Successful Treatment With Insulin Analog Lispro in IDDM With Delayed Absorption of Subcutaneously Applied Human Regular Insulin and Complicated Intraperitoneal Insulin Infusion

A case report

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OBJECTIVE — To subcutaneously administer the insulin analog lispro in a patient with delayed absorption of subcutaneously applied human regular insulin whose continuous intraperitoneal insulin infusion (CIPII) with a percutaneous access device had required multiple surgical interventions because of complications.

RESEARCH DESIGN AND METHODS — In a 35-year-old woman with long-term IDDM and delayed absorption of subcutaneously applied human regular insulin, a 3-year CIPII with human regular insulin via a percutaneous access device was complicated by three catheter obstructions and one subcutaneous abscess. Each complication required the implantation of a new percutaneous access device. During a 2-day trial with continuous subcutaneous insulin infusion (CSII) of the insulin analog lispro at basal infusion rates of 0.5–1.1 U/h, stable metabolic control was achieved. A 5-h intermediate attempt with human regular insulin in CSII, however, increased blood glucose concentrations from 6.0 to 28.8 mmol/l, despite identical basal rates and additional injection of 16 U of human regular insulin. Restarting with CSII of the insulin analog lispro reinforced stable metabolic control.

CONCLUSIONS — It is suggested that the insulin analog lispro is a promising approach in the treatment of IDDM with delayed absorption of subcutaneously applied human regular insulin and a suitable alternative therapy for patients with complications attributed to percutaneous access devices for CIPII.

An implantable percutaneous access device (Percuseal; Percuseal Medical, Huskvarna, Sweden) designed to deliver insulin from an external pump to the abdominal cavity has been reported to be beneficial in IDDM patients with delayed absorption of subcutaneously applied human regular insulin (1–4). However, alternative therapeutic approaches are required because of potential complications attributed to the device (1–4).

The first available insulin analog, lispro (Lilly, Bad Homburg, Germany), which is characterized by a faster onset of action and a shorter half-life (5) due to an interchange of the positions of the amino acids B28 (proline) and B29 (lysine) that results in a rapid dissociation of the insulin hexamer directly to its physiological active monomer structure, has been suggested to be a promising therapeutic approach in diabetic patients with subcutaneous insulin resistance (6–8). It has also been shown that the insulin analog lispro can be successfully applied with continuous subcutaneous insulin infusion (CSII) in IDDM (9).

We report a case of an IDDM patient with delayed absorption of subcutaneously applied human regular insulin and multiple complications attributed to the percutaneous access device for continuous intraperitoneal insulin infusion (CIPII) who was successfully treated with CSII of the insulin analog lispro.

RESEARCH DESIGN AND METHODS

— Because *1*) 20 U of human regular insulin (Alt-Insulin, Hoechst, Frankfurt/Main, Germany) did not result in a significant decrease of plasma glucose within 4 h, 2) severe hypoglycemia occurred after this period, and 3) the response to intravenous insulin was normal, delayed absorption of subcutaneously applied human regular insulin was diagnosed in a 35-year-old woman with IDDM (BMI 20 kg/m^2, duration of diabetes 19 years) (2). During subsequent 3-year CIPII with an implantable percutaneous access device (Percuseal) and application of human regular insulin (H-Tronin 100; Hoechst), three obstructions of the intraperitoneal catheter and one subcutaneous abscess, each requiring surgical reimplantations, occurred.

Because of the frequency of severe complications with the percutaneous access device for CIPII in the patient, a 2-day trial of CSII with the insulin analog lispro (Lilly) was performed (Fig. 1); meal-related subcutaneously applied insulin doses and basal infusion rates (0.5–1.1 U/h), both with the insulin analog, were identical to those previously applied with CIPII. During 32 h of CSII with the insulin analog lispro, stable blood glucose concentrations (range 3.8–9.2 mmol/l) were obtained. At 8:00

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Abbreviations: CIPII, continuous intraperitoneal insulin infusion; CSII, continuous subcutaneous insulin infusion.

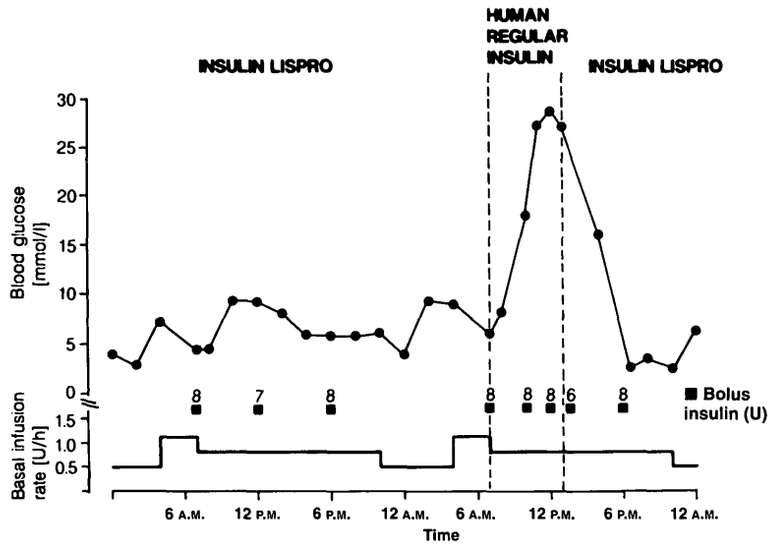

Figure 1—*Blood glucose levels during CSII with the insulin analog lispro and human regular insulin in an IDDM patient with delayed absorption of subcutaneously applied human regular insulin.*

A.M. of the following day (preprandial blood glucose 6.0 mmol/l), CSII with the insulin analog lispro was switched to human regular insulin (H-Tronin 100), but insulin doses were not changed. At 10:00 A.M., blood glucose concentration had increased to 18.0 mmol/l. Because, despite repeated additional injections of 8 U of human regular insulin, blood glucose concentrations further increased to 28.8 mmol/l at noon and 27.2 mmol/l at 1:00 P.M., CSII with human regular insulin was stopped. At this time, the patient presented with ketonuria. Restarting with CSII of the insulin analog lispro normalized blood glucose levels within 5 h. Stable metabolic control was subsequently achieved (Fig. 1).

CONCLUSIONS — We report successful CSII of the insulin analog lispro in a female IDDM patient with delayed absorption of subcutaneously applied human regular insulin who had experienced multiple complications attributed to a percutaneous access device for CIPII.

The phenomenon of delayed absorption to subcutaneously applied human regular insulin remains poorly understood, and different pathogenetic mechanisms can be hypothesized: chemical alterations after subcutaneous injection could cause immunogenic activation and degradation of the human regular insulin molecule (10). Furthermore, inactivation of human regular insulin molecules by proteases in the subcutis could contribute to the phenomenon of delayed subcutaneous absorption (11).

The accelerated dissociation of the hexamer structure to the monomer structure of the insulin analog lispro, as compared with human regular insulin (12), hypothetically results in both a reduction of antibody formation and lack of subcutaneous destruction processes. Also, rapid absorption from the subcutaneous tissue itself could reduce the risk of inactivation or destruction of the insulin analog. Recently, it has been demonstrated that high levels of antibodies against human regular insulin decrease after treatment with insulin analog lispro (6). Comparable levels of antibodies against insulin analog lispro and human regular insulin have also been reported (13, 14). However, it is conceivable that efficacy of therapy with insulin analog lispro in delayed absorption of subcutaneously applied human regular insulin is attributable to its different physical properties.

In conclusion, in IDDM patients with delayed absorption of subcutaneously applied human regular insulin, CSII with the insulin analog lispro is a promising alternative treatment to the frequently complicated CIPII with a percutaneous access device.

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