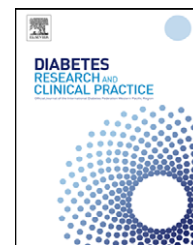




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Brief report

Successful desensitization by glargine administration in a patient with insulin allergy: A case report

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ABSTRACT

The patient was a 56-year-old man with type 2 diabetes and insulin allergy. He was administered glargine, which did not produce any allergic reactions, except for a small non-pruritic wheal. Thereafter, other insulin preparation could be administered. We consider this the first case of successful insulin desensitization by glargine administration.

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1. Introduction

The introduction of recombinant human insulin has dramatically reduced but not completely suppressed the incidence of insulin allergy. The only cure for insulin allergy is desensitization. Frequent administration of small, incremental doses of insulin is commonly used for desensitization. Here, we report the case of a patient with insulin allergy who was successfully desensitized using a simple method involving glargine—a long-acting insulin analogue. To the best of our knowledge, this is the first reported case in which desensitization to insulin was achieved by glargine administration.

2. Case report

A 56-year-old man with insulin allergy was admitted to our hospital for glycemic control. He was diagnosed with type 2 diabetes more than 10 years ago and had been receiving human insulin (biphasic isophane insulin) since 5 years. After 18 months of human insulin therapy, he noticed frequent wheal-and-flare reactions at the sites of insulin injections. These reactions gradually worsened: flares occurred 10 min after each injection, reached a diameter of 8–12 cm, and persisted for 3–5 h; finally, generalized pruritic erythema developed. Therefore, insulin was discontinued, and an oral hypoglycemic agent was adminis-

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tered. Glycemic control was lost after the discontinuation of insulin therapy.

On admission, the patient's fasting blood glucose and glycosylated hemoglobin A1c (HbA1c) levels were 307 mg/dL and 8.9%, respectively. Skin-prick tests were positive for regular, neutral protamine Hagedorn (NPH), and lispro insulin preparations and negative for insulin aspart and glargine. The serum anti-insulin-specific immunoglobulin (Ig)E autoantibody level was increased (0.92 UA/mL); eosinophilia was not detected. The binding capacity of anti-insulin IgG antibody was 89.2%.

On the basis of the results of the skin-prick tests, 2 U aspart was administered in combination with maleate dexchlorpheniramine, an antihistamine agent. However, 10 min after the injection, erythema and wheal (diameter, 5 cm) with marked pruritus appeared at the injection site. Therefore, aspart was discontinued. After 4 days, we administered glargine once a day, starting at a dose of 1 U. Glargine administration induced a mild non-pruritic local reaction (diameter, 2 cm); further, the severity of the reaction gradually decreased despite the gradual increase in the daily dose. Five days after the introduction of glargine, aspart administration before meals was restarted, and now aspart induced only a mild non-pruritic local reaction. After 3 weeks, the skin reaction was no longer observed. The patient was discharged, and the antihistamine was discontinued without any aggravation of the skin reaction. The serum anti-insulin-specific IgE level reduced to 0.64 UA/mL at 5 months after discharge. Although the binding capacity of anti-insulin IgG antibody is currently high, insulin therapy is now effective, and the HbA1c level has decreased from 8.9% to 6.0%.

3. Discussion

Not only insulin but also the constituents of insulin preparations, such as protamine and zinc, are allergenic. In our patient, specific IgE antibody to insulin was detected, while those to protamine and latex were not. Further, the patient was allergic to several insulin preparations that were produced by different manufacturers and contained different additives. Hence, we concluded that in this patient, the allergy to insulin preparations was induced by insulin itself.

Desensitization is the only cure for insulin allergy. Frequent subcutaneous administration of small, incremental doses of insulin is a commonly used method for desensitization [1]. Recent reports suggest that continuous subcutaneous insulin infusion (CSII), which enables the continuous administration of minute amounts of insulin, is also effective for desensitization [2]. As reported in this paper, desensitization with glargine administered using a proprietary injector device is an alternative protocol that is simple and inexpensive.

We present two possible mechanisms underlying insulin desensitization mediated by glargine administration. The first is as follows: glargine forms precipitates after it is subcuta-

neously injected, and these precipitates dissolve at a slow and constant rate. Therefore, the pattern of antigen presentation after glargine injection resembles that after CSII. Another possible explanation is that the differences in the amino acid composition of glargine could inhibit the immune reaction. Successful use of glargine to produce desensitization has previously been reported in 2 patients with insulin allergy [3,4]. One of these patients was allergic to several insulin preparations, excluding insulin lispro and glargine, and was successfully treated with lispro and glargine without any allergic reaction. It was speculated that the low immunogenicity of glargine was attributable to its amino acid sequence. The second patient was treated with glargine, which did not induce any allergic reaction, and was then desensitized to other insulin preparations. Therefore, in these cases, the success of glargine therapy was attributed to the difference in the amino acid compositions of glargine and human insulin, and not to desensitization. The author of the latter study speculated that desensitization to other insulin preparations resulted from epitope spreading. In contrast, in our patient, although the skin test for glargine was negative, glargine administration initially resulted in a mild allergic reaction. Therefore, we assume that in our patient, the favorable effect of glargine was due to desensitization and not due to the amino acid composition of glargine.

In conclusion, we report a case of insulin allergy in which successful desensitization was achieved by glargine administration. Glargine administration using a proprietary injector device is an easy and cost-effective method for desensitization, and might be a good therapeutic alternative in patients with insulin allergy.

Conflicts of interest

There are no conflicts of interest.

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