(SSTR) subtype 2 specific somatostatin analogues (SSA). Pasireotide is a newer multiple SSTR binding SSA with actviity primarily at SSTR5 and SSTR2, which has not been widely studied in AIP mutated patients. **Clinical case and results.** A male patient was diagnosed aged 29 with a GH-producing pituitary macroadenoma (25×18×23 mm); he was from a FIPA kindred and his sister also had acromegaly due to a pituitary macroadenoma (25 mm) at age of 24 and was cured by neurosurgery. A familial AIP mutation p.Gln217X was revealed in the index patient, his sister and an unaffected nephew. The patient underwent transsphenoidal surgery, with partial resection of a GH and prolactin positive adenoma. He was treated for post-operative corticotroph, thyrotroph and gonadotroph deficiencies but GH hypersecretion by the residual tumor required adjuvant medical treatment. He was treated with SSTR2 specific agents (lanreotide autogel and octreotide LAR), but without hormonal control. Addition of cabergoline did not improve hormonal suppression. An increase of tumor residue size was observed on SSA treatment and the residual tumor approximated the chiasma, which precluded safe surgery and pegvisomant therapy, while the patient declined radiotherapy. The patient began pasireotide LAR and was uptitrated to 60 mg/month. The clinical signs of acromegaly improved, GH/IGF-1 was controlled and tumor size was stable. Pasireotide was associated with worsening of existing impaired glucose control and treatment with metformin, gliclazide and liraglutide was required. After 2 years of treatment the dose of paseriotide was decreased to 40 mg/4 weeks and further follow-up showed tumor shrinkage and an empty sella. However, glucose metabolism worsened over time despite existing therapy and exogenous insulin treatment was required. **Conclusion.** In this patient from an AIP-mutation positive FIPA family, resistance to surgery, SSTR2-spcific SSA and cabergoline was seen. Pasireotide permitted clinical, hormonal and tumoral improvement, albeit at the cost of long-term worsening of hyperglycemia requiring increasing antidiabetic therapy.

KEYWORDS: somatotropinoma, acromegaly, AIP, FIPA family, pasireotide LAR.

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CARBOHYDRATE METABOLISM IN PATIENTS WITH CUSHING DISEASE AND ACROMEGALY: A GLANCE AT THE INCRETIN SYSTEM

Lubov Matchekhina

Endocrinology Research Centre, Moscow, Russia

Introduction. The relevance of carbohydrate metabolism studying in patients with Cushing disease (CD) and acromegaly can be explained by frequent occurrence of glucose metabolism disturbances on the one hand, and difficulties in glucose-lowering therapy in these patients on the other. The effectiveness of hyperglycaemia treatment may be reduced due to difficulties in remission/cure of the underlying disease, as well as to the use of specific drug-therapy, leading to hyperglycaemia. There is a growing interest in research aimed at studying the role of incretin system in the pathogenesis of secondary hyperglycemia associated with neuroendocrine diseases recently. **Aim of the study.** To analyze the rhythm and levels of incretins and neuropeptides secretion in patients with CD and acromegaly and therefore to specify the pathogenesis of carbohydrate metabolism disturbances. **Material and methods.** 42 patients with Cushing disease and acromegaly were included; the mean age was 37.5 years. All of the patients were newly diagnosed with Cushing disease (using urinary free cortisol levels, evening saliva cortisol levels and low-dose dexamethasone suppression test) and acromegaly (in absence of GH suppression during OGTT and high IGF-1 levels); none of them had a history of previous drug therapy, radiotherapy or pituitary surgery. All patients underwent OGTT, during which glucose, glucagon, GLP1, GLP2, GIP, ghrelin were measured at 0, 30 and 120 min respectively. **Results.** During OGTT glucose levels were not significantly different in all groups. The mean HbA_{1c} level was 5.8% (5.3—6.2). However the relevance of prediabetes was higher in CD patients. In CD patients glucagon levels were significantly higher at all cut off points compared to controls (p=0.001). In acromegaly patients, no significant differences were found. GIP secretion was slightly lower in CD patients; in acromegaly patients, no differences were found. Acromegaly group was characterized by inverse rhythm of GIP secretion, with no peak level at 30': GIP 0 min — 194.2 pg/ml, GIP 30 min — 178.8 pg/ml/. GLP-1 levels were significantly higher in CD patients (p=0.047). In acromegaly group, no significant differences in GLP-1 secretion were found. GLP-2 levels were significantly higher in CD patients compared to acromegaly and controls (p=0.001). Ghrelin levels were significantly higher in CD (p=0.013) and acromegaly (p=0.023) patients. **Conclusion.** More pleotropic actions of glucocorticoids can possibly explain higher relevance of carbohydrate metabolism disturbances in CD patients. This can be also explained by higher levels of glucagon secretion, which does not depend on type of carbohydrate metabolism disorder and is stimulated by a direct action of glucocorticoids on glucagon receptor. GIP and GLP-1 secretion in CD and acromegaly patients are characterized by inverse rhythm with no peak levels which means that these hormones are not playing the crucial role in carbohydrate disturbances development in these patients. On the contrary, GLP-2 and ghrelin seem to influence and potentially regulate glucose homeostasis in CD and acromegaly patients.

KEYWORDS: Cushing disease, acromegaly, glucose metabolism disturbances, hyperglycemia, incretin system.

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