A STUDY OF KETOPROFEN IN RHEUMATOID ARTHRITIS

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SUMMARY
Experience with ketoprofen, using the oral and rectal routes, was reviewed. The value of ketoprofen in rheumatoid arthritis was confirmed and the drug was usually well tolerated.

The activity of ketoprofen was the subject of an ‘open’ trial carried out on a group of patients with rheumatoid arthritis, admitted to the Rheumatology Clinic, Montpellier.

PATIENTS AND METHODS
The trial included 54 patients (10 men and 44 women) with classical rheumatoid arthritis according to the criteria of the American Rheumatism Association. The distribution of the cases according to age-group and to radiological and clinical findings is shown in Table I. The Waaler–Rose test was positive in 33 cases.

TABLE I
DISTRIBUTION OF PATIENTS BY AGE-GROUP AND RADIOLOGICAL AND CLINICAL FINDINGS

<table>
<thead>
<tr>
<th>Age groups (years)</th>
<th>Group I</th>
<th>Group II</th>
</tr>
</thead>
<tbody>
<tr>
<td>11–20</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>21–30</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>31–40</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>41–50</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>51–60</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>61–70</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>71–80</td>
<td>8</td>
<td>12</td>
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<tr>
<td></td>
<td>5</td>
<td>5</td>
</tr>
</tbody>
</table>

Two groups of patients were considered:

Group I
25 patients treated with ketoprofen orally in a dosage of 200 to 300 mg per day. The average duration of treatment was 26.2 days (range 7 to 112 days).

Group II
29 patients treated with ketoprofen rectally (suppositories containing 100 mg). Eleven of these patients received 200 mg and five others had 300 mg of ketoprofen rectally for an average period of 27.7 days (range 5 to 77 days). The remaining 13 patients were given combined treatment with 100 mg of ketoprofen rectally at bed-time and 100 mg (7 cases) or 200 mg (6 cases) of the same drug by mouth. The average duration of the treatment in these cases was 18.9 days (range 7 to 43 days).

None of these patients received any analgesic or anti-inflammatory drug other than ketoprofen. If gold therapy had been instituted a long time before the beginning of this clinical trial, it was continued.
Assessment of the results

In the assessment of the results the analgesic, anti-inflammatory and antipyretic effects of ketoprofen were taken into account. Systematic questioning of the patients made it possible to assess the influence of the drug on the pain syndrome, particularly pain at night and on movement. Clinical examination made it possible to follow the progress of the objective signs, which were studied on the joint showing the greatest clinical involvement, the local course of the inflammatory syndrome, joint effusion and joint mobility being observed. The joint with the greatest clinical involvement and the proximal interphalangeal joints of the index fingers of both hands were measured systematically. In addition, skin temperatures were measured by thermistor, so that any changes in the local inflammatory state could be assessed objectively. The influence of ketoprofen on the biological aspects of the inflammatory syndrome was studied systematically by means of determinations of the erythrocyte sedimentation rate before and after the clinical trial.

The results were classified as follows:
- Very good: symptomatic recovery, with disappearance of the objective clinical signs and the pain.
- Good: subjective and objective improvement by more than 50%.
- Moderate: subjective improvement of less than 50% with or without detectable objective improvement.
- Nil: no improvement.

Cardiovascular, gastro-intestinal, hepatic, cutaneous, renal and neurological tolerance to ketoprofen were assessed in all cases by questioning and clinical examination of the patients. Local tolerance of the suppositories was also studied systematically. The possible biological effects of ketoprofen were investigated by means of the following laboratory examinations; carried out before and after the therapeutic trial: erythrocyte sedimentation rate, blood picture, serum transaminases, serum alkaline phosphatases, prothrombin level, blood-sugar, blood, non-protein nitrogen, blood uric acid, and protein content of the urine.

RESULTS

Group I

In this group of 25 patients with rheumatoid arthritis treated solely with ketoprofen by mouth, the results were: very good in three (12%), good in nine (36%), moderate in five (20%), and nil in eight (32%) (Table II). The percentage of very good or good

![Table II](https://academic.oup.com/rheumatology/article-abstract/15/5/67/1780771/15671780771)
results is thus 48. Including the cases with a moderate result, the percentage in which ketoprofen had a favourable effect was 68. In these cases an analgesic and anti-inflammatory action could be demonstrated. We did not observe an antipyretic effect when rectal temperatures were read morning and evening.

**Group II**

*Treatment by the rectal route only*

Sixteen patients were included in this group. We recorded six good results (37.5%), five moderate results (31.2%), and five failures (31.2%) (Table II). Ketoprofen had a favourable effect in 68.7% of the patients in this series. Nonetheless, the absence of any excellent results is to be noted.

*Combined treatment*

In this group of 13 patients (100 mg rectally associated with 100 mg or 200 mg by mouth) we obtained two very good results (15.3%), three good (23%), seven moderate (53.8%) and one failure (7.6%) (Table II). An excellent or good result was thus observed in 38.2% of the cases. The high percentage of moderate results is to be emphasized. The results in this small series do not appear to have been clearly influenced by the dosage of ketoprofen given by mouth.

*Combined results for Group II*

These results are also shown in Table II. The effects of the treatment were very good in 6.8% of the cases, good in 31%, and moderate in 41.3%. We recorded 20.6% failures. Thus, ketoprofen given solely as suppositories or as combined treatment (100 mg by suppository and 100 to 200 mg by mouth) gave a very good or good result in 37.8% of cases. Furthermore, in 41% of the cases this treatment led to less outstanding improvement, as it was incomplete, but it was nonetheless real.

**CLINICAL TOLERANCE**

In the first group of patients receiving only ketoprofen by mouth, clinical tolerance was excellent in 24 out of 25. In the exceptional case, epigastric pain in the presence of a hiatus hernia necessitated discontinuation of the treatment. Gastro-intestinal tolerance was very good in four patients with a history of epigastric pain—due to oesophageal diverticulum in one, non-steroidal anti-inflammatory agents in two, and an old gastric ulcer in one. We also observed an eruption on the face in one case and transitory nausea, regressing spontaneously, in another.

In group II, clinical tolerance was less satisfactory. Poor local or regional tolerance of the suppositories was observed in eight cases: anal burning, with rejection of the suppository, in six, and colic in two. The incidence of local intolerance was much higher in the patients receiving ketoprofen by the rectal route only (six out of eight patients) than in those having combined treatment (two out of eight patients). Epigastric pain occurred in six patients treated with ketoprofen as suppositories (200 mg per day). In one case there was a hiatus hernia; in two cases an exacerbation of an old gastric ulcer developed. Lastly, a state of nausea occurred in one case. In the whole group, treatment had to be interrupted in eight of 29 patients on account of poor local tolerance of the suppositories and this was associated with epigastric pain in six cases. It is to be noted, however, that local tolerance of the suppositories was excellent in a patient usually showing poor tolerance of non-steroidal anti-inflammatory agents given rectally.
BIOLOGICAL TOLERANCE

Biological tolerance was excellent in both groups of patients treated. The following abnormalities were observed: increase in serum transaminases to the upper limit of normal in two cases; slight decrease in prothrombin level (minimum level 45%) in four cases; increase in alkaline phosphatase to 85 mU in one case; slight increase in blood non-protein nitrogen (50 and 66 mg/l) in two cases.

The erythrocyte sedimentation rate, which was raised in all the cases studied, had definitely diminished at the end of the treatment in one case and had become normal in two cases. It was not affected by the treatment in any of the other cases.

DISCUSSION

Taking into consideration all the results obtained with ketoprofen in this study, whatever the route of administration used (Table II), it is seen that very good or good results occurred in 42.5% of cases, a moderate result in 31.4% of cases and failure in a quarter of the patients treated.

In rheumatoid arthritis, the initial treatment generally requires a dosage of 300 mg daily by mouth. Subsequently, combined administration (100 mg of ketoprofen rectally together with 100 to 200 mg by mouth) can constitute a useful means of treatment.

Systemic tolerance to ketoprofen was satisfactory on the whole, whatever the method of administration. Treatment had to be interrupted in seven of 54 cases (13%) on account of epigastric pain. Poor local tolerance to the suppositories was observed in 37% of the cases when only the rectal route was used. With combined treatment this figure decreased to 15%.

Ketoprofen is a useful anti-inflammatory agent in rheumatoid arthritis, particularly when given orally. Combined treatment with a suppository of 100 mg at bed-time and 100 to 200 mg by mouth in divided amounts during the day is also useful.