TITLE

Long acting somatostatin analogs in the management of congenital hyperinsulinism in cases with poor compliance to conventional therapy

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OBJECTIVES

Congenital hyperinsulinism(CHI), is the most common cause of severe hypoglycaemia in neonates and infants. The cornerstone of medical therapy is diazoxide. Octreotide, a somatostatin analogue, is the second therapeutic option in diazoxide unresponsive cases. However, due to its short half-life and requirement of multidose application, lack of compliance may cause recurring hypoglycaemia and related neurological deficits, particularly for the family with low socioeconomic status. Long acting somatostatin analogs that provide good glycaemic control by a monthly injection, might help in the management of CHI patients who have poor compliance with conventional medical therapy. Herein, we report the management of 5 patients with diazoxide unresponsive CHI who have poor compliance, using the long-acting somatostatin analogue, octreotideLAR(oLAR).

PATIENTS

Patient details are summarized in Table 1. Patients 1, 2 (two siblings) and 3 had been diagnosed in the neonatal period and were diazoxide unresponsive but, octreotide responsive. All developed severe neurodevelopmental deficits and epilepsy due to recurring hypoglycaemic episodes as a result of the non-compliance. Patient 4 was the first cousin of patient 3 and had another sister with CHI due to identical mutation and severe mental-motor retardation. We therefore commenced oLAR in this patient at a younger age resulting in more favorable blood measurements and neurological development. Patient 5 was also started on oLAR therapy at a younger age and had a good glycaemic control, consequently normal neurological development. In all 5 patients diazoxide and multidose octreotide was weanned off successfully. Furthermore, we have not observed any severe acute or long-term side effects requiring treatment withdrawal (Table 1).

Table 1. Presenting caharcteristics, gentics and and follow up of patients

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Age of diagnosis	1st week	1st week	1st week	2nd week	1st week
Age at oLAR therapy	5.8	9.8	4.0	1.3	1.9
Mutation	c.3512del (*ABCC8)*	c.3512del (*ABCC8)*	c.3554C>A (*ABCC8*)	c.3554C>A (*ABCC8)*	NA
Octreotide dose (mcg/kg/day)	10	5	13.3	20	10
Diazoxide dose (mg/kg/day)	10	10	7.5	15	15
OctreotideLAR (mg/28 day)	30	30	30	30	30
TFT's initial/follow up	Euthyroid	Euthyroid	Euthyroid	Euthyroid	Euthyroid
TFT's follow up	Euthyroid	Euthyroid	Euthyroid	Euthyroid	Euthyroid
Lineer growth	Normal	Normal	Normal	Normal	Normal
IGF1/IGFBP3 initial (µg/L)	108/3000	241/4030	53/3140	NA/4280	101/3020
IGF1/IGFBP3 folow/up (µg/L)	NA/NA	NA/NA	136/NA	NA/NA	167/4180
Gallbladder pathology	No	No	No	No	No
Side effect (other)	No	No	No	No	No

CONCLUSION

Administration of long acting somatostatin analogs(28 daily) results in better compliance and thereby prevents recurring hypoglycaemic episodes and related neurological deficits. In case of low scoieconomic status and poor compliance long acting somatostatin analogs may potentially be the first option in the medical therapy of CHI.

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