

Growth hormone & hypopituitarism

Abstract

Growth Hormone (GH) deficiency due to hypopituitarism may occur in adulthood or childhood. The disease spectrum is complex and requires thorough clinical assessment before actual GH replacement. If left untreated, may result in various complications. We discuss the basic approach in managing such a condition, in adult and pediatric age group.

Keywords: hypopituitarism, growth hormone, deficiency, replacement

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Abbreviations: GH, growth hormone; QOL, quality of life;
 IGF, insulin-like growth factor; BMD, bone mineral density

Introduction

Hypopituitarism is defined as either partial or complete deficiency of anterior or posterior pituitary hormone secretion or both. Growth hormone (GH) deficiency is one of the most important aspects among them. GH deficiency due to hypopituitarism may occur in adulthood or childhood. Childhood-onset disease is mostly idiopathic or genetic, whereas, in adults, the hypopituitarism is caused mainly by causes like a pituitary tumour, irradiation, inflammation, apoplexy, pituitary surgery etc. The most commonly associated clinical features are short stature or growth failure (in children) and increased lean muscle mass, increased visceral /central fat, lack of energy and exercise (in adults) etc. GH deficiency is also associated with insulin resistance and increased cardiovascular risk. In untreated patients, there is high morbidity, usually as a sequel to conditions like myocardial infarction, cerebrovascular disease, and malignancies. Both adult-onset and child-onset types have different treatment protocols. In children, GH replacement is usually given in growth promoting dose and whereas in adults, it's given at a 'metabolic dose' to cure symptoms.

Mini Review

Traditionally, GH was recommended only in children, but following the development of recombinant GH, it could also be used in improving disease status adults. Such improvements are with regard to body composition, bone mineral density, exercise capacity and psychological well-being. According to National Institute for Health and Care Excellence (NICE) guidance on Human GH (Somatropin) in case of Severe GH deficiency (during an insulin tolerance test peak GH response <9mU/L); Quality of life (QoL) assessment of GH deficiency in adults (QoL-AGHDA) report at least 11 (Impaired QoL); and among Patients who are already on replacement therapy of any other pituitary hormone deficiency.

Treatment is self-administered by a daily subcutaneous injection. Initially, 0.2-0.3mg daily is started and the dose is titrated according to serum IGF-1 level for first 2-3 months and then maintenance dose continues with 0.4mg daily, which decreases with age. The symptoms of GH deficiency decrease with treatment, although some adverse effect may be reported e.g. peripheral edema, myalgia, arthralgia,

impaired glucose tolerance etc. However, treatment is contraindicated in critically ill-patients, pregnancy, lactation, and in a patient with tumor activity (GH can increase the tumor growth). Follow-up is usually based on QoL status, which is to be reassessed after 9 months of initiating therapy. Treatment should be discontinued if no improvement is observed in 7-point QoL-AGHDA score. However, there is a predominant improvement of QoL in the first year of treatment and successive positive changes occur thereafter, usually seen after 8 years of treatment.

It is to be noted, that physical development in early adulthood (between linear growth completion and 25 years age), treatment should be continued (if criteria for severe deficiency matched) till adult peak bone mass gained. Several studies have pointed that treatment continued throughout life is beneficial [1-8]. Moreover, elderly patients are more sensitive to Insulin-like growth factor-1 (IGF-1), so they require less dose of recombinant GH to achieve safer and effective level of IGF-1. Periodic monitoring by measuring indices like weight, BP, IGF-1, fasting glucose, glycated hemoglobin (HbA1c), lipid profile, waist-hip ratio, and bone densitometry (in patients with initial low BMD) are to be done periodically.

According to the NICE guidance on Somatropin for treatment of growth failure in children (2010), the treatment should be immediately started in a diagnosis of childhood-onset GH deficiency (short stature due to hypopituitarism). In such cases, Somatropin is self-administered at a dose of 23-39 mcg/kg daily or 0.7-1mg/sqm daily to be taken subcutaneously. In the 1st year of therapy, height velocity often increases to 10 -12 cm/year, however, growth is slower in the later period although the levels are always greater than pre-treatment value. Treatment is to be discontinued in cases where the growth velocity increases less than 50% from baseline in the first year of treatment; the growth velocity is < 2cm of total growth in 1 year; the final height is achieved (Closure of epiphysis); and problem of treatment adherence.

Although GH replacement protocols are distinctly different in adult and children, there are few common criteria which must be adhered to in either group namely: The thyroid, adrenal and gonadal functions are to be restored to normal first and to be checked for every 3-6 months after start of the treatment, since introduction of GH replacement may unmask both incipient adrenal insufficiency and central hypothyroidism; If the glucocorticoid and thyroxine replacement are

simultaneously administered, the dose must be titrated upwards as GH can influence such hormone metabolism; An adequate nutrition must be confirmed; If there is a history of tumour activity, treatment must be initiated after 2 years of 'no growth' of a tumour evidence; The GH replacement dose must be titrated according to the anthropometric data. however, the inter- and intra-observer variation in height measurements should not exceed 3cm and 5mm respectively; The IGF-1 must be monitored every 6 months to avoid over-replacement and the gradual dose titration is to be done every 4-6 weeks according to clinical and biochemical responses (IGF1 SD score).

A trial period of 6 months is usually recommended after initial 3 months period of dose adjustment. In case the desired height velocity is not optimal within 6 months, doubling of the dose is recommended. However, high dose therapy warrants extra caution due to the concern of few major adverse events, particularly in children. Treatment should be discontinued in conditions like slipped capital femoral epiphysis, benign intracranial hypertension, enlarged adenoids, worsening of scoliosis and increased blood sugar levels. Generally, males respond better than females, so the dose in females is required to be more. This is likely as estrogen inhibits IGF-1 function and testosterone enhances it.

Conclusion

GH replacement in hypopituitarism, is distinct area and therapeutics is to be directed via an evidence-based approach. This includes proper diagnostic evaluations, including appropriate biochemical assessments and specific therapeutic decisions to decrease the risk of co-morbidities due to hormonal over-replacement or under-replacement, and managing hypopituitarism throughout all age groups.

Acknowledgments

None.

Conflicts of Interest

None.

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