Congenital Hyperglycinemia; Demonstration of a Minor Metabolic Defect in the Parents

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Oral glycine loading test to the parents of a patient with congenital hyperglycinemia revealed that the elevation of glycine was more remarkable and that of serine less remarkable. It is, therefore, suggested that the parents have a minor block in the conversion of glycine to serine and that they are heterozygous for the disorder.

Idiopathic hyperglycinemia, first discovered by Childs et al.,1 is thought to be an inherited metabolic disorder, because of onset of the clinical symptoms and presence of metabolic anomaly in the early period of life and probable familial occurrence of the disorder.1-3

In our preceding studies on this particular disorder,4 the following results were obtained: 1) The fasting serum level of glycine was found to be slightly but significantly higher in the parents of a patient with hyperglycinemia than in controls. 2) In oral glycine loading test (0.5 g/kg), the parents showed significantly higher levels of serum glycine at 1, 2 and 3 hours following the test dose as compared with those of controls.

These results suggested that the parents were heterozygous for the disorder.

Basing upon these results, we have suggested that the term “congenital hyperglycinemia” is more appropriate for this disorder rather than “idiopathic hyperglycinemia.3,4

In this paper, further evidence of heterozygosity will be reported.

METHODS AND MATERIALS

Glycine loading test was carried out in the parents of a patient with congenital hyperglycinemia who was previously reported3 and in control individuals. Control subjects were all healthy adults working in the hospital; 0.5 g of glycine per kg of bodyweight was orally administered in the fasting state. Blood specimens were
drawn two hours after the ingestion of the amino acid, because the previous studies showed that serum glycine reached the maximal level one to two hours following the loading.

The levels of glycine and serine in serum were determined by the use of Automatic Amino Acid Analyzer (Beckman-Spinco type). Since the separation of serine from glutamine is incomplete by using the standard procedure of Spackman et al., a procedure modified by Yamane and Mitsuhashi was applied in order to make more accurate determination of serine. The standard procedure on the 150 cm column was modified as follows. The pH of the first buffer was kept at 2.50, and it was changed to the second buffer (pH 3.25) after \(9\frac{1}{2}\) hours and again changed to the third buffer (pH 4.24) after \(16\frac{1}{2}\) hours. The temperature change from \(30^\circ\)C to \(50^\circ\) was made after 13 hours. The speed was set at the normal rate of 30 ml/hr. Under this condition, serine was eluted between 325 and 340 ml and glycine between 450 and 465 ml, tracing a sharp peak, respectively.

**RESULTS AND DISCUSSION**

The results were shown in Table I. The levels of serum glycine following the glycine loading were significantly higher in the parents than in controls. These results are in agreement with those obtained by colorimetric determination in the previous experiment. The levels of serum serine were significantly lower in the parents than in controls. Accordingly, the ratio of glycine to serine was definitely higher in the parents than in the controls.

Congenital hyperglycinemia is characterized by a striking elevation of glycine in serum, urine and spinal fluid. Such an elevation of glycine is supposed to be attributed to a certain metabolic defect involved in glycine. Nyhan and Childs demonstrated, with the use of isotopically labeled glycine, that the conversion of glycine to serine was slower in a patient with hyperglycinemia than in the control individuals and they suggested that fundamental abnormality of the disorder might exist in conversion of glycine to serine. Since the degradation of glycine is thought to be mainly taken place through its conversion to serine,
the block in this conversion may reasonably result in an elevation of glycine in body fluid. The serine levels following the glycine loading are noticeably high, as is indicated in the present results, as compared with the fasting level of serine which has been reported to be ranging from 76 to 194 μmoles/l in normal adults. This supports that the conversion of glycine to serine is in vivo actually taken place. However, the present results show that the elevation of glycine is more remarkable and that of serine less remarkable following the glycine loading in the parents of the hyperglycinemic patient than in control individuals. It is, therefore, suggested that the parents also have a minor block in the conversion of glycine to serine and that they are heterozygous for the disorder.

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Literature

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