Insulin injection sites in diabetes—a neglected area?

The process of injecting insulin is deceptively simple and has accordingly been neglected.1 The demonstration that the absorption of insulin varies between different anatomical sites2 is likely to be important clinically, and abnormalities at injection sites may modify insulin absorption.2,4 In anticipation of the need to offer new guidelines on injection procedure we have reviewed current practice and problems.

Patients and results

The practice of insulin administration and the prevalence of injection site abnormalities were studied in 224 patients selected at random from a diabetic clinic. Initially all patients had been instructed to administer insulin using the standard injection areas (arm, leg, and abdomen) in regular rotation and to use multiple injection sites within these areas. The current sites of injection were documented, and the degree of adherence to a system of rotation of injection sites between or within areas was established. All injection sites were examined and abnormalities were classified as lipoatrophy (subcutaneous hollows) or lipohypertrophy (soft subcutaneous swelling).

The leg was used most frequently for injection (195 patients) while the abdomen (74) and the arm (56) were less favoured. Most patients (140) restricted injections to only one of these areas and 87 patients always used localised injection sites within one such anatomical area. Most patients (152) had some routine of changing the site of insulin injections, even if this was just using alternate sides of the body, but the remainder injected in a random manner with no premeditated plan.

Conventional insulins had been used at some time by 176 patients, of whom 106 (60%) had been aware of some problem at the injection site with using this insulin. By contrast, only 3% of the 48 patients who had used only the highly purified insulins noticed abnormalities. Inspection of the areas used for injection showed that the patients who were still taking conventional insulins had a lower proportion of problems than reported, while those using highly purified insulins had a higher prevalence, with lipohypertrophy being found in 27 (21%) (table). There were more women among those with lipoatrophy, and 32 of the 41 patients now taking highly purified insulins who had reported lipolysis while using conventional insulins were women. No sex or age difference was associated with lipohypertrophy (table). Almost all patients with lipohypertrophy used only one anatomical area for injection with a restricted injection site, whereas the corresponding proportions for those with lipohypertrophy were much lower (table). Twenty-three patients who had lipohypertrophy when taking highly purified insulins had taken conventional insulins previously, and 18 of these patients had experienced lipoatrophy.

Prevalence of lipoatrophy and lipohypertrophy and factors associated with their development in 224 insulin-dependent diabetic patients aged 12-83 years (mean 38 years). Results expressed as number (%) of patients

<table>
<thead>
<tr>
<th></th>
<th>Lipoatrophy</th>
<th>Lipohypertrophy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients using conventional beef insulin (n = 98)</td>
<td>16 (16)</td>
<td>14 (14)</td>
</tr>
<tr>
<td>Patients using highly purified pork insulin (n = 126)</td>
<td>0 (0)</td>
<td>27 (22)</td>
</tr>
<tr>
<td>Total</td>
<td>16</td>
<td>41</td>
</tr>
</tbody>
</table>

Of patients with complications:

<table>
<thead>
<tr>
<th></th>
<th>Lipoatrophy</th>
<th>Lipohypertrophy</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of men</td>
<td>5 (31)</td>
<td>21 (51)</td>
</tr>
<tr>
<td>No of women</td>
<td>11 (69)</td>
<td>20 (40)</td>
</tr>
<tr>
<td>No who used only one anatomical injection area</td>
<td>9 (56)</td>
<td>38 (93)</td>
</tr>
<tr>
<td>No who used restricted injection site</td>
<td>10 (63)</td>
<td>33 (61)</td>
</tr>
</tbody>
</table>

Comment

This survey confirms the clinical impression that few patients rotate the injection of insulin to all three anatomical areas as initially instructed. Lipohypertrophy was confined to those patients using conventional insulins, while a similar proportion and sex distribution was found in those in previous reports.4 Lipohypertrophy, however, was present in about 20% of patients taking the highly purified pork insulins, and this high prevalence has not been documented previously. Lipohypertrophy was associated with the repeated use of a restricted injection site within a single anatomical area, and there was no sex difference. It is possible that the continued use of one particular area may achieve consistency of absorption of insulin.2 It is not known whether the presence of the lesions of lipohypertrophy influence insulin absorption, though there is some suggestion that this may be so.2,4 Since few patients are aware of lipohypertrophy or report its presence unless it is severe we suggest that injection sites should be reviewed at regular intervals.

We are grateful to Mrs S Dickson for secretarial help and to Mrs M Oliver for typing the manuscript.


(Accepted 13 May 1981)

Diabetic Department, Royal Infirmary, Edinburgh EH3 9YW

R J YOUNG, MB, MCPr, registrar
J M STEEL, MB, MCPr, senior registrar
B M FRIER, MB, MCPr, senior registrar
L J F DUNCAN, FCP(c), consultant physician

Toxic confusional state and choreiform movements after treatment with anabolic steroids

Oxymetholone is a C-17-substituted steroid with minimal androgenic effects. It is used, often illicitly by athletes, for its anabolic activity and is also used as a narrow stimulant in treatment of aplastic anaemia. Its value in aplastic anaemia is not completely established, but many authorities regard it as the treatment of choice.1 Response may be delayed for up to six months, and it has several side effects: cholostatic liver dysfunction is common, as are hirsutism and deepening of the voice in women. A coarse tremor is often associated with high doses, and, rarely, hepatocellular carcinoma and possibly acute leukaemia may be induced. Neither psychosis nor extrapyramidal syndromes have been recorded previously.

We describe a patient who developed a toxic confusional state and choreiform movements after treatment with anabolic steroids.

Case report

A 66-year-old man presented in September 1979 with the features of severe anaemia. Apart from pallor and breathlessness, the only clinical finding was of perivascular haemorrhages in the fundi. He had been a vegetarian for three years and had a schizophrenic daughter and a severely affected haemophilic son. Despite these provocations, he had no history of psychiatric illness. Full blood count showed a haemoglobin concentration of 5 g/dl, white blood count of 4.1 × 10⁹/l, with 53% neutrophils, mean cell volume of 110 fl, and platelet count of 22 × 10⁹/l. Serum B₄ and folate concentrations were normal, and bone marrow biopsy showed aplastic anaemia. The only other abnormality found was a deficiency of serum IgA.

He was given a transfusion of six units of packed red cells and started on oxymetholone 200 mg daily. Despite this his haemoglobin concentration continued to fall so that he required repeated transfusions, and his platelet count fell to less than 10 × 10⁹/l, which was associated with purpura and spontaneous bruises. Oxymetholone was increased to 250 mg daily in December and to 300 mg daily in March 1980. From February 1980 he was treated with tranexamic acid 1.5 g daily in an attempt to reduce his transfusion requirement. In June 1980 his haemoglobin concentration started falling, his platelet count began to rise, and the tranexamic acid was stopped. By July his blood count was essentially normal, though still slightly macrocytic. During this time he had suffered none of the known side effects of oxymetholone. In August, oxymetholone was reduced to 250 mg daily and in September to 200 mg daily.

On 22 September 1980 he was readmitted in a severely confused state. This had come on gradually over the course of 10 days, starting with feelings of dizziness and difficulty in driving. He had become progressively more restless, making uncontrolled movements and talking in a morbid and uncontrolled manner. He had ideal of imminent death and strong guilt feelings. On examination his speech was disjointed and incoherent and he...
Effect of prostaglandins I2 and E1 on red cell deformability in patients with Raynaud’s phenomenon and systemic sclerosis

The deformability of red blood cells measured by a filtration technique using whole blood has been found to be decreased in some patients with Raynaud’s phenomenon and greatly improved by plasmapheresis.1 Prostaglandins E1 and I2 (PGI2) administered intravenously have produced prolonged benefit in patients with symptomatic Raynaud’s phenomenon associated with systemic sclerosis. To elucidate the possible mechanism of action of these drugs we measured red cell deformability in plasma-free conditions in 12 patients with systemic sclerosis and Raynaud’s phenomenon.

Subjects, methods, and results

Red cell deformability was measured in 12 patients with Raynaud’s phenomenon and systemic sclerosis and 12 normal controls matched for age and sex. It was also measured immediately before and after the infusion of PGI2 (seven patients) and PGE, (five patients). PGI2 and PGE, were administered as infusions through centrally placed intravenous catheters (total duration 72 hours). The dose of PGI2 varied from 5 to 7.5 μg/kg/min, and the dose of PGE, was increased from 6 to 12 ng/kg/min by increments of 2 ng/kg/min. Red cell deformability was measured using the original technique of Schmid-Schonbein et al2 with Reid’s technical modification. Plasma-free conditions were used to ensure that the observed effects were on the red cells and not other constituents of whole blood.

Red blood cells were obtained from heparinized venous blood by centrifugation and washed three times in phosphate-buffered saline (pH 7.4) containing 0.25% human albumin. The final red blood cell suspension (10% v/v) was resuspended through a Nucleopore polycarbonate sieve of pore diameter 3 μm, with a negative pressure of 10 cm water. After a steady flow through the filter had been achieved the filtration time per ml volume was measured from 1 ml to 10 ml volume and plotted on semilog paper. The slope of this line represented the deformability (ml/min). Standard conditions were used. Tripleclic determinations were performed on each sample of venous blood, the assay being performed in all cases within two hours of venepuncture at a temperature of 21 ± 1°C.

Results

Raynaud’s phenomenon was significantly different between the patients and controls, the mean ± SEM blood flow/min being 0.257 ± 0.02 ml/min in the patients (two women, 10 men) compared with 0.512 ± 0.04 ml/min in the controls (p < 0.001).

Mean blood flow/min measured by filtration immediately before the infusion of PGI2 (seven patients) and PGE, (five patients) for Raynaud’s phenomenon confirmed the presence of reduced red blood cell deformability in these patients (table). After the 72-hour infusions of PGI2 and PGE, the mean blood flow/min—that is, red blood cell deformability—was increased (p < 0.05 and p < 0.01 respectively).

<p>| Deformability of red blood cells from patients with systemic sclerosis before and after infusions of PGI2 and PGE, |</p>
<table>
<thead>
<tr>
<th>No of subjects</th>
<th>Mean ± SEM red blood cell filtration (blood flow/min)</th>
<th>Effect of infusion</th>
<th>Patients improved</th>
<th>No change</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before</td>
<td>After</td>
<td>Infusion of PGI2</td>
<td>Infusion of PGE</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.269 ± 0.03</td>
<td>0.218 ± 0.01</td>
<td>0.413 ± 0.06</td>
<td>0.400 ± 0.04</td>
</tr>
</tbody>
</table>
*Measured by 3 μm pore diameter filter.

Comment

PGE, affects different functions of platelets, polymorphonuclear leucocytes, and lymphocytes and increases both the deformability and the cyclic adenosine monophosphate content of red blood cells. Moreover, recent evidence suggests a role for cyclic nucleotides in regulating the shape and permeability of red blood cells.3 The effect of PGI2 on red blood cell behaviour has not been described previously. The decreased red blood cell deformability in patients with Raynaud’s phenomenon and systemic sclerosis may have pathophysiological importance, contributing to the microcirculatory insufficiency by increasing the occlusion of small blood vessels and blood viscosity at low shear rates. Possibly the decreased red blood cell deformability in patients with Raynaud’s phenomenon and systemic sclerosis may be linked to a deficiency of cyclic adenosine monophosphate in the red cells of these patients, and the PGI2 and PGE, may increase the red cell deformability by increasing the intra-cellular content of cyclic adenosine monophosphate.


(accepted 13 May 1981)

Departments of Dermatology and Clinical Pharmacology, St Bartholomew’s Hospital, London EC1 7BE

Pauline M Dowd, Bsc, Mrcp, senior registrar
Iren B Kovacs, MD, PhD, research fellow
C J H Bland, MB, ChB, house physician
J D T Kirby, Mrcp, consultant