

Pasireotide-induced hyperglycemia

Abstract

Pasireotide has been shown to be an efficacious therapeutic agent for patients with acromegaly. Its use has also been associated with hyperglycemia. We report a case of pasireotide-induced hyperglycemia and review the recommendations for combatting this side effect.

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Introduction

Pasireotide (Signifor®) is a new-generation, multi-receptor targeted somatostatin analogue approved for treatment of Cushing's disease or acromegaly. It is indicated for patients who are non-surgical candidates or those inadequately treated with surgery.^{1,2} Pasireotide decreases growth hormone (GH) secretion by binding to somatostatin receptor subtypes expressed by somatotroph tumors.³ In a phase 3 study Colao et al.,⁴ evaluated 358 patients with medically naive acromegaly. One year of monthly injections were compared between pasireotide LAR vs. Octreotide LAR. Results favored pasireotide LAR with normalized IGF-1 levels (38.6% vs 23.6%) and attained GH <2.5µg/L (48.3% vs 51.6%). Although most adverse events with pasireotide in this trial were similar to those experienced with other somatostatin receptor ligands (SRLs), the incidence of hyperglycemia-related adverse events was greater in those treated with pasireotide LAR (57.3% vs 21.7%).⁵ As a novel therapeutic agent for acromegaly, pasireotide's potential for adverse events should be considered.

Case presentation

A 38-year-old man with acromegaly underwent endoscopic transphenoidal hypophysectomy in February 2016. A two-month postoperative IGF-1 level remained elevated at 690ng/ml (baseline 280ng/ml). He was started on adjuvant therapy with pasireotide LAR 40units IM every 4weeks. After three doses, the patient presented with symptoms of nausea, polyuria, polydipsia, weakness, vomiting, and syncope. He also had an abrupt 20-pound weight loss. He was treated for DKA, and transitioned to Lantus and As part of note, his HbA1c increased from 6.2% (baseline) to 12.5% (hospital admission) after treatment initiation of pasireotide LAR. He was discharged on a basal bolus.

Discussion

Pasireotide has been associated more with hyperglycemia than any other SRLs in patients with acromegaly or Cushing's disease.³⁻⁶ The hyperglycemia is attributed to reducing insulin secretion and incretin response. On the other hand, glucagon secretion and insulin sensitivity appear to be minimally affected.^{7,8} A phase 3 core study by Sheppard et al. found that more patients with normal fasting plasma glucose (FPG) (<100mg/dL) at baseline developed hyperglycemia at their final assessment on pasireotide compared with octreotide (69% vs 39%).⁹

Treatment options have been proposed. A phase 1 study by Breitschaft et al.,⁸ co-administered pasireotide along with an anti-hyperglycemic to healthy volunteers. GLP-1 agonists and DPP-4 inhibitors were most effective lowering plasma glucose AUC post-OGTT and attenuating decreases in serum insulin.⁸ Furthermore, Gadelha et al.,¹⁰ found that patients with acromegaly and FPG>250mg/dL showed improvement in FPG if anti-diabetic medications were initiated within 2weeks of the first dose of pasireotide LAR.^{3,10}

Conclusion

Our case highlights the need for additional studies to better assess the long-term effects of pasireotide on glucose metabolism. Early initiation of anti-diabetic medications and close glucose monitoring will help improve glycemic control in acromegalic patients treated with pasireotide LAR.

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Conflict of interest

The author declares no conflict of interest.

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