

Intradermal Desensitization with Human Insulin (recombinant DNA) in a Patient with Severe Allergic Skin Reaction due to Insulin

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This is a case report of a 70-yr-old female patient with a severe allergic skin reaction (necroses) due to insulin injections. Because of insulin dependency, desensitization to insulin was mandatory. For desensitization, a schedule with intradermal injections of increasing insulin concentrations (from 0.02 to 2 U per injection) at time intervals of 3 h was used. With highly purified pork insulin, the concentration limit of 0.04 U was reached in spite of 75 injections. After changing to human insulin (recombinant DNA), a rapid desensitization could be performed at the same concentration. Desensitization resulted not only to human insulin but also to highly purified pork insulin, as shown by intradermal testing 6 mo later. *DIABETES CARE* 5 (SUPPL. 2): 165-167, 1982.

Desensitization to insulin is the recommended treatment for patients with severe local or generalized skin reactions and anaphylaxis due to insulin preparations.¹ A pure intradermal desensitization program proved to be very successful in our experience.^{2,3} According to this schedule, eight patients could be treated either with highly purified pork insulin (seven patients) or human insulin (recombinant DNA). In this last patient (reported here) monocomponent pork insulin failed, while human insulin resulted in a fast desensitization.

PATIENT AND METHODS

The 70-yr-old female patient (S.R.) had a diabetic history of 11 yr. She received intermittent insulin therapy twice, 2 yr and 4 mo ago. The second period of insulin treatment had to be interrupted because of severe local allergic reactions to insulin. The type of allergy was described as subcutaneous, indurated, erythematous lesions 12-24 h after the injection of insulin leading to severe necroses after several days. Scars of these necroses are shown in Figure 1. At the time of admission the patient was on glibenclamide therapy; blood glucose was above 400 mg/dl with pronounced glucosuria and ketonuria. Insulin therapy was refused by the patient.

Insulin desensitization schedule. Intradermal tests with a variety of undiluted insulin preparations are performed before starting desensitization. Insulin with the least allergic reaction is used for desensitization in decreasing dilutions of 1:100, 1:50, 1:20, 1:10, 1:5, 1:2, and 1:1. The desensitization

doses are given intracutaneously in 0.05-ml volumes every 3 h. An increase of insulin concentration is not taken before a reaction to the previous injection has been ruled out. The last injections with undiluted insulin are given subcutaneously, followed by the normal insulin regimen with two injections daily of an intermediate-acting insulin.

RESULTS

Intradermal testing. To find out whether an allergy existed even to highly purified pork insulin preparations, intracutaneous tests with the following preparations were carried out: Actrapid (Novo Industries, Copenhagen, Denmark), Monotard (Novo), Velasulin (Nordisk, Copenhagen), Insulatard (Nordisk), and Optisulin 01S (Hoechst, Frankfurt/Main, West Germany). Normal saline (0.9% NaCl) and histamine solutions were injected as controls. At each site of insulin injection positive reactions occurred: after 15-20 min, acute erythema and after 10-12 h, indurations followed and developed into flat necrotic areas after 5-7 days, persisting for several weeks. Figure 2 shows the situation 4 wk after injection.

Desensitization. Desensitization to insulin was started with Actrapid (Novo) in a dilution of 1:100 (0.02 U of insulin). Local reactions could be observed up to the 25th injection; then, we were able to proceed to the next dilution, 1:50 (0.04 U of insulin). Allergic reactions developed for the next 50 injections again, without improvement. Therefore, we decided to use human insulin, also in a dilution of 1:50. After the first four injections some local reactions still oc-



FIG. 1. Scars after subcutaneous necroses due to local allergic reactions to insulin injections in patient S.R.

curred. But then, no further allergic reactions were observed up the final undiluted insulin concentration. The first 2–3 subcutaneous insulin injections led to some minor reactions again. Later on, no further reaction, including the use of the NPH preparation, was seen until now, after 12 mo of treatment. The metabolic situations during this time of hospitalization are shown in Figure 3. Body weight reduction, and glibenclamide and metformin therapy led to an improvement in blood glucose to 200–250 mg/dl, with almost complete reduction of glucosuria. Further improvement was achieved by insulin therapy with blood sugars below 200 mg/dl. The insulin requirement for good metabolic control was 32 U/day in two daily injections. After discharge, the insulin requirement increased to 38 U/day mainly due to poor dietary adherence. HbA_{1c} could be kept constantly at about 10%.

After 6 mo of insulin therapy we performed intracutaneous tests with human insulin and two highly purified pork insulin

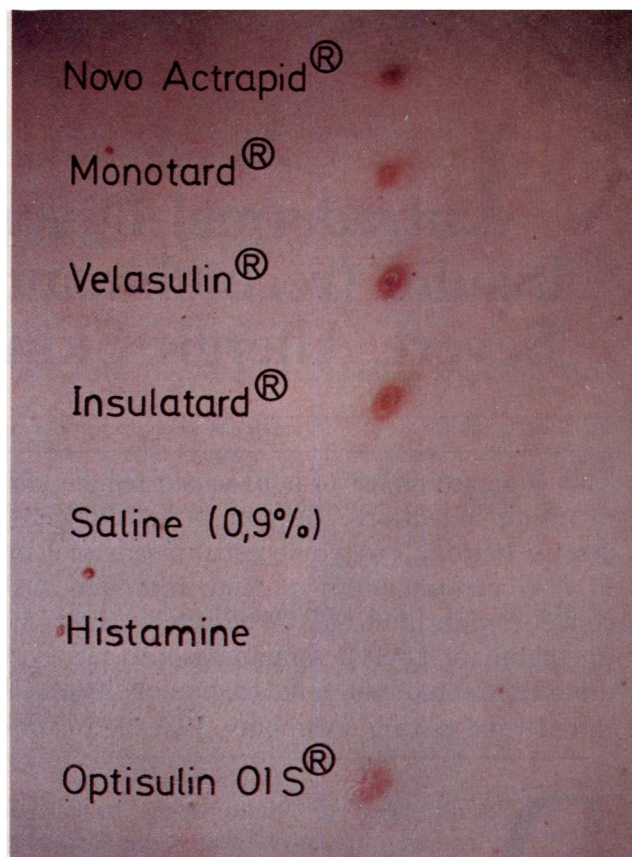


FIG. 2. Skin reactions persisting 4 wk after intradermal injections of various purified pork insulin preparations in patient S.R. with severe local allergy to insulin.

preparations (Actrapid and Velasulin). No allergic reactions to any of these insulins could be observed.

DISCUSSION

In the absolute need of insulin therapy desensitization to insulin is the most successful method of overcoming severe insulin allergy. During the last 4 yr we have been very successful in desensitization to insulin using a program described before.^{2,3} The most important points of this method are an exact 3-h time interval schedule, the pure intradermal injections, and no increment in insulin concentration until the disappearance of any reaction to the previous dose. This may help to improve the desensitization procedure and to avoid the return to the next or even second lowest concentrations that occurs with other regimens.^{1,4} This program and the use of highly purified pork insulin preparations enabled us to successfully treat patients with systemic or severe local allergic reactions³ and anaphylaxis to insulin.² Only in one patient reported here the use of pork insulin failed to obtain desensitization, although 75 injections with insulin dilutions of 1:100 (0.02 U of insulin) and 1:50 (0.04

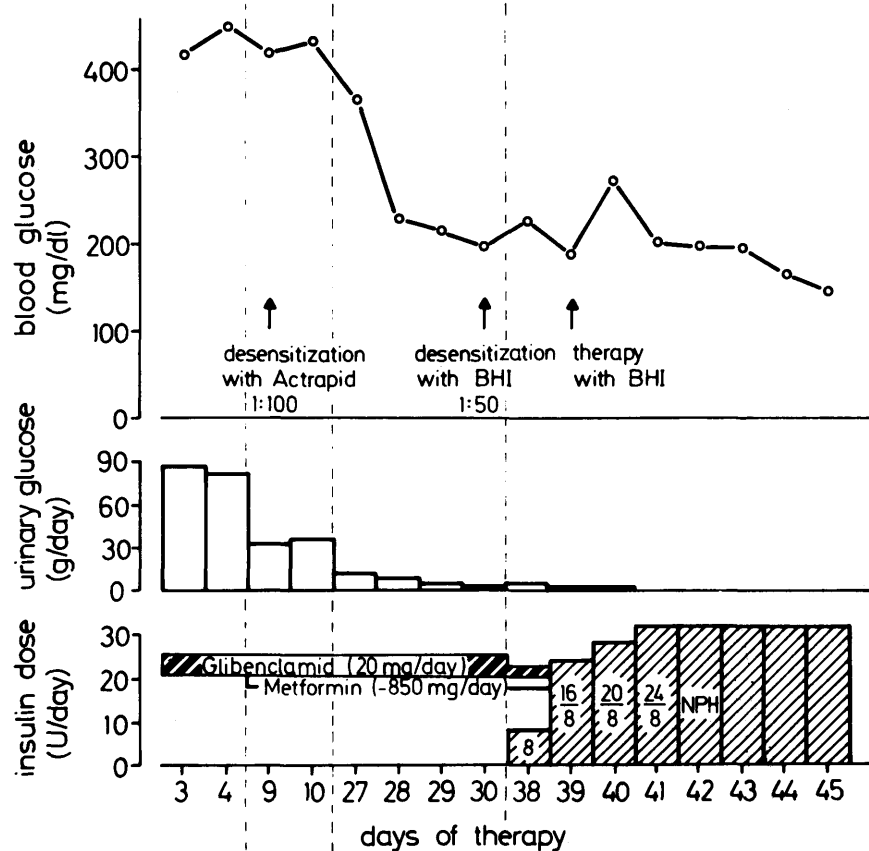


FIG. 3. Changes of postprandial blood glucose (each point represents the mean of 9 a.m. and 1 p.m. values), urinary glucose, and type of treatment in a patient (S.R.) during hospitalization because of desensitization to insulin. Desensitization was started with Actrapid (Novo) and changed to human insulin as a regular preparation. Insulin therapy was performed with a NPH formula.

U) were performed. Although desensitization could also have been achieved by ongoing injections with pork insulin, immediate improvement after changing to human insulin suggests an extraordinary effect of human insulin on desensitization in that patient. Furthermore, with human insulin a desensitization not only to this insulin preparation but to pork insulin as well could be obtained, demonstrated by intradermal testing 6 mo later. The suggestion is raised that human insulin may be helpful in the treatment of insulin allergy, especially in desensitization to insulin, which may at least shorten the desensitization procedure.

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