Decrease in Plasma Insulin Concentration in Lactating Rat

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ABSTRACT. Decreased plasma insulin levels in lactating rats were restored by the treatment with CB-154, but at the same time, lactation ceased. Low plasma insulin levels in lactating rats were also restored by the removal of pups. This rise due to pups-removal was not prevented by prolactin administration. Plasma insulin lowered again with resumption of nursing. Thus, milk production presumably serves to suppress insulin secretion from B-cells. —KEY WORDS: CB-154, insulin, lactation.

Insulin, as many other hormones such as prolactin and corticosteroids, are considered to be indispensable for lactation [3, 10, 12]. However, it has been noted that the plasma insulin levels in pregnant rats decrease during the latter half of pregnancy, and significantly decreased insulin levels continue during the lactational period [2, 5, 6]. We recently found that the decrease in circulating insulin concentration during lactation is due to a decrease in pancreatic insulin secretion, because plasma insulin in the portal vein and peripheral blood were stayed at similar levels and that the insulin secretory response following glucose infusion was not different from that in non-pregnant rats [11]. Since plasma insulin levels increased according to the decrease in litter size and returned immediately to the levels in non-pregnant rats when lactation was stopped, sucking stimulus or milk secretion seems to inhibit insulin secretion. It is suggested that such a decrease in plasma insulin is due to rise in plasma prolactin levels in response to suckling [1, 4, 9]. These reports are based on experimental results showing that decreased insulin levels in lactating rats returned to the levels in virgin rats after administration of CB-154. Administration of CB-154 in rats as in many animals is known to suppress prolactin secretion and stop lactation simultaneously [3]. It remains to be clarified whether as elevation of plasma insulin level in lactating rats after CB-154 injection was caused by a decrease in plasma prolactin level or an abolition of milk secretion.

Female SD rats, 9 weeks old and weighing 230–250 g, from the Charles River Japan Inc. were used. All the animals were allowed free access to a commercial diet (Nihon CLEA, Tokyo) and water. The day of parturition is day 0 of lactation. After parturition, the litter size was adjusted to 10 or 0 (no pups). Immediately after parturition, the mothers with 10 pups received daily subcutaneous injections of 1 mg CB-154 (bromocriptine, provided by Sandoz Ltd, Basel, Switzerland) in 0.2 ml ethanol-0.15M-NaCl (1:1, v/v) alone or with 35 IU sheep prolactin (Sigma, St. Louis) in 0.2 ml 0.15M-NaCl. Blood samples were collected from the tail vein without anesthesia between 11:00 to 13:00 hr. The samples were centrifuged and plasma samples were stored at −20°C until required for assay. Insulin was assayed using the 125I-insulin radioimmunoassay kit supplied by CEA-IRE-
to their mothers on day 2 of lactation, the rise in plasma insulin was arrested, but plasma insulin levels rose, when the pups were removed again on day 5 of lactation. Subcutaneous injections of prolactin to virgin rats, 35 IU/day, over a period of 7 days did not change plasma insulin levels (44.0 ± 7.3 μU/ml).

The decreased plasma insulin levels in lactating rats returned to the levels comparable to unmated rats after administration of CB-154, as previously reported [1, 4, 9]. Thus, prolactin itself appears responsible for the lowered plasma insulin levels in lactating rats. However, the rise in plasma insulin levels observed after the pups-removal was not prevented by the administration of prolactin, suggesting prolactin itself dose not lower plasma insulin levels. The administration of CB-154 to lactating rats which induced a rise in plasma insulin levels, caused the abolishment of milk secretion at the same time. Plasma insulin levels in high-yielding dairy cows are significantly lower than those of low-yielding cows [7, 8].

Milk secretion maintained in the presence of
prolactin will suppress insulin secretion from the pancreas. In our previous report [11], we showed that plasma insulin levels were not decreased when milk secretion was stopped without inhibiting prolactin secretion by sectioning the galactophores. Prolactin administration could decrease plasma insulin levels for only a short period after weaning [9]. Moreover, there was no change in plasma insulin levels when 35 IU of prolactin was injected into virgin rats for 7 days. Prolactin itself does not seem to affect the insulin secretion.

The mechanism or the reason why milk secretion inhibits insulin secretion is not clear. During a lactation period, the mammary tissue must be provided with a large amount of substrate for the synthesis of milk components such as lactose and casein. Most of the substrate is derived from blood glucose and amino acids. The insulin secretion is mainly controlled by a feedback effect of the blood glucose level directly on the pancreas, so that blood glucose and blood insulin levels parallel each other with a remarkable consistency. We found previously that the blood glucose levels in the abdominal vein and insulin levels in the portal vein decreased progressively with increase in little size [11]. On the basis of these findings, we conclude that the decrease in peripheral blood glucose level involved in milk production suppresses the insulin secretion from B-cells.

REFERENCES


要約

泌乳ラットにおける血漿インスリン濃度の低下：溝口順二・今道友則1）（食品薬品安全センター黒野研究所，1）日本農芸衛生大学生理学教室）——泌乳ラットにCB-154を投与すると、血中インスリン濃度は処女ラットの値まで回復したが、同時に泌乳は停止した。泌乳ラットのインスリン濃度は乳仔の除去によって上昇したが、この上昇は同時にプロラクチンを投与しても阻止できず、授乳再開によりインスリン濃度は再び低下した。これらのことから、泌乳ラットでは乳汁分泌がインスリン濃度の低下をもたらすと推察された。