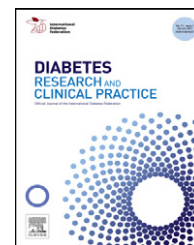




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Brief report

Successful treatment with continuous subcutaneous insulin infusion for the allergy to human insulin and its analogs

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ABSTRACT

Allergy to insulin is rare. We report a type 2 diabetic patient who is allergic to human insulin and its analog preparations and successful treatment with continuous subcutaneous insulin infusion.

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1. Introduction

The adverse effects of insulin are hypoglycemia, edema and weight gain, allergy is rare. The incidence rate of allergy to animal insulin is high, however, the rate is less than 1% when considering human insulin and its analogs [1]. But with extensive usage of insulin, allergy to human insulin and aspart, lispro has emerged [2,3]. Just as we know, the first allergy to glargine has been reported in 2003 [4]. Here we report a type 2 diabetic patient who is allergic to human (Humulin R, Novolin R) and insulin analogs preparations (aspart, lispro, glargine) and successful treatment with continuous subcutaneous insulin infusion.

2. Case report

A 58 years old female patient with type 2 diabetes injected herself aspart and Novolin N to control the glucose level. After 5 months, rhabdion, flare and pruritus appeared at the injection site, they lasted 3–4 h. 7 Months later, rhabdion and flare appeared at the abdominal region, thigh and pruritus appeared all over the body, they lasted 24 h. She was admitted to our hospital due to the location allergy and the poor control of glucose. Because she was allergic to insulin, after informed consent, insulin intradermal test with lispro, Humulin R, aspart, Novolin R, glargine, was performed. This consists in injecting 0.05 ml of 0.25 U insulin, and saline was examined as

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the negative control. After 15 min, rhabdion and flare occurred in location, however, the diameters are 12 mm, 10 mm, 6 mm, 6 mm, 7 mm, respectively, pruritus and light pain occurred in lispro location. There was no reaction in saline location. Auxiliary examination: serum IgG, IgE were negative. Insulin bump was chosen as the way of desensitization. Because she was allergic to aspart in the past, Novolin R was chosen. Basal rate of the first day was 0.05 U/h, in the second day, 0.05 U/h; 0.1 U/h in the third day, and 0.2 U/h in the fourth day. After that, the basal insulin rate was adjusted according to the glucose monitoring system. Repaglinide was used to control postprandial glucose. There was no local allergy reaction appeared. During this period, the patient injected 2 U subcutaneous insulin continuously, pruritus appeared all over the body. The pump was suspended and loratadine was administered. When the symptom disappeared, pump was started again, and the course was repeated. 18 Months later, the glucose was in good control, HbA1c was 6.7%, and no adverse reaction occurred.

3. Discussion

The allergy to insulin causes location reaction and whole-body reaction. Location reaction includes erythema, pruritus or rhabdion in the injection site, it is common but not serious, it would be better during the course of treatment. Whole-body reaction includes allergic shock, acute circumscribed edema or cnidosis, and is rare. Human allergy to one of the insulins was reported, but it was rare that one can be allergic to human insulin and its analogs and glargine. Oh et al. [5] reported one diabetic patient who was allergic to all of the insulin varieties and was treated with islet transplantation. Castéra [3] reported that a 50 years old male diabetic patient who was allergic to Lispro 75/25. Intra-dermal test showed that he was allergy to porcine, human and insulin analog preparations (aspart, lispro, glargine), however, the allergic reaction to lispro was the least, he was successfully treated by continuous subcutaneous infusion of lispro. Other reports also indicated this method may be useful as an alternative treatment in insulin allergy [6–8]. In our study, she was allergic to human insulin, analogs and was treated by constant subcutaneous pump infusion of insulin, but when the blous was injected, rhabdion occurred, and so Repaglinide was administered to control the postprandial glucose.

Currently, the mechanism of allergic reactions to human insulin preparations is not entirely clear, possible causes are: high concentrations of insulin can form polymers, resulting in conformational changes in its space and can lead to its antigenicity. Some patients still sensitive to insulin analogs may be because changes in the amino acid sequence or antigenic types of lead increased. Insulin-induced allergic reactions are mostly of type 1, which is characterized by B lymphocyte antigen to stimulate IgE antibody, the formation of insulin–IgE complex, the complex effect on basophiles and

mast cells to release histamine and other inflammatory mediators [9]. Furthermore, rare allergic reactions are of type III and IV [10–12]. Type II allergic reaction has not been reported.

Though insulin allergy is also a rare clinical situation, its resolution is not so easy. We would like to recommend constant subcutaneous pump infusion of insulin as an alternative choice.

Conflict of interest

The authors declare that they have no conflict of interest.

REFERENCES

- [1] Schernthaner G. Immunogenicity and allergenic potential of animal and human insulins. *Diabetes Care* 1993;16:155.
- [2] Barranco R, Herrero T, Tornero P, Barrio M, Frutos C, Rodríguez A, et al. Systemic allergic reaction by a human insulin analog. *Allergy* 2003;58:536–7.
- [3] Castéra V, Dutour-Meyer A, Koeppl M, Petitjean C, Darmon P. Systemic allergy to human insulin and its rapid and long acting analogs: successful treatment by continuous subcutaneous insulin lispro infusion. *Diabetes Metab* 2005;31:391–400.
- [4] Durand-Gonzalez KN, Guillausseau N, Pecquet C, Gayno JP. Glargine insulin is not an alternative in insulin allergy. *Diabetes Care* 2003;26:2216.
- [5] Oh HK, Provenzano R, Hendrix J, el-Nachef MW. Insulin allergy resolution following pancreas transplantation alone. *Clin Transplant* 1998;12:593–5.
- [6] Sola-Gazagnes A, Pecquet C, Radermecker R, Piétri L, Elgrably F, Slama G, et al. Successful treatment of insulin allergy in a type 1 diabetic patient by means of constant subcutaneous pump infusion of insulin. *Diabetes Care* 2003;26:2961–2.
- [7] Nagai T, Nagai Y, Tomizawa T, Mori M. Immediate-type human insulin allergy successfully treated by continuous subcutaneous insulin infusion. *Intern Med* 1997;36:575–8.
- [8] Eapen SS, Connor EL, Gern JE. Insulin desensitization with insulin lispro and an insulin pump in a 5-year-old child. *Ann Allergy Asthma Immunol* 2000;85:395–7.
- [9] Roest MA, Shaw S, Orton DI. Insulin-injection-site reactions associated with type I latex allergy. *N Engl J Med* 2003;348:265–6.
- [10] Silva ME, Mendes MJ, Ursich MJ, Rocha DM, Brito AH, Fukui RT, et al. Human insulin allergy-immmediate and late type III reactions in a long-standing IDDM patient. *Diabetes Res Clin Pract* 1997;36:67–70.
- [11] Darmon P, Castera V, Koeppl MC, Petitjean C, Dutour A. Type III allergy to insulin detemir. *Diabetes Care* 2005;28:2980.
- [12] Loeb JA, Herold KC, Barton KP, Robinson LE, Jaspan JB. Systematic approach to diagnosis and management of biphasic insulin allergy with local anti-inflammatory agents. *Diabetes Care* 1989;12:421–3.