient receiving either Voltaren plus ibuprofen placebo or Voltaren placebo plus Ibuprofen, with treatments commencing in a random fashion. Diclofenac was presented as 25-mg enteric-coated tablets and ibuprofen was presented as 400-mg film-coated tablets. Treatment was commenced on a dose of 75 mg of diclofenac (one three times a day) or 1200 mg of ibuprofen : (one three times a day) and the dose was adjusted upwards if necessary at the end of weeks one and two. Patients then continued their dose for the three-week test period before changing over to the other medication.

The majority of patients in each group took 100 mg of diclofenac and 1600 mg of ibuprofen for the three-week test period. Patients with significant renal or liver impairment were excluded from the study, but patients on stable doses of prednisolone, gold and D-penicillamine were included. There were four patients on maintenance gold therapy, two patients on D-penicillamine therapy and one patient on prednisolone (10 mg a day). The following assessments were carried out on the patients with rheumatoid arthritis: grip strength according to the method of Lee *et alii*;[3] circumference of the proximal interphalangeal joint;[4] articular index;[5] and the duration of morning stiffness. An analogue pain score was taken on a 10-cm line at the time of final assessment and, for the last three weeks of each treatment period, patients were asked to fill in a daily pain score according to the method of Lee *et alii*.[6] A visual analogue pain score was also carried out in the patients with osteoarthrosis who were also asked to assess the effect of the treatment on pain in their most affected joint (this remained the same throughout the trial) on a five point scale. A daily pain score was also performed for the final three weeks of each treatment period in the osteoarthritic patients. Side effects were assessed at the end of each treatment period by asking the patients to comment as to whether they had noticed anything abnormal during the test period.

RESULTS

Rheumatoid Arthritis

Twenty-six patients entered the trial. Two dropped out: one because of failure to control symptoms of pain (on ibuprofen); and one because of indigestion (diclofenac). There were 10 males and 16 females with a mean age of 52 years and a mean duration of disease activity of nine years. The results of the clinical measurements in the rheumatoid arthritic patients are shown in Table 1.

Table 1 : Results of Clinical Assessments

Tests	Results*		
	Diclofenac	Significance	Ibuprofen
Patients with rheumatoid arthritis (n=24)			
Grip strength (kPa)†			
Right hand ..	14.9 ±7.0 (112 ±53)	NS	13.8 ±6.0 (104 ±45)
Left hand	13.0 ±6.5 (98 ±49)		14.5 ±5.9 (109 ±44)
Ring size (mm)			
Right hand ..	296 ±30	NS	294 ±29
Left hand	292 ±29		292 ±28
Pain score (analogue)	4.7 ±3.5	NS	4.9 ±3.7
Articular index ..	11 ±8	NS	10 ±8
Duration of morning stiffness (hours) ..	1.7 ±2.5	NS	2.4 ±3.3
Daily pain score ..	2.5 ±0.8	NS	2.6 ±0.7
Patients with osteoarthritis (n=12)			
Patient assessment ..	3.4 ±0.8	P 0.05	2.9 ±1
Analogue pain score ..	4.2 ±3	P 0.025	7.6 ±2
Daily pain score ..	2.4 ±7	P 0.05	2.8 ±2

▪ Mean values ± standard deviation.
† mmHg in parentheses.
NS-not significant.

Osteoarthrosis

Fourteen patients with osteoarthrosis entered the study. Two dropped out: a 64-year-old man with a previous history of myocardial infarction died suddenly after an episode of central chest pain two weeks after commencing treatment; and one patient dropped out because the test medication (ibuprofen) caused an itchy skin rash. The results of the clinical assessments in the osteoarthritic patients are shown in Table 1.

At the end of the trial, patients were asked for a global assessment of the two treatment periods. Both the rheumatoid arthritic patients and osteoarthritic patients strongly favoured diclofenac over ibuprofen. In the rheumatoid group, 12 of 24 patients favoured diclofenac and eight found the drugs of equal efficacy. Of the osteoarthritic group, eight of 12 patients favoured diclofenac and four patients rated the treatments equally.

From Table 1, it can be seen that for patients with rheumatoid arthritis there is no significant difference in the clinical parameters measured, though the analogue daily pain score during the three-week test period and the duration of morning stiffness are less during the diclofenac period. In those patients with osteoarthrosis there is a significant difference in the clinical parameters measured in favour of diclofenac.

Side effects occurred in 13 of the 40 patients entering the trial, but required a cessation of treatment in only two patients (one on diclofenac and one on ibuprofen).

CONCLUSION

In this double-blind crossover trial, diclofenac was shown to be equally efficacious to ibuprofen for patients with rheumatoid arthritis. In those patients with osteoarthrosis diclofenac was shown to be significantly better than ibuprofen in all clinical parameters measured. Seven patients on diclofenac and eight patients on ibuprofen developed side effects during the trial, though in all but two cases, patients were able to continue the trial with disappearance of the side effect. Diclofenac, with its small tablet size, tolerability and efficacy will certainly be a useful additive to the non-steroidal anti-inflammatory drug range for the treatment of osteoarthrosis and rheumatoid arthritis. Further trials against the new propionic acid derivatives are awaited to assess its proper place in the antirheumatic armamentarium.

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