Long acting somatostatin analogue for the treatment of refractory RA

We read with interest the article by Paran and colleagues on a pilot study of a long acting somatostatin analogue for the treatment of refractory rheumatoid arthritis (RA).\(^1\) The role of peptidergic sensory neurones and the “neurogenic inflammation” in RA and, particularly, in the involvement of substance P (SP) in the articular destruction in experimental arthritis has been demonstrated.\(^2\) High levels of SP have been detected in synovial fluid and plasma samples of patients with RA. It has also been shown that somatostatin inhibits SP release from sensory nerves.\(^3\) Matucci-Cerinic et al. have demonstrated that intra-articular somatostatin induces clinical improvement in patients with RA.\(^4\)

We would like to report our experience, based on a pilot study of treatment for RA with somatostatin analogue (sandostatin). Eleven female patients with classical or definite RA according to American Rheumatism Association criteria were selected for this study with a mean age of 57.4 years and average duration of disease period of 14.5 years. All the patients had previously received multiple disease modifying antirheumatic drugs, but complete remission could not be achieved. Patients who had received any drug except non-steroidal anti-inflammatory drugs during the eight weeks before the start of the study, who had severe renal, pulmonary, renal, or hepatic disease, and who were hypersensitive to both penicillin analogues were not included in the study group. During this treatment, patients were allowed to receive piroxicam and indometacin group NSAIDs.

Sandostatin (Sandostatin) is a synthetic octapeptide derivative of naturally occurring somatostatin.\(^5\) It has also been shown that somatostatin inhibits SP release from sensory nerves.\(^6\) Intra-articular somatostatin analogue for the treatment of refractory rheumatoid arthritis (RA) was reported by Drs. Koseoglu and colleagues in a pilot study on the effect of somatostatin analogue treatment in refractory rheumatoid arthritis in their paper published in the Annals of the Rheumatic Diseases.\(^7\) Evidence that substance P is a mediator of antidromic vasodilatation using somatostatin” as a release inhibitor.\(^8\) A pilot study of a long acting somatostatin analogue for the treatment of refractory rheumatoid arthritis.\(^9\)

Table 1: Patients’ characteristics at the beginning of the study

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Duration of RA</th>
<th>Disease stage*</th>
<th>Drugs used before somatostatin</th>
<th>Drugs used while taking somatostatin</th>
<th>Rheumatoid factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>60</td>
<td>13</td>
<td>III</td>
<td>1, 2, 6, 7, 9</td>
<td>Indometacin</td>
<td>+</td>
</tr>
<tr>
<td>2</td>
<td>66</td>
<td>20</td>
<td>III</td>
<td>1, 2, 6, 7, 9</td>
<td>Indometacin</td>
<td>+</td>
</tr>
<tr>
<td>3</td>
<td>70</td>
<td>25</td>
<td>III</td>
<td>1, 2, 4, 6, 8, 9</td>
<td>Indometacin</td>
<td>+</td>
</tr>
<tr>
<td>4</td>
<td>60</td>
<td>7</td>
<td>III</td>
<td>1, 3, 6, 9</td>
<td>Piroxicam</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>63</td>
<td>30</td>
<td>III</td>
<td>1, 2, 6, 9</td>
<td>Indometacin</td>
<td>–</td>
</tr>
<tr>
<td>6</td>
<td>55</td>
<td>8</td>
<td>II</td>
<td>1, 3, 6, 7, 9</td>
<td>Indometacin</td>
<td>+</td>
</tr>
<tr>
<td>7</td>
<td>60</td>
<td>15</td>
<td>III</td>
<td>1, 4, 6, 7, 9</td>
<td>Indometacin</td>
<td>+</td>
</tr>
<tr>
<td>8</td>
<td>42</td>
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<td>III</td>
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<td>Piroxicam</td>
<td></td>
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<tr>
<td>9</td>
<td>55</td>
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<td>II</td>
<td>1, 2, 6, 8, 9</td>
<td>Indometacin</td>
<td>+</td>
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<tr>
<td>10</td>
<td>57</td>
<td>14</td>
<td>III</td>
<td>1, 2, 3, 6, 9</td>
<td>Indometacin</td>
<td>+</td>
</tr>
<tr>
<td>11</td>
<td>55</td>
<td>6</td>
<td>II</td>
<td>1, 5, 6, 9</td>
<td>Indometacin</td>
<td>+</td>
</tr>
</tbody>
</table>

*Classified using the criteria of Steinbrocker, et al.

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Authors’ response

We read with interest the letter by Drs Koseoglu and Koseoglu, in which they report a pilot study on the effect of somatostatin analogue treatment in refractory rheumatoid arthritis (RA). Their study is similar to our
study in size and patient characteristics but differs in three major points: the dose of somatostatin analogue and the preparation used; the length of the study; and the criteria employed to assess a therapeutic response.

The dose of octreotide (sandostatin) used in their study was low (100 µg once a day). When using subcutaneous octreotide 100 µg/day injections to treat other conditions, such as acromegaly, the accepted dose is 100 µg three times a day owing to the peptide’s short half life. A dose of subcutaneous octreotide 100 µg/day may not be sufficient to achieve a significant effect. This may explain the more marked effect seen in our study, where octreotide was given as a long acting preparation that produces therapeutic doses of octreotide (equivalent to 100 µg subcutaneously three times a day) for a period of four weeks after injection.

Koseoglu and Koseoglu conducted a shorter study of only eight weeks as compared with our 14 week study, where we saw continued improvement after eight weeks.

Moreover, accepted American College of Rheumatology criteria for the evaluation of response to treatment in patients with RA were not used, making it difficult to compare the results. Despite the different methodology Koseoglu and Koseoglu showed a similar, significant beneficial effect of somatostatin analogue treatment on the assessment of pain: “pain intensity”, and “joint sensitivity”, with only mild adverse effects.

This pilot study supports our conclusion that treatment with a somatostatin analogue may be beneficial in the treatment of RA, and that further, large, placebo controlled studies are required to evaluate this drug as a potential disease modifying antirheumatic drug for patients with RA.

D Paran, O Elkayam, H Paran, M Yaron, D Caspi
Department of Rheumatology, Tel-Aviv Sourasky Medical Centre, 6 Weizmann Street, Tel-Aviv 64329, Israel

Correspondence to: Dr D Paran; paran620@weizmann.ac.il

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Further details can be obtained from: Miss Lisa McClair, ARC Epidemiology Unit, Stopford Building, University of Manchester, Oxford Road, Manchester, M13 9PT, UK. Tel: (0) 161 275 5993, Fax: (0) 161 275 5043. Email: Lisa@fs1.serner.man.ac.uk

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F Koseoglu and T Koseoglu

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