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The effect of VIP and PHI-27 on oxytocin release in vitro

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Key words: vasoactive intestinal peptide (VIP), peptide histidine isoleucine (PHI-27), oxytocin, hypothalamo-pituitary complex, perifusion.

Abstract

The effect of vasoactive intestinal peptide (VIP) and peptide histidine isoleucine (PHI-27), peptides of the glucagon-secretion family, on oxytocin release were examined in a perifusion system by perifusing the hypothalamo-pituitary complex from normal female rats in diestrus. VIP at 10^{-7} M had no significant effect on oxytocin release from the hypothalamo-pituitary complex. Medium containing 10^{-7}M PHI also induced no significant release of oxytocin. These date indicate that VIP and PHI in a dose range which stimulates prolactin secretion have no effect on oxytocin release in vitro.

Introduction

The distribution and concentration of peptide histidine isoleucine (PHI), a new member of the glucagon-secretion family[1], in the brain were found to be similar to those of vasoactive intestinal peptide (VIP)[2][3]. Moreover, the concentrations of these two hormones have recently been reported to be equally high in the hypophyseal portal blood[4]. The concentration of VIP in the posterior lobe of the pituitary gland is higher than that in the anterior lobe[5]. These findings suggest that VIP and PHI are involved in regulation of the function of the pituitary gland, especially the posterior lobe. However, there are few reports concerning their action on oxytocin secretion[5].

In the present study we examined the effects of VIP and PHI on the release of oxytocin from the rat hypothalamo-pituitary complex in an in vitro perifusion system.

Materials and Methods

Cycling 200-250g female Wistar-Imamichi rats in diestrus of the estrous cycle were used. The animals were decapitated at 12:00 h and their hypothalamo-pituitary complex was removed and perifused in a perifusion system as described previously[6]. The complex was placed in a 0.1ml plastic chamber, and perifused with Medium 199 (Handai Biken, Japan) saturated with 95% O_2−5% Co_2 at 37°C at a flow rate of 3ml per hour. After 2.5 h equilibration, the effluent was collected in 0.5 ml fractions at 10-min intervals for 1 h, and then medium with 10^{-7}M VIP (Sigma, St. Louis, Mo) or newly synthesized PHI[7] was perifused for 30 min. Eighteen fractions were collected in 3 h and stored at −20°C until assay. Eight experiments were done on each group. Oxytocin in effluent fractions was measured by radioimmuno-assay as reported previously[6][8]. The minimum detectable dose and within-assay coefficients of variation were 1μU/tube and 7.5%, respectively, In each experiment, the mean oxytocin concentration in the first 6 fractions collected in the 1 h before each treatment was used as the basal value for each group, and change in efflux of oxytocin was expressed as percentage change from the basal value. Statistical analyses were performed by analysis of variance.

Results

The mean (±SEM) basal concentration of oxytocin in th perifusion efflux from the hypothalamo-pituitary complex in all groups was 66.4 ± 6.8 μU/ml and there was no significant difference among values for the three groups. Changes in oxytocin concentrations in the perifusion efflux from the hypothalamo-pituitary complex are show in Fig. 1. The oxytocin level in the control group tended to decrease gradually during the first hour and increase during the last two hours. The changes in the oxytocin concentrations in the efflux on treatments with VIP and PHI were within 25% of the mean basal levels. Neither 10^{-7}M VIP nor PHI induced significant increase of oxytocin release from the perifused hypothalamo-pituitary complex over that in the control group.

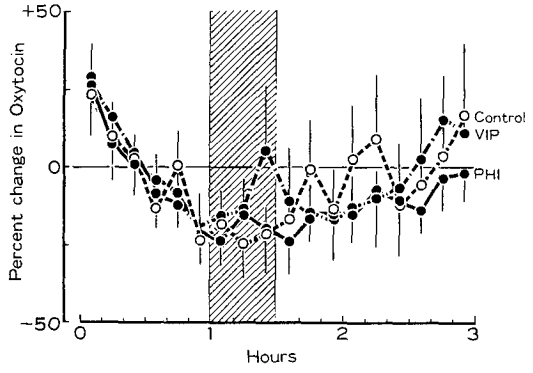

Fig. 1 oxytocin changes in the perifusion effluent from the hypothalamo-pituitary complex after administration of 10^{-7}M VIP or PHI in Medium 199. The mean oxytocin concentration of 6 fractions collected in 60 min before each treatment was taken as the basal value. Values are shown as percentage changes from the basal level in each group. Points are means (±SEM) for 8 experiments.

Discussion

The perifusion system used in the present experiment has been reported to be useful for study of the secretions of LH-RH, LH or oxytocin from the hypothalamo-pituitary axis[6)9)10)]. Using this system, we demonstrated that sodium induced oxytocin release from rat pituitary[6)].

The present in vitro study showed that 10^{-7}M VIP and PHI, members of glucagon-secretion family, did not affect oxytocin release from the hypothalamo-pituitary complex. Both VIP and PHI in the concentration range of 10^{-7}M used in the present study have been demonstrated to stimulate prolactin release from pituitaries in vitro[11)12)]. There are some possibilities that VIP and PHI in higher concentration may induce the oxytocin release. However, the limitation of available materials did not allow to confirm these possibilities.

Ottensen et al., however, observed the increase of plasma oxytocin levels following VIP administration in vivo[5)]. In the cat, infusion of 0.6 nmol/ml VIP into the common carotid artery caused an increase in the concentration of oxytocin from a mean of 7.9 μU/ml to a maximum of 34.9μU/ml in the jugular vein plasma. The difference between the present in vitro findings and their in vivo results may be caused by the experimental conditions and/or the animal species used. There is another possibility that VIP may act on the oxytocin nerve via the outside of hypothalamo-pituitary region.

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