BIOLOGICAL DETERMINATION OF ANTIDIURETIC ACTIVITY IN TISSUES OF THE HUMAN EMBRYONIC HYPOTHALAMUS, PITUITARY, AND HUMAN PLACENTA

S. E. Levina and E. A. Ivanova

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The antidiuretic activity of tissues of the hypothalamus and pituitary of 49 human fetuses between 12 and 40 weeks of development and of the placenta between the 7th and 40th weeks of pregnancy was investigated. Activity of the hypothalamic tissue can be detected after the 14th week and it increases after the 21st and 22nd week. In the pituitary of fetuses aged 12-15 weeks activity is found in one-quarter of cases, increasing after 21st week. The placental tissue possesses antidiuretic activity throughout embryogenesis, from the 7th until the 40th week of pregnancy. Variations in activity are independent of age or sex of the fetus.

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Antidiuretin (AD) is of interest not only as the hypothalamic factor regulating water and salt metabolism and pressor reactions. According to several workers, AD liberates pituitary adrenocorticotropin (ACTH-1). These results were obtained in experiments on adult rats. Meanwhile, the role of AD in embryonic development of mammals is still unexplained. We do not know when ACTH secretion in ontogenesis becomes dependent on CRF (the hypothalamic ACTH-releasing factor).

Information is likewise lacking on the role of AD in early human ontogenesis. It has been shown that ACTH is formed in the human pituitary after the 9th-10th week of embryogenesis [2]. Marked atrophy of the adrenals has been described in all human anencephalic fetuses (which possess varying amounts of adenohypophysis but never a hypothalamus).

These facts suggest that hypothalamic control over ACTH secretion by the pituitary is established in the early stage of human embryogenesis. In this connection, information on a substance which, like AD, possesses high CRF activity and can be subjected to direct endocrinologic testing is of considerable interest.

The object of the present investigation was to determine the antidiuretic activity of hypothalamic and pituitary tissues of human embryos and placenta.

EXPERIMENTAL METHOD

AD was tested by its effect on diuresis of male albino mice weighing 18 g over a period of 4 h after intraperitoneal injection of the test tissue and of 1 ml physiological saline. Acetone-treated hypothalamic or pituitary tissue was investigated from 40 fetuses of both sexes at the 12th-40th week of development, and placental tissue from 30 fetuses aged 7-40 weeks. Before the beginning of the investigation the fetuses were kept for 4-24 h in the cold. A pharmacopoeial preparation of pituitrin P was used as standard.

Sometimes the hypothalamus was divided by a frontal incision into anterior and posterior parts. In such cases the total activity obtained for the anterior and posterior parts is indicated. Control mice received injections of acetone-treated brain tissue from the same fetuses.

[illegible] by Active Member of the Academy of Medical Sciences of the USSR A. L. Prozorovskii. Translated from [illegible] Eksperimental'noi Biologii i Meditsiny, Vol. 65, No. 6, pp. 81-82, June, 1968. Original article submitted [illegible] 18, 1967.

EXPERIMENTAL RESULTS

The first investigations of hypothalamic tissue were made from fetuses at the 14th week of development. From this time until the 19th week, 0.45-0.55 unit AD was consistently determined in the hypothalamus of fetuses of both sexes. From the 20th-21st week the AD content in the hypothalamus increased to 1.0-1.3 units, and at the same time considerably variability of the results appeared: in some fetuses not more than 0.35-0.4 unit AD was found at the 24th, 27th, and 34th weeks. There were no fetuses with absence of AD activity.

Investigations of the pituitary began in 12-week fetuses. In one male fetus at the 12th week of development 0.084 unit AD was found. Of 7 fetuses at 13-15 weeks, no AD was found in the pituitary of one male and one female fetus. In the other 5 fetuses 0.05-0.09 unit AD was found. Later, until the 20th week, 0.1-0.4 unit AD was discovered (the same in fetuses of both sexes).

The AD content in the pituitary began to increase after the 21st week, reaching 0.9-1 unit by the 22nd-23rd week of development, 1.3-1.7 units by the 25th-28th week, and 4.5-4.8 units at birth. However, just as during investigation of the hypothalamus, after the 21st week the variability of the AD concentration in the pituitary began to increase: in one-quarter of all fetuses investigated at this age the AD activity did not exceed 0.3-0.4 unit. Absence of AD from the pituitary was not found in any fetuses over 14 weeks old, and sexual dimorphism likewise was not found. The AD content in the placenta was high, but no regular changes in its level depending on age or sex of the fetus could be detected, although the individual variability was fairly high.

At the 7th week of pregnancy the placental tissue contained 1.7 units* AD, and in three cases at 12-13 weeks of pregnancy the figure was between 0.6 and 2.8 units. The AD content in the placenta at 15-19 weeks varied from 0.7 to 3 units, at 20-25 weeks from 1.05 to 4 units, and from the 26th to the 40 th week from 0.5 to 1.6 units.

The role of AD in fetal development is not clear, particularly remembering the considerable factual evidence of insensitivity of the kidney to AD in early ontogenesis [1]. The role of pressor factors and regulators of water and salt metabolism during intrauterine development likewise is unexplained, although the need for them (especially in the placenta) seems very probable. So far as the close relationship between AD and CRF is concerned, attention is drawn to the synchronous increase in AD and ACTH content in the embryonic pituitary (starting from the 20th week of development).

However, this phenomenon cannot be regarded as of decisive importance, because the 20th week is a milestone in human embryogenesis after which important changes take place in the whole development of the fetus and, in particular, in the development of its endocrine system.

LITERATURE CITED

1. M. G. Zaks and L. K. Titova, Abstracts of Proceedings of the Second Scientific Conference on Evolutionary Physiology [in Russian], Leningrad (1959), p. 76.
2. Yu. B. Skebel'skaya, Probl. Endokrinol., No. 4, 77 (1965).

*The AD content in the placenta is expressed per 100 mg dry weight (corresponding to approximately 700-720 fresh weight).