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Glucose Administration Does Not Modulate Prolactin Response to Exercise, TRH or Haloperidol Injection

M. VIGAŠ, D. JEŽOVÁ

Institute of Experimental Endocrinology, Slovak Academy of Sciences, Bratislava, Slovak Republic

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Summary

Glucose was found to exert an *In vitro* regulatory effect on prolactin secretion. Its role in the modulation of stimulated secretion of prolactin in man is, however, not clear. To evaluate the effect of hyperglycaemia on prolactin release, three stimulatory tests with different mechanisms of stimulation were employed. Healthy male subjects served as volunteers during submaximal exercise, TRH test (0.2 mg i.v.) and administration of haloperidol (2 mg i.v.). Glucose (100 g in 400 ml) or an equal volume of water was given 30 min before the tests. Blood for glucose and prolactin analysis was taken *via* an indwelling catheter. The plasma prolactin concentration increased in response to each of the stimuli applied. However, the prolactin increase during hyperglycaemia did not differ from values obtained in tests performed in normoglycaemia after water administration. These results indicate that prolactin release in healthy man is not modulated by hyperglycaemia.

Key words

Prolactin response – Exercise – TRH – Haloperidol

Introduction

Prolactin is a protein similar to the growth hormone in its primary structure as well as in its phylogenetic development (Kawauchi *et al.* 1990). Release of these hormones during increased demands of glucose (hypoglycaemia) or energy substrates (exercise) is well established. However, the opposite situation, i.e. the effect of glucose on hormone secretion is clear only in case of growth hormone. Administration of glucose inhibits the growth hormone response to several pharmacological (Mims *et al.* 1973) and physiological stimuli (Glyck *et al.* 1965). Little information is available on the influence of glucose on prolactin release. A suppressed prolactin response to TRH during hyperglycemic clamp in patients with type II diabetes was reported (Vierhapper *et al.* 1983). A comparison with a non-diabetic group was, however, not included in this trial. Glucose infusion (Lugari *et al.* 1986) or ingestion (Ajlouni *et al.* 1976) was without effect on basal, non-stimulated plasma prolactin levels. Recently, Langford *et al.* (1992) suggested that glucose concentrations may regulate prolactin release from pituitary lactotrophs *in vitro*. The effect of hyperglycaemia on stimulated prolactin secretion in healthy humans has not yet been studied.

The aim of our investigation was to clarify the effect of an acute increase in plasma glucose concentration on the prolactin response to different stimuli of hypothalamic-pituitary lactotropic function. For this purpose, the prolactin response to submaximal exercise, to the hypothalamic hormone thyreoliberin (TRH) and to the dopaminergic antagonist haloperidol was examined during concomitant hyperglycaemia in healthy subjects.

Material and Methods

Subjects

Healthy non-obese male volunteers aged 23–30 years gave written consent for participation in the study. The investigations started at 07.30 h after an overnight fast. An indwelling catheter was inserted into the cubital vein for blood sampling and the first blood sample was not taken earlier than 30 min after inserting the catheter. Each subject underwent the

same test twice, one week apart, after water and after glucose ingestion (100 g in 400 ml), with the order of the tests being randomized. The tests started 30 min after glucose or water ingestion.

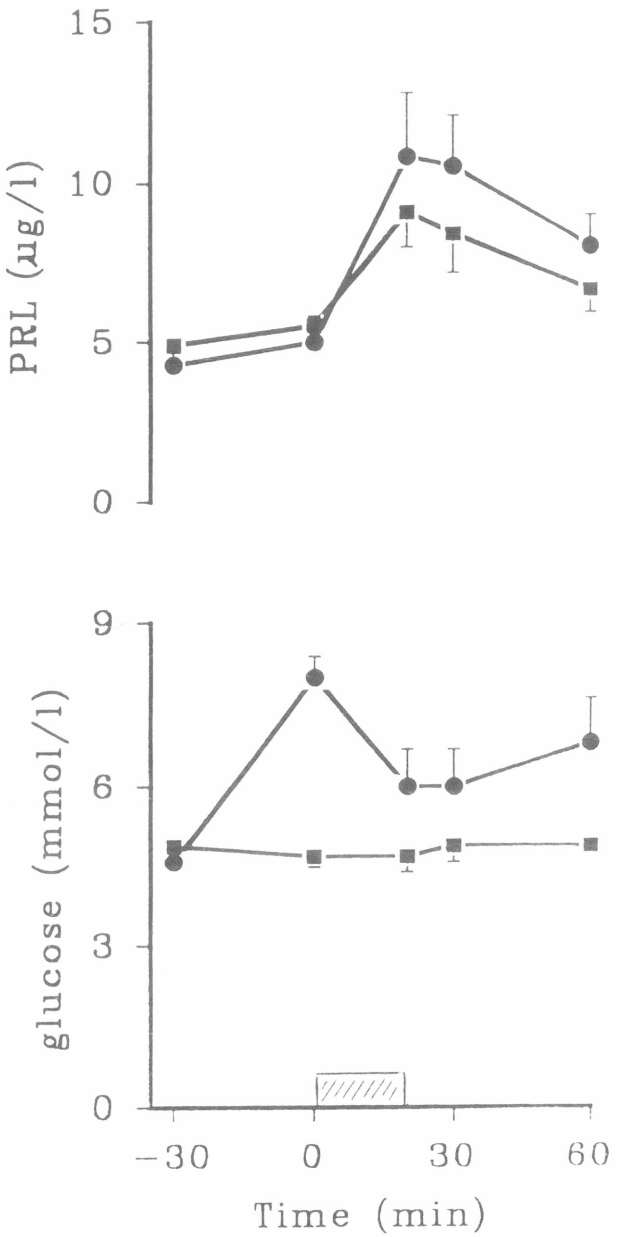

Fig. 1
Prolactin response to submaximal exercise in six subjects after glucose (closed circles) or water (closed squares) ingestion. Glucose or water were given at −30 min, exercise was performed from 0 to 20 min. The differences in plasma prolactin concentration between the tests were not significant.

Exercise

Six volunteers received glucose or an equal volume of water and 30 min later they performed an exercise on a bicycle ergometer. The exercise test consisted of three periods with work loads increasing from 1.5 to 2.0 and 2.5 W/kg. Each period lasted 6 min with one-minute rest in between. Plasma prolactin and glucose levels were determined in blood collected at intervals indicated in Fig. 1.

Administration of TRH

Six volunteers received glucose or an equal volume of water. TRH (Thyreoliberin, SPOFA, 0.2 mg) was injected intravenously 30 min later and blood samples for prolactin and glucose determination were taken at intervals shown in Fig. 2.

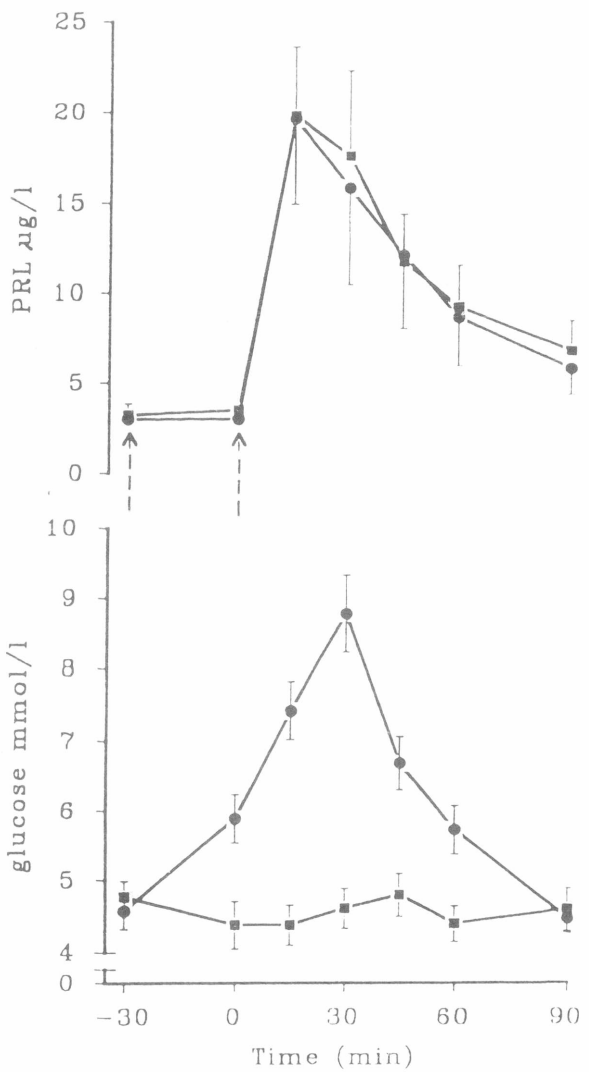

Fig. 2
Prolactin response to TRH in six subjects after glucose (closed circles) or water (closed squares) ingestion. Arrow at −30 min indicates glucose or water administration whereas TRH was given at 0 min. The differences in plasma prolactin concentration were not significant.

Administration of haloperidol

Eight volunteers received glucose or an equal volume of water. Thirty minutes later, haloperidol (RICHTER, 2 mg) was administered intravenously. Plasma samples assayed for prolactin and glucose concentration were obtained at time intervals indicated in Fig. 3.

Hormone measurements

The concentration of plasma prolactin was measured by radioimmunoassay using commercial kits (UVVR, Prague). Plasma glucose was analyzed by the glucose oxidase method (Oxochrom, LACHEMA). All samples of one trial were run in duplicates in the same assay.

The data (Means ± S.E.M.) were statistically evaluated by analysis of variance (ANOVA) followed by pairwise comparisons according to Dunn and Dunnet.

Results

Exercise

Glucose given orally 30 min before the work load on a bicycle ergometer led to hyperglycaemia which declined rapidly during exercise. After exercise, plasma glucose tended to increase, probably as a result of absorption of glucose from the digestive tract, which had been slowed down during muscle work. Hyperglycaemia, however, did not influence the prolactin response to exercise (Fig. 1) .

Administration of TRH

Plasma glucose concentration was increased at the time of TRH administration and hyperglycaemia culminated during the first 15–30 min of the TRH test. The plasma prolactin increase after glucose ingestion did not differ from the values obtained in the control investigation after water administration.

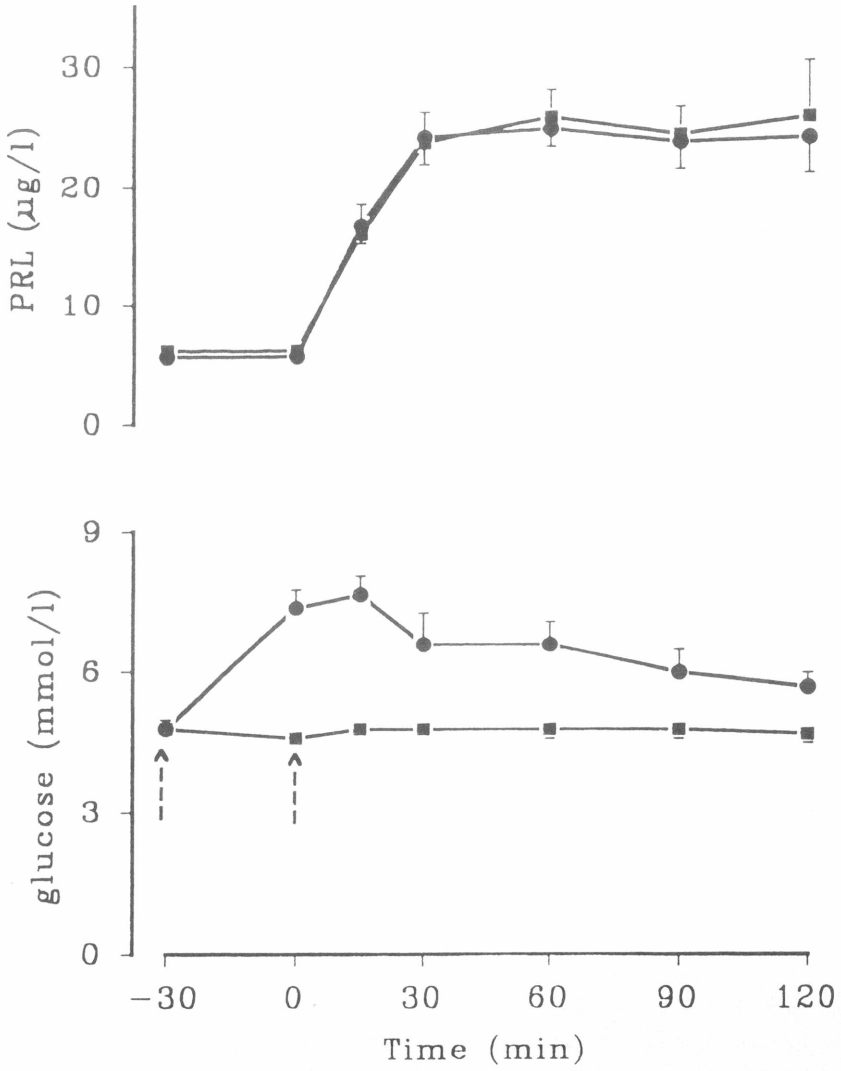

Fig. 3
Prolactin response to haloperidol administration in 8 subjects after glucose (closed circles) or water (closed squares) administration. Water or glucose were given at −30 min, haloperidol at 0 min. The differences in plasma prolactin concentration between the tests were not significant.

Administration of haloperidol

As expected, blockade of dopamine receptors by haloperidol injection resulted in a significant rise in prolactin release. Hyperglycaemia induced by glucose ingestion did not affect haloperidol-induced prolactin secretion (Fig. 3).

Discussion

Glucose administration very effectively inhibited growth hormone release to the majority of pharmacological or pathophysiological stimuli tested (L-dopa – Mims *et al.* 1973, growth hormone-releasing hormone administration – Masuda *et al.* 1985, exercise – Hunter *et al.* 1965, surgery – Vigaš *et al.* 1977). However, information on the role of glucose in preventing the response of other pituitary hormones to stimulation is limited. Glucose ingestion was without any detectable influence on basal values of β-endorphin, ACTH and cortisol (Balon-Perin *et al.* 1991). In our previous investigation, the administration of glucose failed to affect stress-induced activation of adrenocorticotropic function. However, ingestion of glucose inhibited the plasma cortisol increase after pharmacological stimulation with L-dopa (Ježová-Repčeková *et al.* 1980). Glucose infusion or ingestion did not reduce the basal concentration of plasma prolactin in normal subjects (Lugari *et al.* 1986, Ajlouni *et al.* 1976). Langford *et al.* (1992) recently found that glucose modulated prolactin secretion *in vitro* from pituitary lactotrophs. However, the increase of glucose concentration in the medium was followed by increased or decreased prolactin secretion, depending on the plasma insulin concentration of rat donors.

For elucidation of the role of glucose in the prolactin response, three different tests were used in the present investigation. Glucose administration before exercise enables to test the effect of hyperglycaemia on hypothalamic regulation of prolactin secretion. The other two tests assessed the effect of glucose on the secretion of prolactin by pituitary lactotrophs. From the point of view of cellular mechanisms of prolactin secretion, each test operates in a different way. TRH is supposed to stimulate prolactin release mainly by activating the phosphoinositide cascade (Martinez de la Escalera and Weiner 1992). Vasoactive intestinal peptide (probably mediating prolactin secretion during stress – Abe *et al.* 1985) exerts its effect by activating adenylyl cyclase, while the dopaminergic antagonist haloperidol is blocking the effect of dopamine, which inhibits adenylyl cyclase and also lowers cytoplasmic Ca^{2+} by decreasing its influx (Martinez de la Escalera and Weiner 1992).

During exercise, the signal for activation of endocrine functions can be generated by forward regulation from motor centres in the brain (Kjaer *et al.* 1987), or by feedback regulation by metabolic error signals, the most important probably being a decrease in glucose availability (Galbo 1983). However, glucose administration failed to modify the regulation of prolactin secretion during exercise. The failure of hyperglycaemia to affect the prolactin response to exercise indicates that (1) the glucose deficit is not the signal for activation of the lactotropic function during exercise, and (2) glucose does not exert any effect on secretory mechanisms operating during exercise.

In our investigation, hyperglycaemia failed to modify haloperidol or TRH-induced prolactin release in healthy male subjects. On the other hand Vierhapper *et al.* (1983) found a moderate inhibition of TRH-induced prolactin release during hyperglycaemic clamp in diabetic subjects. This interference of glucose with the TRH effect in pituitary lactotrophs of patients with type II diabetes may be due to some metabolic consequences of this disease. Similar differences were found in the effect of prolactin on glucose metabolism between healthy subjects and patients with prolactinomas. Pathological hyperprolactinaemia exerted diabetogenic effects (Landgraf *et al.* 1977), while hyperprolactinaemia induced in healthy subjects by physiological or pharmacological stimulation of prolactin release failed to affect glucose homeostasis (Vigaš *et al.* 1993).

Our results suggest that glucose does not modulate the prolactin response to stimuli operating *via* hypothalamic (exercise) or pituitary (TRH, haloperidol) regulatory mechanisms in healthy subjects.

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Reprint Requests

M. Vigaš, M.D., D.Sc., Institute of Experimental Endocrinology, Slovak Academy of Sciences, 83306 Bratislava, Vlárska 3, Slovak Republic.