Double-blind study of erbium 169 injection (synoviorthesis) in rheumatoid digital joints

C.-J. MENKES, A. LE GÔ, P. VERRIER, M. AIGNAN, AND F. DELBARRE

Summary A double-blind study of erbium 169 injection into rheumatoid digital joints was carried out with saline as control. 201 joints in 36 patients were studied (137 metacarpophalangeal, 64 proximal interphalangeal). Erbium 169 was injected into 121 joints and saline water into 80 joints. Local injection of corticosteroids was given to both groups. A definite improvement was observed in 55% to 58% of cases with erbium 169 (+prednisolone acetate) and in 26% to 28% of cases with saline (+prednisolone acetate). The difference was highly significant.

Intra-articular injection of radioisotopic β emitter is used to control synovial inflammation and to prevent osteoarticular damage, or is given when drug therapy has failed (Ansell et al., 1963; Makin et al., 1963.) New isotopes have been developed that permit treatment of any inflamed joint whether joint effusion is present or not (Table 1) (Delbarre et al., 1972; Gumpel, 1973). Yttrium 90 (90Y) has a high penetrating capacity and is used mainly for the treatment of the knee joint in rheumatoid arthritis. A double-blind study has proved the effectiveness of 90Y as compared to saline water and nonradioactive yttrium (Delbarre et al., 1974).

Smaller joints such as the wrist, elbow, shoulder, ankle, or hip can be treated with gold 198 (198Au), or better with rhenium 186 (186Rh) which is an almost pure β emitter (Delbarre et al., 1973). For the small digital joints, erbium 169 (169Er) has been chosen. It is a radioisotopic β emitter of limited effect and penetration.

A large clinical trial with 1261 digital joints treated with 169Er between 1969 and 1973 gave very good and good results in 54-6% of cases after one year (Menkes et al., 1974). As corticosteroid injection was used simultaneously, it was thought necessary to assess the exact therapeutic value of 169Er using a double-blind study with saline water as control.

Methods

Isotopic Injections

The digital joints were randomly allocated to two groups. Two mg of prednisolone acetate were given the local injection of erbium 169 (169Er) and saline water used as control.

The injection was given to the in the proximal interphalangeal (PIP) (synoviorthesis) in 55% to 58% of cases with erbium 169 (+prednisolone acetate) and in 26% to 28% of cases with saline (+prednisolone acetate). The difference was highly significant.

The injection dose was 1 mCi 169Er for the metacarpophalangeal joint (MCP) and 0.5 mCi 169Er for the proximal interphalangeal joint (PIP). Colloidal 169Er citrate, pH 7 (Commissariat à l'énergie atomique-Saclay), was used. The mean diameter of particles is 100 Å and physical properties of 169Er are given in Table 1.

The parameters used for comparison between groups were duration of disease, clinical stage, radiological stage, modification of the ESR, and Rose-Waaler test titration.

Each joint was tested for synovial thickness, synovial effusion, and range of movement. Global measure of the joint volume was made with the ring method for PIP joints and with a compass for MCP joints. In most cases patients were re-examined after 3 months and then again between 6 months and 1 year. The notation was: ‘excellent’ for an apparently normal joint, ‘good’ for marked improvement of subjective parameters and of mobility associated with decreased joint effusion, ‘fair’ for improvement of some tests, and ‘poor’.

Statistics

Comparisons between groups were done using Student’s 't' and χ² tests. All the binary coded data were processed on 36 091 IBM computer* using principal components multifactorial analysis. These

*Centre d'Etudes Nucléaires - Fontenay-aux-Roses, Prof. Roucayrol.
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Table 1  Isotopes used for synoviorthesis

<table>
<thead>
<tr>
<th>Isotope</th>
<th>Duration (d)</th>
<th>Type of radiation</th>
<th>Maximum energy of radiation (MeV)</th>
<th>Tissue penetration (mm)</th>
<th>Cartilage penetration</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Mean</td>
<td>Maximal</td>
<td>Mean</td>
</tr>
<tr>
<td>169Er</td>
<td>9-5</td>
<td>β</td>
<td>0.34</td>
<td>1</td>
<td>0.2</td>
</tr>
<tr>
<td>198Au</td>
<td>2-7</td>
<td>γ</td>
<td>0.96</td>
<td>1.2</td>
<td>0.9</td>
</tr>
<tr>
<td>186Rh</td>
<td>3-7</td>
<td>γ (rare)</td>
<td>0.98</td>
<td>3.7</td>
<td>1</td>
</tr>
<tr>
<td>90Y</td>
<td>2-7</td>
<td>β</td>
<td>2.2</td>
<td>11</td>
<td>2.8</td>
</tr>
</tbody>
</table>

analyses are designed to work in connection with all parameters and to give a graphic outline of the results.

Patients

244 digital joints in 41 patients suffering from classical rheumatoid arthritis, according to the American Rheumatic Association criteria, were treated. 201 joints of 36 patients (12 had negative latex and Rose-Waaler tests) were studied. The other 5 patients were not studied as medical treatment had to be modified during follow-up (i.e. drug side effects, flare-up of the disease in other joints). 169Er (+prednisolone acetate) was injected into 121 joints, and saline water (+prednisolone acetate) into 80 joints. Of 137 MCP joints, 85 were injected with 169Er and 52 with saline water. Of 64 PIP joints, 36 were injected with 169Er and 28 with saline water.

Results

We found no statistically significant difference between the two groups of patients for any parameter before treatment, nor any difference between parameters. But 3 months after the injections there was a significant difference between the two groups with regard to 'poor' results (35% injected with saline, 17.8% injected with 169Er, P<0.05). Between 6 months and one year the difference between the two groups was more striking since with 169Er 58% 'excellent' or 'good' results were seen compared with only 28.5% with saline water (P<0.01) (Fig. 1).

In 27 patients several joints were treated with either 169Er or saline water. Results were excellent or good in 55% of those treated with 169Er and in

Table 2  Changes in results between the 1st estimation (3 months) and the 2nd estimation (6 months–1 year)

<table>
<thead>
<tr>
<th>Improvement of results</th>
<th>Saline</th>
<th>169Er</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excellent/Good (%)</td>
<td>50.0</td>
<td>26.9</td>
<td>NS</td>
</tr>
<tr>
<td>Fair/Poor (%)</td>
<td>1/18</td>
<td>11/30</td>
<td></td>
</tr>
</tbody>
</table>

*Exact probability
only 26.5% treated with saline. The difference between the two treatments was highly significant (P<0.001), giving strong evidence for the therapeutic value of $^{169}$Er (Fig. 2).

Comparison of the results between the first follow-up (at 3 months) and the second (at 6 months – 1 year) in the same patients shows a marked improvement with time in the joints treated with $^{169}$Er (P<0.02). Moreover, impairment of excellent and good results occurs less frequently (26.9%) with $^{169}$Er than with saline water (50%), though the difference is not significant (Table 2).

Usually the results of intra-articular radioactive colloid injection closely parallel the radiological lesions as for synovectomy. Better results are seen when the joint is not destroyed. However, in this study there was no significant difference between subgroups according to the Steinbrocker classification (Table 3).

The graphic outlines of multifactorial analysis allow three subgroups of patients to be distinguished according to clinical changes and radiological lesions.

<table>
<thead>
<tr>
<th>Steinbrocker classification</th>
<th>Results</th>
<th>Excellent/Good</th>
<th></th>
<th></th>
<th>Fair</th>
<th></th>
<th></th>
<th>Poor</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>20</td>
<td>62.5</td>
<td>9</td>
<td>28.1</td>
<td>3</td>
<td>9.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>21</td>
<td>51.2</td>
<td>14</td>
<td>34.2</td>
<td>6</td>
<td>14.6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3+4</td>
<td>27</td>
<td>56.3</td>
<td>15</td>
<td>31.3</td>
<td>6</td>
<td>12.5</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Discussion

The activity of $^{169}$Er can be compared to other radioisotopes which have been proved to be very useful in the management of rheumatoid arthritis. A definite improvement was observed in 56% to 58% of cases. According to statistical analysis, the improvement rate was significantly higher with $^{169}$Er compared to corticosteroid therapy with saline water. The doses chosen (1 mCi for MCP joints, 0.5 mCi for PIP joints) seemed to be optimal, at least for moderately inflamed joints.

References


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