PLACENTAL ENDOCRINE FACTORS INVOLVED IN INTRAUTERINE GROWTH

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Abstract: *Placenta shows hormonal functions like: progestational, fetal and placental growth, regulatory. Progestational role factors are progesterone, estrogen, chorionic gonadotropic hormone (hCG), inhibin (A, B) and activin (A, B), CRH. Progestational hormones promote growth of the placental mass, allowing implantation and maintaince of the pregnancy and represent fetal substrate for fetal synthesis of glucocorticoids, mineralocorticoids, testosterone promoting growth of the alveolar cells and lobules in the breast. The placental hormones with a preponderant role in fetal growth are: HPL, HGH-V, growth factors IGF I, II. Placental Lactogen (chorionic somatotropin) (HPL / HCS-A, B) occurs in the first part of pregnancy whereas variant placental growth hormone (hGH-V) in the second part. They regulate fetal growth by sparing glucose and amino acids for the fetus, modulating the insulin resistance and mobilization of fatty acids for metabolic needs of the mother.*

Cuvinte cheie: *placenta, hormoni progestaţionali, hormoni de creştere fetală*

Rezumat: *Placenta prezintă funcţii hormonale de tip progestational, de creştere fetala, placentara şi reglatorie. Factorii cu rol progestaţional sunt progesteronul, estrogenii, hormonul corionic gonadotrop (hCG), inhibina (A, B) şi activină (A, B), CRH-ul. Hormonii progestaţionali promovează creşterea masei placentare, permit implantarea şi menţinerea sarcinii, reprezintă substrat fetal de sinteză fetala de glucocorticoizi, mineralocorticoizi, testosteron (rol maturant fetal), creşterea celulelor alveolare şi a lobulilor la nivelul sânilor. Hormonii placentari cu rol preponderant de creştere fetala sunt: hPL, hgh-V, factori de creştere insulin-like IGF I, II. Lactogenul placentar (somatotropina corionica) (hPL/hCS-A,B) intervine în prima parte a gestaţiei şi hormonul de creştere placentar variant (hGH-V) în partea a doua, reglând creşterea fetală prin cruţarea glucozei şi aminoacizilor pentru făt, modularea rezistenţei la insulină şi mobilizarea preponderentă a acizilor grai pentru nevoile metabolice ale mamei.*

Endocrine factors involved in intrauterine growth are synthesized both by placenta and by the fetus. Placenta shows very complex hormonal function: progestational, placental, fetal growth and regulatory. **Placental factors with a progestational role** are: progesterone, estrogen, chorionic gonadotropic hormone (hCG), inhibin (A, B) and activin (A,B), CRH.

Progesterone (1,2,3,4) is necessary to enable the maintenance of pregnancy, by relaxing the uterine muscles. It is produced at the beginning of the pregnancy by ovarian corpus luteum, under the hCG action, then follows a transition period (between gestational weeks 6-12), in which it is synthesized by the corpus luteum and placenta (syncytiotrophoblast), after which the placenta becomes the dominant site of synthesis. Levels increase steadily until a few weeks ahead of time (approx. 300mg/day or 400-500 mmol/L).It is urinary excreted in the form of urinary pregnanediol glucuronide. Its maternal functions are:

1. Progestational (relaxes muscles and other uterine smooth muscle and promotes with estrogen the uterine growth, and by the vasodilator effect is increasing the placental mass,
2. It has an immunosuppressive role,
3. It stimulates growth, proliferation of the alveolar cells and lobules in the breast. For the fetus it is the main substrate for the synthesis of glucocorticoids and adrenal gland mineralocorticoids.

Estrogens(1,2,3,4,9) prepare and maintain pregnancy and trigger the parturition. They are synthesized by syncytiotrophoblast and require an effort developed by th fetus, mother and the placenta.

Three major estrogenic compounds occurr in pregnancy estriol (E3) - the major product, estradiol (E2), estrone. The release of the three compounds by maternofetoplacentar unit is predominantly in the maternal circulation. The production level is increased by 1000 times during pregnancy, up to 100 nmol / L, exceeding 80 mg / day of term. By comparison, at the cycle, estrogen levels are 1000 pmol / l. In the past, measurement of maternal serum or urinary estriol is usually made in the third trimester of pregnancy to assess fetal wellbeing, but now it no longer shows the same value. Fetus and mother are protected by high titres of progesterone by the formation of conjugated steroid compounds. Estrogens prepare and maintain pregnancy, cause vasodilation, with an increased flow to the uterus and miometrial hypertrophy; they determine parturition onset (if placental sulfatase is missing it appears a dysfunctional labor). They are designed to promote tissue growth of the birth canal, in order to allow passage of the fetus without trauma, on the breast, estrogens cause proliferation of the ductal system and glandular tissue with progesterone and inhibition of milk secretion.

Chorionic gonadotropic hormone (hCG) (1,2,5,9) has progestational role in maintaining secretion of progesterone

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and oestradiol in the maternal ovarian corpus luteum until the placenta is able to synthesize progesterone. It is secreted by cytotrophoblast, and is detectable in maternal blood 7 to 12 days after conception, and in urine, about 15 days after conception. Urinary concentrations reflect circulating concentrations. HCG levels increase after implantation, reaches a peak (40,000 to 200,000 IU / L) in the weeks 8th and 10th of pregnancy and decreases at nadir. Similar in structure to LH and FSH its role is to stimulate the corpus luteum to continue the production of progesterone until the placenta takes control of progesterone secretion in the 9th gestational week. Other proposed roles are the local stimulation of placental steroidogenesis, secretion of fetal testosterone (it is active early in the fetal testis). **Inhibin (A, B) and activin (A, B)** (1,2,3) are secreted by syncytiotrophoblast and cytotrophoblast cells, predominantly in the maternal circulation. Titers increase, especially in the third trimester, after the 20th gestational week for inhibin, while titers for activin at the onset of labor. Their role in maternal circulation, with estradiol and progesterone, is to suppress FSH secretion. At a placental level they are involved in modulating the synthesis of GnRH, hCG, and progesterone.

CRH (corticotropin releasing hormone) (1,2,3,7,8,9) is secreted by fetal syncytiotrophoblast, but also amnios, chorion and maternal deciduas. CRH is involved in regulating cortisol synthesis, indirectly through the formation of ACTH propiomelanocortin. In labor it enhances the effects of oxytocin on myometrium, with an increased contractility. CRH levels increase in the second trimester with a maximum level between the 36th week and term. High levels are found in the twins, patients with pregnancy-induced hypertension, patients with fetal IUGR, patients with preterm labor. CRH is considered a placental"clock".

Placenta has also the ability of synthesing hormones with an important role related to the fetal growth: HPL, HGH-V, growth factors IGF I, II. In the first part of the pregnancy placental lactogen (HPL) CS-A occurs, whereas in the second part variant GH growth hormone (hCG-V). These hormones increase the synthesis of IGF-1,2 maternal factors.

Placental Lactogen (chorionic somatotropin) (HPL / HCS-A, B) (1,7,8,9)regulates fetal growth, sparing glucose for the fetus and mobilizing fatty acids for metabolic needs of the mother. Placenta synthesizes large amounts of HPL (a molecule with similar biological and chemical site like pituitary GH) both in maternal circulation, and in the fetal circulation. More than 99% of HPL is released in the maternal circulation. Detectable in maternal circulation after 6 weeks of gestation, it reaches the plateau (5-7μg/ml) at the 30th week and the values of about 1 g / day at term; its long-term effects are sparing glucose for the fetus, facilitating the use of fatty acids by the mother. HCS quantity secreted is proportional to the size of placenta (normally it is one sixth of fetal weight). It causes retention of Na, K, Ca. In the fetal circulation is secreted in small quantities 1%. At 20 weeks of gestation the concentration is 5 ng / ml and at birth it reaches 20-30mg/ml. It stimulates the anabolism for carbohydrates, lipids and proteins directly and by enhancing the synthesis of IGF-1, 2 and the release of insulin. It maintains nutrient availability for a long-term for fetus by providing glucose; HPL has an important role in regulating fetal growth and metabolism of normal breast, but this action is permissive (there are cases with no genes for hGH-V and HPL and the pregnancy was successful).

Placental growth hormone (hGH-V) (7,8,9) is synthesized by placenta growth factor only in maternal circulation and is involved in the mobilization of maternal reserves of glucose, fatty acids and ketones in the second part of the pregnancy (with maximum activity in the third trimester). It temporarily replaces mother GH by suppressing pulsed growth hormone release model. It is secreted by syncytiotrophoblast, similar in structure with GH and prolactin, and it is detectable in maternal circulation around the 5th gestational week, according to some authors at week 8, it's level increases gradually, reaching the peak at birth (about. 27.5 mU / l). hGH-V activates lipolysis, with the release of fatty acids, which will be used by the mother (there is "shift" from a mother based on carbohydrate metabolism, to the one based on lipids, sparing the amino acids and glucose for the fetus, regulating fetal growth by modulating nutrients and increasing insulin resistance. It also causes mammary epithelial cell proliferation, production and control of maternal IGF-I, II and it induces placental growth.

BIBLIOGRAPHY

1. Gluckman, P.D., Mark Hanson, The Fetal Matrix – Evolution, Development and Disease, Cambridge University Press, 2005
2. Gluckman, P.D., Insulin-like growth factors and their binding proteins, in: Hanson, M.A., Spencer, J.A.D.,Rodeck, C.H., eds., The fetus and neonate. Vol. III: Growth, Cambridge University Press, 1994
3. Han, V.K.M., Hill, D.J., Growth factors in fetal growth, in: Thorburn, G.D., Harding, R., eds., Textbook of fetal physiology, Oxford University Press, 1994
4. Robinson JS, Owens JA, Owens PC – Fetal growth and fetal growth retardation In: Thoburn GD, Harding R- Textbook of fetal physiology- Oxford University Press, 1994:83
5. Gluckman, P.D., Heymann, M.A., Pediatrics & Perinatology. The scientific basis. Second Edition. Arnold, London,1996
6. Ponte, C., Weill, J., Croissance normale – Croissance pathologiques, Typoform, 1997
7. Gross Ian, D'Alton Mary E. – Seminars in Perinatology, Intrauterine Growth Restriction, 2008, Elsevier
8. Taeusch H. W, Ballard R. Gleason C. - Avery' s diseases of the Newborn 8 th edition, Elsevier, 2004
9. MacDonald, M.G, Avery ' s Neonatology. Pathophysiology and Management of the Newborn. Sixth Edition. J.B. Lippincott Company, Philadelphia, 2005
10. J.C Carel et al. – " Deciphering Growth – Genetic Control of Size at Birth " – D.B.Dunger, C.J.Petry, Springer – Verlag Berlin Heidelberg, 2005
11. Kronenberg H. M et al (editors), Williams Textbook of Endocrinology. 11TH Edition, W.B. Saunders Company, 2008
12. Matzuk M.M, Chester W. Transgenics in Endocrinology Humana Press, 2001
13. Gardner D.C, Dolores S. Greenspan's Basic & Clinical Endocrinology, 8th Edition, Mc Graw-Hill, 2007
14. Bittar E., Bittar N. Principles of Medical Biology, Roger S. - Reproductive Endocrinology and Biology – AI, JAI Press Inc, 1998.