Insulin Effects on Gastric Secretion and Blood Electrolytes Modified by Injected Potassium

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The major action of insulin on gastric secretion is a hypoglycemic vagal stimulation of electrolyte and pepsin secretion. This stimulation is subsequently modified by a direct inhibitory action of insulin on the electrolyte transport systems of the secreting gastric mucosa. The latter action appears to be related to the effects of insulin on K⁺; we have shown that this inhibition can be rapidly reversed or largely prevented by the intravenous injection of KCl. The previous experiments were carried out against a background of continuous histamine infusion; the studies reported below show that KCl is also effective in modifying the inhibitory effect of insulin in the absence of histamine. They also show that the effects of insulin on Na⁺ and K⁺ can be dissociated from its glucotropic action.

MATERIALS AND METHODS

The experiments were done using 8 trained dogs, each with a Komarov esophagostomy and a dependently draining gastric cannula. The general methods have been previously described.

In each dog 2 separate control tests were done using insulin (I) in the dose of 0.6 U./kg. body weight injected intravenously in one dose after a prior 30–45 min. of observation to confirm the absence of basal secretion. Observations were continued for 4 hr. after insulin injection. In a subsequent experiment in each dog, KCl in 50 ml. water (1 mEq. K⁺/kg. body weight) was injected intravenously in a 10-min. period starting 90 min. after the injection of insulin, 0.6 U./kg. body weight (I-K). In a fourth experiment, KCl (0.5 mEq. K⁺/kg./hr.) was injected intravenously continuously from the time the insulin, 0.6 U./kg. body weight, was given until the end of the 4-hr. study (K + I).

Gastric juice was collected continuously from the dependently draining cannula and divided into consecutive 15-min. samples. These were analyzed...
the same day for $\text{H}^+$, $\text{Na}^+$, $\text{K}^+$, $\text{Cl}^-$, osmolality ($O_g$), and pepsin by methods previously detailed. Blood samples drawn in heparinized syringes at 0, 30, 60, 120, 180, and 240 min. were used for hematocrit; sugar (Folin-Wu method); and plasma Na$^+$, K$^+$, Cl$^-$, and osmolality ($O_p$) measurements. Linear interpolations were made for blood values between the points of measurement. Subscripts $p$ and $g$ refer to plasma and gastric juice, respectively, and $E$ to extracellular fluid

RESULTS

BLOOD AND BLOOD ELECTROLYTES

Blood Sugar

The dose of insulin used caused the blood sugar to fall to a low point between 30 and 60 min. after injection, with recovery to control values within 4 hr. (Fig. 1). Neither infusion of KCl nor the single large injection of KCl 90 min. after insulin was given significantly altered the hypoglycemic effects of the insulin. Thus the effects to be described on blood and gastric secretion can not be related to any modification of the blood sugar response to insulin.

Plasma Na$^+$ and K$^+$

The injection of insulin produced the well-known decrease in plasma K$^+$ (Fig. 1). K$_p$ decreased by 1.3 mEq./L. in the first hour, remained at this level for the second hour and then began to recover after 2 hr. to within 0.85 mEq./L. of the control value after 4 hr. Thus the effect of insulin on K$_p$ began to reverse 1 hr. after the start of the reversal of the hypoglycemia, and was still obvious after 4 hr. when the blood sugar had fully recovered. At the same time Na$_p$ rose by 2.25 mEq./L. in the first hour and then fluctuated between 1.2 and 2.25 mEq./L. above control in the next 3 hr. In the first 90 min. of the I-K experiments (i.e., before the injection of KCl) similar values for Na$_p$, K$_p$, and blood sugar were found (Fig. 1).

Despite the continuous infusion of KCl (11.5 mEq. K$^+$/hr.), K$_p$ declined even a little more than in the insulin control, and as in the control, began to rise after 2 hr., being still 0.65 mEq./L. below control values after 4 hr. By contrast with the control studies, however, Na$_p$ rose rapidly (+5.2 mEq./L. at 1 hr., +7.5 mEq./L. at 3 hr.) and leveled off after 3 hr. (Fig. 1). The injection of 1 mEq. K$^+$/kg. body weight in 10 min. after 90 min. caused a more rapid recovery in K$_p$ and a slow increase in Na$_p$ which continued for 2½ hr., reaching +7.2 mEq./L.

Thus under the influence of insulin, relatively large amounts of K$^+$ left the plasma and presumably, the extracellular fluid (ECF), and under the influence of injected K$^+$, an approximately equivalent amount of Na$^+$ entered the plasma and ECF. Assuming that the concentrations of electrolytes in plasma and ECF are equal and using an arbitrary value of 20% body weight for ECF in this group of dogs, but omitting the red blood cells from the estimate (even though red cells are high in Na and low in K), calculations can