

# INSULIN AND GLUCAGON RESPONSES TO VOLATILE FATTY ACIDS AND $\alpha$ -KETO ACIDS IN SHEEP

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## Introduction

It has been shown in ruminant animals that volatile fatty acids(VFA) are potent stimuli for insulin secretion *in vivo* (Manns and Boda, 1967) and *in vitro* (Sasaki et al., 1977), as well as stimulating glucagon secretion. However, the effects of  $\alpha$ -keto acids, which have a similar carbon chain length to VFAs, on insulin and glucagon secretion has not been clarified.

The present study investigates the effects of intravenous infusion of VFAs and  $\alpha$ -keto acids on plasma insulin and glucagon in sheep.

## Materials and Methods

Five cross-bred castrated male sheep (37.5-41.5 kg B.W.) were housed in metabolic cages in a controlled environmental room and were fed alfalfa pellets at 2 % of body weight per day in a single meal daily, at 16:30 h. Water was available continuously. Feed and water were withdrawn on the morning of an experiment. The exteriorized carotid loop were then venupunctured. Each sheep received intravenous infusions of saline and a varying volume of 0.5 mM solutions of acetate, propionate, butyrate, glyoxylate, pyruvate and

$\alpha$ -ketobutyrate to supply of 0.025 m mole/kg/min over 20 min. Base-line blood samples were taken from the carotid artery at -10 and 0 min before starting the infusion. Subsequent blood samples were taken at 5, 10, 15, 20, 30, 45, 60 and 90 min. The concentration of plasma insulin, glucagon and glucose were determined.

The mean of the four values at 5, 10, 15 and 20 min. was taken as the mean concentration during infusion. Mean values for 5 animals are shown with S.E. in table 1. The significance of differences between base-line and mean concentration during infusion was determined using one way analysis of variance.

## Results

The base-line concentration of plasma insulin ranged between  $8.9 \pm 0.6$  and  $12.5 \pm 3.1$   $\mu$ U/ml for each infusion. The infusion of propionate and butyrate brought about marked increases in plasma insulin, whereas acetate had no effect on plasma insulin. The plasma insulin concentration was increased significantly by infusion of  $\alpha$ -ketobutyrate, but was unchanged by glyoxylate and pyruvate.

The basal plasma glucagon concentration was

TABLE 1. MEAN CONCENTRATION OF PLASMA INSULIN, GLUCAGON AND GLUCOSE DURING INFUSION OF VFA AND  $\alpha$  KFTO ACIDS IN SHEEP

	Insulin ( $\mu$ U/ml)	Glucagon (pg/ml)	Glucose ( $\mu$ g/ml)
saline	8.6 $\pm$ 0.5	95.8 $\pm$ 10.0	490.6 $\pm$ 13.1
acetate	14.0 $\pm$ 3.6	108.4 $\pm$ 6.7	539.5 $\pm$ 24.3
propionate	77.5 $\pm$ 8.5**	193.1 $\pm$ 31.5*	608.4 $\pm$ 24.1*
butyrate	122.3 $\pm$ 20.6**	220.0 $\pm$ 36.9*	558.6 $\pm$ 23.6
glyoxylate	7.8 $\pm$ 0.9	91.7 $\pm$ 8.7	472.8 $\pm$ 14.3
pyruvate	10.0 $\pm$ 0.6	88.2 $\pm$ 10.8	502.8 $\pm$ 25.2
$\alpha$ -ketobutyrate	21.4 $\pm$ 2.0**	91.5 $\pm$ 8.0	515.0 $\pm$ 23.2

Values represent mean  $\pm$  S.E. for five sheep.

\*, \*\*, significant differences from baseline values at levels of  $p < 0.05$  and  $p < 0.001$ , respectively.

between  $87.0 \pm 9.9$  and  $107.9 \pm 11.9$  pg/ml for each infusion. The infusion of propionate and butyrate increased the plasma glucagon concentration significantly, but acetate did not affect plasma glucagon. No increase in plasma glucagon occurred after infusions of glyoxylate, pyruvate and  $\alpha$ -ketobutyrate.

The base-line concentration of plasma glucose ranged between  $470.5 \pm 24.4$  and  $543.5 \pm 26.8$   $\mu$ g/ml for each infusion. Propionate infusion produced a significant elevation in the plasma glucose concentration during infusion, followed by a gradual decrease thereafter reaching a level below base-line concentration at 45-90 min. (Data are now shown). The infusions of acetate and butyrate did not alter plasma glucose during infusion. Glyoxylate, pyruvate and  $\alpha$ -ketobutyrate infusions had no effect on plasma glucose.

#### Discussion

The present report that intravenous infusions of propionate and butyrate caused significant increases in plasma insulin and glucagon are in good agreement with earlier studies. The stimulatory

effect of propionate and butyrate on insulin and glucagon secretion has been shown to be specific for ruminant animals. Among the  $\alpha$ -keto acids tested only  $\alpha$ -ketobutyrate stimulated insulin secretion in sheep. To date, insulin and glucagon secretion in response to  $\alpha$ -keto acids has not been examined comprehensively, so that further detailed studies using a range of species will be necessary to characterize any species-related differences in the insulin response to  $\alpha$ -keto acids. It will also be necessary to clarify the mechanism of insulin secretion in response to  $\alpha$ -ketobutyrate. (Key Words: Insulin Secretion,  $\alpha$ -Keto Acids, VFA)

#### Literature Cited

- Manns, J.G. and J.M. Boda. 1967. Insulin release by acetate, propionate, butyrate, and glucose in lambs and adult sheep. *Am. J. Physiol.* 212: 747-755.
- Sasaki Y., T.E.C. Weekes. and J.B. Bruce. 1977. Effects of glucose and butyrate on insulin release from perfused fragments of sheep pancreas. *J. Endocr.* 72:2346-2351.