Scottish Paediatric Endocrine Network (SPEG)

Position statement on the investigation and treatment of Growth Hormone Deficiency in transition

NOTE
This guideline is not intended to be construed or to serve as a standard of care. Standards of care are determined based on all clinical data available for an individual case and are subject to change as scientific knowledge and technology advance and patterns of care evolve. Adherence to guideline recommendations will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgement must be made by the appropriate healthcare professional(s) responsible for clinical decisions regarding a particular clinical procedure or treatment plan. This judgement should only be arrived at following discussion of the options with the patient, covering the diagnostic and treatment choices available. It is advised, however, that significant departures from the national guideline or any local guidelines derived from it should be fully documented in the patient's case notes at the time the relevant decision is taken.

Contents

Purpose of guideline

Guidance for the investigation and management of Growth Hormone Deficiency in young people undergoing transition to adult endocrine services.

- Guidance for the investigation and management of Growth Hormone Deficiency in young people undergoing transition to adult endocrine services.
- **Who should use this document?** Paediatricians, Paediatric Endocrinologists, Adult Endocrinologists – this guideline is not intended for use in primary care.
- **Patients to whom this document applies**. Young people treated with growth hormone therapy.

Definition of Transition

The transition period is defined as the broad set of physical and psychosocial changes starting in late puberty and ending with full adult maturation. This generally refers to the period from mid-to late teens until six or seven years after achievement of final height.

Transition in Children on Growth Hormone Therapy

In patients with childhood onset growth hormone deficiency (GHD), it is essential to reassess the need for ongoing growth hormone (GH) therapy following completion of growth and pubertal development.

Following attainment of final adult height there are the following options to continuation of GH treatment:

Discontinuation of GH Therapy:

- patients with isolated GHD in childhood may not have persisting GHD and so assessment at this stage may lead to discontinuation of therapy.
- in patients with GHD in childhood secondary to low dose radiotherapy, retesting at final adult height reveals a significant proportion of patients who will not meet criteria for adult GHD.

Continuation of GH Therapy

There are certain groups of patients in whom there is a very high probability that GHD is permanent and GH therapy is likely to be continued into adulthood. These groups are:

- patients with severe GHD due to a structural hypothalamo-pituitary abnormality.
- patients with multiple anterior pituitary hormone deficiencies.
- patients with CNS tumours
- patients who have received high dose cranial irradiation; while susceptibility varies, risk of GHD increases with doses of cranial irradiation >18Gy (or total body irradiation in childhood with single fractions >10Gy) while higher doses may be associated with multiple pituitary hormone deficiencies
- patients with genetic causes of GHD

Benefits of GH therapy in Adults

There are several reported benefits to GH therapy during transition (until peak bone mass is attained) and in adults.

These benefits include:

- greater spine bone mineral density (BMD)
- increase in lean body mass
- decrease in fat mass.
- benefits in lipid profile
- improved quality of life

Process for Reassessment of GH therapy

The following approach should be used to investigate GHD in transition (based on Clayton PE et al European Journal of Endocrinology 2005 vol 52, 165-70 see figure 1).

- all patients with childhood onset GHD are evaluated for ongoing GHD once final adult height is achieved and pubertal development is complete. This should be undertaken after discontinuation of GH therapy for at least four weeks
- patients with a high likelihood of persistent GHD, and who have serum IGF-1 more than two standard deviations below the mean should be considered GH deficient and may recommence GH therapy. In these patients, if IGF-1 is not more than two standard deviations below the mean, a GH provocation test should be performed (see below)
- in patients with a lower likelihood of permanent GHD (i.e. all other patients), IGF-1 as well as a GH provocation test should be performed

    - If both are low then GHD is confirmed

    - if both are normal no GH therapy is indicated (though in patients who have been exposed to cranial irradiation, future GHD may later become apparent)

    - If the tests are discordant (i.e. one low and one normal test), follow up is indicated

GH provocation tests

We recommend that the evaluation of GHD in transition, whether it be by measurement of IGF-1 off treatment or by provocation test, should take place in the context of a joint transition service.

The principle of retesting off GH replacement and offering GH during transition for those who have ongoing severe deficiency should be applied in all centres.

It is recognised that regional services will vary but each team should have an agreed policy on whether testing will be led by the paediatric or adult endocrinologist.

The insulin tolerance test (ITT) is seen as the gold standard test and will test the integrity of the whole axis. However, it is contraindicated in certain individuals, such as those with a history of seizures. This may be relevant to patients with growth hormone deficiency secondary to treatment for childhood CNS tumours.

Alternative tests such as the arginine stimulation test, or the Growth Hormone Releasing Hormone GHRH test and glucagon stimulation may also be used. The arginine GHRH test may be unreliable in patients with hypothalamic disease due to its direct stimulation of the pituitary.

When to Treat with Growth Hormone in Transition

- there is no consensus on the cut-off value for severe GHD in transition, and different centres may choose different cut-offs, but ESPE guidance suggests <5µg/l for severe GHD in transition.

GH Dose in Transition

In transition, patients should recommence GH therapy at a dose of 0.2mg-0.3mg daily and titrate to age and gender adjusted IGF-1 levels, bearing in mind clinical response, oestrogen status (use of oral oestrogen is likely to be associated with a requirement for a higher GH dose to reach target IGF-1) and side effects.

Adult GH Therapy

At completion of somatic growth (approximately 25-30 years old), re-evaluation should be undertaken, and treatment offered and monitored in accordance with NICE guidance (HTA 64 August 2003).

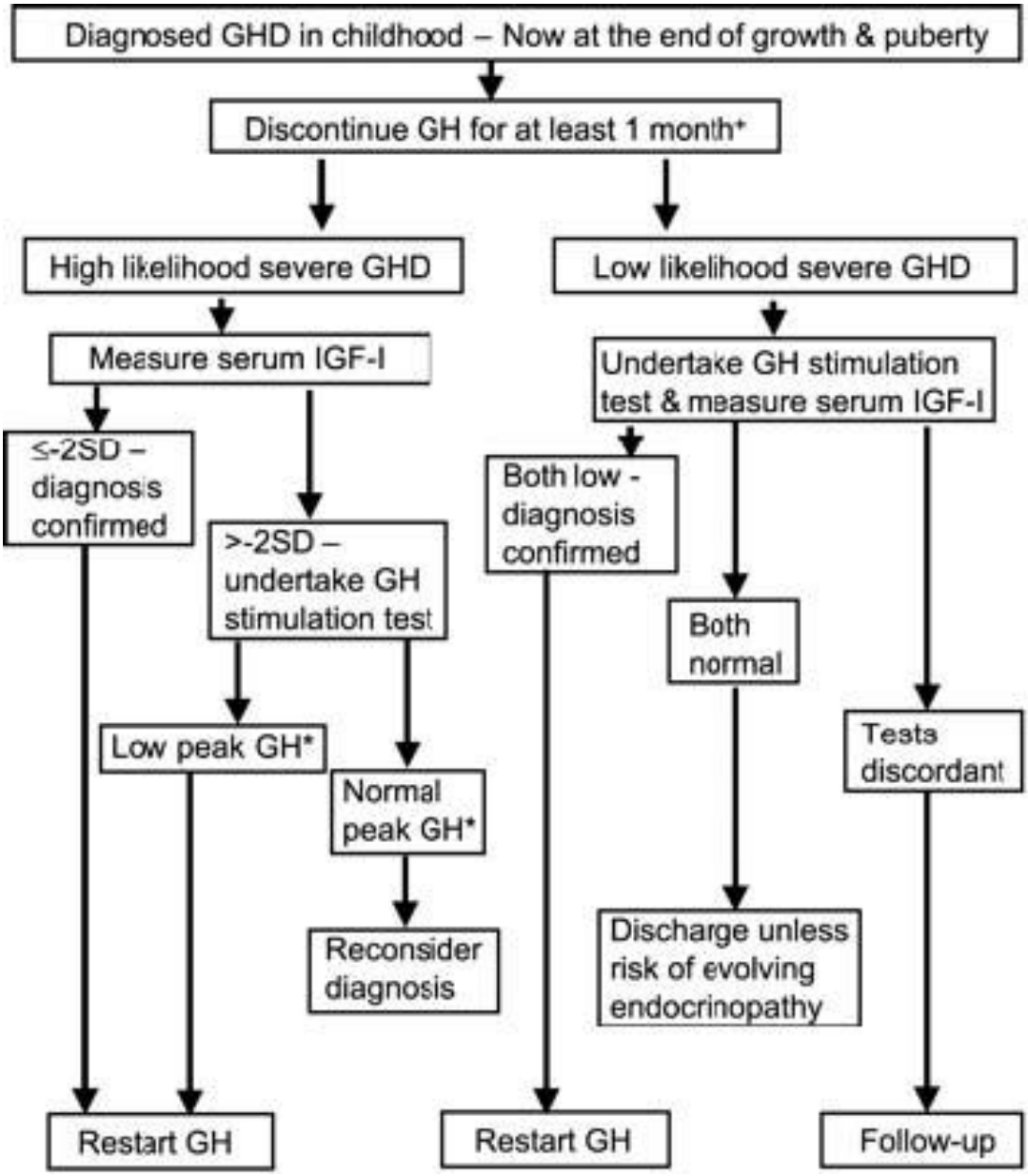

Figure 1
(From Clayton P.E et al, European Journal of Endocrinology 2005 vol. 52, 165-70)

GHD Transition Standards for Future Audit

All children with GHD should be retested after final height has been achieved to assess their need for ongoing GH replacement.

For adolescents and young adults with persistent severe GHD, GH replacement should be offered as standard until the age of 25.

References

1. Human Growth Hormone (somatropin) in adults with growth hormone deficiency. NICE Technology appraisal guidance 64, August 2003. www.nice.org.uk/guidance/ta64
2. Consensus statement on the management of the GH-treated adolescent in the transition to adult care. Clayton P.E et al, European Journal of Endocrinology: 2005; 152: 165-170.