EVALUATION IN MAN OF FENOCLOZIC ACID
(I.C.I. 54,450: MYALEX), A NEW ANTI-INFLAMMATORY AGENT

II. CLINICAL TRIAL IN PATIENTS WITH RHEUMATOID ARTHRITIS

BY

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In the pharmacological evaluation of a new drug much is to be gained by close co-operation between clinical and industrial research. Following initial pharmacological and toxicological testing of the new compound in laboratory animals, the next step is to establish the pharmacokinetic behaviour of the drug in normal human subjects and in patients with the disease in which the drug may have therapeutic potential. The results of such studies with fenclozic acid have been described in the first part of this paper (Chalmers, Pohl, and Platt, 1969).

The purpose of the second part is to report the results of a clinical trial of the drug in the treatment of rheumatoid arthritis. The object of this trial was to compare the effects of aspirin 3-6 g. daily with those of fenclozic acid in dosages of 200, 300, or 400 mg. daily, when each treatment was given in random sequence for a period of 10 days. Concomitant pharmacological studies led to an alteration in trial design whereby clinically unsuspected bias could be diminished.

Material and Methods

Forty patients (38 female and two male), all with classical or definite rheumatoid arthritis as defined by the criteria of the American Rheumatism Association (Ropes, Bennett, Cobb, Jacox, and Jessar, 1959), were admitted to the trial in three groups which were similar as regards average age, body weight, and duration of disease. Eight patients received 200 mg. fenclozic acid daily, eight 300 mg., and 24 400 mg. All patients were in hospital receiving routine conservative treatment with rest in bed, graded exercises, and conventional splintage. Criteria of entry included the presence of clinically active rheumatoid arthritis and the involvement of at least one proximal interphalangeal joint in each hand. Patients receiving corticosteroids were excluded, but treatment with antimalarials was maintained unless very recently commenced.

Patients were allotted randomly on entry to treatment with aspirin or fenclozic acid for a period of 10 days, when the alternative treatment was begun and continued for a further 10 days. Capsules, identical in weight and appearance, were used to facilitate the double-blind design of the trial. The capsules contained 50 or 100 mg. fenclozic acid, 300 mg. aspirin, or non-medicated granules (placebo). To enable identical numbers of capsules to be administered four times daily, the fenclozic acid doses were supplemented with placebo capsules where necessary, and treatments were so arranged that fenclozic acid was given in the first and third doses of any one day, the interval between these doses being approximately 12 hours. Twelve of the patients receiving 400 mg. fenclozic acid daily had a 4-day period of treatment with paracetamol 6 g. daily interposed between the two 10-day periods of trial, as pharmacological studies in the first twelve patients in this group had detected a possible lag effect when fenclozic acid was given during the first treatment period.

Salicylate analgesics were withdrawn and paracetamol 6 g. daily was substituted for 48 hours before entry. The average pre-trial aspirin dosage was 2.4 g. daily.

Clinical assessments were carried out on entry and on days, 5, 10, 15, and 20, except in the case of the twelve patients receiving paracetamol who had an additional assessment before their second 10-day trial period. Patients were assessed at approximately the same hour of the day on each occasion, before routine ward exercises. Assessment included estimation of grip strength, using a dynamometer with the bag inflated to 30 mm. Hg and recording each of three attempts with each hand. Joint size was measured in millimetres (mm.) in the interphalangeal joint of the thumb and in the proximal interphalangeal joint in each finger, excluding from analysis those joints which were clinically normal and using a plastic gauge supplied by Geigy Ltd., as described by Boardman and Hart (1967). The patient's estimate of the duration of morning stiffness and any untoward effects were noted. Patients were allowed additional paracetamol for pain on request and the total number of tablets taken was recorded. At the conclusion of the trial, the patient was asked to indicate in which 10-day period he felt he had made more progress.

Laboratory assessments, on entry and at the end of
each trial period, included measurement of haemoglobin concentration (Hb), the erythrocyte sedimentation rate (ESR), leucocyte and platelet counts, and estimation of prothrombin activity. Biochemical assessment included estimations of serum concentration of salicylic acid and fenclozic acid (Platt, 1969), serum glutamic-oxalacetic transaminase (SGOT: Furuno and Sheena, 1965), isocitric dehydrogenase (ICDH: Bell and Baron, 1960), alkaline phosphatase (Bessey, Lowny, and Brock, 1946), total protein (Henry, 1964), albumin (Briere and Mull, 1964), phosphatase (Lew, Rutenberg, and Scott, 1960), and uric acid (Eichhorn, Zelmanowski, Lew, Rutenberg, and Fanias, 1961). The faeces were tested for occult blood during each period of treatment, and the urine for albumin, glucose, and urobilinogen.

Results

A. Clinical Assessments

The results recorded for grip strength, joint size, duration of morning stiffness, and drug preference are shown in Table I.

Grip strength.—There is little difference between the values obtained with aspirin and those obtained with fenclozic acid at any dosage. In no group of patients is the difference between averages greater than 7 mm. Hg. This equality is also clearly shown in Fig. 1, in which are set out graphically the averages for grip strength obtained from the 24 patients receiving 400 mg. fenclozic acid daily. If given first, fenclozic acid was associated with an improvement comparable with that recorded when aspirin was given first. When given second, fenclozic acid appeared to maintain initial improvement satisfactorily.

Joint Size.—The results of measurement are essentially the same with each drug and show little change from the measurements recorded on entry.

Morning Stiffness.—Changes in the duration of morning stiffness, as estimated by the patient, are more marked, and this subjective index suggests improvement after treatment. The differences noted between the drugs is small, however, being in no group greater than 0-15 hr. The figures show that there is very little, if any, difference between the

Table I

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of Patients</th>
<th>Assessment</th>
<th>Average Grip Strength (mm. Hg)</th>
<th>Average Joint Size (circumference in mm.)</th>
<th>Average Duration of Morning Stiffness (hrs)</th>
<th>Drug Preference</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>8</td>
<td>On Entry</td>
<td>116</td>
<td>57</td>
<td>1-72</td>
<td>No preference</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After aspirin</td>
<td>130</td>
<td>56</td>
<td>0-78</td>
<td>Aspirin</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After Fenclozic Acid 200 mg.</td>
<td>125</td>
<td>56</td>
<td>0-91</td>
<td>Fenclozic Acid</td>
<td>2</td>
</tr>
<tr>
<td>2</td>
<td>8</td>
<td>On Entry</td>
<td>102</td>
<td>53</td>
<td>2-09</td>
<td>No preference</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After aspirin</td>
<td>115</td>
<td>52</td>
<td>1-31</td>
<td>Aspirin</td>
<td>3</td>
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<tr>
<td></td>
<td></td>
<td>After Fenclozic Acid 300 mg.</td>
<td>108</td>
<td>53</td>
<td>1-41</td>
<td>Fenclozic Acid</td>
<td>3</td>
</tr>
<tr>
<td>3A</td>
<td>12</td>
<td>On entry</td>
<td>102</td>
<td>55</td>
<td>2-46</td>
<td>No preference</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After aspirin</td>
<td>121</td>
<td>54</td>
<td>1-25</td>
<td>Aspirin</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After Fenclozic Acid 400 mg. (without interval)</td>
<td>121</td>
<td>54</td>
<td>1-10</td>
<td>Fenclozic Acid</td>
<td>3</td>
</tr>
<tr>
<td>3B</td>
<td>12</td>
<td>On entry</td>
<td>131</td>
<td>56</td>
<td>1-15</td>
<td>No preference</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After aspirin</td>
<td>158</td>
<td>54</td>
<td>0-35</td>
<td>Aspirin</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After Fenclozic Acid 400 mg. (with interval)</td>
<td>158</td>
<td>54</td>
<td>0-44</td>
<td>Fenclozic Acid</td>
<td>2</td>
</tr>
</tbody>
</table>
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effects of the two drugs as measured by the indices employed.

In clinical trials of this kind carried out in patients in hospital, “spontaneous improvement” unrelated to the treatment under trial, may be considerable (Hajnal, Sharp, and Popert, 1959). The method of statistical analysis which these authors recommend measures not only the difference in the effects of two drugs, but also the effect of such “spontaneous improvement”, and this method of analysis has been applied in this present trial to the results obtained for grip strength in the group of patients receiving 400 mg. fenclozic acid daily.

The results of this analysis are shown in Table II. Clearly, aspirin 3·6 g. daily and fenclozic acid 400 mg. daily have the same degree of effectiveness and any difference between them is not statistically significant.

Similarly, the measures of “spontaneous improvement” are not large enough to be considered significantly different from zero in any of the separate dose groups, but combining the results gives an average measure of “spontaneous improvement” which is statistically significantly greater than zero (P<0·05) as might be expected. Expressing the increases in grip strength noted as a percentage of pre-treatment level leads to similar conclusions.

The observations made on drug preference are included in Table I. Seventeen patients preferred aspirin, ten preferred fenclozic acid, and thirteen indicated no preference. No greater preference for fenclozic acid emerged with increasing dose, but it is of interest to note that, in the group of patients who had a 4-day interval on paracetamol interposed between trial periods, preference for aspirin was less marked.

With regard to supplementary analgesic tablets, it was found that patients had requested a total of 203 paracetamol tablets for pain relief while taking aspirin during the trial, and 278 tablets of paracetamol while taking fenclozic acid. The demand from those taking the higher dose of fenclozic acid (79 tablets for 24 patients) was, however, much smaller than that from patients receiving the lower dosage regimes (199 tablets for 16 patients).

SIDE-EFFECTS
These are listed in Table III (overleaf). No serious side-effects were encountered and none severe enough to necessitate withdrawal from the trial. The Table shows that fenclozic acid was associated with fewer side-effects than aspirin but was not entirely free from minor gastrointestinal disturbances.

| TABLE II |
| ANALYSIS OF DRUG EFFECT AND “SPONTANEOUS IMPROVEMENT” |

<table>
<thead>
<tr>
<th>Group 3A (400 mg. Fenclozic acid without interval)</th>
<th>Mean of 1st and 2nd Assessments</th>
<th>Mean of 3rd and 4th Assessments</th>
<th>Drug-Aspirin A-B</th>
<th>3rd and 4th Assessments — 1st and 2nd</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fenclozic Acid given First</td>
<td>131·8</td>
<td>131·7</td>
<td>0·1</td>
<td>0·1</td>
</tr>
<tr>
<td>Aspirin given First</td>
<td>110·2</td>
<td>116·1</td>
<td>5·9</td>
<td>5·9</td>
</tr>
<tr>
<td>Combined Mean</td>
<td>3·0</td>
<td>2·9</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Drug effect (A-B), mm. Hg. = 3·0±3·4 (standard error).
“Spontaneous Improvement” = 2·9±3·4 (standard error).
(3rd and 4th—1st and 2nd assessments).

<table>
<thead>
<tr>
<th>Group 3B (400 mg. Fenclozic acid with interval)</th>
<th>Mean of 1st and 2nd Assessments</th>
<th>Mean of 4th and 5th Assessments</th>
<th>Drug-Aspirin A-B</th>
<th>4th and 5th Assessments — 1st and 2nd</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fenclozic Acid given First</td>
<td>132·2</td>
<td>140·4</td>
<td>-8·2</td>
<td>8·2</td>
</tr>
<tr>
<td>Aspirin given First</td>
<td>176·9</td>
<td>179·3</td>
<td>2·4</td>
<td>2·4</td>
</tr>
<tr>
<td>Combined Mean</td>
<td>-2·9</td>
<td>5·3</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Drug effect (A-B), mm. Hg. = -2·9±3·4 (standard error).
“Spontaneous Improvement” = 5·3±3·4 (standard error).
(P<0·1)
4th and 5th—1st and 2nd assessments.)
Laboratory Investigations

Serum concentrations of fenclozic acid and salicylic acid

On the tenth day of treatment with fenclozic acid, i.e., after nineteen doses, the average maximum serum concentration was 62 μg/ml. (range 42-77) at 100 mg. twice daily, 87.5 μg/ml. (range 42-128) at 150 mg. twice daily, and 126 μg/ml. (range 46-230) at 200 mg. twice daily (Table IV). There was a linear relationship between the average dose (mg/kg) and the average maximum serum concentration in the three groups of patients.

By comparing the accumulated serum concentration after nineteen doses with the average level of 7.9 μg/ml. found for a single dose of 1 mg/kg.

in the initial studies, an estimate of the serum half-life in each patient was made. The mean results are shown in Table IV. There was no significant difference between the means of the three groups, the overall mean being 35 hrs (range 10-100); more than 90 per cent. of the calculated values fell within the range 10-60 hrs, and 72.5 per cent. were within the range 20-50 hrs. Although these calculated values may be subject to considerable error, they serve to indicate the range of serum half-life likely to be encountered in practice.

The average salicylate level after 10 days' treatment at 900 mg. four times a day, i.e., after 37 doses, was 181 μg/ml. (range 73-310). Using a similar calculating technique to the one above, the mean serum salicylate half-life was 11 hrs (range 3-22), in good agreement with the range of 3-20 hrs quoted by Levy (1965).

Clinical haematology

No significant alterations in any of the parameters investigated were observed as a result of fenclozic acid or aspirin treatment.

Clinical biochemistry

The patients had normal serum total protein concentrations but the majority had low normal or

<table>
<thead>
<tr>
<th>Side-Effects</th>
<th>with Aspirin</th>
<th>with Fenclozic Acid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal</td>
<td>15</td>
<td>7</td>
</tr>
<tr>
<td>Tinnitus; Deafness</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Headache</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Drowsiness</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Urinary Frequency</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

**Table III**

**SIDE-EFFECTS**

**Table IV**

**SERUM CONCENTRATIONS AND CALCULATED SERUM HALF-LIVES OF FENCLOZIC ACID AND SALICYLIC ACID IN PATIENTS WITH RHEUMATOID ARTHRITIS**

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean Dose (mg/kg, twice daily)</th>
<th>Mean maximum Serum Concentration after Dose 19 (μg/ml.)</th>
<th>Mean Calculated Half-life (hrs)</th>
<th>Mean Dose (mg/kg, four times daily)</th>
<th>Mean maximum Serum Concentration after Dose 37 (μg/ml.)</th>
<th>Mean Calculated Half-life (hrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.88±0.11 (8)</td>
<td>62±4.5 (8)</td>
<td>31.9±3.5 (8)</td>
<td>16.9±1.1 (8)</td>
<td>205±25 (8)</td>
<td>12±2.2 (8)</td>
</tr>
<tr>
<td>2</td>
<td>2.68±0.14 (8)</td>
<td>87.5±10 (8)</td>
<td>31.2±4.5 (8)</td>
<td>16.1±0.8 (8)</td>
<td>165±20 (7)</td>
<td>9.5±1.3 (7)</td>
</tr>
<tr>
<td>3</td>
<td>3.54±0.11(24)</td>
<td>126±8.3(24)</td>
<td>37.3±4.2(24)</td>
<td>16.0±0.5(24)</td>
<td>178±13 (24)</td>
<td>11±1.1(24)</td>
</tr>
<tr>
<td>All Groups</td>
<td>35±2.9(40)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Samples taken 2 to 3 hrs after the dose indicated (10th day of treatment period); Results expressed as mean ± S.E. (number of observations).

**Table**

**SGOT, ICDH, AND ALKALINE PHOSPHATASE**

<table>
<thead>
<tr>
<th>Group</th>
<th>Pre-trial</th>
<th>Fenclozic Acid</th>
<th>Aspirin</th>
<th>Pre-trial</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>18.5±2.1 (8)</td>
<td>20±3.1 (8)</td>
<td>54.5±28 (8)</td>
<td>5.8±0.2 (8)</td>
</tr>
<tr>
<td>2</td>
<td>23.5±5.8 (8)</td>
<td>16.5±3.4 (8)</td>
<td>28±7.2 (8)</td>
<td>8.6±1.8 (8)</td>
</tr>
<tr>
<td>3</td>
<td>22.5±3.1(24)</td>
<td>21±3.4(24)</td>
<td>72±17 (22)</td>
<td>8±2.0±6.24</td>
</tr>
<tr>
<td>All Groups</td>
<td>22±2.3 (4)</td>
<td>20±2.1(38)</td>
<td>59±11 (38)</td>
<td>7.7±0.5(40)</td>
</tr>
</tbody>
</table>

*Results expressed as means ± S.E. (No observations).

Normal ranges: SGOT 5-35 Babson units; ICDH, 3-12 international units; Alkaline phosphatase, 1-0-2.5 Bessey-Lowry-Brock units.
subnormal albumin levels and hence low albumin: total protein ratios.

Average values for serum enzyme activity are shown in Table V. Serum alkaline phosphatase activity was frequently higher than normal both before and during the trial; treatment with fenclozic acid had no further effect on the activity of this enzyme. Treatment with aspirin induced a six-fold increase in one patient to 12.2 units but had no effect in any of the other patients.

Treatment with aspirin for 10 days was associated with marked elevations of both SGOT and ICDH activities; in six cases, SGOT was raised above 100 units, and in nine cases the level was between 40 and 100 units. A further seven cases showed marginal elevations in the range of 34 to 40 units. There was a highly significant (P = < 0.001), positive correlation between the SGOT and ICDH activities, r = 0.95 (Fig. 2), indicating the liver as the source of these aspirin-induced enzyme changes. Only two abnormal SGOT values were observed after 10 days' treatment with fenclozic acid (40 and 89 units). In the latter case, no value was obtained after treatment with aspirin, which, in this case, preceded the fenclozic acid period. i.e. the elevated SGOT and ICDH levels were probably a reflection of a prior change due to aspirin. In five cases, high SGOT and ICDH levels were seen before the start of the trial, presumably related to previous aspirin therapy; in each case, subsequent treatment with fenclozic acid gave normal levels of both enzymes.

Treatment with aspirin 3.6 g. daily was associated with the uricosuric effect expected at this dosage (Sirota, 1957) with significant reduction of serum uric acid concentrations. In eleven of the 33 recorded pre-trial levels, the uric acid was low because of previous aspirin treatment. Subsequent treatment with fenclozic acid restored the levels to the middle of the normal range, i.e. fenclozic acid is neither uricosuric, nor does it cause uric acid retention.

Aspirin, but not fenclozic acid, was associated with a marginal rise in serum urea concentration in many cases, but these levels rarely fell outside the normal range.

**Discussion**

The necessity for the thorough clinical assessment of any new compound before it is made generally available is now accepted, and the initial part of such testing is best conducted in hospital, where patients can be under careful supervision. With a new anti-inflammatory compound such as fenclozic acid, the significance of the conclusions drawn from the results of these preliminary trials is perhaps limited. For example, the duration of such a trial is of necessity limited by the duration of the patient's total stay in hospital and, moreover, improvement in the patient's condition during this time may result from factors other than the drug under trial. With these reservations in mind, can one say whether the object of the present trial has been achieved?

From the results obtained it would appear that fenclozic acid in the dosages employed can be substituted for aspirin in the routine treatment of
patients with rheumatoid arthritis without detriment to their progress while in hospital, but that it shows no superiority over aspirin in providing symptomatic relief. The possible advantages of the drug to emerge from this short-term study may lie in its comparative freedom from side-effects and in the less frequent doses required to maintain effective blood levels. It would appear justifiable to proceed to the next step in the evaluation of a new drug of this type, namely, the careful assessment of its effects in the maintenance therapy of rheumatoid arthritis in out-patients, with the appropriate haematological and biochemical screening.

With regard to the results of the laboratory studies, three features merit comment.

(1) The first is the successful forecasting, from experiments in animals, of the dosage likely to be required in man to achieve therapeutic effect. It was suggested that a dose of 100-200 mg. twice daily would give serum levels of the order found necessary for significant anti-inflammatory activity in animal experiments, and, on trial, this dose has proved clinically effective.

(2) The second point of interest emerged from the concomitant studies of drug levels carried out before and during the trial. In the earlier studies, among five patients with rheumatoid arthritis receiving 100-300 mg. fenclozic acid daily, the half-life of the drug was found to be 46 ± 7 hours, considerably longer than in normal subjects. During the trial this finding of a longer half-life of the drug in patients with rheumatoid arthritis was confirmed, and in the first group of twelve patients receiving 400 mg. of the drug daily, the average half-life was calculated to be 38 ± 6 hours (range 10-100 hours). This average is more than three times the average half-life calculated for salicylate for all groups (11 ± 0-8 hours), and when fenclozic acid was given first in the trial, its prolonged half-life might have resulted in an additive anti-inflammatory effect during the second period, with the introduction of bias in favour of aspirin.

(3) Thirdly, from the biochemical screening, it is noteworthy that the disturbances in enzyme activity noted occurred in the majority of cases after treatment with aspirin. Manso, Taranto, and Nydick (1956) showed similar parallel increases of SGOT and SGPT activity in children receiving long-term aspirin therapy, with rapid reversal to normal on withdrawal of the drug. In five patients in the present trial, levels of SGOT activity were raised before entry. All five had recently been taking aspirin in varying dosage, and this point emphasizes the importance of establishing biochemical data before a patient enters any trial of this kind.

Summary

(1) The effects of fenclozic acid, a new anti-inflammatory compound, given in dosages of 200, 300, or 400 mg. daily, have been compared with those of aspirin, 3·6 g. daily, in a double-blind cross-over trial in in-patients with rheumatoid arthritis.

(2) Clinical assessment detected little difference between the drugs. Seventeen patients preferred aspirin, ten preferred fenclozic acid, and thirteen declared no preference.

(3) Side-effects were fewer with fenclozic acid and no toxicity was found on haematological and biochemical screening.

(4) It is concluded that, in the dosages employed, fenclozic acid can be substituted satisfactorily for aspirin in affording symptomatic relief to patients with rheumatoid arthritis during treatment in hospital, and it would appear justifiable to proceed to an evaluation of the drug's potential for maintenance therapy in out-patients.

We wish to thank Sister E. Mellor and the nursing staff of the Devonshire Royal Hospital, Buxton, Derbyshire, for their help with these studies, and Miss N. Atkinson, Miss E. Hewitt, and Mrs. A. Winstanley for their technical assistance. We are also indebted to Dr. Colin Clark, of Imperial Chemical Industries, for the statistical analysis.

REFERENCES


L'évaluation chez l'homme de l'acide fenclozique (I.C.I. 54.450: Myalex), comme nouvel agent anti-inflammatoire

II. Un essai clinique chez des malades atteints de polyarthrite rhumatoïde

(1) Les effets de l'acide fenclozique, un nouveau produit anti-inflammatoire, donné en dosages de 200, 300 ou 400 mg. par jour ont été comparés à ceux de l'aspirine, 3,6 g. par jour dans un essai d'après la méthode “double-blind and cross-over” chez 40 malades atteints de polyarthrite rhumatoïde hospitalisés.

(2) L'évaluation clinique a montré très peu de différence entre les deux médicaments; 17 malades préféraient l'aspirine, 10 préféraient l'acide fenclozique et 13 n'avaient pas de préférence.

(3) Les effets secondaires ont été moins nombreux avec l'acide fenclozique et aucune toxicité n'a été démontrée par examen biochimique ou hématoLOGique.

(4) Il a été conclu que, aux dosages employés, l'acide fenclozique peut être substitué de façon satisfaisante à l'aspirine et donne un soulagement symptomatique aux malades atteints de polyarthrite rhumatoïde pendant leur traitement à l'hôpital et il paraîtrait justifiable de procéder à une évaluation de l'effet de ce médicament dans le traitement d'entretien chez les malades qui viennent consulter à la clinique.

Evaluación en el hombre de acido fenclóxico (I.C.I. 54.450: Myalex), un nuevo agente antiinflamatorio

II. Prueba clínica en pacientes con poliartritis reumatoide

(1) Los efectos del ácido fenclóxico, un nuevo compuesto antiinflamatorio, administrado en dosis de 200, 300 o 400 mg. diariamente, han sido comparados con los de la aspirina, 3,6 g. diariamente, en una prueba cruzada dobleciego con pacientes internos que padecen poliartritis reumatoide.

(2) El cálculo clínico descubrió poca diferencia entre las drogas. Dieciséis pacientes prefirieron aspirina, diez ácido fencloúsico y trece declararon no tener preferencia alguna.

(3) Los efectos secundarios fueron menores con el ácido fenclóxico y no se descubrió toxicidad en los análisis hematológicos y bioquímicos.

(4) Se llega a la conclusión de que, en las dosis empleadas, el ácido fenclóxico puede ser sustituido por aspirina para producir alivio sintomático en pacientes con poliartritis reumatoide durante tratamiento hospitalario, y parecería justificable proceder a una evaluación de las posibilidades de la droga como terapia de apoyo en pacientes externos.
T M Chalmers, J H Kellgren and D S Platt

doi: 10.1136/ard.28.6.595

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