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Short Communications

Insulin Effect in Chronic Alcoholics During Alcohol Withdrawal

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Summary. Insulin effect was investigated in 20 chronic alcoholics by use of an insulin and glucose infusion which suppressed endogenous insulin secretion. It was found that the effect of insulin was lower during the first week than the second week of alcohol withdrawal.

Key words: Insulin effect, chronic alcoholics, diabetes.

Mild hyperglycaemia is often observed in alcoholics during the first few days after admission to hospital following a period of heavy alcohol consumption. It has been claimed that this disturbance in glucose metabolism in alcoholics is due to alcohol-induced liver disease or adrenal and sympathetic stimulation [5]. However, transient diabetes has been reported in alcoholics without demonstrable liver or pancreatic disease [7]. Therefore alcoholism itself could be diabetogenic.

Diabetogenic factors, such as obesity, Cushing's syndrome and acromegaly are accompained by decreased insulin sensitivity [4]. In this study we report on the insulin effect in alcoholics recently admitted to hospital following a period of excessive alcohol intake.

Subjects and Methods

Subjects

One female and 19 male chronic alcoholics, aged 25–65 years, were studied. On admission to hospital they all displayed alcohol withdrawal signs, including tremor, tachycardia, perspiration and anxiety. Their mean ideal body weight was 96% (range 74–129%) [3].

None of the subjects had evidence of hepatic cirrhosis or pancreatic disease according to physical examination, serum bilirubin, aspartate and alanine aminotransferase, amylase and protrombin index. All the patients were treated with tranquillizers (clometiazol, propiomazin and nitrazepam). None of the patients were receiving drugs known to influence insulin effect. They were given a normal hospital diet whose caloric content was approximately 9200 kJ (50% carbohydrate, 30% fat and 20% protein). All had adequate nutrition before the study.

The subjects were informed of the nature, purpose and risks involved in the study before their participation and the study was approved by the local Ethical Committee.

Protocol

The patients were studied in the morning after an overnight fast for 10 h. They were given a constant infusion of glucose (330 mg/min), insulin (14 mU/min), adrenaline (6 μg/min), and propranolol (0.08 mg/min) into an antecubital vein for 3 h. Blood samples were drawn from a contralateral antecubital vein through an indwelling Teflon catheter, which was kept patent by a slow physiological saline infusion. Blood samples were drawn before and 60, 120, 150, 165 and 180 min after the start of the infusion. Under these conditions, endogenous insulin secretion is suppressed and steady state blood glucose and insulin levels are reached by 90 min [9]. The mean blood glucose values obtained from 120 to 180 min were used as a measure of the effect of insulin.

In the method described by Reaven et al. [9], insulin was infused at a rate of 80 mU/min. With this dose of insulin, we have found that in some healthy subjects, the steady state glucose level tends to fall below fasting levels. Under these conditions, counter-regulatory responses, might influence the insulin effect. In order to avoid the blood glucose falling below its fasting level, we used a lower insulin dose (14 mU/min) which resulted in rather low steady state serum insulin concentrations (about 30 mU/l). To prove that the steady state glucose level reflected the effect of insulin in these subjects, six were given the infusion mixture without insulin.

In all subjects, identical infusion mixtures were given twice. The first infusion was given 3–5 days after admission to hospital and the second infusion one week later.

Chemical Analysis

Whole blood glucose was determined in duplicate with a glucose oxidase method (Glox, AB Kabi, Sweden). Serum β-hydroxybutyrate was determined according to Persson [6]. Serum immunoreactive insulin (IRI) was determined by a slight modification of the double antibody technique, described by Soeldner and Slone [10]. The sensitivity was 0.5 mU/l, coefficient of variation was 7.9% for insulin values between 6–14 mU/l and 3.8% for insulin values between 16–48 mU/l. Serum growth hormone (HGH) and serum C-peptide were assayed with commercial kits (Phadebas HGH Prist, Pharmacia, Sweden and Diachic Radioisotope Laboratories, Tokyo, Japan). The sensitivity for HGH was 0.5 mU/l and coefficient of variation was 4.6% for values between 0.5–56 mU/l. The sensitivity for C-peptide was 0.1 nmol/l and coefficient of variation was 4.5% for values between 0.2–2 nmol/l.

Student's paired t test was used for statistical evaluation.

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Table 1. Fasting and steady state values at first (I) and second (II) examination

	Fasting		Steady state	
	I	II	I	II
Glucose (mmol/l)	5.0 ± 0.22	4.5 ± 0.12[a]	15.3 ± 0.58	12.9 ± 0.4[b]
Insulin (mU/l)	22.0 ± 1.8	17.0 ± 2.1[a]	30.0 ± 4.6	30.0 ± 4.4
C-peptide (nmol/l)	1.2 ± 0.2	1.1 ± 0.2	1.3 ± 0.3	1.2 ± 0.2
HGH (mU/l)	7.0 ± 2.4	4.7 ± 2.7	12.7 ± 3.6	10.6 ± 5.0
β-hydroxy-butyrate (mmol/l)	0.38 ± 0.13	0.09 ± 0.02[c]	–	–
Patients not given insulin (n = 6)				
Glucose (mmol/l)	–	–	16.3 ± 1.2	15.9 ± 0.95
Insulin (mU/l)	–	–	21.8 ± 3.2	24.2 ± 4.3

Results expressed as mean ± SEM
Significantly different from first examination
([a] $p < 0.01$, [b] $p < 0.001$, [c] $p < 0.05$)

Results (Table 1)

Mean fasting glucose and mean steady state glucose were significantly lower at the second examination compared with the first examination ($p < 0.01$ and $p < 0.001$). The mean steady state insulin concentration were increased above the fasting level and equal during both infusions.

In subjects given the infusions without insulin, the mean steady state glucose values were not significantly different during both infusions.

Discussion

In this series of alcoholics, we have examined the effect of insulin during an infusion of insulin and glucose which suppressed endogenous insulin secretion [9]. In order to examine this effect, it is important that endogenous insulin secretion is suppressed. The venous C-peptide levels did not change from the fasting levels, demonstrating that the glucose infusions had not increased endogenous insulin secretion. In the six subjects studied without exogenous insulin, the venous insulin concentration was continously low and similar at both examinations. Therefore it is unlikely that variations in endogenous insulin secretion could have influenced the results.

In the subjects given the infusion without the addition of insulin, no difference in steady state glucose concentrations was observed between the first and second examinations. In the subjects given the infusion containing insulin, higher steady state venous glucose levels were observed at the first examination, indicating a transient decrease in insulin action.

Previous studies indicate that the combined infusion of insulin, glucose, propranolol and adrenaline inhibit hepatic glucose output [1, 8, 9]. However, these studies were done on healthy subjects with normal liver function. Although none of the patients in this series of alcoholics displayed overt evidence of liver cirrhosis, most of them probably had impaired liver function. Therefore it is possible that changes in insulin action on liver glucose output were responsible for the difference observed in steady state venous glucose levels.

In healthy subjects, hyperglycaemia and hyperinsulinaemia induced by infusions of glucose and insulin are reported to cause a small net uptake of glucose by the splanchnic bed, despite stimulation of total glucose utilization [2]. In view of these findings, it is possible that in this series of alcoholics, the glucose infused was metabolized mainly by peripheral tissues. If this is the case, the difference in steady state venous glucose levels might reflect changes in peripheral insulin sensitivity.

In conclusion, our findings indicate that the action of insulin is reduced in the alcohol withdrawal state. This decrease may be due to impaired glucose handling by the liver and/or decreased peripheral insulin sensitivity.

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