CASE REPORT

Unexplained Hyperglycemia in a Patient on Insulin Pump Therapy; Transient Insulin Failure?

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Abstract

Hyperglycemia may occur with no apparent medical, dietary, insulin delivery or pump failure reasons. We herein present a case of persistent hyperglycemia secondary to transient insulin failure in a 24 year old lady with type 1 diabetes mellitus who is being treated with continuous subcutaneous insulin infusion.

Key words: CSII, Insulin pump, Hyperglycemia, Diabetes

Introduction

The list of potential causes of unexplained hyperglycemia is extensive (1). In patients on insulin pump these include problems with mechanical evaluation of the pump, basal/bolus review, reservoir/tubing, catheter site selection/placement, and insulin compatibility/stability (1,2). Transient insulin failure for inexplicable reasons has not been reported previously. We herein present the case of a 24-year old women with type 1 diabetes treated with insulin pump who suffered persistent hyperglycemia secondary to transient insulin failure.

Case presentation

A 24-year-old lady with type1 diabetes diagnosed in 2007 was initially treated with Insulin Glulisine (Apidra, Sanofi) and Insulin Glargine (Lantus, Sanofi) using insulin pens. In 2011, the patient was placed on continuous subcutaneous insulin infusion (CSII) - insulin pump therapy- and continued using Insulin Glulisine. Over the following two years her diabetes control was well maintained with HbA1c consistently <6.5% and no diabetes complications were detected. Average total insulin requirement was 25 to 35 units in 24 hours. On July 20th 2013, the patient started experiencing symptomatic hyperglycemia with post-prandial blood glucose levels ranging between 18 and 23 mmol/l; meanwhile the insulin pump did not display any error code or unusual alarm at all. As educated, and being a medical student herself, she recalculated her carbohydrate proper-

ly, examined the insertion site, changed the reservoir and the pump infusion set, which looked normal with no air bubbles, and then refilled her insulin from the pharmacy. All these measures only resulted in very minimal improvement in her blood glucose levels. Furthermore, the patient increased the basal insulin rate by 0.05 units every hour and continued to monitor blood glucose levels to assess the reponse. The total basal insulin dose was increased gradually from 16 to 70 units per day, to bring the blood glucose to be around 11.1mmol/ l at best. Meanwhile, the patient experienced increased urination, nausea, blurry vision, increased appetite and unsatisfactory general condition. Over a 10 day period, she gained 3 kg's and did not have any hypoglycemic episodes. The patient monitored her ketones using urine strips, and the results were trace to negative. At this stage, the patient decided to change her Insulin Glulisine to Insulin Aspart (Novorapid, Novo Nordisk) because it was more readily available at the nearest pharmacy to her residence. Assuming her requirements would be the same, she started the infusion with 2 units per hour as a basal rate with a concurrent blood glucose of 14 mmol/l. To her surprise, she developed symptoms of hypoglycemia two hours later. Glucose meter readings confirmed blood glucose levels of 2.9 mmol/l. She immediately reduced the total basal insulin to 20 units per day. The patient felt a remarkable improvement in general health as symptoms of hyperglycemia rapidly abated. Over the following 4 weeks, patient went back to her original weight of 56 kg, her basal insulin daily requirement decreased to 15.6 units. Blood glucose levels ranged between 4.5 to 6.0 mmol /liter in the fasting state and 6.5 to 8mmol/ liter after meals. In October 2013 the same "old- ineffective" batch of insulin Glulisine was cautiously retried. However, on this occasion, it was fully effective.

Discussion

Unexplained hyperglycemia is defined as blood glucose levels above 16.7 mmol/ l that persist for more than four hours with no apparent medical, dietary, insulin dosage or pump failure reason. A recent 13-week study by van Bon et al. revealed that percentages of subjects with at least one unexplained hyperglycemia and/or infusion set occlusion were 68.4% for Glulisine insulin, 62.1% for Aspart insulin and 61.3% for Lispro insulin, all were not significantly different when compared head to head according to investigators (3,4). The present patient was previously well-controlled and had no plausible explanation for the event since she was healthy, afebrile, not pregnant, with stable weight, had no recent stressful life events and used no new medications or herbs that might affect blood glucose levels. Although she could have switched to insulin pens and waited to see her care provider, she elected to handle the matter herself in a systematic way. She recalculated her carbohydrate intake accurately, changed the reservoir and the pump infusion set, refilled the insulin, increased the basal insulin gradually and continued to monitor blood glucose levels and urine ketones, all with minimal improvement. Eventually, the patient opted to shift to different instant acting insulin. Immediate clinical and biochemical improvement with the new insulin suggested that the previous insulin was not fully effective. Our patient failing control on Glulisine insulin was fully responsive to Aspart insulin negating insulin failure due to systemic illness or pump malfunctioning. The recovering of full effect of same previously-ineffective-batch of Glulisine insulin 3 month later is inexplicable and might point to transient insulin failure, may be due to the development of short-lived antibodies against Glulisine insulin specifically.

Diabetes self-management education and frequent blood glucose monitoring are integral parts of diabetes treatment plan in order to manage potential risks to patients using insulin pumps including hypo and hyperglycemias. The most common causes of hyperglycemia in "otherwise healthy" diabetics are food related, mechanical difficulties and physiological counter-regulatory hormone response (2). Food related hyperglycemia may occur due to the slower absorption of carbohydrates secondary to the presence of high fat and protein content or delayed gastric emptying. Employment of the extended bolus/dual wave bolus features on insulin pumps are used to offset this process. Mechanical difficulties that might cause hyperglycemia include expiration of insulin, conditions where insulin or insulin pump are left out in extreme weather thereby causing the insulin to be denatured, miscalculation of insulin dose, hypertrophy of injection sites that prevent or delay insulin absorption, leakage of insulin at the insertion site, tubing obstruction due to insulin instability or kinked tubing and finally failure of pump hardware. Physiologic counter-regulatory response causes hyperglycemia because of increased release of epinephrine, norepinephrine, cortisol, endogenous glucagon, or growth hormone. Other hormones such as testosterone, progesterone, estrogen and human chorionic gonadotrophin can also cause hyperglycemia. Included in this category are exercise that might rarely cause hyperglycemia, dawn phenomenon and the Somogyi effect.

In summary, unexplained hyperglycemia is a real

challenge to patients and physicians as it can lead to serious and life threatening complications such as diabetic ketoacidosis. Careful evaluation of the circumstances, physical examination and examining the techniques in pump programming can uncover many potential causes of hyperglycemia. Transient insulin failure should be considered as a cause of unexplained hyperglycemia and physicians should consider changing the type of short acting insulin when otherwise healthy diabetics develop persistent hyperglycemia.

References

1. Ponder SW, Skyler JS, Kruger DF, Matheson D, Brown BW. Unexplained hyperglycemia in continuous subcutaneous insulin infusion: evaluation and treatment. Diabetes Educ. 2008;34(2):327-33.
2. Cogen, F. The top causes of unexplained hyperglycemia. [cited 2013 November 1]. available from: http://www.healthcentral.com/diabetes/c/651280/121374/hyperglycemia/.
3. Hoogma RP. Schumicki D. Safety of insulin glulisine when given by continuous subcutaneous infusion using an external pump in patients with type 1 diabetes. Horm Metab Res 2006;38:429-33
4. van Bon AC. Bode BW. Sert-Langeron C. Devries JH. Charpentier G. Insulin glulisine compared to insulin aspart and to insulin lispro administered by continuous subcutaneous insulin infusion in patients with type 1 diabetes: a randomized controlled trial. Diabetes Technol Ther 2011;13:607-14.