Short Report

Hyperglycinemia and Propionate Carboxylation*

KEIYA TADA and TSUNEORI ARAKAWA
Department of Pediatrics, Tohoku University School of Medicine, Sendai

TADA, K. and ARAKAWA, Ts. Hyperglycinemia and propionate carboxylation. Tohoku J. exp. Med., 1970, 102 (3), 313-314 — The oxidation of propionate and methylmalonate was investigated in leukocytes from a patient with hyperglycinemia. It was found that the patient's leukocytes could oxidize both propionate and methylmalonate normally. These findings suggest that hyperglycinemia consists of primary type and secondary type.

Hyperglycinemia; propionate carboxylation; methylmalonic aciduria

In 1969, we reported that the primary lesion of hyperglycinemia of nonketotic type was a defect in glycine cleavage reaction which gives rise to the formation of CO₂, methylene-tetrahydrofolate and ammonia from glycine, as a result of enzymatic studies of the liver biopsied from the patient.

On the other hand, Hsia et al. found a defect in the carboxylation of propionate to methylmalonate in leukocytes from a patient with ketotic hyperglycinemia.

It is, therefore, of significance to investigate the carboxylation of propionate in leukocytes from our patient with hyperglycinemia due to a defect in the glycine cleavage reaction.

MATERIALS AND METHODS

The patient with hyperglycinemia reported previously was subjected to the present studies. He was 3 years of age at the time of the present examination and showed a persistently elevated levels of serum glycine (7 to 15 mg/100 ml) for the past two years.

Fasting blood was taken from the index patient and two healthy controls. Leukocytes were isolated by dextran sedimentation procedure. About 1 x 10⁶ leukocytes suspended in 1.0 ml of isotonic phosphate buffer (pH 7.4) were incubated for 3 hours at 37°C with 2 μmoles of propionate-3-¹⁴C (specific activity 1.0 mCi per mmole) by using Warburg manometric flasks. In the same way, leukocytes were incubated with 10 μmoles of methylmalonate-methyl-¹⁴C (specific activity 0.2 mCi per mmole). Cell-free blanks were run for each experiment. The incubation was ended by the addition of sulfuric acid. ¹⁴CO₂ formed during the incubation was absorbed in 0.2 ml of 20% KOH placed in the center well of the flask and converted into BaCO₃ by precipitation with BaCl₂. Radioactivity of BaCO₃ was assayed by a gas-flow counter and the observed counts per minute were corrected for cell-free blank and self-absorption.

RESULTS

The results were shown in Table 1. There was no significant difference in the

* Supported by grants from Fundation for Metabolic Studies (Japan).
$^{14}$CO$_2$ formation from propionate or methylmalonate between the patient's leukocytes and controls' leukocytes.

**Table 1. Oxidation of propionate and methylmalonate from a patient with hyperglycinemia**

<table>
<thead>
<tr>
<th></th>
<th>$^{14}$CO$_2$ from propionate-$^{14}$C cpm per $10^6$ leukocytes</th>
<th>$^{14}$CO$_2$ from methylmalonate-methyl-$^{14}$C cpm per $10^6$ leukocytes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient with hyperglycinemia</td>
<td>3,066</td>
<td>1,048</td>
</tr>
<tr>
<td>Controls</td>
<td>2,838</td>
<td>1,134</td>
</tr>
</tbody>
</table>

**Discussion**

In 1968, Lindbald et al. described that the ketotic type of hyperglycinemia and methylmalonic acidemia might be the same disorder because of the similarity of clinical symptoms and the elevation of serum glycine often found in cases of methylmalonic acidemia. But the absence of the methylmalonic acid accumulation in the urine of the patients with hyperglycinemia clearly differentiated the two conditions.

Hyperglycinemia may consist of primary disorder of glycine metabolism due to a defect in the glycine cleavage reaction and secondary disorder due to other metabolic disturbance. The latter includes methylmalonic acidemia, propionic acidemia or hyperammoninemia. In secondary hyperglycinemia, the elevation of serum glycine is intermittent, whereas the patient with primary hyperglycinemia shows a persistent elevation of serum glycine.

Our previous studies, together with the present study, unquestionably indicate the existence of primary hyperglycinemia.

**References**