Recurrent apnea in a boy suffering from congenital hyperinsulinism in the course of diazoxide treatment.

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Authors declare nothing to disclose

Introduction

Congenital hyperinsulinism (CHI) is a rare disease caused by **mutations in genes responsible for regulation of insulin secretion**. The most common are mutations of K_{ATP} channel. Nowadays we are still not aware of knowledge of exact mutations in 20% of all patients. **All of those disregulations lead up to inadequate excessive secretion of insulin (fig.1). It is the cause of frequent hypoglycemias in individuals suffered from this disease** . Prevalence of CHI is estimated at 1:2500 to 1:50000 live births.

First line treatment is a *diazoxide* therapy. In a case of bad metabolic control or occuring serious side effects of a therapy **somatostatine analogs, rapamicine or nifedipine might be used instead of diazoxide.**

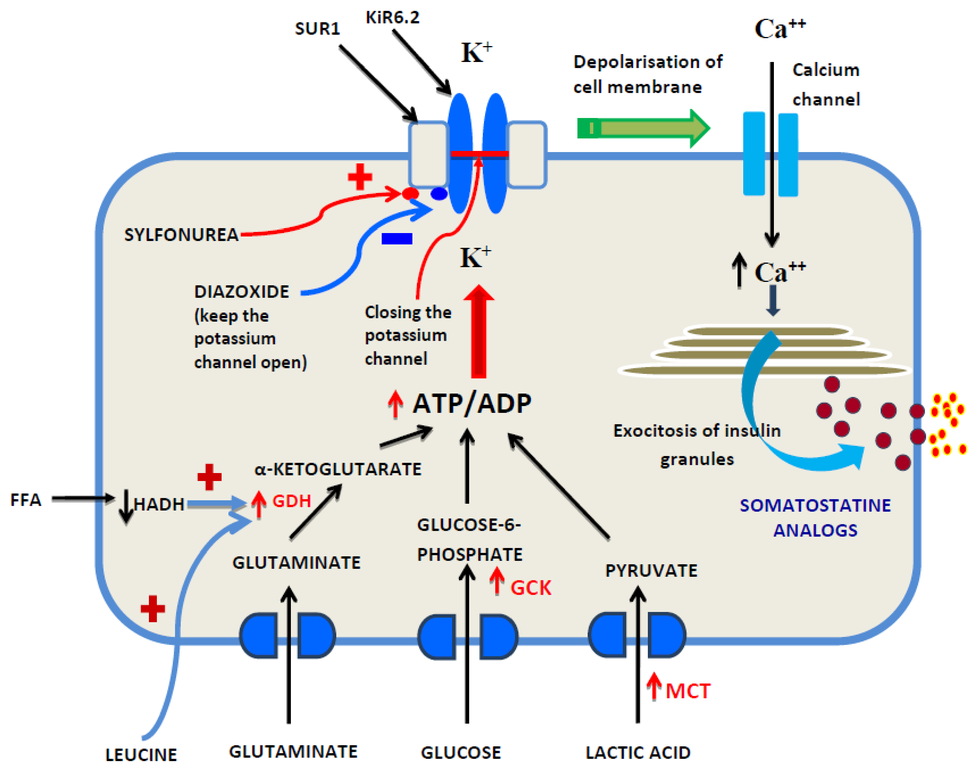

Fig.1 Regulation of insulin secretion in pancreatic beta cell with the most common disregulations leading to CHI (*B.Skwrońska, J.Nowaczyk et al. Wrodzony hiperinsulinizm, Endokrynologia wieku rozwojowego, PZWL 2018*) - own modification

Case report

Our male patient was reffered to the hospital for a first time at the age of 2 months because of episodes of faintness accompanied by hypoglycemia. Laboratory tests confirmed diagnosis of hyperinsulinemic hypoglycemia (***Tab. 1***).

Glucose (mg/dl)	Insulin (µIU/ml)	Cortisol (µg/dl)	Growth hormone (ng/ml)	Amonate (µg/dl)	Lactic acid (nmol/ml)	fT4 (ng/dl)	Ketone bodies in urine
26	15,5	15,9	2,77	<15	2,8	1,33	None

Tab. 1 Laboratory test results

We **denied different** diagnosis like a **inborn metabolic errors**. At the beginning he was treated with diazoxide with a good effect. **Patient achieved normalization of glycemias and the treatment was well tolerated.** Unfortunatelly **in december 2017** he had **first episode of apnea** which was **not connected with hypoglycemia**.

Since december 2017 the boy presented next 3 episodes of apneas not related to hypoglycemia, **they always appeared once the dose of diazoxide was increased (Fig.2)**.

FDA warns of pulmonary hypertension in infants treated with diazoxide

FDA is warning that pulmonary hypertension has been reported in infants and neonates who received diazoxide (Proglycem—Teva) for treatment of hypoglycemia. The condition resolved or improved in all cases after treatment was stopped.

However in the case of our patient during a whole diagnostic process **we didn't find any cardiological (no signs of pulmonary hypertension), neurological (no abnormalities in MRI and EEG) or gastroenterological reasons of apnea.**

Because of intolerance to diazoxide we decided to change the way of his treatment and recommended octreotide in multiple daily injections therapy. At the beginning we observed very good reaction and good glycemic control, but after a few days we observed tendencies to hypoglycemia. Because of lack of a good response to the octreotide by itself, we decided to combine two ways of the therapy – and recently the boy is succesfully treated with diazoxide in smaller dose (2,9 mg/kg) and octreotide received via personal insulin pump (5,7 mcg/kg). Because of secondary adrenal cortex insufficiency caused by octreotide action he also needs to take hydrocortisone orally in supplementary dose. When the dose of diazoxide was decreased no other apnea occured and he's got good metabolic control (Fig.3).

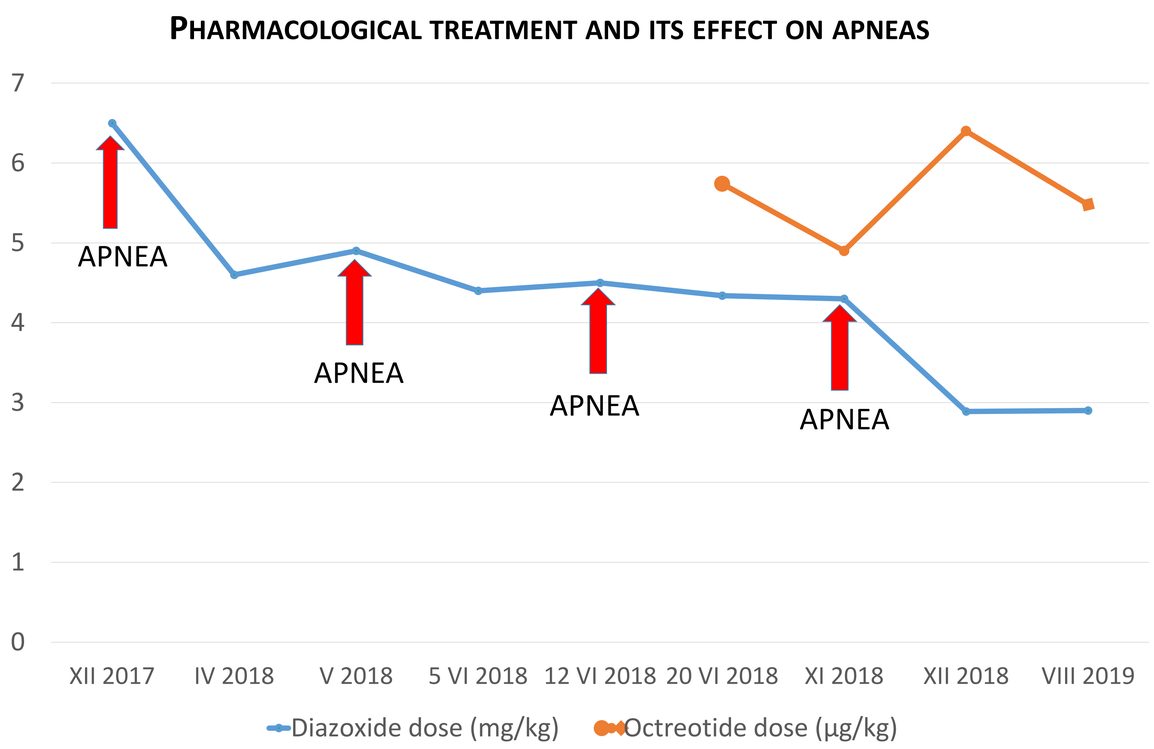

Fig.2 Pharmagological treatment and its effect on apneas

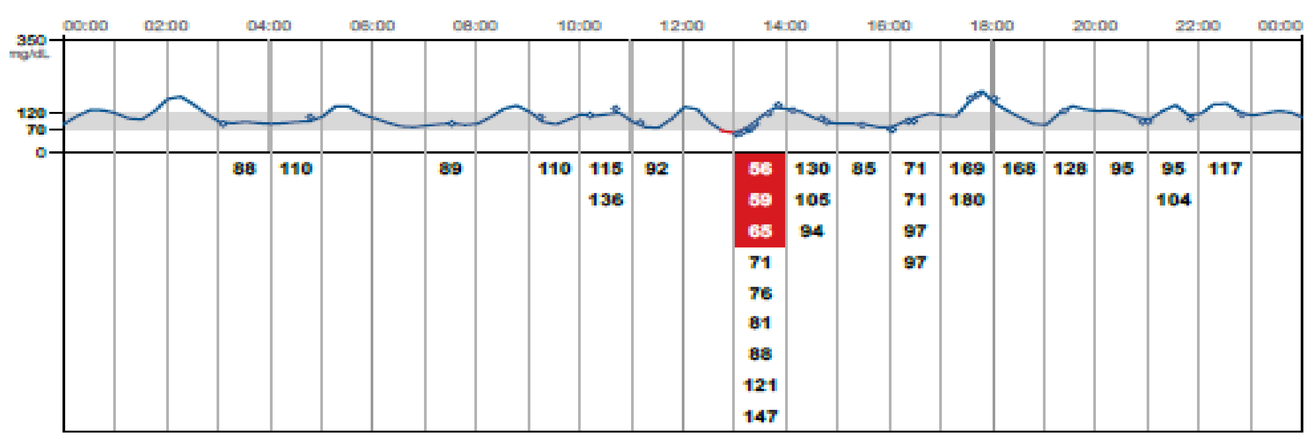

Fig.3 Flash glucose monitoring system report of a patient

Conclusions

There are some reports of kids treated with diazoxide who presented episodes of apneas caused by pulmonary hypertension. In case of our patient **we've never noticed any features of pulmonary hypertension in echocardiography and physical examination as well as other causes of apnea. It prooves that diazoxide might trigger an apnea in different mechanism which is still unknown.**

Patients treated with somatostatine analogs might develop supression of counterregulatory systems (e.g. pituitary-adrenal cortex axis) what complicates management of a patient and indicates implemantation of supplementary hormonal therapy.

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Fetal, neonatal endocrinology and metabolism (to include hypoglycaemia)

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