Comparative toxicity of gold preparations in
treatment of rheumatoid arthritis

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toxicity of gold preparations in treatment of rheumatoid arthritis. Patients with rheuma-
toid arthritis have been treated alternately with aurothioglucose and aurothiomalate. In
the earlier part of the study an oily suspension of aurothioglucose and an aqueous
solution of aurothiomalate were used, but later an aqueous solution of aurothioglucose
was alternated with the oily suspension and an oily suspension of aurothiomalate with
the aqueous solution. Skin eruptions, stomatitis, and albuminuria were significantly
more common in patients treated with the aqueous solution than with the oily suspension.

Although a number of gold compounds have been used in the treatment of rheumatoid arthritis, few
comparisons have been made of their relative toxicity. Oily suspensions were introduced around
1933 in an attempt to produce a more even concentration of gold in the tissues but clinicians tended to
avoid such preparations for fear that excretion might be delayed in the event of side effects arising.
It is now known that excretion is very slow whatever preparation is used, and it must be considered
whether slow absorption, by avoiding peaks in the blood levels, may not be more advantageous.
Rothermich, Bergen, and Philips (1967) have shown that where gold is given at 2- or 3-week intervals in
maintenance therapy the plasma gold level becomes negligible if a soluble salt is used but the decline is
avoided if an oil-depot preparation is used.

Method

Patients with rheumatoid arthritis attending a rehabilitation clinic were allocated consecutively to one of four
treatment groups.

1. Sodium aurothiomalate in aqueous solution.
2. Sodium aurothionolate in oily suspension.
3. Aurothioglucose in oily suspension.

Dosage in the four groups was identical, varying from
50 to 200 mg weekly, being based on the activity of the
disease as determined by the plasma fibrinogen level
(Lawrence, 1953). When the plasma fibrinogen, estimated
monthly, fell below 450 mg/100 ml on three consecutive
occasions a maintenance dose of 50 mg every second
week was given. Results were assessed after two years’
treatment.

Results

The disease was considered to have become quiescent
when joint pain and swelling had subsided and the
plasma fibrinogen level had returned to normal. No
significant difference was observed in the 2-year
assessment between the four treatment groups with
regard to the number becoming quiescent or im-
proved (Table). The erythrocyte sedimentation rate
attained normal levels and remained so for at least
3 months in 60% of those on an aqueous preparation
and in 62% on an oily suspension. There was thus
no difference in therapeutic effectiveness between
oily and aqueous preparations.

Toxicity, on the other hand, showed very signifi-
cant differences. Skin eruptions were four times as
common in those treated with aqueous preparations,
stomatitis three times, and albuminuria more than
to five times as common in this group. The greater
toxicity with the aqueous preparations applied both
to those treated with aurothiomalate and with
aurothioglucose, and the skin eruptions were
significant with the former.

Discussion

The number of patients treated with aqueous
aurothioglucose and oily aurothiomalate is small
<table>
<thead>
<tr>
<th>Preparation</th>
<th>Total no. of patients</th>
<th>Results</th>
<th>ESR</th>
<th>Toxicity</th>
<th>Skin eruptions</th>
<th>Albuminuria</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Quiescent</td>
<td>Improved</td>
<td>No change</td>
<td>Worse</td>
<td>Stopped attending</td>
</tr>
<tr>
<td>Aurothioglucose</td>
<td>51</td>
<td>9 (18%)</td>
<td>32 (62%)</td>
<td>0</td>
<td>0</td>
<td>10 (20%)</td>
</tr>
<tr>
<td>Oily</td>
<td>11</td>
<td>2 (18%)</td>
<td>5 (46%)</td>
<td>0</td>
<td>0</td>
<td>4 (36%)</td>
</tr>
<tr>
<td>Aqueous</td>
<td>12</td>
<td>5 (42%)</td>
<td>5 (42%)</td>
<td>0</td>
<td>0</td>
<td>1 (8%)</td>
</tr>
<tr>
<td>Oily</td>
<td>51</td>
<td>13 (25%)</td>
<td>28 (55%)</td>
<td>5 (10%)</td>
<td>0</td>
<td>4 (8%)</td>
</tr>
<tr>
<td>Aurothioglucose</td>
<td>63</td>
<td>14 (22%)</td>
<td>37 (59%)</td>
<td>0</td>
<td>0</td>
<td>11NS (17%)</td>
</tr>
<tr>
<td>Total oily</td>
<td>62</td>
<td>15 (24%)</td>
<td>33 (53%)</td>
<td>5 (8%)</td>
<td>0</td>
<td>8NS (13%)</td>
</tr>
<tr>
<td>Total aqueous</td>
<td>62</td>
<td>11 (18%)NS</td>
<td>37 (60%)</td>
<td>0</td>
<td>0</td>
<td>14 (22%)</td>
</tr>
<tr>
<td>Total aurothioglucose</td>
<td>63</td>
<td>18 (29%)NS</td>
<td>33 (52%)</td>
<td>5 (8%)</td>
<td>0</td>
<td>5 (8%)</td>
</tr>
</tbody>
</table>

* P = 0.02 (Fisher's exact test). † P < 0.001. NS, P > 0.05. Data from an earlier trial in which an oily suspension of aurothioglucose was compared with an aqueous solution of aurothiomolate have been included in this table.
since discontinuance of aqueous aurothioglucose preparation by the manufacturers put a stop to the trial. The results, however, already showed a greater toxicity from this preparation and are confirmed significantly by the comparison between aqueous and oily aurothiomalate. In addition to the side effects shown in the Table, two patients developed purpura, one on oily aurothioglucose, the other on aqueous aurothiomalate. The condition subsided in 2 weeks. One patient on aqueous aurothiomalate developed peripheral neuritis. Apart from these 3, and one patient on aqueous aurothiomalate in whom dermatitis and stomatitis persisted for more than 4 months after stopping treatment, it was possible to resume the gold injections at a lower dose level.

Most skin reactions to gold and probably also stomatitis and albuminuria must be regarded as immune reactions in which gold acts as a hapten, since these reactions may occur at any stage of the treatment and are unrelated to levels of excretion (Lawrence, 1961; Gottlieb, Smith, and Smith, 1972). In the present series side effects occurred after a total dosage varying from 0.03 to 4 g and the range was comparable in the various treatment groups.

References


LAWRENCE, J. S. (1953) *Ann. rheum. Dis.*, 12, 129 (Factors in gold dosage and toxicity)


ROthermich, N. O., BERGEN, W., and PHILIPS, V. K. (1967) *Arthr. and Rheum.*, 10, 308 (Use of plasma gold levels in determining dose frequency, type of gold salt and impending toxicity)
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