Correspondence

Systemic effects of intra-articular steroid preparations

Sir,
The beneficial, long-lasting local effect of triamcinolone hexacetonide versus other intra-articularly administered steroids is explained by the very low solubility of the drug in synovial fluid. Indeed, the low solubility of triamcinolone hexacetonide in water was demonstrated by Hollander. Accordingly one would expect systemic effects of this preparation to be minimal and their appearance to be delayed. We were therefore surprised at the results published by Bird et al. showing early onset of systemic effects of intra-articular triamcinolone hexacetonide injections, slowly abating after 4 weeks.

We have studied 10 ambulatory patients with rheumatoid arthritis, none of them having received steroid treatment before. All patients had synovial fluid aspirated before receiving an intra-articular injection of 20 mg triamcinolone hexacetone (Lederspan) in 1 ml in one affected knee, just as described in Bird’s publication, who tested 10 of their patients with the same preparation.

The only limitation imposed on our patients after injection was to reduce their physical activity for 24 h and to wear an elastic knee bandage for that period, modified from the customary advice after local yttrium-90 treatment.

We followed the systemic effects of the steroid injection on the pituitary-adrenal axis. Blood samples for plasma cortisol and ACTH were always taken at 10 am on the days indicated, and assayed by standard radioimmunoassay. Results see Table.

Thus, contrary to the report by Bird et al., we found no early suppression of endogenous cortisol (corroborated by the results obtained with ACTH) Our finding of systemic effects of borderline significance on cortisol at 14 days fits the expected late effects due to low solubility of triamcinolone hexacetone. One possible explanation for the late occurrence of systemic effects in our patients may be due to reduction of movement in the injected knee by limiting physical activity and mild splinting. Bird et al. did not describe such precautions. These measures may have caused less of the injected steroid to leave the joint and thus reduced leaking of the drug into the systemic circulation, resulting in attenuated systemic effects.

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References


<table>
<thead>
<tr>
<th>ACTH (pg/ml)</th>
<th>Plasma cortisol (µg/100 ml)</th>
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<tbody>
<tr>
<td>Day 0 (before inj.)</td>
<td>28-2-9-3</td>
</tr>
<tr>
<td>Day 2-3</td>
<td>30-6±13-2</td>
</tr>
<tr>
<td>Day 5-7</td>
<td>29-0±14-3</td>
</tr>
<tr>
<td>Day 10</td>
<td>29-0±14-3</td>
</tr>
<tr>
<td>Day 14</td>
<td>36-9±15-4</td>
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<tr>
<td>Day 21</td>
<td>(—)</td>
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</table>

All values are expressed as mean ± SD. None of these differences were statistically significant, except cortisol day 0 versus day 14, which reaches borderline significance (t=2.38; P=0.05).

This letter has been shown to Dr Bird, whose reply follows.

Sir,

In our study of intra-articular steroid preparations blood samples for plasma cortisol were taken at 10.30 a.m. ± 30 minutes and assayed in random order without knowledge of patients or drugs. The difference between our results and those of Dr Weiss et al. appears a real one, though the depression of endogenous cortisol we observed with triamcinolone hexacetonide was less than that seen with the 2 other preparations tested.

The hypothesis that splinting of the joint delays escape of exogenous steroid is the most attractive one. Our inpatients continued immediately with their physiotherapy and the outpatients were encouraged to exercise, instructions prompted by our failure to delay escape of intra-articular methotrexate with immobilisation in a previous study and our wish to simulate the majority of outpatient injection clinics. The suggestion that immobilisation delays escape of intra-articular steroid, not necessarily synonymous with increased therapeutic effect, has economic implications and should be possible to test now that high-pressure liquid chromatography has made exogenous steroid assays easier. Our demonstration of consistent thermographic improvement in the noninjected knees of triamcinolone-treated patients alone, in our double-blind study, remains unexplained. Neither study excludes a rapid leak of triamcinolone within the first 24 hours, though we agree that on theoretical grounds of insolvency this is unlikely.

While triamcinolone hexacetonide with immobilisation may be the steroid treatment of choice in rheumatoid synovitis of the knee, it must be emphasised that neither study was designed to determine whether the 'best' steroid,
by virtue of its insolubility, extended side-chain, or fluorine atom, also carries the ‘best’ side-effects.

H. A. BIRD
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University of Leeds.

References

Visual analogue pain scales
Sir,

We read with interest the paper by Jane Scott and E. C. Huskisson.1 As a result of their study the authors concluded that either the horizontal or the vertical visual analogue scale (VAS) is satisfactory in the measurement of pain. Unfortunately they did not give any details about the patients used for their study, mentioning only that they suffered from painful conditions.

In our experience the vertical VAS can be misinterpreted by patients suffering from spinal diseases. Recently we studied the vertical and horizontal VAS in 200 consecutive, unselected cases of degenerative spinal diseases. None of them had seen any type of scales before. A standard explanation of the method was given to all of the patients by the same observer. One hundred patients were asked to complete the horizontal VAS and the other 100 patients the vertical one. In addition a simple descriptive pain scale was also used for comparison. It was found that in 6 cases using the vertical VAS there was a clear contradiction between the results of the vertical pain scale and the simple descriptive one. As it turned out, these patients considered the vertical VAS to be a representation of the spinal column, the upper end representing the cervical part and the lower one the lumbosacral region. They labelled the spinal level of their pain on the vertical line, misunderstanding the aim of the method. Therefore we would advise against the use of the vertical VAS in cases with painful spinal conditions.

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References

Systemic lupus erythematosus and pulmonary manifestation
Sir,

Grennan et al.1 reported in this journal a high frequency of clinical evidence and abnormalities of lung function in patients with systemic lupus erythematosus (SLE) suggestive of pulmonary involvement. Fourteen out of 22 SLE patients had respiratory symptoms, but in only 4 patients were abnormalities of chest radiographs observed. Fourteen patients revealed reduced transfer factor, 5 of them in association with restrictive defects.

We have investigated 31 patients with SLE in regard to pulmonary involvement and found our results to be different from those in the above mentioned study. We observed respiratory symptoms only in 10 patients (32%), whereas chest radiographs showed abnormalities in 21 patients (68%) (Table 1). We found concomitant obliteration of costophrenic angle and diaphragmatic elevation or segmental atelectasis and diaphragmatic elevation in 6 cases each.

Lung function analysis included spirography, plethysmography, measurement of diffusing capacity and of compliance (for details in methods see Scherthaner et al.). The results are shown in Table 2. Eight patients (26%) had normal results of lung function analysis. Seventeen patients showed restrictive ventilatory defects, 18 patients had a diminished lung compliance, and 12 patients had reduced diffusion capacity. In 9 of these patients restriction was observed in association with loss of compliance and reduced transfer factor, and in 5 patients restriction occurred together with decreased compliance. Restrictive defects alone were observed in 4 patients, disturbance of compliance alone in 4 patients, and reduced transfer factor in 2 patients. Restriction and loss of compliance showed the highest frequencies.

Grennan et al.1 observed restrictive defects in a similar percentage but lung compliance was not performed. In contrast to the results of Grennan et al.1 we observed a lower incidence of reduced diffusing capacity despite the lack of correction for alteration in haemoglobin concentration. The reason for this difference is not clear. However, our results of transfer factor are in good agreement, with other reports.4,5

Like Grennan et al.1 we could not observe a low incidence of lupus nephritis in patients with pulmonary involvement as mentioned by Holgate et al.6 In our study patients with restriction, loss of compliance, and/or

Table 1 Radiological features of 31 SLE patients

<table>
<thead>
<tr>
<th>Number of cases</th>
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<tbody>
<tr>
<td>Normal chest radiograph</td>
</tr>
<tr>
<td>Obliteration of costophrenic angle</td>
</tr>
<tr>
<td>Pleural effusion</td>
</tr>
<tr>
<td>Segmental atelectasis</td>
</tr>
<tr>
<td>Diaphragmatic elevation</td>
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<td>Reticulo-nodular shadowing</td>
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</table>

Table 2 Lung function analysis in 31 SLE patients

<table>
<thead>
<tr>
<th>Abnormal</th>
<th>Vital capacity (% predicted value)</th>
<th>Specific compliance (ml/cmH2O l)</th>
<th>Specific diffusion capacity (ml/min/Torr l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MV±SD*</td>
<td>84.8±23.1</td>
<td>0.53±0.012</td>
<td>4.85±1.48</td>
</tr>
<tr>
<td>4/10*</td>
<td>54.8</td>
<td>38.0</td>
<td>38.7</td>
</tr>
</tbody>
</table>

*Mean value ± standard deviation.
**Percentage of patients with abnormal lung function parameter.