Cromolyn Sodium for Insulin-Induced Lipoatrophy: Old Drug, New Use

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**OBSERVATIONS**

Cromolyn Sodium for Insulin-Induced Lipoatrophy: Old Drug, New Use

Local insulin-induced lipoatrophy, an immune-mediated loss of subcutaneous adipose tissue at insulin administration sites, is now a rare complication of insulin therapy in patients with diabetes. Lipoatrophy incidence, previously noted in 10–55% of patients using animal-derived insulins (1), declined considerably with the advent of improved purity of modern insulins. Yet, it continues to be reported with insulin analogs (2,3) and poses a clinical challenge owing to erratic insulin absorption at affected areas and distressing cosmetic issues.

We previously demonstrated increased degranulating tryptase/chymase-positive mast cells in biopsies from insulin-induced lipoatropic sites and reported that topical cromolyn sodium (prepared with 4% cromolyn sodium in petrolatum solvent for topical administration twice daily to affected areas) was efficacious therapy in a small series (4). Since this report, we were contacted by 34 health care providers, caregivers, and patients worldwide, to whom we administered surveys to standardize evaluation of their treatment experiences. The study was approved by the institutional review board of the Joslin Diabetes Center.

Twenty-one responded, providing data on 24 patients with insulin-induced lipoatrophy. Ten patients used cromolyn, while the remaining attempted other therapeutic interventions or observation (Table 1). Ten respondents reported a trial of cromolyn administration. Of the 10 cromolyn users, all had type 1 diabetes and 70% were male, with mean age 16.1 ± 5.0 years, age of diabetes diagnosis 6.1 ± 4.4 years, age when lipoatrophy was first noticed 12.2 ± 6.4 years, duration of insulin use prior to onset of lipoatrophy 6.1 ± 5.2 years, and duration of lipoatrophy 3.9 ± 3.4 years. Three patients had Hashimoto thyroiditis and one other had hyperthyroidism as associated autoimmune diseases.

Insulin preparations associated with lipoatrophy included aspart (n = 4), lispro (n = 5), regular human insulin (n = 1), NPH insulin (n = 1), glargine (n = 2), and detemir (n = 1), with three patients reporting use of more than one insulin preparation. Lipoatrophy occurred in regions corresponding to common insulin injection sites: abdomen (n = 6), thighs (n = 5), and buttocks (n = 3), with sizes ranging from 2 × 2 cm to 8 × 10 cm. Eight patients reported multiple lipoatrophic sites.

Among the 10 cromolyn users, 3 initially attempted to treat lipoatrophy by switching insulins, while 2 changed from injections to continuous subcutaneous insulin infusion without improvement. All patients who used cromolyn found it to be at least partially effective; six reported complete resolution of lipoatrophy 3.9 ± 2.7 months. No side effects or adverse events were attributed to cromolyn use by the health care providers or patients. The mean time from initiating cromolyn to noticeable clinical response was 3.1 ± 0.9 months.

Switching insulins and cromolyn were the most frequent therapeutic interventions for lipoatrophy in this series. Cromolyn was reported to be more successful in enabling complete resolution of lipoatrophy than other interventions.

To our knowledge, this is the largest case series to date of patients with insulin-induced lipoatrophy. The retrospective study design, patient/provider qualitative response, and use of multiple interventions for lipoatrophy in noncromolyn users could have restricted the interpretation of results. Nonetheless, topical cromolyn sodium appears to be a well-tolerated and effective option for managing insulin-induced lipoatrophy.

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Patients</th>
<th>Complete resolution</th>
<th>Partial resolution</th>
<th>No change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Topical cromolyn sodium</td>
<td>10</td>
<td>6</td>
<td>4</td>
<td>0</td>
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<tr>
<td>Noncromolyn users*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Changed insulin preparation</td>
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<td>2</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Continuous subcutaneous insulin infusion</td>
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<td>2</td>
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<td>0</td>
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<tr>
<td>Glucocorticoid use</td>
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<td>1</td>
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<tr>
<td>Spontaneous resolution</td>
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<td>1</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Data are n. *Noncromolyn users exceed 14 cases, as patients may have used more than one treatment option.

References
2. Holstein A, Stege H, Kovacs P. Lipoatrophy associated with the use of insulin analogues.
