Growth hormone

General about STH

__Growth hormone (general)

Secretion STH

__Growth hormone (secretion)

Effects of STH

The main effect of STH is to stimulate linear growth (most of the growth effect is mediated by IGF-I):

1. STH increases proteosynthesis via IGF-I bye increasing amino acids uptake and directly increasing transcription and translation mRNA.
2. STH reduces proteocatabolism by mobilising fat (as a more efficient energy source). It directly induces the release of fatty acids from fatty tissue (thus promoting ketogenesis) and enhances their conversion to acetyl-CO.
3. STH also acts on carbohydrate metabolism. It is diabetogenous because it increases glycogen output from the liver and has an anti-insulin effect in the muscles.

Insulin-resistance

Its excess reduces carbohydrate utilisation (inhibits glucose phosphorylation) and disrupts cell glucose uptake. This insulinoresistance appears to be caused by a post-receptor defect in the action of insulin. As a result, TH worsens clinical diabetes and 25% of patients have diabetes when they overproduce growth hormone (tumour of the adenohypophysis that secretes TH). Growth hormone does not directly stimulate insulin secretion, but hyperglycaemia, it causes stimulates the pancreas secondary to growth and may eventually lead to B-cell depletion (reduction of insulin production). Growth hormone produces a positive balance of nitrogen and phosphorus. It increases plasma phosphate levels and decreases urea nitrogen and amino acids in the blood. Independently of the adrenal gland (aldosterone), Na+ and K+ excretion (these electrolytes are directed into growing tissues) is reduced. Furthermore, resorption of Ca2+ in the digestive system and elimination of 4-hydroxyproline (due to increased collagen variation) increase.

Growth and growth hormone

The role of growth hormone in prenatal growth is probably only marginal (although the STH levels in the plasma of the hair are high). During intrauterine life, foetal growth is thought to be controlled via IGF-I. Fetal IGF-I is regulated via placenta glucose transport, which also controls the release of foetal insulin. The glucose-insulin-IGF-I axis is thus primarily used in prenatal growth. Post-natal growth is regulated by the growth hormone-IGF-I axis, which is why IGF-I levels rise after birth. At birth, STH concentrations are increased, but IGF-I concentrations are relatively low in newborns. Thereafter, resting levels of MET decrease, but there are STH secretion pulses, especially in puberty (sex steroids increase the amplitude of STH secretion pulses). This increases **IGF-I levels** during childhood and **peaks at 13-17 years**. However, IGF-II levels do not change during postnatal life.

Prenatally

The IGF-I and II system and its binding proteins are one of the endocrine and paracrine growth systems that regulate foetal and placental growth. IGFs and IGFBPs are significantly influenced by the level of nutrition in the foetus. With insufficient nutrition, IGF-I and IGFBP-3 levels fall and IGFBP-2 levels rise. Babies with a mutation in the IGF-I gene are born with low birth weight, suffer from postnatal growth disorder, mental retardation and insulin-resistence. During intrauterine life, IGF-I levels in the growing foetus gradually increase from 18 to 40 weeks of gestation. In infants born at low birth weight, there is already significantly lower IGF-I and IGFBP-3 levels in cord blood compared to age-appropriate infants (while IGFBP-1 levels are significantly higher in these infants).

For a number of diseases in adulthood, which include hypertension, coronary heart disease or type 2 diabetes mellitus, their onset, course, and prognosis are thought to depend on the combined action of environmental factors and genetic endowments. Risk factors include intrauterine foetal growth disorder, resulting in lower birth weight and baby length at birth.

IUGR

Intrauterine growth retardation (IUGR) and low birth weight and length relative to gestational age (SGA) occur in approximately 3% of children. Intrauterine growth is influenced by a variety of fetal, maternal, placental and demographic factors. It seems that the IGF-I system could be a suitable candidate system for linking intrauterine growth disorder to certain diseases in adulthood, IGF-II and their binding proteins (IGFBP), as well as some polymorphisms in the IGF-I gene promoter.

Postnatally

In young people whose growth slits are not yet fused with long bone diaphyses, growth may be stimulated by or inhibited by growth hormone deficiency. With prolonged exposure, gigantism arises. Once the epiphysical crevices are closed, it is no longer possible to grow in length. If the MET is then in excess, it causes characteristic deformities of both bones and soft tissues, known as acromegaly.

__STH amount disturbances

Treatment in the Czech Republic

Since 1992, growth hormone treatment in the Czech Republic has been fully covered by health insurance (with treatment of one hypophysical nanic costing us around 250 000-400 000 a year). The indication for the treatment of STH produced by recombinant DNA technology (see below) is congenital or acquired growth hormone deficiency in childhood (see above); Turner syndrome, since 1995

growth failure due to chronic renal insufficiency (there is some resistance to the action of STH and IGF-I), since 2001 Prader-Willi syndrome and since 2003 postnatal growth failure resulting from intrauterine growth retardation (the newborn has a low birth weight or length, in 10-15% of such affected children do not experience postnatal growth acceleration due to reduced growth hormone production or reduced susceptibility to STH). In severe growth hormone deficiency, due to its metabolic effects, it is continued at a small dose even after growth has ceased during adolescence and in adult life. As of 2020, it is also indicated in RASopathy such as Noonan syndrome.

Children are treated in **12 paediatric centres** in the Czech Republic. Children with chronic renal insufficiency are being treated in centres where they are being treated with dialysis at the same time. Growth hormone is injected daily at bedtime (to mimic the natural rhythm) into the subcutaneous tissue by means of pens that ensure accurate dosing. Treatment children are regularly monitored for possible adverse reactions of therapy - glucose tolerance disorder, natrium and water retention, epiphysiolysis of the femoral warhead, Turner syndrome lymphoedema recurrence, in isolated cases.

Recombinant DNA technology

By 1986, the only classical method to treat STH deficiency was replacement therapy with human STH (hSTH) from dead donors. In 1985 and later Creutzfeldt-Jakob disease was diagnosed, a degenerative neurological disease (otherwise rare in young patients) that arose in the 10-15 years since they received natural hSTH. Because it was possible that the pituitary glands of human donors were contaminated with prions and caused their death after transmission to MET-deficient patients, natural growth hormone was withdrawn from circulation from all sources. Growth hormone is now obtained by recombinant DNA technology. Commercial growth hormone, now commonly available, has 191 amino acids in natural sequence (somatropin) and 192 amino acids in methionyl form (somatrem). GRH was first isolated from a pancreatic tumour stimulating STH secretion (GRH from pancreatic tumours has the same structure as hypothalamic GRH). IGF-I is also now produced by recombinant DNA technology.

End

Growth hormone levels must be constantly regulated. Both high and low concentrations of STH cause serious health disturbances. Growth hormone therapy has a positive effect in patients who are indicated for this treatment. It is important to start treatment quickly, which provides a chance for a better overall effect of the therapy. Early detection of growth disorder in the child, correct diagnosis and early growth hormone therapy fundamentally influence the overall health and final height of paediatric patients.

Links

Related articles

- Hypophysis
- Diseases of adenohypophysis
- Investigation of pituitary function

External links

- Growth hormone (https://www.rustovyhormon.cz/)

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