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Case Report

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Allergy to Insulin Glargine: A Case Report

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Abstract

We present here a 12-year-old girl with type 1 diabetes and allergy to insulin glargine with no allergy to other types of insulin. Patient developed generalized pinpoint erythematous skin rash with marked pruritus that resolved completely by switching glargine to NPH insulin. This is the first report of selective allergy to insulin glargine in English literatures.

Keywords: Insulin; Allergy; Glargine

Introduction

Since the introduction of human insulin and its analogues, allergy to insulin became rare and currently reported in less than 1% of diabetic patients [1]. In most cases, allergic reactions are restricted to the site of insulin injection. However, systemic, potentially life-threatening reactions such as anaphylaxis have also been reported [2]. Allergic reactions to insulin may result from the insulin molecule itself and/or from preservatives or additives such as protamine or zinc, which are used in many preparations to delay insulin absorption [3]. Management of this condition can be very difficult. Treatment options for insulin allergy are symptomatic therapy with antihistamines, use of an alternative insulin preparation, addition of glucocorticoids to insulin, insulin desensitization using small doses of insulin subcutaneously or through a continuous subcutaneous insulin infusion (CSII) [4], use of monoclonal antibodies (omalizumab) [5], and pancreatic transplantation for severe resistant cases [6].

Here, we report the case of a patient with allergy to insulin glargine who was successfully treated by switching glargine to Neutral Protamine Hagedorn (NPH). To the best of our knowledge, this is the first report in the English literatures of selective allergy to glargine with good tolerance to other insulins.

Case Report

A 12-year-old girl was admitted to the hospital with diabetic ketoacidosis and new onset type 1 diabetes. She was treated appropriately with intravenous infusion of regular insulin and intravenous fluids. On discharge patient was commenced on BID subcutaneous insulin regimen consisting of regular and NPH insulin before breakfast and supper. After 2 weeks, patient was seen in the out patient clinic and her insulin regimen was changed to basal-bolus insulin regimen for better control; insulin aspart before meals and glargine at bedtime. Three days later, the patient developed generalized skin rash with marked pruritus. Despite that, she continued to take her insulin regimen until she came to the clinic visit one week later. She had no previous history of allergy to any medication and she denied taking any drug other than aspart and glargine insulin. She had no history of fever or joint pains. Her examination at that time revealed generalized pinpoint erythematous skin rash. Her vital signs were stable and she had no evidence of infection. An allergy to insulin was suspected. Skin-prick tests to insulin glargine and other insulins as well as assays for IgE and IgG against insulin glargine and other insulins were not done because these are not feasible in our clinic. Therefore, for a simpler approach, we elected to discontinue glargine, restarted NPH insulin twice daily and continued insulin aspart before each meal. In addition, patient was given antihistamine to alleviate her intense itching. One week later, patient came to clinic with complete resolution of her rash. The tolerance to the new regimen was excellent, with no signs of insulin allergy over an 11-month period. A re-trial of switching NPH back to glargine when the patient developed recurrent nocturnal hypoglycemia from

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NPH, as insulin detemir is not a hospital drug formulary, led to the same skin rash with marked pruritus.

Discussion

The introduction of recombinant human insulin has dramatically reduced but not completely suppressed the incidence of insulin allergy. Structural changes leading to these insulins were initially thought to result in a decrease in immunogenicity. Rapid acting insulin analogues, insulin lispro, insulin aspart and insulin glulisine, were used successfully, as an alternative insulin preparation, to treat people with insulin allergy [7-10]. However, recent studies with both insulin lispro [11] and insulin aspart [12] report results supporting similar immunogenicity of the two analogues when compared to human regular insulin. An allergy to the new rapid-acting insulin analogue glulisine has not been reported yet.

New long-acting insulin analogues such as insulin glargine and insulin detemir offer the potential advantage of better basal insulin coverage over a 24-h period as compared to insulin NPH, with less hypoglycaemic events. A few cases showed that insulin glargine could resolve a generalized allergy to human insulin in diabetic patients [13-15]. However, glargine cannot always be considered as an alternative in insulin allergy. Indeed, there are three cases in English literature describing allergy to insulin glargine [16-18]. The first case of allergy with glargine insulin was reported in 2003, an 81-year-old man with type 2 diabetes who presented with allergic reaction to Mixtard 30. He had local induration and pruritus at the insulin injection site and generalized urticaria 10 to 15 min after the injection. Skin-prick tests (5 UI/ml) were positive for human and porcine insulin and insulin analogues, glargine and lispro, and negative for insulin aspart and all additives [16]. The second case described a type 2 diabetic patient who presented with local reactions and then anaphylactic shock after the introduction of insulin analogue premixes. Intra-dermal reactions with porcine, human and insulin analogues preparations (aspart, lispro, glargine) were all positive [17]. The third report was a 60-year-old type 2 diabetic patient who had skin reactions in form of red indurated areas at the injection site associated with severe pain shortly after each injection of human mixtard 30 that lasted for 12 h and was associated with sweating and fever. Insulin was changed to Humulin M3, Novomix 30 and Humalog Mix 25, all of which led to the same reactions. Skin provocation testing was positive for actrapid, mixtard, aspart but not for the additives. Insulin lispro led to a less marked response, but nevertheless positive. A therapeutic trial of insulin glargine was undertaken in that patient and led to similar reactions to the other insulins [18]. All of the aforementioned cases described a local reaction to glarigine. The current case is different from the previous reported cases as it described a patient with generalized skin allergy to glargine. Allergy to the new long-acting insulin analogue detemir has also been reported [19, 20].

In conclusion, although insulin analogues are used sometime to treat insulin allergy, all types of insulin can induce allergy; there is no data on insulin glulisine so far. Patients react differently, i.e., patients can develop insulin allergy to some types of insulin but not to the others. Hence, switching from one type of insulin to another is a simple approach to treat insulin allergy in a limited clinical settings.

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