

Allergy to insulin in a woman with gestational diabetes mellitus: transient efficiency of continuous subcutaneous insulin lispro infusion

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SUMMARY

We report the case of a 31-year-old pregnant woman. She required insulin for the treatment of gestational diabetes from 27 weeks of amenorrhoea to delivery. An allergy to insulin was suspected because she presented with local symptoms at insulin injection sites and a decrease in efficiency of insulin. This diagnostic was confirmed by skin-prick tests. A treatment with subcutaneous continuous lispro insulin analogue infusion was initiated with an oral antihistaminic drug without local reaction. Seven weeks after the initiation of insulin pump, local reactions reappeared. The insulin analogue lispro is not always an alternative in insulin allergy. However, in the case we report, the lack of allergy during a few weeks allowed the birth of a normal infant.

Key-words: Allergy to Insulin · Insulin Analogue Lispro · Adverse Effects.

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RÉSUMÉ

Allergie à l'insuline au cours d'un diabète gestationnel : efficacité transitoire de l'insulinothérapie continue sous cutanée par Lispro

Nous rapportons le cas d'une femme enceinte âgée de 31 ans. Un traitement par insuline a été instauré pour le traitement d'un diabète gestationnel à partir de la 27 semaines d'aménorrhée jusqu'à l'accouchement. Une allergie à l'insuline a été suspectée devant l'apparition de lésions cutanées aux sites d'injection de l'insuline et une diminution de l'efficacité de l'insuline. Des tests de sensibilité cutanée ont confirmé ce diagnostic. Un traitement par pompe externe utilisant l'analogue de l'insuline lispro a été débuté sans réaction cutanée allergique. Sept semaines plus tard, les lésions cutanées ont réapparu. L'analogue de l'insuline lispro n'est pas toujours une alternative thérapeutique en cas d'allergie à l'insuline. Cependant, dans notre cas clinique, l'absence d'allergie pendant quelques semaines a permis la naissance d'un enfant normal.

Mots-clés : Allergie à l'insuline · Analogue de l'insuline lispro · Effets secondaires.

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Allergy to insulin is rare with human recombinant insulin, and is now reported for less than 1% of the diabetic patients [1, 2]. Clinic symptoms are usually local and appear a few minutes after the injection. A decrease in the efficiency of the insulin is usually associated with these symptoms. Different methods have been proposed for the treatment of insulin allergy including the use of oral antihistaminics, the addition of glucocorticoids to insulin, and the change to human insulin analogues. We report one case of allergy to insulin during a gestational diabetes, transiently controlled by insulin lispro in pump.

Case report

A 31-year-old pregnant woman (weight 92 kg, BMI 35) was diagnosed as having a gestational diabetes at 25 weeks of amenorrhoea. She had no other diseases and no history of any allergy. She has been twice pregnant before without gestational diabetes clearly identified.

She was first treated by a normocaloric diet but insulin was required to achieve normoglycaemia. Intermediate insulin at bed time (Insulatard HM: 20 UI) and regular insulin (Actrapid HM: 18 UI) before each meal were initiated. No local reaction was observed.

Two weeks later, the patient was admitted for uncontrolled diabetes and urticarian lesions at insulin injection sites. An allergy to insulin was then suspected.

Leukocytes and eosinophilias were within the normal range ($9.6 \times 10^9/l$ and $0.25 \times 10^9/l$ respectively). The specific human insulin IgE antibody (CAP-SYSTEM RAST FEIA) was high (4.12 KUI/l). Skin-prick tests (5 UI/ml) were positive for human and porcine insulin and negative for all additives (protamine, paraben, metacresol, phenol, zinc and isophane) using the Novo Insulin allergy kit (Novo Nordisk). These tests confirmed the allergy to insulin (Table I).

A new treatment with subcutaneous continuous lispro insulin analogue infusion was initiated together with an oral

antihistaminic drug (Cetirizine 10 mg daily). No local reaction was observed, and glycemic control gradually improved until 34 weeks of amenorrhoea. At that time, local reaction reappeared at catheter implantation site, and insulin requirements continuously increased up to 150 UI per day. The obstetric scan revealed a foetal macrosomia and an interventricular septum of 5 mm. A caesarean was performed at 35 weeks. The newborn was healthy, with a weight of 4.020 g. Insulin was rapidly decreased and finally stopped as a normal glycemic control was achieved.

Discussion

Insulin allergy has increasingly decreased with the use of human recombinant insulin and is now reported in less than 1% of diabetic patients treated with insulin [1, 2]. Similar cases of insulin allergy in patients with gestational diabetes have been previously reported [3, 4].

Generally, local clinic symptoms (i.e., red blotch, induration, pruritus, burning sensation) appear a few minutes after insulin injection. Local reactions appear at insulin injection sites. Patients present rarely with general reactions like urticarian, wheezing, and anaphylactic shock. A decrease in the efficiency of the insulin is usually associated with these reactions.

Allergy to insulin is confirmed by skin-prick tests. Elevation of insulin-specific IgE antibodies in the serum may also be useful.

Different methods have been proposed for treating patients with insulin allergy, such as oral antihistaminics, addition of glucocorticoids to insulin, different models of desensitisation, and changing the type of insulin. Human insulin is beneficial for most diabetic patients with insulin allergy. However, cases of local or generalized allergic reactions to human insulin have been previously reported [5]. In most patients with insulin allergy, insulin lispro, a genetically engineered insulin analogue (Humalog, Lilly, Indianapolis IN) is well tolerated and can be safely used because of less antige-

Table I

Skin prick tests with insulin and different additives in a patient with allergy to insulin.

	1/1000		1/100		1/10		Pure	
	Papule (mm)	Redness (mm)	Papule (mm)	Redness (mm)	Papule (mm)	Redness (mm)	Papule (mm)	Redness (mm)
Human insulin	0	0	0	0	7	15	10	20
Porcine insulin	0	0	0	0	0	0	10	20
Paraben	0	0	0	0	0	0	0	0
Phenol	0	0	0	0	0	0	0	0
Metacresol	0	0	0	0	0	0	0	0
Zinc	0	0	0	0	0	0	0	0
Isophane	0	0	0	0	0	0	0	0
Protamine	0	0	0	0	0	0	0	0

nicity due to increased clearance of insulin analogue monomers from injection sites [6, 7]. Continuous subcutaneous insulin infusion with lispro insulin has been recently reported to resolve an allergy to human insulin [8, 9]. However, cases of allergy to lispro insulin have been recently reported and treated with another human insulin analogue aspart (Novorapid, Novo Nordisk, Bagsvaerd, Denmark) [10, 11]. By contrast, allergic reactions to both insulin analogues have been reported in another case [12]. Therefore, lispro and aspart insulin are not necessarily an alternative for the treatment of insulin allergy. In our observation, we describe an intolerance case with lispro insulin appearing 7 weeks after the initiation of insulin pump. However, the lack of allergy during a few weeks allowed the birth of a normal infant.

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