INSULIN, GLUCAGON AND GROWTH HORMONE RESPONSES TO AMINO ACIDS IN SHEEP

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Introduction

Several amino acids are known to affect the secretion of metabolic hormones such as insulin, glucagon and growth hormone(GH). As these hormones are central to the regulation of amino acid metabolism, it is worthwhile to quantify the extent to which each amino acid could stimulate the secretion of these hormones. In ruminants, however, the effects of very few amino acids on the secretion of insulin and GH has been studied (Davis, 1972). In the present experiment, using sheep, we investigated the secretory response of insulin, glucagon and GH to intravenous infusion of 17 amino acids.

Materials and Methods

Six cross-bred castrated male sheep were used. They were housed in metabolic cages and offered alfalfa pellets once daily and water ad libitum. Sheep were intravenously infused with solution of individual amino acids through a jugular venous catheter at a rate of 3 mmol/kg of body weight over a period of 30 min. Infusion solutions were adjusted to pH 7.4, except for the solution of Leu to pH 2.5. The amino acids used for infusion are shown in table 1. Blood samples were obtained from a carotid artery surgically placed in a loop of skin, from 20 min before to 90 min after starting the infusion, and were transferred into heparinized test tubes containing benzamidine, and centrifuged. Plasma sample were stored at $-20^{\circ}C$ until radioimmunoassay. Plasma glucagon and GH were assayed using antiserum G-42 E and NIADDK-anti-oGH-2, respectively. The incremental hormone areas enclosed by hormone concentration curves above basal levels were calculated between 0 and 90 min, and significant differences in hormone areas between amino acids were analyzed by Duncan's multiple range test using General Linear Model of the SAS program package.

TABLE 1. INSULIN, GLUCAGON AND GH RESPONSE TO AMINO ACIDS

Amino Acids	Insulin Area ($\mu u \cdot min \cdot ml^{-1}$)	Glucagon Area ($pg \cdot min \cdot ml^{-1}$)	GH Area ($ng \cdot min \cdot ml^{-1}$)
Ala	64.8± 7.4^{ab}	307.5±62.7^{a}	1.1±0.3^{bcd}
Arg	25.5± 4.5^{bcd}	139.2±20.0^{b}	1.0±0.4^{bcd}
Asn	25.5±13.8^{bcd}	135.8±20.8^{b}	1.9±0.5^{bcd}
Asp	−3.6± 1.2^{cd}	−3.5±14.4^{cf}	9.8±2.0^{a}
Gln	15.0± 3.4^{cd}	99.6±19.4^{bc}	2.5±1.2^{bcd}
Glu	7.8± 3.7^{d}	4.3±11.0^{def}	3.2±0.8^{bc}
Gly	101.6±19.2^{a}	295.5±57.1^{a}	1.1±0.6^{bcd}
His	−1.9+ 1.2^{cd}	3.7± 5.8^{def}	0.4±0.2^{d}
Ile	6.1± 0.7^{cd}	−10.8± 5.6^{f}	0.2±0.4^{d}
Leu	99.8±38.5^{a}	8.8± 5.0^{f}	1.2±0.5^{bcd}
Lys	17.2± 1.9^{cd}	45.8±14.5^{cdef}	0.2±0.2^{d}
Met	36.1+11.9^{bc}	62.7± 8.1^{bcdef}	0.8±0.3^{cd}
Phe	37.6± 8.3^{bc}	77.3±15.1^{bcde}	3.3±0.8^{b}
Pro	21.4± 2.9^{cd}	83.8± 9.5^{bcd}	0.6±0.5^{d}
Ser	88.9±18.9^{a}	242.5±44.6^{a}	1.2±0.3^{bcd}
Thr	26.8± 5.2^{bcd}	90.7±11.1^{bc}	0.7±0.2^{d}
Val	3.7± 0.5^{cd}	23.8± 3.2^{cdef}	0.4±0.5^{d}

Values represent Mean ± SE.
^{a,b,c,d,e,f}Mean values in the same vertical column not sharing common letters differed significantly ($p < 0.05$).

Results

Large differences were observed in the responses of plasma insulin, glucagon and GH concentrations to individual amino acids. Insulin secretion induced by Gly, Ser or Leu infusion was significantly ($p < 0.05$) greater than that induced by other amino acids. Most amino acids increased the plasma insulin concentration above the basal level, while His, Asp and Glu produced slight decreases in plasma insulin. Glucagon secretion was significantly ($p < 0.05$) augmented by infusion of Ala, Gly or Ser, which were much more potent than other amino acids, plasma glucagon remaining

elevated even after cessation of infusion. The intravenous infusion of Asp caused the greatest enhancement of GH secretion among the amino acids tested.

Discussion

The results of the present experiment show that Gly, Ser and Leu were the most potent amino acids for stimulating insulin secretion, while Ala, Gly and Ser were most effective for glucagon and Asp for GH in sheep. Unlike Leu or Asp, which stimulate only insulin or GH secretion respectively, no amino acid was found that only induce glucagon secretion in this study. It has been well documented that Arg has a remarkable effect in enhancing insulin (Floyd et al., 1966) and GH (Knopf et al., 1966) secretion, so that Arg has been commonly used as a standard secretagogue. We suggest, however, that it would be reasonable to use Leu for specifically inducing insulin secretion and to use Asp rather than Arg as the secretagogue to induce GH secretion, at least in castrated male sheep.

This study was supported by a Grant-in Aid for Scientific Research from the Ministry of Education, Science and Culture of Japan (No. 62480077)

(**Key Words:** Amino Acids, Metabolic Hormones)

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