
The Use of Growth
Hormone Replacement
in Adult Patients
with Severe Growth
Hormone Deficiency

A Position Statement

from the



Society for Endocrinology

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1 Introduction

Many countries, including the UK (1996), have approved the use of GH replacement therapy in adults with growth hormone deficiency (GHD). This approval is based on the increasing body of evidence that adults with GHD have impaired health. This document is published with the aim of assisting purchasing authorities and health-care professionals to understand the rationale underpinning the decision to treat GHD and also to encourage a cohesive nationwide approach to providing GH replacement for patients with hypopituitarism.

This document has been developed by the Society for Endocrinology, the body which represents endocrinology in the UK.

Aspects covered include:

- the features of GHD
- the rationale behind the selection of patients for GH therapy
- treatment options - commencement and maintenance of GH replacement

2 Growth Hormone Deficiency – the disease

Cause

- In adults, GHD is commonly due to pituitary tumours or their treatment
- Cranial irradiation may also cause GHD

Epidemiology

- Indirect estimates based on the incidence of pituitary tumours suggest an incidence of 10 per million annually for adult onset GHD

Morbidity

- Altered body composition (reduced lean mass and increased fat mass, especially in the trunk)
- Osteopenia/osteoporosis
- Dry skin – reduced sweating
- Reduced muscle strength and exercise capacity
- Reduced quality of life (especially reduced energy levels)
- Lipid abnormalities (especially elevated LDL cholesterol)
- Insulin resistance
- Increased levels of fibrinogen and plasminogen activator inhibitor
- Increased thickness of the intima media
- Cardiac dysfunction

Mortality

- Adults with hypopituitarism have reduced life expectancy compared with that of healthy controls; mortality from cardiovascular disease is more than twice as high in these patients.
- It has been proposed that GHD accounts for this increased mortality. This is consistent with the abnormalities in cardiovascular risk factors reported in patients with severe GHD.

3 Rationale for treatment

The rationale for providing GH replacement therapy is based on the fact that people with severe GHD have:

- Adverse cardiovascular risk factors, which are believed to contribute to increased mortality
- Increased risk of bone fracture
- Decreased quality of life (QOL)

The philosophical attitude of endocrinologists towards adult GH replacement varies. Therapeutic studies have lent some support to the “treatment for all” position. In general, GH replacement improves the profile of cardiovascular risk factors, and two years of GH replacement significantly increases bone mineral density in patients in whom it is reduced. Nonetheless, a reduction in cardiovascular mortality and fracture rate in response to GH replacement therapy remain to be established. The majority view among UK endocrinologists is that the cardiovascular changes alone are not persuasive enough at the present time to recommend GH replacement for all adults with severe GHD. The skeletal indication is also important, but careful patient selection for GH therapy remains necessary. If osteopenia is the primary indication for treatment then the trial of GH therapy should continue for at least 2 years.

We believe that reduced QOL should be a major indication for offering GH replacement to patients with severe GHD. Thus, the selection of whom to treat will be heavily influenced by the attitude of the patients as well as that of the doctors. This is analogous to the situation in paediatric GHD patients, where GH replacement is provided in order to improve QOL, via an increase in growth. In order to assess which adult patients would benefit from GH replacement, patient-perceived impairment of QOL should be assessed in clinical interviews. Validated questionnaires to assess QOL objectively include generic questionnaires, such as the psychological general well-being schedule (PGWB) and the disease-specific adult GHD assessment (AGHDA).

4 Treatment of Growth Hormone Deficiency

GH replacement is administered by a daily subcutaneous injection. The average cost of GH replacement in the UK for an adult with GHD is between £3000–4000 annually. Adult patients commence GH replacement with an initial dose of 0.6 – 0.9 units (0.2 – 0.3 mg) daily, independent of weight or surface area. The appropriate GH dose is determined by monthly assessments over an initial period of two to three months, using measurements of GH-dependent hormone markers and assessments of side effects. This low-dose GH titration regimen decreases the incidence of side effects.

Once the appropriate maintenance-dose of GH has been achieved (usually within three months), patients being treated primarily for reduced QOL should be reassessed after six months of maintenance-dose GH therapy. If patients show improvement, determined by QOL questionnaires and subjectively, then they should be offered the opportunity to continue GH therapy on a long-term basis with a clinical review on an annual basis.

GH replacement therapy will be withdrawn if the patient perceives no benefit after a six month trial or if the patient is non-compliant.

5 Recommendations

Where recommended by an endocrinologist, GH therapy should be made available to any patient with severe GHD. This will be the primary therapy. It is recommended that all patients who start GH therapy be entered prospectively into a multicentre surveillance programme.

Therapy should be administered and supervised in accordance with shared care protocols which may be designed and arranged to suit local practices.

PATIENT SUPPORT GROUP

This group provides information leaflets on pituitary disease and medical developments. It also provides contacts with other patients through regional support groups:

The Pituitary Foundation

PO Box 1944, Bristol BS99 2UB. Tel: 0117 927 3355

SOCIETY FOR ENDOCRINOLOGY

The Society for Endocrinology is a registered charity. It is the leading UK body representing the science and medicine of endocrinology. For further details, contact Tom Parkhill on 01454 201612.

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DUALITY OF INTEREST

Members of the working group have no direct interest in growth hormone producing pharmaceutical companies, but the departments of several of the members have received research grants.

FURTHER READING

Carroll PV, Christ ER, *et al* Growth hormone deficiency in adulthood and the effects of growth hormone replacement: a review. *Journal of Clinical Endocrinology and Metabolism*, 1998, **83**:382-395.
