

ENDOCRINE FACTORS INVOLVED IN INTRAUTERINE FETAL GROWTH

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Keywords: Fetal growth factors, factors for maturation, intrauterine growth

Abstract: Major fetal hormones involved in regulating fetal growth are fetal growth factors (IGF insulin-like growth factor, insulin, GH's - growth hormone) or hormones for maturation (steroid hormones, thyroid hormones and catecholamines). IGF-II are involved in early gestation, IGF-I in late gestation both growth factors regulate growth by IGF-I receptor. Insulin increases fetal secretion of IGF-I, GH determines the correct number and size of various organs without being a major determinant of growth (eg weight fetuses anencephalic / almost normal length at birth). Thyroid hormones, adrenal hormones, corticosteroid hormones have an important role in bone, lung, heart maturation.

Cuvinte cheie: factori de creștere fetală, factori maturanți, creștere intrauterină

Rezumat: Hormonii fetală majori implicați în reglarea creșterii fetale sunt factori de creștere (IGF-factori de creștere insulin like, insulină, GH-ul - hormonul de creștere) sau hormoni maturanți (hormonii steroidieni, hormonii tiroidieni și catecolaminele). IGF-II intervin în gestația timpurie, IGF-I în gestația târzie ambii factori de creștere reglând creșterea prin receptorul IGF-I. Insulina intensifică secreția fetală de IGF-I, GH-ul determină numărul și dimensiunea corectă în diferite organe fără a fi însă determinantul major al creșterii (ex fetușii anencefalici cu greutate/lungime aproape normală la naștere). Hormonii tiroidieni au rol în maturarea osoasă, neurologică, a plămânului, a cordului alături de hormonii corticosuprarenalieni și medulosuprarenalieni.

INTRODUC

Major hormones involved in regulating fetal growth are fetal growth factor (IGF insulin-like growth factor, insulin, GH's - growth hormone) or hormones for maturation (steroid hormones, thyroid hormones and catecholamines).

Insulin-like growth factor (IGF-I, II) (1,2,3,4) are synthesized mainly in fetal liver. IGF-I and IGF-II may be taken from human tissue from the 12th week and are found in circulation in the 15 week of gestation. Circulating concentrations of IGF-I and IGF-II increase with gestation, but remain lower than in maternal plasma at birth. They have a very important role in placental growth. Setting the IGF level is both autocrine and by other hormones (stimulating the secretion of IGF is triggered both by hGH-V and insulin, the inhibitor effect is made by cortisol secretion).

IGF-II occurs early in gestation. Experiments have demonstrated that mice without IGF-II genes had a fetal and placental growth retardation after 11 days of gestation, but resumed a growth rate parallel to that of the control group after day 18th. Fetuses were detected with high concentrations of circulating IGF-II receptor in early gestation. Double null mice model IGF-I, IGF-II (without genes encoding IGF-I, II) are very similar in terms of growth retardation with models without genes encoding IGF-I receptors, suggesting that both IGF-I and IGF-II act through IGF-I receptor to regulate fetal growth.

IGF-I occurs in late gestation. Fetal levels of IGF-I and fetal cord blood correlate with birth size. Fetal production of IGF-I is regulated primarily by glucose and insulin, GH fetus's having a minor role. Studies in mice without IGF-I gene showed that the subjects had serious problems and subsequent intrauterine growth postnatally; growth disorders were higher in

cases without IGF-I receptor genes.

Circulating levels of IGF - I and IGF - II (ng / ml) increases up to birth as follows:

Age	IGF - I	IGF - II
Fetus of 20 weeks	50	400
Fetus of 40 weeks	150	600
newborn	36	237

Insulin (1,2,3,4) plays an essential but permissive role in regulating fetal growth and can also serve as intermediary in regulating fetal IGF secretion by providing nutrients. Its presence is essential for normal fetal development. In the few reported cases of pancreatic agenesis, birth weight was approximately 2000g. Excess insulin can lead to pathological fetal growth as seen in children with diabetic mothers, and children with Beckwith-Wiedemann syndrome. This weight gain is clearly the result from an increase in fat cell mass, because the increase in muscle mass is minor.

The insulin enhances the secretion of fetal IGF-I but binds poorly at high concentrations to IGF-I receptors. It stimulates fetal growth indirectly by enhancing production of IGF-I and IGF-BP at the physiological limits of concentrations of substrates. The pituitary GH (GH - growth hormone) (9,10,11,12,13,14) is found in fetal circulation in the 10th week of gestation, and is only pituitary in origin. Modulation of GH secretion is made by GHRH (stimulation) and SRIF (GH inhibiting factor) IGF-I (inhibition).

In the mid-gestation, serum concentrations are in the range of 100 ng / ml the highest dose measured in any moment of time before or after birth. Decreased serum concentrations of GH occur in late gestation and appears to be related to the

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Article received on 25.05.2010 and accepted for publication on 01.06.2010

ACTA MEDICA TRANSILVANICA June 2010; 2(2)285-286

development of inhibitory tone on hypothalamic-pituitary axis. (increase in IGF-I, SRIF). GH receptors in fetal hepatocytes grow on the 30 week of gestation and can be responsible for initiating the synthesis of IGFBP-term 3. Inhibiting influences will increase resulting in a gradual loss of concentration and the appearance of the pulsating model at birth .

Despite the abundance of GH hormone, it was not considered a major endocrine determinant of fetal growth (anencephalic fetuses have a relatively normal body weight). Recent studies on cases of congenital GH deficiency, have shown a reduced birth length and relative obesity. In experimental models, fetal GH deficiency is associated with reduced long bone length and low levels of IGF-I. GH receptors were demonstrated in a variety of fetal cells in the second trimester and pituitary axis is important in producing the correct number and size in different organs.

Thyroid hormones (T3, T4, TSH, TRH). (11,12,13,14). TRH, TSH and thyroid hormones operates in 10 gestational week and fetal thyroid function is characterized by excessive synthesis of rT3 (reverse triiodothyronine) compared to triiodothyronine (T3), although it seems that rT3 has no significance for fetal development. Levels of T3, T4 will increase later in gestation because of the effect of cortisol on hepatic deiodinase. This is important in fetal lung maturation and explain the high incidence of respiratory distress syndrome in congenital hypothyroidism (serve with estrogen and cortisol on pulmonary surfactant synthesis. Fetal hypothyroidism results in delayed neuronal and bone maturation but has no significant effect on total body length. Thyroid hormones are β - adrenergic with an important role in fetal heart development. They have either the synergistic effect with catecholamines or act directly by normal hypertrophic growth.

The regulation of thyroid hormone secretion is made by hCG initially, then at week 10 of gestation by TRH, but also by the fetal cortisol. Maternal TRH crosses the placenta, TSH and stimulates the fetal TSH. This treatment was used for fetal lung maturation with intraamniotic administration of T4.

Adrenal corticosteroid hormones (5,8,9,10,11,12) have the most important role in tissue maturation. Cortisol is produced in the adrenal fasciculated zone of fetal and maternal placenta, but is produced also by placenta. The fetal adrenal gland, synthesized cortisol by ACTH stimulation starting with the 10th week of gestation. His role is to maturate a large number of enzymes involved in adapting the tissues and organs for extrauterine life: it accelerates lung structural development and surfactant synthesis (in several species increases adrenergic agonist. β lung receptors, lung receptors for insulin, EGF. At a heart level (the sheep fetus), it decreases sensitivity of ductus arteriosus to the dilator role for prostaglandins, facilitating ductal closure in response to oxygen concentration. It stimulates hepatic glycogen deposit, enzymatic gluconeogenic activity or the catalyation of the transformation of T4 in T3 (in animals and probably not experience the human fetus) the nervous system influence the myelinization rate; sheep fetus to placental synthesis promotes the synthesis of estrogen with F2 α consecutive synthesis and the initiation of parturition.

Catecholamines (CA) (1,2,3,8,9,10,11) are involved in the third trimester with functions in the lung, heart, and energy metabolism. Catecholamine levels are low in the intrauterine life, and the sympathetic tone is increased (intrauterine production but also the clearance rate are increased by 2 to 4 times compared with adult body). Production rate will increase once the labor is starting, ensuring a successful transition to postnatal life. T3 enhances the action of catecholamines and cortisol (cortisol receptors β density increases). Cellular response to catecholamines will normally increase in the third

trimester . In the lungs, CA increase the production and synthesis rate and reduce the pulmonary liquid; at the heart level, they cause increased myocardial contractility and systemic vascular resistance; catecholamines triggers thermogenesis by mobilizing energy chemicals (glucose and fatty acids).

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