

Growth Hormone Deficiency in Abdominal Obesity

OVERVIEW

Obesity, which is defined by a Body Mass Index greater than $30\text{kg}/\text{m}^2$ (weight divided by height squared), is increasing in North America at an alarming rate. The focus on total fat mass and overall weight is not in itself sufficient to determine an increase in health risk to an individual. There is an association between abdominal adiposity, and more specifically, visceral adipose tissue (VAT) which is deep fat densely packed around the organs, and cardiovascular (CV) disease.¹

A majority of growth hormone (GH) deficient subjects have excess VAT and are abdominally obese, a combination of factors which increases CV risk even more significantly in this group.

Excess VAT is associated with insulin resistance, abnormal lipids and systemic inflammation, which play an important role in cardiovascular disease. Not only is abdominal obesity associated with increased CV disease but it also is strongly associated with all-cause and cause-specific mortality, further emphasizing that it is not only important to maintain a healthy overall weight but that a healthy waist measurement is also key². Therefore, it is believed that specifically reducing VAT is a more relevant approach to improving the health risks in obese subjects rather than total weight loss, or targeting a reduction in Body Mass Index.³

DESCRIPTION AND CLINICAL IMPACT

- GH deficiency is a disorder that involves the pituitary gland (a small gland located at the base of the brain), which produces growth hormone and other hormones. In adults, when the pituitary gland does not produce enough growth hormone, metabolic and body composition abnormalities occur.
- GH deficiency results in a decrease of lean body mass, increase in body fat, abnormal bone density, diminished muscle strength and higher lipid levels. In adults, low or absent GH can also cause symptoms such as fatigue and lack of motivation, which can impact the quality of life in those people with GH deficiencies.
- GH deficiency is associated with a marked increase in body fat.⁴

¹ Zhang, C. et al. 2008 Circulation 117:1659-1667.

² Zhang, C. et al. 2008 Circulation 117:1659-1667.

³ Bays H.E. et al. 2008 Expert Rev. Cardiovasc Ther 6:343-368.

⁴ Pijl, H. et al. 2005 JCEM 56:5509-5515

POTENTIAL THERAPEUTIC OPTIONS

- There is currently no approved treatment for patients with a moderate GH deficiency (5-8 ng/mL) and the only therapeutic solution for patients with severe GH deficiency (<5ng/mL) is growth hormone. However, GH treatment is associated with several undesirable side-effects, including fluid retention (swelling), significant muscle and joint pain as well as high blood sugar.
- A potential therapeutic approach involves the use of human Growth Hormone Releasing Factor (GRF), which induces an increase in endogenous GH generally within the physiological range. One therapy under development is a synthetic form of GRF. Clinical studies have shown that it significantly reduces abdominal fat (in particular, visceral fat), without compromising glycemic control (the regulation of blood sugar levels); increases muscle mass; and is associated with fewer side effects than administration of pharmacological doses of GH.

INTERESTING REFERENCES

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