
IBUPROFEN IN THE TREATMENT OF RHEUMATOID ARTHRITIS AND OSTEO-ARTHRITIS

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Ibufenac (4-isobutylphenylacetic acid) was reported by Chalmers (1963) to be an effective anti-rheumatic agent, 1-8 g. daily being comparable with aspirin 3-6 g. daily in rheumatoid arthritis. Side-effects on Ibufenac were fewer, and gastro-intestinal haemorrhage measured by 51Cr was insignificant in the majority of patients (Tudhope, 1964). The possibility that Ibufenac might be responsible for hepatic damage was raised by the occurrence of jaundice in 1 per cent. of the first 500 patients treated (Morton, 1964), and raised serum transaminase levels were reported in 20 to 30 per cent. of cases treated for 6 weeks or more (Hart and Boardman, 1965). Because of this, related compounds have been studied which possess comparable anti-inflammatory properties in standard pharmacological animal experiments. This report presents the results of trials of one analogue, Ibuprofen (2, 4'-isobutylphenylpropionic acid), in rheumatoid arthritis and osteo-arthritis.

The aim of this study was to compare Ibuprofen 0-9 g. daily with placebo in rheumatoid arthritis, and to compare 0-6 g. daily with placebo in osteo-arthritis.

Material and Methods

In the twenty patients with rheumatoid arthritis, Ibuprofen 0-9 g. daily was compared on a double-blind cross-over basis with placebo, each preparation being given in random order for 7 days. All had classical or definite rheumatoid arthritis (American Rheumatism Association, 1959). Their mean age was 56 years; twelve were female and eight male. The Waaler-Rose titre was positive in sixteen patients. They were assessed by serial weekly recordings of grip strength, size of the proximal interphalangeal joints of the hands, and individual preference.

All nineteen patients with osteo-arthritis had the characteristic radiological changes in association with pain. Their mean age was 57-7 years; fourteen were female and five male. Ibuprofen 0-6 g. daily was compared on a double-blind basis with placebo, each being given for 14 days. Assessment was based on the symptomatic response, recorded in three grades as improved, no change, or worse. Preference was recorded at the end of the trial.

Side-effects were recorded. All other therapy remained constant during a baseline period of 14 days and throughout both trials.

Results

In the twenty patients with rheumatoid arthritis, there was no statistically significant difference in grip strength, joint size, or preference on Ibuprofen compared with placebo.

In the nineteen patients with osteo-arthritis there was slight but not significant preference for Ibuprofen. There was no significant difference in the number improving, remaining unchanged, or deteriorating on the two preparations.

Side-Effects.—Dyspepsia was noted by two patients on Ibuprofen, and three on placebo. Other complaints on Ibuprofen were: rash (1), nocturnal frequency of micturition (1), heavy perspiration (1), headache (1), nausea (1), and giddiness (1). Complaints on placebo were: headache (1), constipation (1), heavy perspiration (1), and heartburn (1). All were mild and transient.

Discussion

The dose of 0-9 g. daily was chosen because preliminary investigation had suggested that benefit was greater on 0-6 than on 0-3 g. daily. High dosage was considered most likely to provide a definite answer. Lack of therapeutic effect, however, was noted with both 0-6 and 0-9 g. daily.

It is possible that the trial period of 7 days was too short to give a reliable answer, but this limited duration was decided upon as it had been found adequate in previous studies to demonstrate differences with rapidly-acting anti-inflammatory
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agents. There was no sign of significant improvement in the second week compared with the first week in the patients with osteo-arthritis on Ibuprofen. In these trials there was no significant difference between Ibuprofen and placebo. There was probably slight symptomatic improvement in the patients with osteo-arthritis treated with Ibuprofen, but it is unlikely that the degree of improvement is of clinical significance.

Side-effects were no problem.

Summary

(1) At the relatively high dose of 0·9 g. daily, Ibuprofen (2, 4'-isobutylphenylpropionic acid) did not exhibit a significant therapeutic effect in twenty patients with rheumatoid arthritis during a 7-day treatment period compared with placebo given for the same period.

(2) Clinically significant improvement was not obtained in nineteen patients with osteo-arthritis who were given a dose of 0·6 g. daily for 14 days.

(3) Side-effects occurred in approximately one-third of patients on both Ibuprofen and placebo; in no instance were they troublesome.

(4) Unless development of therapeutic activity occurs on more prolonged periods of treatment, Ibuprofen appears to be of no value in the treatment of rheumatoid arthritis or osteo-arthritis.

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REFERENCES

Hart, F. Dudley, and Boardman, P. L. (1965). Ibid., 24, 61 (Ibufenac (4-isobutylphenyl acetic acid)).

L'Ibuprofen dans le traitement de l'arthrite rhumatismale et de l'ostéarthrose

RéSUMÉ

(1) A la dose quotidienne relativement élevée de 0,9 g., l'Ibuprofen (ácido 2,4'-isobutilfenilpropriónico) n'a pas montré d'effet thérapeutique significatif chez vingt malades ayant une arthrite rhumatismale pendant une cure de 7 jours, comparé à l'effet d'un placebo administré pendant la même période.

(2) On n'a pas obtenu d'amélioration clinique significative chez 19 malades ostéarthrosiques, qui avaient reçu une dose quotidienne de 0,6 g. pendant 14 jours.

(3) Des effets secondaires sont apparus dans à peu près un tiers des cas aussi bien avec l'Ibuprofen que le placebo; ils n'étaient en aucun cas gênants.

(4) A moins qu'une activité thérapeutique ne se manifeste après un traitement plus prolongé, l'Ibuprofen paraît n'être d'aucun secours dans le traitement de l'arthrite rhumatismale et de l'ostéarthrose.

Ibuprofen en el tratamiento de la artritis reumatoide y de la osteoartritis

SUMARIO

(1) Con dosis diaria relativamente alta de 0,9 g., Ibuprofen (ácido 2,4'-isobutilfenilpropriónico) no manifestó efecto terapéutico significativo en veinte enfermos con artritis reumatoide durante siete días de tratamiento, en comparación con un placebo administrado durante un periodo similar.

(2) No se obtuvo mejora clínica significativa en 19 enfermos con osteoartrosis tratados con una dosis diaria de 0,6 g. durante 14 días.

(3) Efectos secundarios sobrevinieron en cerca de una tercera de los enfermos tratados tanto con el Ibuprofen como con el placebo; en ningún caso fueron estos efectos molestos.

(4) A no ser que una actividad terapéutica se manifieste después de un tratamiento más prolongado, Ibuprofen parece tener poco valor en el tratamiento de la artritis reumatoide o de la osteoartrosis.