European Journal of Therapeutics

DOI: 10.5152/EurJTher.2017.293

Case Report

Diabetic Ketoacidosis Occurring in Patient on Newly Started Insulin Glargine U300

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ABSTRACT

Insulin glargine U300 is a 3-fold, concentrated, long-acting insulin analog providing a more stable effect compared with insulin glargine U100. However, stable plasma insulin concentration is reached on day 4 of the treatment. Patients with type 1 and type 2 diabetes mellitus with decreased insulin reserve are at an increased risk of diabetic ketoacidosis when there is insufficient exogenous plasma insulin concentration. Herein, we present a case of diabetic ketoacidosis occurring in a patient with insulin glargine U300 and emphasize the pharmacokinetic properties of insulin glargine U300.

Keywords: Glargine U300, diabetic ketoacidosis, pharmacokinetic

INTRODUCTION

Basal insulin secretion is essential for the maintenance of fasting glucose levels, especially through inhibition of excessive hepatic glucose output. Insulin glargine U300 is a novel long-acting basal insulin formulation that provides more stable effect than glargine U100. Because of the pharmacokinetic properties of glargine U300, the expected plasma insulin concentration is not achieved during the first 4 days of treatment. We report a case of diabetic ketoacidosis on the first day of glargine U300 administration due to low plasma insulin concentration.

CASE PRESENTATION

A 62-year-old female patient diagnosed with type 2 diabetes mellitus (DM) for 25 years, hypertension, hyperlipidemia, hypothyroidism, and previous history of cerebrovascular accident consulted our hospital for routine control. Her medications include insulin aspart 12 unit 3 times daily, insulin detemir 22 unit once daily, metformin 1000 mg twice daily, linagliptin 5 mg, levothyroxine 100 mcg, acetylsalicylic acid 300 mg, perindopril/indapamide 10 mg/2.5 mg, and atorvastatin 20 mg. According to the patient's anamnesis, it was noticed that in addition to the especially night hypoglycemia, the blood glucose levels of fasting and postprandial in the evening were high and she said that did not adhere to her diet. Physical examination revealed that her body mass indexwas 33 kg/m^2. Laboratory findings were as follows: HbA1c: 10.3%, c-peptide: 0.07 µg/L, Hb: 9.2 g/L, MCV: 89 fL, ferritin: 7.93 µg/L. The patient was hospitalized to regulate her blood glucose and to investigate anemia etiology. Insulin detemir, which was used by the patient, was replaced with glargine U300 U/mL, 30 units once daily because of the hypoglycemia at night and the high blood sugar levels in the evening. On the second day of treatment, abdominal ultrasound examination was required from the patient to research anemia etiology. Blood glucose was measured 450 mg/dL after returning from the ultrasound when she had not eaten breakfast. Ketones were detected in the urine along with pH: 7.29 and hCO3: 14 mmol/L in the blood gas of the patient with complaints of nausea and fatigue. There was no pathology except minimal abdominal tenderness on the physical examination. Tests performed for etiology showed 0.8 mg/dL C-reactive protein (normal: 0-0.8) and 0.02 ng/mL procalcitonin (normal: 0-0.5). Urine leukocyte esterase was negative and the electrocardiogram showed normal sinus rhythm. Insulin infusion was initiated by considering mild diabetic ketoacidosis (DKA) in the patient. Subcutaneous insulin therapy was switched on when the blood sample was taken at the 6th hour of the infusion with pH: 7.36 and hCO3: 19 mmol/L. The next morning, the patient underwent urea breath test and was examined using glucose-insulin-potassium (GIK) solution because the patient was still hungry. During this time, the blood glucose of the patient who followed the hourly basis was between 150 and 200 mg/dL. From the third day of the treatment onward, it was observed that the patient had steady blood glucose levels and night hypoglycemia was absent. Patient with erosive gastritis and H. pylori infection as anemia etiology was discharged.

DISCUSSION

Diabetic ketoacidosis is one of the acute metabolic complications of uncontrolled DM. A combination of hormonal disturbances causes DKA. In the setting of insulin deficiency, increased counter-regulatory hormones lead to increased extracellular glucose, decreased glucose use, and hyperglycemia (1). Inadequate dosing of insulin and infections are the most common causes of DKA (2). Other causes include pancreatitis, myocardial infarction, cerebrovascular accident, and drugs that interfere with carbohydrate metabolism such as corticosteroids (2). In this case, there

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Received: 15.12.2017 • **Accepted:** 03.01.2018

were no other causes of DKA except inadequate dose of basal insulin, which is the most common cause of the DKA.

Basal insulin therapy is primarily important for regulating fasting glucose levels by inhibiting increased hepatic glucose output (3). It is known that patients who have received treatment with insulin detemir, in particular, should be given two doses daily to achieve fasting glycemic control (4). Considering the night hypoglycemia, evening fasting hyperglycemia and the high HbA1c level, our patient was treated using insulin glargine U300 U/mL because of the insufficient duration of single-dose insulin detemir treatment and hypoglycemia due to peak effect. However, for treatment of insulin glargine U300 U/mL to be stable, 4 days must pass (5).

CONCLUSION

In conclusion, for the first 4 days, it may be seen the diabetic ketoacidosis on the patients who have type 1 DM and, as in this case, long-term type 2 DM with decreased insulin reserve, who are newly administered insulin glargine U300 due to inadequate plasma basal insulin. When rapid-acting insulin is not applied in such patients, the GIK solution must be given especially for the first 4 days after insulin glargine U300 U/mL treatment is newly started.

Informed Consent: Informed consent was not obtained due to the retrospective nature of the report.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - L.K.; Design - L.K.; Supervision - C.O.K.; Resources - L.K.; Data Collection and/or Processing - C.O.K.; Analysis and/or Interpretation - S.H.İ.; Literature Search - S.H.İ.; Writing Manuscript - C.O.K.; Critical Review - S.H.İ.

Conflict of Interest: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

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How to cite:

Kıraç CO, İpekçi SH, Kebapcılar L. Diabetic Ketoacidosis Occurring in Patient on Newly Started Insulin Glargine U300. Eur J Ther 2018; 24(4): 266–7.