Journal Digest for Congenital Hyperinsulinism

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A Chinese cohort of patients with CHI (n=50) were characterised; 52% were diazoxide unresponsive. Gene variants suggestive of pathologic changes were identified in 48% which is similar to EU and US rates of genetic diagnosis in CHI. In this enriched cohort, 32% had focal lesions, although not all (75%) were cured by lesionectomy surgery. The presence of hotspots in *ABCC8* and *KCNJ11* for Chinese patients was noted [1]. This study confirms and reinforces existing knowledge that ATP-sensitive K+ channel mutations are the predominant causes of CHI not only in the EU and US but also in China.

Hypoglycaemia is often observed in children following gastric procedures, such as gastrostomy. The cause for hypoglycaemia is not well known but is generally labelled as post prandial hypoglycaemia. In adults undergoing bariatric surgery, hypoglycaemia is well recognised. A retrospective observational study from a large surgical centre involving 333 obese patients undergoing various gastric procedures noted the high frequency of hypoglycaemia (25%). While this finding is not directly relevant to children, the frequency of hypoglycaemia in children following gastric surgery is not well known. Given the findings from adults, it may be important to assess hypoglycaemia due to hyperinsulinism in children undergoing gastric surgery [2].

Diazoxide is commonly used in CHI but has a range of side effects. Following a recent publication by the group from Philadelphia[3], a recent publication from a group from Texas also showed a relatively high rate of pulmonary hypertension (4.8%), and a similar frequency with neutropaenia[4].

In a new study in Journal of Pharmacology and Experimental Therapeutics[5], the authors have described potential novel treatment of hyperinsulinism. While diazoxide is the only licensed treatment of CHI, it suffers from off target effects and consequently has an adverse safety profile. VU007 1063 is a novel compound discovered in a high throughput screen that is a scaffold activator of Kir6.2/SUR1. The drug is noted to be a more potent opener of ATP sensitive K+ channels than diazoxide; in time, this drug may come to clinical trial and may be utilised as new treatment for hypoglycaemia[5].

Sirolimus had been introduced as an oral drug in 2014 to be used as third line medication in an effort to minimise the need for subtotal pancreatectomy. However, several publications did not support efficacy and suggested the risk of serious adverse effects. A recent paper from the same group as the original NEJM publication[6] has now been published 5 years from the original publication [7]. This is a retrospective study of 22 children in whom 20 showed partial response, one showed complete response and one showed no response. Most children suffered from infection complications (n=17, 77%); in those with infections, sirolimus was stopped in 13 patients, suggesting that infection risk was unacceptable. In this paper, the authors report partial response in the majority of patients treated with sirolimus; by inference, this implies inadequate efficacy and high risk of adverse effects to justify the use of sirolimus in children with CHI.

References:

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