Treatment of hyperinsulinaemic hypoglycaemia with nifedipine

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Abstract We report on two children with mild persistent hyperinsulinaemic hypoglycaemia. In both, oral nifedipine treatment (0.7 and 2.0 mg/kg per day respectively) had a significant clinical effect. In one case, nifedipine monotherapy prevented hypoglycaemia; in the second case, the dosage and the side-effects of other substances could be reduced, thus circumventing surgical therapy.

Conclusion Nifedipine treatment has a favourable effect on the clinical course of patients with mild hyperinsulinism. It represents a valuable new substance for the treatment of this disorder.

Key words Nifedipine · Hypoglycaemia · Hyperinsulinism · Nesidioblastosis · Persistent hyperinsulinaemic hypoglycaemia of infancy

Abbreviation PHHI persistent hyperinsulinaemic hypoglycaemia of infancy

Introduction Persistent hyperinsulinaemic hypoglycaemia of infancy (PHHI) is a rare, heterogeneous disorder of glucose metabolism affecting approximately 1 in 50000 individuals [1, 6]. PHHI presents with variable clinical phenotype including cases with mild or very severe hypoglycaemia. Since the risk of neurological damage is high, early diagnosis and appropriate treatment have a pivotal role in long-term outcome. Although a surgical management is frequently required, some milder cases respond to a protein-restricted diet and/or to medical treatment with diazoxide or/and the somatostatin analogue octreotide [4]. However, side-effects of these drugs such as anorexia, nausea, vomiting, fluid retention with oedema, and hypertrichosis are limiting factors and in many cases surgical treatment cannot be circumvented. Here we report on two children with hyperinsulinaemic hypoglycaemia with a favourable response to the calcium channel blocker nifedipine.
nifedipine (0.7 mg/kg per day) and diazoxide in a reduced dose (6 mg/kg per day) was therefore introduced and was effective. Glucose infusion could be terminated without the recurrence of hypoglycaemia (Fig. 1a,b). With the exception of tolerable hypertrichosis, the side-effects of diazoxide disappeared and this therapy has been continued for more than 2 years. Before discharge from hospital the parents were instructed to monitor the child’s blood glucose (with a minimum of three and up to 12 determinations per day). Repeatedly, a decline in plasma glucose level, without reaching hypoglycaemic levels, has been observed. This could be reversed by an adjustment of the drug dosage to the increasing body weight, suggesting that hyperinsulinism is persistently present.

Case 2

This patient is the second child of non-consanguineous German parents. Her mother, the maternal grandmother, and a maternal aunt also suffer from persistent hypoglycaemia suggesting a dominant trait [3]. An activating mutation in exon 10 of the glucokinase gene as reported by Glaser et al. [2] was not detectable. The girl was born at term with a birth weight of 2800 g. During the newborn period tetralogy of Fallot was diagnosed. At that time no hypoglycaemia was noted. At the age of 15 months the patient had a first hypoglycaemic seizure (plasma glucose 36 mg/dl). Since the age of 19 months hypoketotic hypoglycaemia with a minimum plasma glucose concentration of 16 mg/dl was repeatedly documented during periods of prolonged fasting and after protein-rich feeds. During hypoglycaemic episodes, plasma insulin concentration was repeatedly elevated up to a value of 16.9 μU/ml. Consequently, the insulin [μU/ml]/glucose [mg/dl]-ratio was elevated (0.54 normal < 0.4). An oral provocation test with leucine (150 mg/kg) resulted in severe hypoglycaemia with an inappropriately high insulin/glucose-ratio of 0.9. Since the patient’s mentally retarded mother was considered to be unable to prepare a protein-restricted diet with frequent feeds, medical treatment was started. After increasing oral monotherapy with nifedipine to a dosage of 2 mg/kg per day, no further episodes of hypoglycaemia could be documented (Fig. 1c,d).

References


![Fig. 1a-d](image)