The role of beta-endorphin in pregnancy and delivery

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Summary: This paper deals with beta-endorphin determination in 20 autopsy specimens of human fetal and neonatal pancreas, as well as in the placental tissue specimens of the same feto-placental units, by means of radioimmunoassay (RIA - Nichols Institute). Peripheral blood samples of 10 healthy non-gravids were taken as controls. Our results present a marked increase of beta-endorphin levels with the progression of gestation, reaching a peak of 3960 pg/g at term. The data obtained indicate that beta-endorphin plays an important role in pregnancy and delivery regulation.

Key words: Beta-endorphin; fetal and neonatal pancreas; pregnancy and delivery regulation.

INTRODUCTION

Developmental patterns of pancreatic opioid peptides, especially beta-endorphin (beta-EP) and islet hormones studied in experimental conditions indicate their surge during the first postnatal week ([1]). Beta-EP containing cells are in close proximity to insulin containing ones in the endocrine pancreas. In has been confirmed that beta-EP stimulates glucagon release and inhibits somatostatin secretion, the effects that can be reversed by naloxone ([2, 3]). Recent studies indicated that beta-EP infusion caused a significant rise in plasma glucose concentrations preceded by a significant increase in peripheral glucagon levels but no changes occurred in the plasma concentrations of insulin and C peptide ([4, 5]). Beta-EP have morphine-like analgesic properties, behavioral effects and neurotransmitter (neuromodulator) functions, but their role in the perinatal period still remains unresolved.

The purpose of this research was to estimate the production and concentration variations of beta-EP in the human fetal and neonatal pancreas during the gestation (third trimester) and in the early neonatal period in order to explain their possible influence on delivery initiation and pancreatic islet cell function.

MATERIALS AND METHODS

The study was carried out on 20 autopsy human fetal (FPG) and neonatal (NPG) pancreas gland tissue specimens, obtained imme-

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diately after spontaneous preterm labor. The gestational ages were, respectively: eighth (4), eighth and a half (4), ninth (4) and ninth and a half (4) months of gestation as well as term delivery (4). Peripheral blood samples of 10 nongravid healthy people were taken as controls. Placental tissue specimens of the same feto-placental units were also examined. After removing, pancreatic and placental tissue specimens were placed directly into liquid nitrogen and transported to the laboratory. One gram of tissue was cut and, after the microdismembranation process (6), put in 5 ml of homogenization buffer. Beta-EP determination was based on the evaluation of concentration in both membranes and cytosol of the pancreatic and placental cell substrate by using radioimmunoassay techniques (RIA-Nichols Institute). Results were expressed in picograms of beta-EP in one gram of wet tissue weight, mean ± SD. Beta-EP concentrations in peripheral blood were determined using RIA Nichols kits. The obtained data were analyzed by Student's t and chi-square test.

RESULTS

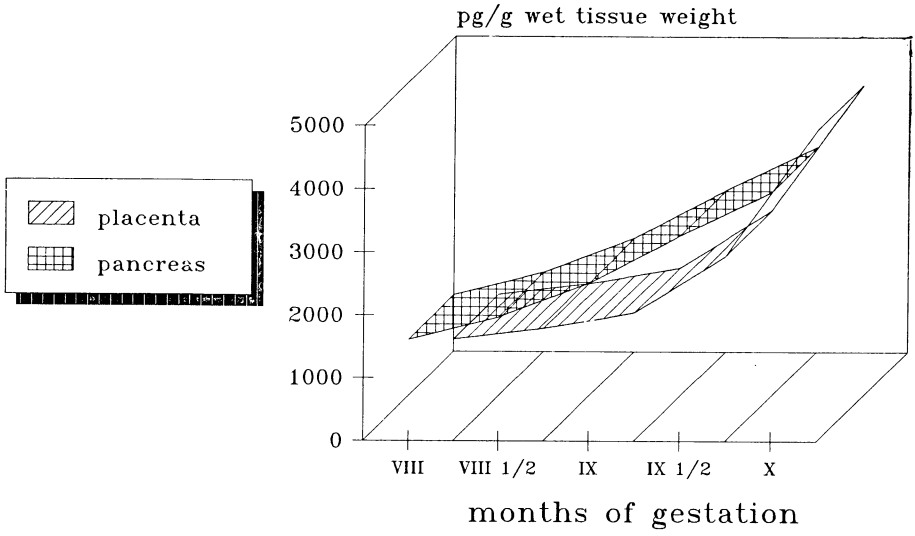
This study presented a marked increase of beta-EP level in human pancreatic cellular substrates with the progression of gestation. This finding was particularly expressed at term, reaching a peak of 3960 ± 637 pg/g (fig. 1). Beta-EP concentration was also high in placental compartment (4234 ± 840 pg/g), while its level in the peripheral blood of nonpregnant women was 45 ± 8 pg/ml.

DISCUSSION

The pancreas is found to be a very important source of many hormones and opioid peptides during fetal and neonatal life (1). In pregnancy, and particularly during labour, which represents an extremely stressful situation, maternal and fetal production of blood beta-EP is increased (7), which our study confirmed. There is a putative bidirectional network carrying information between the endocrine and reproductive systems (8). The pancreas is incorporated in the hypothalamic-pituitary-gonadal axis and production (secretion) of opioid peptides during gestational period is likely to be increased (9). Results of this investigation indicate that opioid peptides - beta-endorphins are components of the intrapancreatic regulatory system, that means beta-EP of pancreatic origin may function as ultra-short-loop or autocrine regulator of pancreatic islet cells, because their concentration rises during gestation, throughout the intrapartal period and in the early neonatal life.

While hypophyseal and gonadal hormones feedback information to the pancreatic islet cells exists, providing a modulatory system for the regulation of pancreatic cell maturation and peptides production, the pancreas and its peptides secretion can exert a modulation of gonadotropin secretion via a direct action at the hypothalamic LHRH level (8).

Neurohormone beta-EP appears to have a significant physiological role as a regulator of pain perception, by increasing the threshold of this perception and as an endocrine factor in human reproduction. Beta-EP stimulates the secretion of prolactin, growth hormone and vasopressin, and inhibits the production of oxytocin, dopamine, folliculostimulating and luteinizing hormone, resulting in the depression of copulative effects, that is, it exerts an antireproductive influence both in female and male reproductive tracts (3). It is worth noting that pancreatic islet cells were found to produce several neurohormones, including beta-EP (1), which show antagonistic effects. This interaction has already drawn the attention of investigators in the field of neuroendocrinology. It has been found that beta-EP protects the reproductive system from both the excessive secretion and effects of pituitary trophic hormones. The mechanism of opioid peptide action is via opioid receptors, and can be antagonized by com-



Beta - Endorphins	Month of Gestation				
Wet tissue weight (pg/g, mean +/- SD)	VIII	VIII 1/2	IX	IX 1/2	X
Pancreas	1620 +/- 155	1980 +/- 186	2520 +/- 223	3276 +/- 648	3960 +/- 637
Placenta	910 +/- 198	1086 +/- 212	1336 +/- 288	2243 +/- 548	4234 +/- 848

Fig. 1. — Beta-EP levels in human fetal and neonatal pancreas and placenta.

petitive binding antagonist naloxone. Naloxone and its possible relationship to fetal endorphin levels and fetal distress have been studied by Goodlin ([2]).

The results obtained in this study could suggest that the identified increased beta-EP production in both membranes and cell substrate cytosol from fetal and neonatal pancreas are most probably caused by intrapartal stress. As an alternative hypothesis we propose that beta-EP of the pancreatic origin represents an anti-reproductive factor, throughout intrauterine fetal and early neonatal life. There is no doubt that beta-endorphins of pancreatic origin influence intrapancreatic hormones and other opioid peptides synthesis, which means that beta-EP may function as an ultra-short-loop or autocrine regulator of pancreatic islet cells.

The endocrinology of pancreatic cells requires further research in order to obtain a definitive and exact insight in human reproduction.

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