

The metabolism and action of insulin and glucagon in lactating and non-lactating goats

J. GRIZARD, Claire SORNET, Michèle BALAGE, C. CHAMPREDON

*Laboratoire d'Etude du Métabolisme Azoté et CNRS UA 041123,
I.N.R.A., Theix, 63122 Ceyrat, France.*

Introduction. Insulin and glucagon may be involved in the adaptation of metabolism to lactation (Gill and Hart, 1980 ; Burnol *et al.*, 1985) but the mechanisms are not well understood. The aim of the present study was to analyse the metabolism of insulin and glucagon and their action on blood glucose in lactating and non-lactating goats.

Material and methods. Nine Alpine goats 4 to 7 years old kidded from the end of January to the beginning of March. Their hormonal status was studied at 6-8 weeks postpartum (lactating : L) and at 12-17 weeks postpartum, *i.e.* 3-4 weeks after the animals were dried off (non-lactating : NL). At these times, body weight averaged 56 and 50 kg in L and NL animals, respectively. The former yielded 3-3.7 kg of milk per day. They were fed a diet of meadow hay and concentrates (1 : 1) and daily intake was about 3 kg. The non-lactating animals received only about 1.3 kg of meadow hay. The diet was given twice daily in two equal meals at milking time (8 : 30 a.m. and 4 : 30 p.m.).

Two separate experiments (I and II) were performed. In experiment I (6 goats), unlabelled porcine insulin (MC S 83 81 104 from Novo ; 13 µg/kg body weight) was injected into the jugular vein at around 1 : 30 p.m. Blood samples were collected before injection and at various times during the 3-hour period following injection. One or two days later, 4 goats were injected with unlabelled porcine glucagon (G 4250 batch 109C-0332 from Sigma ; 11 µg/kg body weight) in the same manner, except that the blood was collected over a 1.5-hour period. In experiment II (3 goats), insulin was infused at a constant rate (1.4 µg/kg/h) for a 6-hour period starting at 10 a.m. In order to maintain blood glucose at a basal level, variable amounts of glucose were simultaneously infused. The blood was sampled frequently.

Plasma insulin and glucagon were measured by radioimmunoassay using commercial kits and the double antibody method. Glucose was measured according to a glucose-oxidase method.

Results and discussion. Plasma insulin was similar in lactating and non-lactating goats before insulin injection (about 1.3 ng/ml). In contrast, basal plasma glucagon was significantly higher in lactating than in non-lactating animals (0.11 ± 0.02 vs 0.07 ± 0.01 ng/ml ; SE ; $0.025 < P < 0.050$).

A bi-exponential decay curve showed a fall in hormone concentration over the first 90 min after both hormone injections (Grizard and Szczygiel 1983). Plasma insulin along the disappearance curve was lower in lactating than in non-

lactating goats (significant at 30, 60 and 90 min after injection ; $P < 0.05$). The metabolic clearance rate of insulin was increased during lactation (10.8 ± 0.9 vs. 8.4 ± 0.6 ml/kg/min in L and NL goats, respectively). Indeed, it has been shown that insulin uptake by the mammary gland is greatly increased in lactating animals. A part of this insulin is degraded and the rest passes into the milk. This increased uptake is in keeping with the low plasma insulin which has usually been observed in lactating ruminants (Gill and Hart, 1980). In contrast, the disappearance curves of glucagon were similar in lactating and non-lactating animals.

Basal blood glucose was the same in all the animals. Insulin injection resulted in a high decreased of blood glucose, the minimal levels occurring at 30-90 min after injection, whereas glucagon sharply increased blood glucose (maximal levels at 15-30 min). At almost all times after insulin injection, the effect of insulin was significantly impaired (about - 50 %) in lactating compared to non-lactating goats. However, 2 to 10 min after glucagon injection, the effect of glucagon was moderately, but significantly, improved (about + 12 %) by lactation. Plasma insulin increased 2 to 4-fold when insulin was infused at a constant rate. In order to maintain the blood glucose level, the animals were simultaneously infused with increasing rates of glucose during a 0 to 4-hour period (mean levels of 1.0, 1.5, 1.8, 2.3 mg/kg/min during hours 0-1, 1-2, 2-3, and 3-4, respectively, in group L ; 1.3, 1.8, 2.5 and 2.9 mg/kg/min in group NL) ; the infusion rate was lower in group L than in group NL during the 3-4-hour period ($0.05 < P < 0.10$). Glucose infusion thereafter plateaued at the same value in both groups (about 2.9 mg/kg/min).

The lactating goats exhibited hormonal adaptation which is expected to depress insulin action. Insulin metabolic clearance increased. In addition, the effect of insulin on blood glucose was impaired. This might be due to insulin resistance in the target tissue (muscle). Thus, less substrate might be utilized in those tissues whereas more would be used in the mammary gland. In contrast, the effect of glucagon was improved in lactating goats ; this is in keeping with an increase in the gluconeogenic and ketogenic pathways.

Résumé. L'étude est réalisée chez la chèvre tarie et en lactation. La lactation ne modifie pas l'insulinémie mais augmente la glucagonémie. Elle accroît la clairance métabolique de l'insuline sans changer celle du glucagon. Elle réduit la capacité de l'insuline à promouvoir l'hypoglycémie mais augmente celle du glucagon à stimuler l'hyperglycémie.

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