Lipohypertrophy – a complication of insulin injections

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To the Editor: Lipohypertrophy and lipoatrophy of injection sites was a major problem with the old impure insulins.[1] The problem improved somewhat with the advent of the monocomponent bovine and porcine insulins and the current pure human insulins, such that lipoatrophy in particular is now very rare.[1,2] However it now manifests more subtly, with thickening of the skin rather than the formation of lumps and pitting. Even diabetologists have been known to miss it, when not looking for it carefully. The complication has occurred with the new genetically engineered modified human insulins, with and without continuous subcutaneous insulin infusions.[2-4] The question is whether there will ever be any form of insulin therapy that will be without complications.

Lipohypertrophy occurs because patients inject the same site day after day. It frequently occurs on both sides of the umbilicus or in the mid-thigh areas[1] as these are convenient places to inject,[5] and where the patient's hands reach most naturally. Eventually the area becomes hyposensitive. Once the patient feels pain when injecting elsewhere, but not in the lipohypertrophic area, he or she tends to continue injecting in the same site even if aware of the need to rotate sites.

Some classification systems[6,7] neglect subtle lipohypertrophy that is not visible but only palpable, and also add lipoatrophy as the most severe form. Grouping lipohypertrophy and lipoatrophy together is inappropriate: separate mechanisms have been suggested as a cause – lipoatrophy may result from a local immune reaction against impurities of the insulin preparations, while lipohypertrophy may result from the local trophic action of insulin.[7,8] Furthermore, cases of severe lipoatrophy without pre-existing lipohypertrophy have been described.[2] Rare lipohyper- trophy syndromes associated with diabetes exist and have a poor prognosis;[9,10] the term has been inappropriately used to describe the local occurrence of lipohypertrophy due to injected insulins.[5,7]

The objective of this study was to describe the appearance and prevalence of lipohypertrophy in a paediatric diabetic clinic.

All patients should be closely examined for lipohypertrophy at every clinic visit, using inspection and palpation of injection sites. An audit was done of the files of children attending the Endocrine Clinic, Ga-Rankuwa Hospital, Pretoria. Data collected included patient age, duration of diabetes, number of clinic visits and those visits on which an examination for lipohypertrophy was recorded, presence and severity of the condition, treatment prescribed and the response to treatment.

Twenty-three patients between the ages of 6.5 and 18.5 years were included in the study (11 males and 12 females). The duration of diabetes varied from 1 to 16 years, with 13 patients having had diabetes for less than 5 years and only 2 having had it for more than 10 years. They had attended the clinic for a mean of 20.8 visits, but there was a wide variation, from 2 to 48 visits. Five patients had never been checked for lipohypertrophy, and 3 had only been checked once or twice. However, 10 patients had been checked 9 times or more. Lipohypertrophy had not been detected in 11 patients; this included the 5 patients who had never been checked as well as 3 patients who had only been examined once or twice. The condition therefore had a prevalence rate of 52% in our population. Counting only those patients who had been examined on several occasions, the prevalence rate for lipohypertrophy was 80%. It was mild in 6 patients, moderate in 3 and severe in 2 (1 was not categorised), the categorisation depending on the judgement of the attending doctor. The condition was not present in the 2 patients who had had diabetes for 1 year, while it was present in 3 of the 4 with disease duration of between 1 and 3 years. Of the 12 patients with lipohypertrophy, 4 were told to change injection sites, and 7 were taught a system of site rotation. Seven cases improved.

The significant ($p < 0.05$) correlations (Pearson's correlation coefficient) between the factors (frequency of lipohypertrophy checking, presence of lipohypertrophy, severity, treatment prescribed and response to treatment) were expected, as was the correlation between number of visits and frequency of lipohypertrophy checking. Stepwise multiple linear regressions were performed, with the presence of lipohypertrohy as the dependent factor. Two factors, namely severity of lipohypertrophy and treatment prescribed, were included in the model and described 86% of the variance.

There was a high awareness of the condition among the clinic staff and it was examined for at least once in 78% of the patients. This study found that lipohypertrophy was common, with a prevalence rate of 52% overall, 67% in those patients where examination for lipohypertrophy was recorded, and 80% in those examined frequently for the occurrence of the condition. It was not recognised by patients and parents, which is similar to findings elsewhere.[1] It requires re-education if improvement is to occur. In our study the condition did not develop in the first year, although it occurred very soon thereafter. Where it occurs, it has been shown to develop in half of patients within the first 2 years and three-quarters within the first 5 years.[8]

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Lipohypertrophy has occurred with continuous insulin delivery systems, i.e. subcutaneous indwelling catheters[12] and insulin pump therapy.[2,3] Subcutaneous indwelling catheters are placed for a period of 4 - 5 days.[12] Patients are instructed to avoid areas of lipohypertrophy, but as has been noted above the condition is not necessarily recognised by patients and they may place catheters in areas where early lipohypertrophy is already present.

In the past, lipohypertrophy and lipoatrophy caused obvious changes to the skin, and the effects were cosmetically disturbing for patients. With more subtle presentation, there is less incentive for the patients to try to avoid lipohypertrophy. However, injecting in lipohypertrophic areas affects the rate of absorption of the insulin, contributing to erratic blood glucose control.[11,13]

Rotation schemes may not distribute injections widely over the largest target area. For example, one scheme (left, right thigh and/or left, right abdominal area)[6] results in either 2 or 4 target areas, but leaves where in that area to inject to the discretion of the patient. In that case, insulin may well still be injected in only a few concentrated target areas, a problem noted before.[5] A scheme dividing the abdomen into 9 zones, with 2 imaginary parallel horizontal and vertical lines peri-umbilically, will ensure that an injection is only repeated in an area after about 4 days, and is therefore more likely to be effective than 'site rotation'.

It has been recommended that in order to diagnose the condition sites should be palpated and not just visually examined.[1] In order to feel subtle skin thickening the hand should be stroked firmly over the injection sites in a sweeping motion rather than using traditional techniques of light and deep palpation.

Lipohypertrophy is difficult to recognise. Extensive education is required, firstly of doctors so that they can learn to recognise the problem and be encouraged to examine closely, by palpation, for presence of the disorder. Secondly, patients need to be educated that they can avoid the problem, and to be re-educated where the problem has already occurred.

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