Justified and unjustified use of growth hormone
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Growth hormone (GH) replacement therapy for children and adults with proven GH deficiency due to a pituitary disorder has become an accepted therapy with proven efficacy. GH is increasingly suggested, however, as a potential treatment for frailty, osteoporosis, morbid obesity, cardiac failure, and various catabolic conditions. However, the available placebo controlled studies have not reported many significant beneficial effects, and it might even be dangerous to use excessive GH dosages in conditions in which the body has just decided to decrease GH actions. GH can indeed induce changes in body composition that are considered to be advantageous to GH deficient and non-GH deficient subjects. In contrast to GH replacement therapy in GH deficient subjects, however, excessive GH action due to GH misuse seems to be ineffective in improving muscle power. Moreover, there are no available study data to indicate that the use of GH for non-GH deficient subjects should be advocated, especially as animal data suggest that lower GH levels are positively correlated with longevity.

The therapeutic use of growth hormone (GH) as replacement in GH deficient adults has been shown to produce a beneficial effect on body composition, serum lipid concentrations, bone mineral density, muscle strength, and exercise endurance. It remains to be determined, however, whether or not chronic GH replacement therapy will indeed have beneficial effects on morbidity and mortality. The benefits of chronic use of GH for other potential indications such as ageing, catabolism, diabetes, and morbid obesity are far from clear. However, GH is also used for conditions in which no intrinsic disease is present, for example, cosmetic use for slight adiposity and sports use to improve performance. Obviously, the use of GH for these goals is not promoted by the medical profession, and indeed can have significant and potentially dangerous side effects. In the following sections, an overview is given of the accepted indication for use of daily GH injections, as well as an overview on the misuse of this powerful peptide hormone.

JUSTIFIED USE OF GROWTH HORMONE
In children
In paediatrics, there is no doubt that the use of recombinant human GH for short stature has been very successful. The improved final height for these children has been increased dramatically, with a corresponding increase in quality of life. There is also a place for GH in the management of children with other conditions associated with GH deficiency or lack of GH action, such as Turner’s syndrome and chronic renal insufficiency. Treatment with GH in combination with low dose oestrogens can result in a significant increase in adult height in girls with Turner’s syndrome, even if they start the treatment at a relatively late age. Children with hypochondroplasia having severe short stature and disproportion of the body segments owing to the mutation Asn540Lys respond to GH therapy with an increase in spinal length, and in combination with a surgical leg lengthening procedure it is possible for some patients even to achieve an adult height within the normal range. At present, there is no way of predicting which patient with hypochondroplasia will undergo a normal pubertal growth spurt, therefore, all such patients should be monitored during childhood and GH treatment should be only given to those patients who fail to develop a growth spurt at puberty.

Severe growth retardation can also be observed in children treated with glucocorticoids for conditions such as systemic forms of juvenile chronic arthritis. Studies suggest that GH may partially counteract such adverse effects of glucocorticoids on growth and metabolism in patients with chronic inflammatory diseases, but more long term controlled studies are needed to determine the risks and benefits of GH therapy in this subgroup of GH deficient patients.

In adults
The beneficial effects of chronic replacement therapy in GH deficient adult patients have been addressed by many studies. Because of the existence of several large databases, we are able to show beneficial improvements with GH therapy not only in quality of life, cardiac performance, and anthropomorphic parameters such as body composition, but also on many biochemical parameters such as lipid patterns, coagulation, and glucose metabolism. Elderly patients with end stage renal disease, who often have protein and/or caloric malnutrition that severely affects general wellbeing and mortality, also benefit from GH therapy. It was reported that GH treatment increased serum insulin-like growth factor-1 (IGF-1), fat free mass, and serum concentration of albumin compared with placebo, while the number of patients with hypoalbuminaemia was reduced by a factor of three in the GH treated group.

Abbreviations: GH, growth hormone; IGF-1, insulin-like growth factor-1; IGFBP, insulin-like growth factor binding protein
Belgian study reported that GH treatment had a positive effect in short children with renal allografts, even if started in late puberty. However, in the presence of underlying chronic rejection, GH treatment needed careful monitoring to minimise the risk of graft loss.

Whether or not GH treatment can improve the metabolic state of adult patients with non-pituitary disorders that are characterised by a temporary GH deficient state, for example patients with critical diseases and in perioperative situations, has not been well addressed, although some reports observed dangerous deterioration in patients and increase in morbidity and mortality. However, there are also reports of beneficial effects of supportive GH treatments, for instance, the observation that perioperative GH treatment of younger patients undergoing major abdominal surgery preserved limb lean tissue mass, increased postoperative muscular strength, and reduced long term postoperative fatigue. It was also reported that perioperative GH administration may result in improved cardiac performance during aortic surgery. Studies performed on accidental hip fracture patients were promising but could not be reconfirmed.

Finally, high dose GH treatment increases body weight, lean body mass, and treadmill work output, and appears to be a safe and potentially effective therapy in patients with HIV-associated wasting.

UNJUSTIFIED USE OF GROWTH HORMONE

GH is without doubt a powerful anabolic hormone that affects all body systems and plays an important role in muscle growth. Serum GH levels are variable and are dependent on many factors, such as age, sex, body composition, and exercise itself. The improvements in muscle strength obtained by resistance exercise training in young men or in healthy older men cannot be further enhanced by additional administration of GH. The increases in fat-free mass that can be observed in athletes who use GH for performance enhancement purposes are not due to accretion of contractile protein, but rather to fluid retention or accumulation of connective tissue. In experienced weightlifters and in power athletes, the skeletal muscle protein dynamics are not decreased by short term administration of GH. A placebo controlled study on the efficacy of GH treatment in improving muscle power in power athletes reported no increase in maximum strength during concentric treatment in improving muscle power in power athletes.

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REFERENCES


Tuberous sclerosis associated with giant bilateral bleeding angiomyolipomas

Tuberous sclerosis is a systemic disorder characterised by benign hamartomatous tumours that involve multiple organ systems. Angiomyolipomas are found in about two thirds of the kidneys of patients with tuberous sclerosis at necropsy. A 29 year old woman with tuberous sclerosis presented with diffuse abdominal pain, gross haematuria, and hypotension. At the age of 22 the patient had been admitted to our hospital with acute upper abdominal pain and gross haematuria. Physical examination had revealed bilateral massive abdominal masses with no tenderness. Computed tomography had confirmed the presence of giant bilateral renal masses with the typical appearance of an angiomyolipoma, and a huge retroperitoneal haematoma extending to the pelvis and the left side of the abdomen (fig 1). After arterial embolisation, left radical nephrectomy was performed. The pathological diagnosis was angiomyolipoma without malignant findings, and the patient was discharged two weeks after the operation (fig 2).

During the latest admission, computed tomography of the abdomen showed a giant right renal angiomyolipoma (fig 3). An attempt for selective arterial embolisation failed, and right radical nephrectomy was performed as the patient was becoming haemodynamically unstable. The patient has been started on haemodialysis, and renal transplantation is planned.

Kidneys can be involved in three different ways in tuberous sclerosis: angiomyolipomas, cystic disease, and renal cell carcinomas. The typical angiomyolipoma is a mixture of smooth muscle, fat, and abnormal blood vessels, the relative proportions of which vary widely. Although angiomyolipomas were previously considered to be hamartomas, they have been recently recognised as clonal neoplasms, and it has been proposed that the perivascular epithelioid cell is the progenitor cell. From the clinical point of view, angiomyolipomas are usually silent, but they can rarely cause life threatening haemorrhage. Patients with tuberous sclerosis and angiomyolipomas greater than 4 cm have a high risk of developing symptoms and may require surgery. Because of its sensitivity in detecting small amounts of fat, computed tomography is the imaging modality of choice, although the typical appearance may be altered in predominantly non-fatty angiomyolipomas or in tumours in which haemorrhage has occurred. Long term follow up results of patients with angiomyolipomas treated with selective arterial embolisation have been reported recently. Selective arterial embolisation seems to be ideal in the case of acute haemorrhage in selected patients with renal angiomyolipoma but its indication, safety, and efficacy require further evaluation.

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REFERENCES


IMAGES IN MEDICINE

Tuberous sclerosis associated with giant bilateral bleeding angiomyolipomas

Figure 1 Abdominal computed tomogram showing giant bilateral renal masses consisting predominantly of fat tissue, and a retroperitoneal haematoma.

Figure 2 Histological specimen showing a typical renal angiomyolipoma (haematoxylin and eosin × 200).

Figure 3 Abdominal computed tomogram showing a giant bleeding right renal angiomyolipoma.