INFLUENCE OF ANESTHESIA ON THE RATE OF INSULIN BIOSYNTHESIS

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Hyperglycemia as a result of the action of various anesthetics was shown by several authors. But the mechanism of the development of this state is not yet clear. The increase in blood sugar cannot be explained by reduced activity of the key enzyme of carbohydrate metabolism — hexokinase of various organs and tissues. It cannot be excluded that hyperglycemia under the influence of anesthesia may correspond to inhibition of glucose consumption by peripheral tissues as a result of delayed insulin production or secretion. Some data show the difference in the mode of action of various anesthetics on hormone secretion. BRESSLER and BREDEL found inhibition of insulin secretion under some local anesthetics, but nitrous oxide did not influence the insulin blood level; at the same time ether anesthesia gave rise to a significant increase of hormone blood level.

Thus the characterization of insular apparatus is important not only for the investigation of the mechanism of hyperglycemia, but also for the rational selection of appropriate anesthetics in cases of pancreatic disorders.

We investigated insulin biosynthesis and secretion under anesthesia with the neuroleptanalgetic thalamonal and the barbiturate thiopental, the latter causing deep anesthesia. Additionally we tested the 11-OCS concentration in blood, because blood glucose may be elevated also as a result of corticosteroids release causing increased gluconeogenesis.

MATERIALS AND METHODS

The first group of rats weighing 180-200 g was infected with thalamonal [1:1:N-2-fentanyl-4N-propionylaniline-piperidine 0.05 mg/ml and 1,3-(4-fluorobenzoylpropyl)-4(2-oxo-1-benzymideazolylil)-1,2,3,6-tetrahydropyridine 2.5 mg/ml] 0.1 ml/g. Rats of the second group were given thiopenral sodium [5-(1-methyl-butyl)-5-ethyl thiobarbimrate sodium] 7 mg/100 g body weight. Once a state of general anesthesia was reached (with thalamonal this occurred after 5-10 min, with thiopental after 2-3 min) rats were given i.p. 0.1 μCi/100 g 14C-glycine (specific activity 170 μCi/mg) and sacrificed after 30, 60 and 120 min.

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90 min. Unanesthetized rats receiving the same dose of labeled amino acid served as control. 11-OCS was tested in blood plasma by a fluorimetric method, and immuno-reactive insulin by the double antibody method.

Insulin isolated from pancreas by acid alcohol extraction at pH 2.0 was repeatedly reprecipitated at the isoelectric point of insulin (by using crystalline insulin as a carrier) and additionally purified by double gel-filtration on Sephadex G-50 (column 1×50). Eluates of fractions corresponding to the insulin peak were pooled and evaporated. Protein and radioactivity were determined in aliquot parts. Total proteins were isolated from part of the pancreas. For this purpose 200 mg of tissue were homogenized in 2 ml 5% TCA. TCA-precipitate was prepared for detection of radioactivity of total proteins. Radioactivity of TCA-supernatant was tested after discarding of TCA (three times by triple volumes of ether) and was used as indicator of the presence of free amino acid in the pancreas.

Twenty intact rats and 60 rats in each experimental group (20 rats each time point) were used for investigation of levels of insulin and 11-OCS in blood. Ninety rats in each experimental group (45 intact rats and 45 ones under each kind of anesthesia — 15 rats each time point) were used for investigation of rate of insulin and total protein synthesis.

RESULTS

Plasma 11-OCS content was shown to be altered under the neuroleptanalgesia during the intervals employed (tab. 1). Investigation of the rate of $^{14}$C-glycine incorporation into insulin has shown that under thalamonal-induced anesthesia the biosynthesis of insulin is slightly delayed (fig. 1), because the maximum incorporation of labeled amino acid was reached by 60 min (in control animals by 30 min). Insulin blood content was decreased (tab. 2).

In order to evaluate the specificity of thalamonal-induced alterations of the rate of insulin synthesis we investigated the rate of synthesis of total proteins in pancreas. Fig. 1 shows the rate of synthesis of total proteins to be delayed similarly to that of insulin. Permeability of cellular membranes may be altered under neuroleptanalgesia thus disturbing the uptake of labeled precursor and consequently changing the rate of synthesis; it was therefore interesting to determine the rate of uptake of labeled amino acid by the tissue at the above mentioned intervals.

Radioactivity assay in the protein-free filtrate (fig. 2) showed that uptake of labeled amino acid was not changed at the time of testing (curves were similar in control and test animals although absolute values of radioactivity at all points were higher in the latter group).

<table>
<thead>
<tr>
<th>anesthetic</th>
<th>control</th>
<th>time after injection of anesthetic (min)</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>30</td>
</tr>
<tr>
<td>thalamonal</td>
<td>21.0±2.0</td>
<td>21.7±1.8</td>
</tr>
<tr>
<td>p</td>
<td>&gt; 0.2</td>
<td>&gt; 0.5</td>
</tr>
<tr>
<td>thiopental</td>
<td>21.0±2.0</td>
<td>12.2±1.1</td>
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<tr>
<td>p</td>
<td>&lt; 0.05</td>
<td>&lt; 0.01</td>
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</tbody>
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Table 1 - Influence of thalamonal and thiopental on plasma 11-OCS (μg%; M±m).