Upsala J Med Sci 78: 215–216, 1973

Plasma Insulin Content and Glucose Tolerance in Homocystinuria

Short Communication

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ABSTRACT

The plasma insulin level and glucose tolerance were studied in five patients with homocystinuria. Two of them showed a marked hyperinsulinemia and a concomitant pathologic glucose tolerance, while the remaining three showed a normal glucose tolerance, two of them, however, had plasma insulin values in the upper level of the normal range. These preliminary results support the earlier hypothesis that the pancreatic islets β-cells are particularly sensitive to an imbalance in the sulfhydryl levels of the organism since homocystinurics have an increased plasma methionine level due to an inborn error of the methionine metabolism.

INTRODUCTION

Homocystinuria, an inborn error of transsulfuration in the methionine to cystine pathways, results in connective tissue abnormalities, thrombosis, and mental retardation (4). In addition, seizures with early onset are often observed. They have usually been ascribed to "cerebral thrombosis" (2). However, it is known that patients with familial hypermethioninaemia can have islet cell hyperplasia and hypoglycaemia (5). As homocystinuria is associated with an accumulation of methionine (4), the ensuing hypermethioninaemia might elicit an islet cell hyperplasia with hyperinsulinaemia and hypoglycaemic convulsions also in homocystinuria.

The pathogenesis of these signs of putative functional islet tissue alterations in homocystinuria has been investigated previously in experimental studies from one of our laboratories on the effect of excess methionine on both the exocrine and endocrine pancreas (1) and on the role of sulfhydryl compounds in the pathogenesis of diabetes mellitus (3).

In order to test this working hypothesis, plasma insulin assays and glucose tolerance tests were made in 5 patients with homocystinuria and hypermethioninaemia. Two patients (cases 1 and 2) were 23–24 years old, 3 (cases 3–5) were between 10 and 16, and the clinical picture was typical for homocystinuria in all 5 cases.

Table 1. *Plasma methionine and plasma insulin contents, as well as glucose tolerance, in patients with homocystinuria*

	Case 1 24 ♂	Case 2 23 ♂	Case 3 16 ♀	Case 4[b] 12 ♂	Case 5[b] 10 ♀	Normal range
Methionine (μmoles/l)	449	367	316	644	242	13–29
Insulin (μU/ml)	25	20	29	40	45	5–25
Glucose tolerance	normal	normal	n.p.[a]	pathological	pathological	

[a] n.p. = not performed.
[b] Siblings.

METHODS

The determinations of the plasma methionine concentrations were performed by ion exchange chromatographic analysis. The plasma insulin assays were made in patients fasted overnight, using a commercial radioimmunoassay technique (Phadebas®, Pharmacia, Uppsala, Sweden). Glucose loading was performed by oral ingestion of 1 g of glucose per kg body weight.

RESULTS AND DISCUSSION

The plasma insulin content far exceeded the normal range in cases 4 and 5 (Table I). High values, close to (or even above) the upper level of the normal range, were obtained in cases 1 and 3, whereas the insulin content was normal in case 2. The glucose tolerance tests were pathological in cases 4 and 5, showing an initially steep elevation of the blood glucose level, followed by an abrupt decrease within the first hour, tallying with a state of hyperinsulinism.

A more detailed analysis of the glucose tolerance of all the patients is now being made in our laboratories.

The results of this pilot study indicates that the working hypothesis is valid, *viz.* that a state of hyperinsulinism can exist in patients with homocystinuria. It is conceivable that this hyperinsulinism is able to evoke episodes of hypoglycaemia like those occurring in familial hypermethioninaemia (5).

However, it is still not shown in our patients that these episodes of convulsions are in fact due to hypoglycaemia, as no blood glucose assays have been performed in any of them during actual convulsions, malaise, or faintings.

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Received June 15, 1973

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