HYPOGLYCEMIC RESPONSES TO INSULIN IN NORTMOHERMIC AND HYPERTHERMIC YOUNG DOGS

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Summary: The present study was conducted in 10 healthy young dogs in which pattern of hypoglycemia to injected insulin (0.12 *U/kg* I.V.) was studied at normothermic (38.5°C) and hyperthermic (42.5°C) body temperatures.

Average maximum fall in plasma glucose concentration from the control level was 44.3% and 53.8% in normothermic and hyperthermic dogs respectively. The hypoglycemic response to injected insulin was much greater and prolonged in hyperthermic dogs. The recovery of plasma glucose to preinjection level was also very sluggish and incomplete in these dags.

The above changes in hyperthermic animals may be due to enhanced secretion of insulin, as well as an increased sensitivity to injected insulin. The slow recovery of plasma glucose to preinjection level following insulin administration in hyperthermic dogs would indicate inefficient feedback mechanisms which normally operate to raise the plasma glucose during hypoglycemia.

Key words: hyperthermia hypoglycemia insulin sensitivity feedback mechanisms

INTRODUCTION

Hypoglycemia has been obesrved in dogs subjected to hyperthermia, but the cause of hypoglycemia is not very well worked out. Kanter (1,2) attributed this hypoglycemia to utilization of glucose by the respiratory muscles used in panting. Whereas in our earlier study we still observed hypoglycemia in dogs in which panting was very slight. Thus we had suggested that hypoglycemia may be due to enhanced secretion of insulin as evidenced by higher kt values (fractional rate of disappearance of glucose/min) obtained during hyperthermia. However, the possibility of peripheral tissues becoming more sensitive to the action of insulin during hyperthermia could not be ruled out. Therefore, the present investigation was undertaken to observe and compare the pattern of hypoglycemic responses to injected insulin in normothermic and hyperthermic young dogs.

MATERIALS AND METHODS

The present study was conducted on 10 healthy young dogs of either sex with body weights ranging between 2-5 *kg*. Their ages ranged from two to four months. In all the animals, the rectal temperature was recorded by an indwelling rectal thermometer. They were anaesthetized by injecting freshly prepared solution of pentobarbital sodium (Nembutal) intraperitoneally in dosage of 30 *mg/kg*. The animals were fasted for 12 hr prior to the experiment. To produce hyperthermia the body temperature of each animal was raised to 42.5°C by keeping it in a specially designed wooden cabinet fitted with a thermostatically controlled hot air blower.

A fine polythene catheter was introduced into the inferior vena cava via the saphenous vein for injecting insulin as well as collecting blood samples. In each animal 0.12 *U/kg* of insulin was injected rapidly intravenously once at normal body temperature and again after four days at hyperthermic body temperature (42.5°C). After each sample the cannula was washed by heparinized saline. Serial blood samples were withdrawn at 2, 5, 10, 20, 30, 45, 60, 90 and 120 min for determination of blood glucose (4) following insulin administration.

Each experimental animal acted as its own control.

RESULTS

The hypoglycemic responses to intravenous injection of insulin (0.12 *U/kg*) in a typical experiment at 38.5°C and 42.5°C body temperatures are shown in Fig.1. A comparison of the

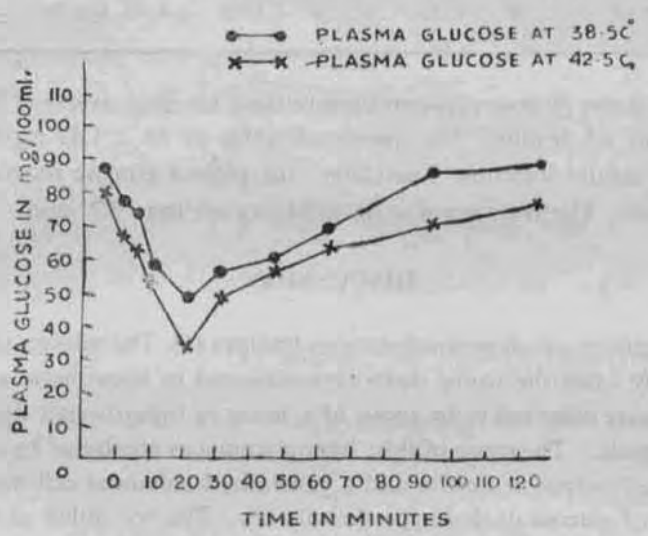

Fig. 1: Time course of hypoglycemic responses to intravenous insulin (0.12 *U/kg*) in a dog at 38.5°C and 42.5°C body temperatures. The insulin injection was given at o time.

two responses elicits that control plasma glucose concentrations were 84 *mg*/100 *ml.* and 78 *mg*/100 *ml* respectively at these temperatures. The maximum fall in plasma glucose which occured after 20 min of insulin injection was 44.0% and 58.9% respectively at the two temperatures. This greater percentage of fall at 42.5°C was found to be statistically significant ($P < 0.05$). Throughout the recovery phase the plasma glucose concentrations remained lower at 42.5°C as compared to those at 38.5°C. Further the return to preinjection level was delayed (120 min) and incomplete (90%) at 42.5°C whereas complete recovery occured in 90 min a 38.5°C. Table I shows the hypoglycemic responses to intravenous administration of insulin at normal body temperature (38.5 ± 0.5°C) and at a body temperature of 42.5°C in ten young dogs. The mean con-

trol plasma glucose concentration in normothermic animals was 88 ± 2.5 *mg*/100 *ml*. It decreased to a minimum value of 49 ± 2.21 *mg*/100 *ml* after 20 min of insulin injection. It returned to preinjection level in 90 min and remained steady at this level upto 120 min.

TABLE I: Mean plasma glucose concentrations (*mg*/100 *ml*) before and after administration of insulin (0.12 *U*/*kg*) at normal (38.5°C) and hyperthermic (42.5°C) body temperatures of ten young dogs.

Body temp.	*Control plasma glucose*	*Plasma glucose concentrations at specific times post injection (Mean ±SEM)*								
		2 min.	*5 min.*	*10 min.*	*20 min.*	*30 min.*	*45 min.*	*60 min.*	*90 min.*	*120 min.*
38.5°C	88.0 ±2.5	79.0 ±1.89	71.8 ±1.64	60.3 ±2.37	49.0 ±2.21	58.7 ±3.28	63.0 ±3.1	72.1 ±2.75	87.9 ±1.91	88.1 ±1.96
42.5°C	78.0 ±0.63	69.5 1.58	63.8 ±1.76	55.9 ±1.66	36.0 ±1.43	44.1 ±3.00	53.9 ±2.34	57.9 ±2.35	65.9 ±2.2	74.0 ±1.37

At 42.5°C, the plasma glucose concentration in these ten dogs averaged 78 ± 0.63 *mg*/100 *ml* before administration of insulin. The minimum value of 36 ± 1.43 *mg*/100 *ml* was observed at 20 min following insulin injection. Thereafter the plasma glucose recovered very slowly to near preinjection level. The recovery was incomplete even upto 120 min.

DISCUSSION

Two salient features are apparent from our findings (1). The plasma glucose concentration decreased significantly when the young dogs were subjected to hyperthermia. Basal plasma glucose concentrations were observed to be about 11% lower in hyperthermic dogs than those found in normothermic animals. The cause of this hypoglycemia as attributed by us earlier appears to be due to an increased output of insulin and a generalized enhanced cell metabolism leading to increased utilization of glucose during hyperthermia (3). The possibility of an increased sensitivity to insulin acquired by the peripheral tissues under the effect of heat may also be an additional cause of hypoglycemia.

(2) The hypoglycemic response to injected insulin was much greater in dogs subjected to hyperthermia than in dogs at normal body temperatures. A comparison of hypoglycemic responses at 42.5°C and 38.5°C (Fig.1) showed that plasma glucose concentrations were lower at 2, 5 and 10 min of insulin administration at 42.5°C. Also the maximum fall in plasma glucose which occured at 20 min was much greater in hyperthermic dogs. The return of plasma glucose concentration to preinjection level was sluggish and incomplete at 120 min following insulin injection in dogs whose body temperature was raised. This exaggerated response to insulin would suggest an increased sensitivity of hyperthermic tissues to insulin since equal amounts of insulin were administered in hyperthermic and normothermic dogs. The slow recovery of plasma

glucose concentration in hyperthermic young dogs may point out that either the removal of injected insulin is slow in these animals or the feedback mechanism which raise the plasma glucose concentration during hypoglycemia are not operating efficiently in young dogs subjected to hyperthermia.

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