Introduction

Lipoatrophy (LA) was commonly seen with insulin use prior to the 1970s, occurring in 25–55% of patients using conventional bovine or porcine insulin.1 The incidence of LA fell to less than 10% with the introduction of highly purified insulin1 and it has been largely unreported and hence considered extremely rare since the development of recombinant human insulin and insulin analogues. In the past decade, however, there has been an increase in reports of LA among patients using various rapid- and long-acting analogue insulin preparations. Lipoatrophy is more commonly seen in young people,1 therefore its incidence is particularly relevant in a paediatric setting. The presence of LA is clinically significant because it may lead to impaired insulin absorption and instability of blood glucose control. Furthermore, its adverse cosmetic effects can cause distress to patients and their carers.

Case reports

We retrospectively collected data on patients identified with LA from our clinic population of 328 patients. Over a two-year period, four patients with type 1 diabetes presented with LA (see Table 1). All four patients were female, and receiving treatment with insulin aspart (NovoRapid) via a continuous subcutaneous insulin infusion (CSII) pump for the management of type 1 diabetes. We did not observe any cases of lipoatrophy in patients receiving multiple daily insulin injections. In examining the effect of lipoatrophy on glycaemic control, we found no detrimental effect of lipoatrophy on the patients’ glycosylated haemoglobin.

Discussion

Lipoatrophy is a rare and likely under-reported complication of insulin therapy, which appears to be re-emerging. Lipoatrophy represents destruction of subcutaneous fat and presents with well demarcated, depressed areas at sites of insulin administration, typically following 6–24 months of regular insulin treatment. We present four cases of LA: all female, and all on CSII with insulin aspart. This raises a number of interesting points.

Abstract

Over the last decade, there has been an increase in reported cases of lipoatrophy as a complication of treatment with analogue insulin preparations. Lipoatrophy causes undesirable cosmetic appearances and may cause variable glycaemic control.

We report a case series of four female patients from a tertiary paediatric diabetes unit presenting with lipoatrophy while on treatment with insulin aspart via a continuous subcutaneous insulin infusion (CSII) pump for the management of type 1 diabetes. We did not observe any cases of lipoatrophy in patients receiving multiple daily insulin injections. In examining the effect of lipoatrophy on glycaemic control, we found no detrimental effect of lipoatrophy on the patients’ glycosylated haemoglobin.

Cases of lipoatrophy should be reported to drug manufacturers and through the appropriate national adverse drug reaction reporting system. This will facilitate observation of trend, and help monitor for associations, informing future research. Copyright © 2014 John Wiley & Sons.

Key words
diabetes; lipoatrophy; paediatrics; CSII

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The precise mechanism of LA is still unknown, although it is considered to be an immunological phenomenon. This theory is supported by the presence of IgM, IgA, C3 and fibrin in LA lesions and a response to steroid therapy in a number of cases.2,3 Our case series suggests that the continuous exposure to insulin via CSII may play a role in inducing the immunogenic response. Reports of LA occurring with insulin analogues via injections2,3 and pump therapy4,5 imply that the mechanism may be independent of the delivery system. However, this observation may not necessarily be applicable to a paediatric population. In theory, infusion of insulin and maintaining the catheter at the same site over a number of days could predispose to the development of LA, since the repeated administration of insulin to a particular area has been identified as a contributing factor.1,2 It is conceivable that, in young children, sites for cannula insertion for CSII may be limited, leading to a decrease in the recommended rotation of insertion sites, compared to rotation of injection sites with multiple daily injections. This is supported by our data series where LA presented only in patients on CSII. In addition, previous studies and reports have described an increased incidence of LA in females,2,3 a point highlighted by the demographics of our case series. Further research by Salgin et al. in 20136 showed that Hashimoto’s thyroiditis and coeliac disease – both autoimmune conditions, and with a higher prevalence in females – were more prevalent in patients with LA. Lipoatrophy was also associated with an increased risk of Hashimoto’s thyroiditis and coeliac disease in female patients.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age (years)</th>
<th>Duration of diabetes (years)</th>
<th>Duration of CSII use (years)</th>
<th>Total daily dose (units/kg)</th>
<th>Site of LA</th>
<th>HbA1c (%) 3 months prior to LA diagnosis</th>
<th>HbA1c (%) at LA diagnosis</th>
<th>Follow up (months)</th>
<th>LA resolved (Y/N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>3</td>
<td>1.5</td>
<td>1.3</td>
<td>0.7</td>
<td>Buttock</td>
<td>7.1</td>
<td>6.9</td>
<td>4</td>
<td>N</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>7</td>
<td>3.3</td>
<td>3.25</td>
<td>0.8</td>
<td>Abdomen</td>
<td>8.3</td>
<td>7.8</td>
<td>8</td>
<td>N</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>8</td>
<td>5.6</td>
<td>2.45</td>
<td>0.7</td>
<td>Thigh</td>
<td>8.9</td>
<td>7.7</td>
<td>25</td>
<td>N</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>10</td>
<td>4.9</td>
<td>1.6</td>
<td>0.4</td>
<td>Abdomen</td>
<td>6.8</td>
<td>7</td>
<td>9</td>
<td>N</td>
</tr>
</tbody>
</table>

Table 1. Demographic data in patients identified with lipoatrophy (LA)

Figure 1. Patient 1: lipoatrophy on buttock (arrowed)

Figure 2. Patient 2: lipoatrophy on abdomen (arrowed)
sites, substituting insulin brands, the use of oral or injected corticosteroids, and the use of topical disodium cromoglycate ointment.\textsuperscript{2,3,7} Noud et al. in 2009\textsuperscript{8} also suggested the novel approach of peritoneal insulin in a patient with intractable LA. At this time, the use of corticosteroids appears to be the most effective method for achieving complete remission of LA.\textsuperscript{5} In our case series, we advised rotation away from the areas of LA as the initial management strategy allowing for a period of observation before resorting to alternative forms of management. All patients continue to be followed up.

Conclusions
Understanding the risk factors for developing LA and ultimately understanding the pathogenesis of LA will be useful in modifying the treatment options in the future.

We recommend further research in this area. Cases of LA should also be reported to drug manufacturers and through the appropriate national reporting system for adverse drug effects. This will facilitate observation of trend, and help monitor for associations, informing further research.

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Declaration of interests
There are no conflicts of interest declared. Source of funding: none.

References