Insulin-induced hypoglycaemia is accompanied by increased pyruvate and lactate levels and decreased inorganic phosphate and potassium levels in the circulating blood. These changes are thought to be attributable to the effect of insulin on sugar metabolism and cell membrane permeability to inorganic ions. Very similar manifestations follow the administration of adrenaline.

Since insulin is also responsible for the release of endogenous catecholamines, the question naturally arises whether these metabolic changes are also dependent on increased catecholamine activity. In an attempt to find an answer to this question, we have studied the effect of β-adrenergic blockade with propranolol on both adrenaline- and insulin-induced modifications of blood sugar, pyruvate, lactate, phosphates and potassium. The present paper offers a summary of our results, part of which have been the subject of notes on single aspects of the problem.

MATERIAL AND METHODS

Eighteen male and 11 female apparently normal, non-obese volunteers aged 19-42 years were used.

Thirteen subjects received 10 μg/min adrenaline acid tartrate for 30 min in basal conditions and after 15 mg propranolol perfused over a period of 10 min (Inderal, Imperial Chemical Industries Pharmaceutical Division, Macclesfield, England); 12 different subjects underwent two insulin tolerance tests (0.15 U/kg body weight Actrapid 10 times recrystallized, Novo, Copenhagen, Denmark, administered within a few seconds), one of which was preceded by the administration of propranolol. The remaining 4 subjects received only propranolol.

Tests were carried out in random order with an interval of at least 4 days between tests in the same subject.

A cannula for blood sampling and perfusion was inserted into the elbow vein (both arms in the adrenaline test) after an overnight-fast in the recumbent subject and, after 15-30 min rest, 100 ml isotonic saline, with or without propranolol, were perfused over a period of 10 min. On completion of perfusion (time 0 min), insulin was given or adrenaline was perfused by means of a constant-rate pump. Blood sampling without

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Stasis was carried out with a heparinised syringe at — 10, 0, 10, 20, 30, 40, 50, 60 and 70 min (tests with propranolol or adrenaline alone, and adrenaline + propranolol) or at 0, 15, 30, 45, 60, 90 and 120 min (insulin and insulin + propranolol tests).

Glucose and inorganic phosphates were determined by the methods of Nelson and Fiske and Subbarow respectively. Potassium was estimated spectrophotometrically, while the enzymatic method was used to assay lactate and pyruvate (lactic acid and pyruvate tests; Boehringer, Mannheim, FRG).

RESULTS

Significant changes in blood glucose, pyruvate, lactate, phosphorus and potassium were not noted in the 4 subjects who received propranolol only. Moreover, the values for these parameters at time 0 in both the adrenaline and the insulin test, whether before or after propranolol, were fully comparable (tab. 1). Comparison can thus be made between the response to these drugs with or without propranolol.

Adrenaline test - Propranolol produced a slight, though significant fall in the hyperglycaemic response to adrenaline. A highly significant decrease was observed after only 10 min. It also abolished the marked adrenaline-induced increase in lactate and pyruvate (fig. 1) and the adrenaline-induced decrease in blood phosphorus and potassium (fig. 2). In the case of pyruvate, this blockade is limited to the period of the catecholamine perfusion.

Insulin test - There was no significant difference in the mean blood glucose curves obtained with and without propranolol (fig. 3), though 4 of the 12 subjects showed a slight delay in the rebound stage when propranolol was given.

Propranolol, on the other hand, significantly reduced the insulin-induced increase in pyruvate at 30, 45 and 60 min (fig. 3). Inhibition of the maximum increase, however, varied considerably (0-94%; mean 44% ± 17.7 SEM). The subject in whom there was no decrease after propranolol also displayed a very low increase after insulin alone.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Without Propranolol</th>
<th>With Propranolol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose (mg/100 ml)</td>
<td>86 ± 2.05</td>
<td>88 ± 1.74</td>
</tr>
<tr>
<td>Pyruvate (mg/100 ml)</td>
<td>0.79 ± 0.53</td>
<td>0.91 ± 0.07</td>
</tr>
<tr>
<td>Lactate (mg/100 ml)</td>
<td>9.6 ± 0.53</td>
<td>10.3 ± 0.67</td>
</tr>
<tr>
<td>Phosphate (mg/100 ml)</td>
<td>2.9 ± 0.12</td>
<td>2.9 ± 0.15</td>
</tr>
<tr>
<td>Potassium (mEq/l)</td>
<td>3.9 ± 0.10</td>
<td>3.8 ± 0.11</td>
</tr>
</tbody>
</table>

Table 1 - Basal blood sugar, pyruvate, lactate, phosphorus and potassium values (mean ± SEM) in the adrenaline and insulin tests, with and without propranolol.