Effect of amylin on prolactin release

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Abstract

OBJECTIVE: Amylin is a 37-amino acid peptide that is secreted from the pancreatic β cells. This peptide is cosecreted with insulin from the pancreas by glucose. Amylin plays a role in glucose homeostasis and in the regulation of lipid metabolism. Amylin receptors were identified in central nervous system of rats. There is no available data on the effects of amylin on the pituitary hormones secretion. The aim of this study was to evaluate the effect of amylin on prolactin release in vivo and in vitro experiments in male adult Wistar Kyoto rats.

METHODS: Amylin in a dose of 1µg/5µl was injected intraventricularly (i.c.v) during 5 min. using automatic pump. The control group received 5 µl cerebrospinal fluid. Amylin was injected intravenously (i.v) in a dose of 10 µg in 300 µl 0,9% NaCl. The control group received 300 µl 0,9% NaCl. In vitro experiment was performed in the pituitary cells culture conditions. Amylin was added to pituitary cell culture in a dose of 1, 10, 100 nM. Prolactin concentrations were determined using RIA methods.

RESULTS: Central or peripheral administration of amylin caused a significant decrease of serum PRL concentrations as compared with control after 120 min. After 240 minute incubation of the pituitary cells culture with amylin in doses of 10 nM and 100 nM a significant inhibition of the release of PRL was found. However we found that the effect of amylin on the release of PRL depended on dose and time of incubation. A significant increase of PRL level was observed in cultured media in the presence of 1 nM of amylin after 60 min.

CONCLUSION: Our results indicate that amylin administrated centrally and peripherally as well in the cell culture inhibits PRL release.
Introduction

Amylin (islet amyloide polypeptide; IAPP) is a 37 aminoacide peptide that is secreted from the pancreatic β cells [1]. The data of Hanabusa et al. [2] revealed that IAPP is cosecreted with insulin from the pancreas. The physiological role of amylin have not been exactly establish. Previous studies have demonstrated an effect of IAPP on glucose metabolism in several species of animals [3, 4, 5, 6, 7, 8, 9]. Authors of previous studies suggested that amylin is unlikely to be of physiological importance in peripheral glucose metabolism [5]. In all of these studies the doses of amylin used were much higher above the physiological range. Arnello et al. [10] using a novel aortic catherisation technique observed that chronic low dose amylin infusion reduces food intake, but has no influence on glucose metabolism. However the results of Wang at al. [11] indicated that amylin is more potent and more effective than glucagon in raising plasma glucose concentrations in fasted rats. Amylin infusion raised both glucose and insulin concentrations and these results may suggest that amylin can induce peripheral insulin resistance [12]. However some authors suggested [13] that hypoamylinemia rather than hyperinsulinemia per se can have directly caused the insulin resistance in the obese LA/N cp rats (insulin resistant Lister Albany rats).

Hettiarachchi [14] demonstrated that the specific amylin antagonist, amylin [8–37]; enhances whole body, liver, and muscle insulin sensitivity with a concomitant decrease of basal plasma insulin in both normal and insulin – resistant, hGH-infused rats. They found that amylin [8–37] infusion was associated with altered lipid distribution. Ye. J. M. et al. [15] observed that amylin stimulates lipolysis in vivo. These results may suggest that amylin plays a role in glucose homeostasis and in the regulation of lipid metabolism.

Moreover amylin inhibits food intake and gastric acid secretion [16]. Amylin receptors were identified in central nervous system in rats [17]. There is no available data on the effects of amylin on the pituitary hormones secretion.

The aim of this study was to evaluate the effect of amylin on prolactin release in vivo and in vitro experiments in male Wistar Kyoto rats.

Material and methods

Male Wistar–Kyoto rats (240–260 g) were maintained under controlled conditions (14L:10D, lights on at 06:00h, temperature at 23 ±1°C) with free access to food and water. All experimental procedures were approved by the First Warsaw Ethic Committee for Experiments on Animals (the M. Nencki Institute of Experimental Biology, the Polish Academy of Science).

Intracerebroventricular (icv) administration of amylin

The animals were anesthetized ip with ketamine and implanted with a stainless-steel guide cannula, 23 gauge cannula was located in the third cerebroventricle. Y e. J. M. et al. [15] observed that amylin infusion reduces food intake, but has no influence on glucose metabolism. However the results of Wang et al. [11] indicated that amylin is more potent and more effective than glucagon in raising plasma glucose concentration in fasted rats. Amylin infusion raised both glucose and insulin concentrations and these results may suggest that amylin can induce peripheral insulin resistance [12]. However some authors suggested [13] that hypoamylinemia rather than hyperinsulinemia per se can have directly caused the insulin resistance in the obese LA/N cp rats (insulin resistant Lister Albany rats).

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In vivo experiment results

Effects of amylin on PRL after intracerebroventricular (icv) administration and intravenous (iv) injection are presented in figures 1, 2.

A significant decrease of PRL in the peripheral blood compared with control after 120 min (p<0.05) after the central administration (icv) of amylin was observed. Intravenous (i.v) injection amylin significantly decreased PRL level after 120 min. (p<0.01)

Discussion

It has been known that amylin displays 50% homology with calcitonin gene-related peptide (CGRP) and it is co-localized with somatostatin in endocrine cells of the gastric fundus. Amylin participates in the regulation of gastric endocrine (somatostatin, histamine)
Effect of amylin on prolactin release and exocrine (acid) secretion. Amylin enhances somatostatin secretion via autocrine mechanism and leads to inhibition of histamine and acid secretion [23].

Amylin antagonizes insulin action and causes in vivo insulin resistance, but amylin did not affect the level of plasma glucagon, epinephrine, norepinephrine and corticosterone and metabolism clearance rate of insulin [24]. Amylin modulates aminergic neurotransmitters in the hypothalamus and inhibits food intake, through inhibition of dopamine release without affecting norepinephrine or serotonin [25].

Moreover, amylin inhibits NPY, a potent feeding stimulating peptide, and leads to weight loss [26]. Nyholm et al. [27] demonstrated that amylin analog AC 137 caused a rise in circulating cortisol and GH release during hypoglycemia in patients with insulin – dependent diabetes mellitus.

In our experiments we observed that amylin administered centrally (icv) and peripherally (iv) produced a significant decrease in prolactin release. However, effects of amylin on PRL release from cultured pituitary cells were dependent on dose and time of incubation. We found inhibiting effects of amylin (in doses 10; 100 nM) on PRL release after 120 and 240 min. of incubation. Transitory stimulating effect of amylin in a dose of 1nM was observed only after 60 min. of incubation.

Paganii et al. [28] investigated the effect of amylin and salmon calcitonin (sCT) on β endorphin secretion induced GH and PRL secretion in male rats. They found that amylin inhibited β endorphin – that induced GH secretion. Where as sCT was able to inhibit β endorphin induced prolactin secretion. Amylin and sCT may act through various receptors and this finding may explain the differences in action on GH and PRL release.

Some factors may be involved in the mechanism of inhibiting effects of amylin on PRL release in our experiments in vivo and in vitro. It has been reported that amylin modulates neurotransmitters and neuropeptides activity. Effects of amylin on dopaminergic activity NPY (Neuropeptide Y) and VIP (vasoactive intestinal peptide) activity may be involved in the inhibition of PRL release. Fernandez at al. [29] indicated that IGF I and VIP induce lactotrophs proliferation and PRL release.

Conclusions

Direct and indirect inhibitory effects of amylin on PRL release were found.

REFERENCES

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