

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.^{3,4} 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 while using this insulin. By contrast, only three 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 lipoatrophy 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 lipoatrophy 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

	Lipoatrophy	Lipohypertrophy
Patients using conventional beef insulin (n = 98)	16 (16)	14 (14)
Patients using highly purified pork insulin (n = 126)	0 (0)	27 (22)
Total	16	41
Of patients with complications:		
No of men	5 (31)	21 (51)
No of women	11 (69)	20 (49)
No who used only one anatomical injection area	9 (56)	38 (93)
No who used restricted injection site	10 (63)	33 (81)

Comment

This survey confirms the clinical impression that few patients rotate the injection of insulin to all three anatomical areas as initially instructed. Lipoatrophy was confined to those patients using conventional insulins, with a similar prevalence and sex distribution to those in previous reports.⁵ 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.^{3,4} Since few patients are aware of lipohypertrophy or report its presence unless it is severe we suggest that injection sites should be inspected at regular intervals.

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¹ Anonymous. Subcutaneous injections and absorption of insulin. *Lancet* 1980;ii:1005-6.

² Koivisto VA, Felig P. Alterations in insulin absorption and in blood glucose control associated with varying insulin injection sites in diabetic patients. *Ann Intern Med* 1980;92:59-61.

³ Balodimos MC, Williams RH. Absorption of 131 I insulin from subcutaneous tissue in diabetic patients. *Am J Med Sci* 1962;243:103-10.

⁴ Root HF, Irvine JW, Evans RD, Reiner L, Carpenter TM. Absorption of insulin labelled with radioactive iodine in human diabetes. *JAMA* 1944;124:84.

⁵ Reeves WG, Allan BR, Tattersall RB. Insulin-induced lipoatrophy; evidence for an immune pathogenesis. *Br Med J* 1980;280:1500-3.

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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 marrow 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: cholestatic 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 5.0 g/dl, white blood count of $4.1 \times 10^9/l$, with 53% neutrophils, mean cell volume of 110 fl, and platelet count of $22 \times 10^9/l$. Serum B_{12} 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 $10 \times 10^9/l$, 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 stopped 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.

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 ideas of imminent death and strong guilt feelings. On examination his speech was disjointed and incoherent and he