Effect of Glucagon Infusion on Plasma Magnesium, Glucose, and Insulin in Bull Calves

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ABSTRACT
Two Holstein bull calves each were infused intravenously with 1 mg glucagon in .9% sodium chloride, and two were given saline alone; 1 wk later treatments were reversed. Glucagon increased concentrations of insulin and glucose but decreased potassium in blood plasma and moderately increased urinary magnesium and calcium losses. When only saline was used, there was no effect. A hypothesis relating elevated glucagon to grass tetany is proposed.

INTRODUCTION
Hypoglycemia and ketosis may accompany grass tetany (6, 10), which suggests that an imbalance in intermediary energy metabolism may be involved. With the exception of reduced carbohydrate intake (13), however, there has been no fitting hypothesis relating these disorders to grass tetany. Recently there has been interest in the insulin-glucagon regulation of glucose metabolism in both nonruminant (9, 12) and ruminant (1) animals. The purpose of this study was to investigate the effects of elevated plasma glucagon on insulin, glucose, magnesium, potassium, and calcium of plasma in calves and to evaluate these factors in relation to the grass tetany syndrome.

EXPERIMENTAL PROCEDURE
Four Holstein bull calves weighing 102 ± 10 kg (mean ± SD) were allotted randomly to intravenous infusion with 500 ml of sterile nonpyrogenic physiological saline3 or with 1 mg beef-pork glucagon4 dissolved in 500 ml saline in a simple changeover experimental design (4). Calves were kept in metabolism stalls 7 days prior to and during the infusion period. They were fed 1.4 kg red clover-orchard grass hay and 5 g salt daily at 0800 and 1530 but were not fed for 24 h prior to infusion. Indwelling polyvinyl catheters were placed in both left and right external jugular veins at least 2 h before initiation of infusion. Heparin (control) or glucagon solutions were infused into the left catheters for 50 min at 10 ml/min by an intravenous injection set.5

Heparinized blood samples were drawn from right catheters at 30 min and immediately prior to infusion; at 15, 30, and 45 min during infusion; and 10, 40, 70, and 130 min postinfusion. Sodium fluoride also was added to samples intended for glucose but not insulin measurement. Blood samples were placed in an ice bath during collection; plasma later was separated and stored frozen. Urine was collected for 4 h prior to infusion and again for 4 h after infusion was initiated. Plasma was analyzed for immunoreactive insulin5 and glucose6 by commercial kits and for Mg, Ca, and K by atomic absorption spectrophotometry.7 Urinary Mg, Ca, and K also were measured.7 Differences between preinfusion, during infusion, and postinfusion periods were tested by analysis of variance (4).

RESULTS
Glucagon infusion produced a rapid increase (P<.01) in plasma glucose concentration fol-
# TABLE 1. Effect of glucagon or saline infusion on magnesium, calcium, and potassium concentrations in plasma and losses in urine of calves.

<table>
<thead>
<tr>
<th>Period of infusion</th>
<th>Material infused and mineral measured</th>
<th>Control&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Glucagon&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mg (mg/100 ml)</td>
<td>Ca (mg)</td>
<td>K (mg)</td>
</tr>
<tr>
<td></td>
<td>Pre 2.1 ±.1</td>
<td>10.4 ±.5</td>
<td>16.2 ±.4</td>
</tr>
<tr>
<td></td>
<td>During 2.0 ±.1</td>
<td>10.1 ±.3</td>
<td>16.0 ±.3</td>
</tr>
<tr>
<td></td>
<td>Post 2.1 ±.1</td>
<td>10.1 ±.4</td>
<td>16.0 ±.3</td>
</tr>
<tr>
<td>Plasma (mg/100 ml)</td>
<td>Pre 85.4 ±27.8&lt;sup&gt;d&lt;/sup&gt;</td>
<td>3.5 ±1.4</td>
<td>888 ± 232</td>
</tr>
<tr>
<td></td>
<td>During 70.1 ±13.3</td>
<td>2.3 ±.4</td>
<td>559 ± 154&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup>Saline solution (.9% NaCl) infused at 10 ml/min.

<sup>b</sup>Glucagon (1 mg in 500 ml .9% NaCl) infused at .02 mg/min.

<sup>c</sup>Plasma mineral concentrations are means ± SE of four calves.

<sup>d</sup>Total for 4 h. Each value is the mean ± SE of four calves.

<sup>e,f,g</sup>Statistically significantly different from preliminary period: e, P<.01; f, P<.05; g, P<.10.
lowed closely by elevated ($P<.01$) insulin (Fig. 1). Although plasma concentrations of glucose and insulin declined rapidly after termination of glucagon infusion, they remained above ($P<.05$) preinfusion values for 130 min. Neither glucose nor insulin was affected ($P>.25$) by infusion of normal saline.

Exogenous glucagon decreased ($P<.01$) plasma K but did not alter significantly either Mg or Ca (Table 1). Plasma K concentrations rapidly returned to preinfusion levels ($P>.25$) during the postinfusion period. Normal saline alone did not significantly ($P>.25$) alter Mg, Ca, or K in plasma. Urinary Mg and Ca losses increased moderately ($P<.10$) during glucagon but not during saline administration (Table 1). Urinary K output was decreased ($P<.01$), however, by saline alone.

**DISCUSSION**

Glucagon infusion had a prominent hyperglycemic-glycogenolytic stimulatory effect in our calves accompanied by a marked increase in plasma insulin (Fig. 1). Hyperglycemic effects of glucagon are well recognized in nonruminants (9), but our results do not establish whether plasma insulin was elevated directly by glucagon or indirectly through high plasma glucose. Insulin in turn has an important physiological role in the regulation of concentration of plasma K (7). It appears, therefore, that reduced plasma K during and following glucagon infusion (Table 1) was an indirect effect of glucagon stimulation through insulin release (Fig. 1).

Exogenous glucagon did not increase urinary losses or reduce plasma concentrations of Mg and Ca in calves (Table 1) to the extent observed in nonruminants (2, 3, 11, 14). However, the glucagon infusion period was much shorter for the calves than for the nonruminants. Increased urinary Mg loss due to prolonged flooding of glucagon into circulating blood at a time when available dietary Mg is low might eventually result in hypomagnesemia.
Possible Involvement of Elevated Glucagon in Grass Tetany: A Hypothesis

Well fertilized, vegetative spring grass is frequently high in K and low in Mg (6) and readily available carbohydrate (13). Elevated K and reduced Mg in plasma of ruminants grazing such forage (6) could increase insulin secretion (8) which in turn might stimulate glucagon release (1, 5). Prolonged elevation of glucagon during a period when carbohydrate reserves in rapidly growing grasses are low (13) eventually could deplete precursors of glucose and accelerate lipid breakdown (9), resulting in ketosis. The problem would be further complicated by increased urinary Mg loss caused by glucagon.

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REFERENCES