IBUPROFEN IN RHEUMATOID ARTHRITIS

CLINICAL STUDY OF ANALGESIC AND ANTI-INFLAMMATORY ACTIVITY

BY

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Ibuprofen (2-4'-isobutylphenylpropionic acid) is one of a series of phenylalkanoic acids which have been found to possess analgesic, anti-inflammatory and antipyretic properties. The first of these to be successful in the treatment of rheumatoid arthritis was Ibufenac (isobutylphenylacetic acid) (Chalmers, 1963; Thompson, Stephenson, and Percy, 1964; Hart and Boardman, 1965) and the most recent of the series is Ibuprofen. Pharmacological studies have shown that the compound is between two to eight times more potent than aspirin (Adams, Cliffe, Lessel, and Nicholson, 1967).

In this paper we report a double-blind cross-over study of the analgesic and anti-inflammatory activity in rheumatoid arthritis of a daily dose of 750 mg. Ibuprofen compared with aspirin 5g./day and prednisolone 15 mg./day; each drug being administered orally for a period of one week.

Material and Methods

Nine patients (seven females and two males) with "definite" or "classical" rheumatoid arthritis according to the diagnostic criteria of the American Rheumatism Association (Ropes, Bennett, Cobb, Jacox, and Jessar, 1959) were studied. Their mean age was 49.5 years (range 37 to 67). The mean duration of arthritis was 2.8 years (range 1 to 6). All patients had positive tests for rheumatoid factor by the sheep cell agglutination method (Heller, Jacobson, and Kolodny, 1949) in titres ranging from 1:32 to 1:1024, and joint erosion was present radiologically. The patients had received various analgesics before this study, but none had received corticosteroid therapy at any time in the course of their disease.

The patients were given four courses of treatment each lasting one week: Ibuprofen 750 mg./day, aspirin 5 g./day, prednisolone 15 mg./day, and lactose as placebo. All four compounds were given by mouth in identical capsules, three capsules being taken five times daily. The courses of treatment were allocated at random, some

patients starting with Ibuprofen, some with aspirin, some with prednisolone, and some with placebo. The sequence in which the four compounds were given in the nine patients is shown in Table I, where it can be seen that the schedule of administration was reasonably randomized. The study was performed in a double-blind fashion, the physicians assessing the patients' response being unaware of which treatment was being given. The patients were assessed at the end of each week's treatment.

TABLE I
PLAN OF ADMINISTRATION OF IBUPROFEN (Ib),
ASPIRIN (A), PREDNISOLONE (P), AND LACTOSE (L)

Patient No.	Sex	Week 1	Week 2	Week 3	Week 4
1		L	A	P	Ib
2	F	Ib	P	A	L
3	F	A*	P	Ib*	L*
4		P	Ib	L	A†
5		Ib	P	A†	P
6	M	L	L	Ib	A
7	F	A	L	P	Ib
8		A	Ib	P	L
9		L	Ib	P	A

Notes: *Therapy had to be discontinued (See text).

†Dose of drug was reduced on account of tinnitus and deafness (See text).

The patients were questioned regarding the overall severity of their joint pain and stiffness, four categories being recognized: 0 nil; +1 mild; +2 moderately severe; +3 severe.

An attempt was made to quantitate joint pain by devising a "pain index". The joint pain experienced by the patient was graded arbitrarily as follows: 0 no pain; +1 mild pain; +2 moderately severe pain; +3 severe pain. Some joints were considered as single units such as: the temporomandibular joints, the cervical spine, the sterno- and acromio-clavicular joints, the metacarpophalangeal and proximal interphalangeal joints in each hand, and the mid-tarsal and metatarsophalangeal joints in each foot. The pain index was calculated as the sum of scores for the different joints. The maximum possible pain score for an individual was +78.

An "articular index" was based on the response of the patient to firm pressure over the joint (Ritchie, McInnes,

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Jasani, Dalakos, Greiveson, Boyle, and Buchanan, 1968), the pain response being graded as follows: 0 no pain; +1 patient complains of pain; +2 patient complains of pain and winces; +3 patient complains of pain and withdraws. Certain joints were examined by passive movement, *e.g.* the cervical spine, hips, and mid-tarsal joints, and the joints considered as single units in the pain index were also regarded as single units for the articular index. This index gave a measure of joint tenderness, the maximum possible score for an individual patient being +78. The articular index has been shown to have an acceptable degree of intra-observer reproducibility; the mean intra-observer error difference in eighteen patients examined by the same observer within 30 minutes being of the order of 1.2 score units and the standard error of this difference being 1.1 score units (Ritchie and others, 1968). This articular index has also been shown to compare favourably with the articular score employed by the Co-operating Clinics Committee of the American Rheumatism Association (1965), the correlation coefficient being 0.89 (Ritchie and others, 1968).

Grip strength was measured for each hand using a mercury dynamometer with the cuff inflated to 30 mm. Hg, the mean result of three readings being recorded.

Joint size was measured in millimetres (mm.) using a plastic gauge supplied by Geigy Ltd., in a manner similar to that described by Boardman and Hart (1967). The circumference of the interphalangeal joint of each thumb and of the eight proximal interphalangeal joints was measured, and the total circumference of five joints of each hand was recorded.

In addition to these clinical parameters, a number of laboratory investigations were also performed at the end of each treatment period. These included: haemoglobin concentration, erythrocyte sedimentation rate (Westergren), serum albumin and globulin concentrations, sheep cell agglutination titres of rheumatoid factor, serum transaminases (SGOT and SGPT), urinalysis, and blood urea. A record of possible side-effects was also made at each assessment. All the patients were kept in hospital during the period of study.

Results

The results are summarized in Tables II to IV.

Ibuprofen therapy had to be discontinued in Patient 3 (Table I) after the fifth treatment day because of troublesome gastro-intestinal symptoms.

TABLE II
SUMMARY OF FINDINGS IN SUBJECTIVE IMPROVEMENT DURING TREATMENT WITH LACTOSE, IBUPROFEN, ASPIRIN, AND PREDNISOLONE, EACH GIVEN FOR ONE WEEK

Patient No.	Lactose		Ibuprofen		Aspirin		Prednisolone	
	Joint Pain	Joint Stiffness	Joint Pain	Joint Stiffness	Joint Pain	Joint Stiffness	Joint Pain	Joint Stiffness
1	+3	+3	+1	+1	+2	+1	0	0
2	+3	+2	+2	+1	+1	+1	0	0
3	+3	+1	+2	0	+1	+1	0	0
4	+3	+3	0	+1	+2	+2	+1	+1
5	+3	+3	+1	+1	+1	0	0	+1
6	+3	+3	+2	+3	+1	+3	0	0
7	+3	+1	+2	+3	+2	+3	+1	+1
8	+3	+3	0	+1	+2	+1	0	+1
9	+3	+1	+2	+1	+2	+1	0	0
P value			<0.01	N.S.	<0.01	N.S.	<0.01	<0.01

Joint Pain and Stiffness is graded: 0 = none, +1 = mild, +2 = moderately severe, +3 = severe. P values are based on the Sign test of Siegel (1956).

SUMMARY OF ASSESSMENT OF JOINT PAIN, JOINT TENDERNESS, GRIP STRENGTH, AND ESR DURING TREATMENT

Patient No.	Lactose				Ibuprofen			
	Pain* Index	Articular Index†	Grip Strength (mm./Hg)	ESR (mm./hr)	Pain Index	Articular Index	Grip Strength (mm. Hg)	ESR (mm./hr)
1	16	20	310	71	12	17	242	58
2	14	26	495	—	17	13	435	38
3	37	38	385	58	41	34	380	28
4	22	28	—	55	9	24	—	28
5	4	56	110	114	1	24	110	46
6	36	39	175	15	24	26	235	10
7	45	55	190	127	28	50	215	118
8	12	33	262	60	3	21	346	28
9	40	48	210	40	29	36	215	38
Mean ± S.E.	25.1 ± 4.9	38.1 ± 4.3	267.1 ± 32.3	67.5 ± 13.0	18.2 ± 4.4	27.2 ± 3.7	272.2 ± 37.5	45.4 ± 11.4
P value					<0.05	<0.01	N.S.	<0.05

The P values have been calculated from the mean difference between the values on lactose and after treatment with Ibuprofen, aspirin, and prednisolone.

TABLE IV
SUMMARY OF MEASUREMENTS OF PIP JOINT CIRCUMFERENCE (mm.)

Patient No.	Side	Lactose	Ibuprofen	Aspirin	Prednisolone
4	R	304.0	295.5	287.5	282.5
	L	303.0	296.5	291.5	280.0
5	R	292.5	288.5	279.5	270.0
	L	275.0	273.5	266.0	259.0
6	R	344.5	329.5	334.5	321.5
	L	329.0	320.0	324.0	317.0
7	R	293.5	288.5	289.5	291.5
	L	287.5	269.0	271.5	277.5
9	R	279.0	275.5	268.9	259.0
	L	272.0	270.0	265.4	258.5
Mean		298.0	290.6	287.8	281.5
±S.E.		±7.4	±6.5	±7.6	±7.2
P			<0.01	<0.001	<0.001

The P values have been calculated from the mean differences of the values on lactose and after treatment with Ibuprofen, aspirin, and prednisolone and their standard deviation, and not from the differences between the means (see text).

Similar symptoms forced this patient to discontinue aspirin also after the fourth treatment day. Patients 4 and 5 experienced tinnitus and deafness after their third treatment day during Weeks 4 and 3, respectively (Table I); in both patients a blood sample was taken for serum salicylate which was found to be raised, and the dose was reduced to nine capsules per day for the remaining week.

All patients completed the week on prednisolone without any complaints.

Lactose therapy had to be discontinued in Patient 3 only because of unbearable joint pain.

When a treatment had to be discontinued the clinical and laboratory measurements were carried out and the next treatment was started at once.

Joint Pain (Table II)

All nine patients experienced severe (+3) articular pain during lactose therapy. After one week's treatment with Ibuprofen two patients were free of

pain (0), two had only mild pain (+1), and five experienced moderately severe pain (+2). Analysis of these results using the Sign test for non-parametric data described by Siegel (1956) showed these differences to be significant at the 1 per cent. level. Significant improvement in joint pain occurred with aspirin and prednisolone compared with lactose ($P < 0.01$ and $P < 0.002$ respectively); during aspirin therapy four patients had mild and five patients moderately severe pain, and on prednisolone seven patients had no pain and two patients had mild pain. Ibuprofen therapy was not significantly better than aspirin therapy, but prednisolone was significantly better than either of them ($P < 0.05$ and $P < 0.01$ respectively).

Joint Stiffness (Table II)

All patients experienced joint stiffness while on lactose: one mild (+1), two moderately severe (+2), and five severe (+3). With Ibuprofen three patients

TABLE V
TREATMENT WITH LACTOSE, IBUPROFEN, ASPIRIN, AND PREDNISOLONE EACH GIVEN FOR ONE WEEK

Aspirin				Prednisolone			
Pain Index	Articular Index	Grip Strength (mm. Hg)	ESR (mm./hr)	Pain Index	Articular Index	Grip Strength (mm. Hg)	ESR (mm./hr)
12	20	250	67	6	13	365	52
4	10	478	—	1	9	545	—
13	30	370	51	4	11	500	38
17	20	—	100	12	20	—	56
0	35	110	85	2	12	150	49
31	34	165	5	0	17	520	6
30	34	220	120	15	34	215	85
20	31	345	40	11	24	294	43
14	21	220	40	0	6	260	27
15.6	26.1	269.7	61.6	5.7	16.2	357.4	46.7
±3.6	±2.9	±31.3	±1.9	±1.9	±2.9	±39.1	±8.6
<0.05	<0.01	N.S.	N.S.	<0.01	<0.01	<0.001	<0.05

and their standard deviation, and not from the differences between the means (see text).

had no stiffness, four mild, and two severe. With aspirin two patients had no stiffness, five mild, and two severe. With prednisolone only one patient had mild stiffness. The result with Ibuprofen and aspirin were not significantly different compared with that with placebo treatment, but prednisolone therapy led to a significant improvement in joint stiffness compared with lactose, Ibuprofen, and aspirin ($P < 0.002$, $P < 0.05$, $P < 0.05$ respectively).

Since the experimental design of this study consisted of treating the same patients with lactose, Ibuprofen, aspirin, and prednisolone, the results of the pain index, articular index, grip strength measurements, and erythrocyte sedimentation rate (Table III) and joint size measurements (Table IV) have been analysed using the "t" test applied to a paired comparison as described by Hill (1961).

Pain Index (Table III)

Compared with lactose, Ibuprofen, aspirin, and prednisolone improved joint pain as measured by the pain index. The mean difference in the pain index between lactose and Ibuprofen, 6.9 (S.D. ± 7.3) was significant ($P < 0.02$, Table III). The corresponding values for aspirin and prednisolone treatments were 9.4 ± 10.7 and 19.4 ± 15.2 respectively, and these were also significant ($P < 0.05$, $P < 0.01$). Improvement in joint pain was significantly greater with prednisolone than with Ibuprofen or aspirin ($P < 0.05$, $P < 0.01$ respectively), but the results with Ibuprofen therapy did not differ significantly from those with aspirin.

Articular Index (Table III)

Comparison of the articular index values obtained after Ibuprofen with those after lactose therapy shows that there was a significant improvement ($P < 0.01$) in joint tenderness with Ibuprofen, the mean fall in the articular index being 10.9 (S.D. ± 9.0). Aspirin and prednisolone therapies were also accompanied by a significant fall in the articular index, the mean fall being 10.9 ± 9.6 ($P < 0.01$) on aspirin and 22.1 ± 13.6 ($P < 0.01$) on prednisolone. A significantly greater improvement in joint tenderness occurred during prednisolone therapy compared with that with Ibuprofen and with aspirin ($P < 0.02$, $P < 0.01$ respectively) but there was no difference between the results with Ibuprofen and with aspirin.

Grip Strength (Table III)

The strength of grip for each patient was recorded as the sum of the mean of three grip strength readings for each hand. There was no significant

difference in grip strength with Ibuprofen and with aspirin compared with lactose, but a highly significant improvement ($P < 0.001$) was noted with prednisolone compared with lactose (mean rise 89.0 mm. Hg ± 34.0).

Erythrocyte Sedimentation Rate (Table III)

A significant fall in the ESR was noted after Ibuprofen and prednisolone. The mean fall with Ibuprofen compared with lactose was 22.1 mm. ± 22.4 (S.D.) in the first hour and following prednisolone compared with lactose it was 21.2 mm. ± 21.3 in the first hour, both results being significant at the 5 per cent. level.

Joint Size Measurements (Table IV)

The total circumference of the four proximal interphalangeal joints and the interphalangeal joint of the thumb was recorded for each hand in each of the patients. The mean difference in joint circumference between Ibuprofen and lactose, 7.4 mm. $\pm$ S.D. 5.6 , was significant at the 1 per cent. level. The mean differences between aspirin and lactose (10.6 mm. ± 5.0) and between prednisolone and lactose (16.4 mm. ± 7.0) were highly significant ($P < 0.001$). As reflected by the above changes, reduction in joint size obtained with Ibuprofen was not significantly different from that with aspirin, but a highly significant reduction occurred with prednisolone compared with Ibuprofen and aspirin ($P < 0.001$, $P < 0.02$ respectively).

Serum Glutamic-oxaloacetate (GOT) and Glutamic-pyruvic (GPT) Transaminase Determinations

These were performed routinely before commencing the drug trial and at the end of each treatment week. Retrospective analysis of the results (Table V) revealed no uniform trend but compared with the serum enzyme concentrations at the end of lactose week a mean rise of 2.9 units per ml. ± 7.8 (S.D.) in the GOT activity and 3.9 units per ml. ± 14.3 (S.D.) in the GPT activity was observed with Ibuprofen therapy. Aspirin induced a mean fall (4.0 ± 46.0 and 5.0 ± 39.3) and prednisolone treatment resulted in a mean rise (5.0 ± 39.3 and 3.0 ± 28.6 respectively). None of these differences achieved statistical significance.

Two out of eight patients, however, did have serum transaminase levels above the upper limit of normal (Table V, opposite).

Patient 6 (Table V), a male, had raised GOT and GPT levels after lactose treatment (Week 1, Table I). In him, prednisolone therapy (Week 2) caused a definite fall in the activity of both the enzymes but after Ibuprofen (Week 3) they were again raised, whereas after aspirin they were approximately the same as after prednisolone.

TABLE V
SUMMARY OF CHANGES IN SERUM GLUTAMIC-OXALOACETIC (GOT) AND
GLUTAMIC-PYRUVIC (GPT) TRANSAMINASE (units/ml.)

Patient No.	Lactose		Ibuprofen		Aspirin		Prednisolone	
	GOT	GPT	GOT	GPT	GOT	GPT	GOT	GPT
1	32	26	29	26	24	24	39	31
2	29	10	—	—	17	19	13	15
3	20	10	18	22	28	25	34	28
4	21	19	20	23	24	19	48	30
5	17	12	20	21	26	25	28	22
6	73	105	71	81	31	41	22	37
7	59	17	77	41	56	15	54	21
8	17	11	24	11	28	16	45	48
9	22	15	25	23	20	15	27	20
Mean	32.2	25.0	35.5	31.0	28.2	22.1	34.4	28.0
±S.D.	±21.0	±30.5	±23.8	±21.8	±10.2	±8.8	±14.8	±10.1

Normal range for Serum GOT level 5-40 units/ml. and for Serum GPT level 5-35 units/ml.

Patient 7 (Table V), a female, had a higher than normal level of serum GOT before the start of the trial and this remained abnormal except for a slight fall after aspirin, lactose, and prednisolone in that order. The GPT showed no change. After Ibuprofen a further rise in GOT was associated with a rise above normal in GPT.

In one patient the transaminases were not determined after Ibuprofen.

Other Laboratory Investigations

No significant differences were noted in the haemoglobin concentration, serum albumin and globulin levels, and sheep cell agglutination titres. None of the patients developed albuminuria or showed a rise in the blood urea during treatment with Ibuprofen.

Side-effects or Toxic Effects of Ibuprofen

One patient (Patient 2, Table I) complained of slight nausea but continued the therapy for the full week.

Another female patient (Patient 3, Table I) had troublesome nausea, heartburn, and epigastric discomfort as well as transient episodes of giddiness and buzzing in the ears. As these symptoms persisted despite lowering the daily dose to nine capsules, she had to discontinue therapy after 5 days. She had similar symptoms during aspirin therapy which had to be discontinued after 4 days.

The remaining patients gave no history of similar or other untoward symptoms. There were no cases of skin rash, albuminuria, or raised blood urea.

Discussion

On treatment with Ibuprofen the patients as a group experienced a significant improvement in joint pain and tenderness, and a significant reduction in joint swelling, which suggests that the drug has a clinically demonstrable anti-inflammatory activity (Boardman and Hart, 1967). The erythrocyte sedimentation rate also fell significantly.

Aspirin given in full therapeutic doses also resulted in a significant improvement in joint pain and tenderness and a reduction in joint size, but not in ESR. With this exception no significant differences were noted. This would suggest that Ibuprofen

and aspirin are approximately equipotent in their analgesic and anti-inflammatory effects in the doses employed in this study.

Prednisolone given in a high dose of 15 mg./day produced a significant improvement in all the parameters studied, the degree of improvement being significantly greater than that with Ibuprofen or aspirin. It would be interesting to compare the effects of Ibuprofen and aspirin with those of the generally-used dose of 7.5 mg. prednisolone administered in divided doses as in this study.

A rise in serum glutamic-oxaloacetic transaminase (GOT) and glutamic pyruvic transaminase (GPT) levels was reported during long-term use of Ibufenac in clinical trials carried out by Thompson, Stephenson, and Percy (1964) and Hart and Boardman (1965). Both groups of workers referred to the development of jaundice in association with the disturbed GOT and GPT levels, the incidence being less than 1 per cent. of all patients in one series (Hart and Boardman, 1965). Ibufenac has now been withdrawn from the market, the last reported case having developed a fatal hepatic coma. In the present study, two out of nine patients developed higher than normal serum levels of GOT and GPT after Ibuprofen therapy. Although such increases were present in both these patients after lactose and in one after prednisolone, great caution should be exercised in the use of Ibuprofen, especially in view of the known hepatotoxicity of the earlier phenyl-alkanoic acid Ibufenac. The therapeutic usefulness of Ibuprofen will very much depend upon its hepatotoxicity during long-term use.

Summary

In a double-blind cross-over study the analgesic and anti-inflammatory action of Ibuprofen 750 mg./day in cases of rheumatoid arthritis has been compared with aspirin 5g./day and prednisolone 15 mg./day. Lactose was used as a placebo. Each

compound was administered in identical capsules and in a totally random order to all the patients studied. Subjective improvement in the patients' joint pain and stiffness and changes in joint tenderness, grip strength, joint size, and erythrocyte sedimentation rate were assessed before and after one week's treatment with each drug.

Ibuprofen was found to have a significant analgesic and anti-inflammatory effect in the patients studied and the incidence of side-effects was low.

The analgesic and anti-inflammatory activity of 750 mg. Ibuprofen, the dose employed in the present

study, was found to be approximately equipotent to that of the effective therapeutic dose of aspirin 5 g./day in rheumatoid arthritis. Prednisolone in a relatively higher dose of 15 mg./day was significantly more potent than Ibuprofen or aspirin.

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REFERENCES

- Adams, S. S., Cliffe, E. E., Lessel, B., and Nicholson, J. S. (1967). *J. pharm. Sci.*, **56**, 1686 (Some biological properties of 2-(4-Isobutylphenyl)-propionic acid).
- Boardman, P. L., and Hart, F. Dudley (1967). *Brit. med. J.*, **4**, 264 (Clinical measurement of the anti-inflammatory effect of salicylates in rheumatoid arthritis).
- Chalmers, T. M. (1963). *Ann. rheum. Dis.*, **22**, 358 (Clinical trials of a new drug, Ibufenac, in the treatment of rheumatoid arthritis. A preliminary report).
- Co-operating Clinics Committee of the American Rheum. Ass. (1965). *Arthr. and Rheum.*, **8**, 302 (A seven-day variability study of 499 patients with peripheral rheumatoid arthritis).
- Hart, F. Dudley, and Boardman, P. L. (1965). *Ann. rheum. Dis.*, **24**, 61 (Ibufenac (4-isobutylphenyl acetic acid)).
- Heller, G., Jacobson, A. S., and Kolodny, M. H. (1949). *Proc. Soc. exp. Biol. (N.Y.)*, **72**, 316 (A modification of the hemagglutination test for rheumatoid arthritis).
- Hill, A. Bradford (1961). "Principles of Medical Statistics", 7th ed., p. 149. Lancet, London.
- Ritchie, D. M., Boyle, J. A., McInnes, J. M., Jasani, M. K., Dalakos, T. G., Grieson, P., and Buchanan, W. W. (1968). *Quart. J. med.* (in press) (Clinical studies with an articular index for the assessment of joint tenderness in patients with rheumatoid arthritis).
- Ropes, M. W., Bennett, G. A., Cobb, J., Jacox, R., and Jessar, K. A. (1959). *Ann. rheum. Dis.*, **18**, 49 (1958 Revision of diagnostic criteria of rheumatoid arthritis).
- Siegel, S. (1956). "Nonparametric Statistics for the Behavioral Sciences", p.68. McGraw-Hill, New York.
- Thompson, M., Stephenson, P., and Percy, J. S. (1964). *Ann. rheum. Dis.*, **23**, 397 (Ibufenac in the treatment of arthritis).

L'action antalgique et anti-inflammatoire de l'Ibuprofen dans la polyarthrite rhumatoïde

RÉSUMÉ

On a comparé dans des cas de polyarthrite rhumatoïde par la méthode de *double-blind cross-over* l'action antalgique et anti-inflammatoire de l'Ibuprofen, 750 mg. par jour, avec celle de l'aspirine 5 g. par jour et de prednisolone 15 mg. par jour. La lactose était usée comme placebo. Tous ces produits furent administrés en capsules identiques et la répartition des malades parmi les groupes de traitement fut fortuite. L'amélioration de la douleur, de l'enraidissement et de la sensibilité douloureuse au niveau des articulations, la force de la main, les dimensions des articulations et la VSG furent déterminées avant et après une semaine de traitement par chaque produit.

On a trouvé que l'Ibuprofen exerçait une action antalgique et anti-inflammatoire significative chez les patients étudiés et que la fréquence des effets secondaires gênants était basse.

L'action antalgique et anti-inflammatoire de 750 mg. d'Ibuprofen, dose employée dans cette étude, s'avéra à peu près équivalente à celle de 5 g. d'aspirine par jour, dose thérapeutiquement efficace dans la polyarthrite rhumatoïde. La prednisolone, à la dose quotidienne relativement plus forte de 15 mg. fut significativement plus puissante que l'Ibuprofen ou l'aspirine.

Acción analgésica y anti-inflamatoria de Ibuprofen en la poliartritis reumatoide

SUMARIO

Se compararon, en casos de poliartritis reumatoide, por el método de *double-blind cross-over*, las acciones analgésica y anti-inflamatoria de 750 mg. diarios de Ibuprofen con la de 5 g. diarios de aspirina y 15 mg. diarios y la de prednisolona. La lactosa fué empleada como placebo. Todos estos productos fueron administrados en cápsulas idénticas y asignados a enfermos en un orden fortuito. La mejoría del dolor, de la rigidez y de la sensibilidad dolorosa en las articulaciones, la fuerza de asimiento, el tamaño de las articulaciones y la velocidad de sedimentación eritrocitaria fueron determinadas antes y después de una semana de tratamiento con cada producto.

Se halló que Ibuprofen desempeñaba una acción analgésica y anti-inflamatoria significativa en los enfermos estudiados y que la frecuencia de los efectos secundarios molestos era baja.

La acción analgésica y anti-inflamatoria de 750 mg. de Ibuprofen, dosis empleada en esta investigación, se reveló aproximadamente equivalente a la dosis diaria de 5 g. de aspirina, terapéuticamente eficaz en la poliartritis reumatoide. La prednisolona, en dosis diaria relativamente más fuerte de 15 mg., fué significativamente más poderosa que Ibuprofen o aspirina.