

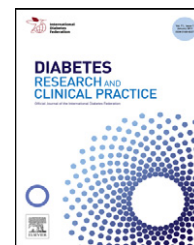


Contents lists available at ScienceDirect

Diabetes Research and Clinical Practice

journal homepage: www.elsevier.com/locate/diabres

International
Diabetes
Federation



Letter to the Editor

Insulin glulisine may ameliorate nocturnal hypoglycemia related to insulin antibody – A case report

A 70-year-old man was admitted to our hospital in January 2010. His chief complaint was poor glycemic control with nocturnal hypoglycemia. He had been diagnosed with type 2 diabetes 35 years ago, and treated with a sulfonylurea. In 2006, he started insulin therapy with insulin lispro mix 50 because of hyperglycemia (HbA1c 11.9%), then basal-bolus therapy with insulin lispro and detemir was introduced in June 2009. Since then, he had suffered from nocturnal hypoglycemia with daytime hyperglycemia. Switching insulin detemir to NPH insulin did not correct the unsatisfactory glycemic control, with the HbA1c level being 8.3% at the time of admission.

After admission, introducing a bed-time snack and discontinuing NPH insulin did not reduce nocturnal hypoglycemia. Fasting plasma glucose, insulin and C-peptide levels were 58 mg/dl, 109 mU/l and 1.5 ng/ml, respectively.

The main causes of hypoglycemia are anti-diabetic medications, hepatic or renal failure, hormone deficiency, or tumors [1]. These possibilities were ruled out and hypoglycemia due to insulin autoimmunity syndrome [2] was suspected. His insulin antibody titer was high (binding ratio 85.2%), and scatchard analysis revealed low affinity-high binding capacity of the antibody ($k_1 = 0.0071 \times 10^8 \text{ M}^{-1}$, $b_1 = 261 \times 10^{-8} \text{ M}$, $k_2 = 0.0001 \times 10^8 \text{ M}^{-1}$, $b_2 = 146 \times 10^{-8} \text{ M}$). We concluded that his nocturnal hypoglycemia was related to insulin antibody.

Even after switching insulin from lispro to regular human insulin (0.38 U/kg/day), nocturnal hypoglycemia with daytime hyperglycemia persisted. However, after switching from regular insulin to insulin glulisine three times a day (0.47 U/kg/day), his nocturnal hypoglycemia disappeared and his glucose fluctuations improved. One year after switching to insulin glulisine, although his insulin antibody titer remained high (binding ratio 87.5%), scatchard analysis showed higher affinity and lower binding capacity of the antibody ($k_1 = 0.294 \times 10^8 \text{ M}^{-1}$, $b_1 = 11.7 \times 10^{-8} \text{ M}$, $k_2 = 0.0050 \times 10^8 \text{ M}^{-1}$, $b_2 = 10.7 \times 10^{-8} \text{ M}$), suggesting preferable change of antibody characteristic.

Insulin glulisine is a fast-acting human insulin analogue engineered by changing two amino acids in human insulin (3^BLys-29^BGlu-human insulin), and shows stability in monomeric and dimeric forms in solution in the absence of zinc [3].

Ozaki and Oiso reported a patient with type 1 diabetes and severe insulin allergy whose allergy symptoms completely subsided after insulin lispro was replaced with glulisine [4]. However, to our knowledge, there has been no report on the efficacy of insulin glulisine for treatment of hypoglycemia due to insulin antibody. Here, we experienced a patient whose nocturnal hypoglycemia due to insulin antibody was resolved by switching to insulin glulisine. Although its mechanism remains unknown, insulin glulisine may be considered as a therapeutic option for poor glycemic control due to insulin antibody.

Conflict of interest

The authors declare that they have no conflict of interest.

REFERENCES

- [1] Cryer PE, Axelrod L, Grossman AB, Heller SR, Montoro VM, Seaquist ER, et al. Evaluation and management of adult hypoglycemic disorders: an Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab* 2009;94:709–28.
- [2] Uchigata Y, Hirata Y, Omori Y. A novel concept of type VII hypersensitivity introduced by insulin autoimmune syndrome (Hirata's disease). *Autoimmunity* 1995;20:207–8.
- [3] Becker RH. Insulin glulisine complementing basal insulins: a review of structure and activity. *Diabetes Technol Ther* 2007;9:109–21.
- [4] Ozaki N, Oiso Y. Immunologic tolerance to the insulin analogue glulisine. *Diabetes Care* 2010;33:e39.

Arata Itoh
Department of Internal Medicine,
Keio University School of Medicine,
Tokyo, Japan

Yoshifumi Saisho*
Department of Internal Medicine, Keio University School of Medicine,
35 Shinanomachi, Shinjuku-ku, Tokyo 160-8582, Japan
Masanori Mitsuishi
Department of Internal Medicine,
Keio University School of Medicine, Tokyo, Japan

Yoichi Oikawa
*Department of Internal Medicine, Saiseikai Central Hospital,
Tokyo, Japan*

Toshihide Kawai
*Department of Internal Medicine,
Keio University School of Medicine, Tokyo, Japan*

Masami Tanaka
*Department of Internal Medicine,
Keio University School of Medicine, Tokyo, Japan*

Akira Shimada
*Department of Internal Medicine,
Saiseikai Central Hospital, Tokyo, Japan*

Hiroshi Itoh
*Department of Internal Medicine,
Keio University School of Medicine, Tokyo, Japan*

**Corresponding author. Tel.: +81 3 3353 1211x62383;
fax: +81 3 5269 3219*

E-mail address: saish@sc.itc.keio.ac.jp
(Y. Saisho)

24 December 2010

0168-8227/\$ – see front matter
© 2011 Elsevier Ireland Ltd. All rights reserved.
[doi:10.1016/j.diabres.2011.04.001](https://doi.org/10.1016/j.diabres.2011.04.001)