East Kent Prescribing Group

Shared Care Guidelines, Growth Hormone – Paediatric Patients

Recommendation

The EKPG has approved the shared care guidelines for growth hormone for paediatric patients.

Approved by: East Kent Prescribing Group *(Representing Ashford CCG, Canterbury and Coastal CCG, South Kent Coast CCG and Thanet CCG)*
Date: Dec 2014
Address: c/o *Canterbury and Coastal CCG, Ground Floor, Council Offices, Military Road, Canterbury, Kent,CT1 1YW*
Contact: T: 01227 791267 | E: accg.eastkentprescribing@nhs.net

Shared Care Guidelines

Growth Hormone – Paediatric Patients

Indications for GH Therapy in Children (as per NICE guidelines May 2002)

1. Short stature due to growth hormone deficiency
   - Idiopathic isolated GH deficiency
   - Congenital hypopituitarism eg anomalies of the pituitary gland such as septo-optic dysplasia
   - Acquired hypopituitarism eg craniopharyngioma & post cranial irradiation & neuro-surgery

2. Severe constitutional short stature amenable to GH therapy in
   - Turner Syndrome (confirmed by chromosome analysis)

3. The treatment of growth failure associated with chronic renal failure (on dialysis or post renal transplant).

4. The treatment of children with Prader-Willi syndrome.

Diagnostic Criteria for GH Deficiency in Children

The early recognition of growth failure is an essential component of a national strategy leading to rational and effective use of GH. Monitoring of growth (height and weight) should be part of all health surveillance of children in primary care and in school.

1. Short stature that is inappropriate for the parental heights.
2. Subnormal growth rate: ie a height velocity of below the 25th centile or less than 4cm/yr over two successive years than 3rd centile over one year in a pre-pubertal children, <8cm/yr in puberty.
3. As part of multiple pituitary hormone deficiencies.
4. Growth delay confirmed by delayed skeletal maturation. Clinical and / or imaging evidence of a structural disorder of the hypothalamo-pituitary axis: this includes previous cranial irradiation.
5. Exclusion of other genetic, psychosocial and systemic causes of growth failure.
6. Biochemical evidence of GH deficiency.

GH deficiency: 0.7 – 1.0 mg/m^2/day or 0.025 – 0.035 mg/kg/day given as a daily subcutaneous injection (0.5 units/kg/body weight/week (15 units/m^2/wk) divided into 7 daily doses). (*Upper end of dosing scale for pubertal child)*

Turner Syndrome: 1.4 mg/m^2/day or 0.05 mg/kg/day given as a daily subcutaneous dose (1.0 units/kg body weight/week (28-30 units/m^2/wk) divided into 7 daily doses).

Prader-Willi Syndrome (PWS): 1.0 mg/m^2/day or 0.035 mcg/kg/day (max. 2.7 mg/day).

Prescribing of Growth Hormone (generic name Somatropin)

Patients are offered a choice based on the type of device they would like to use as this has been shown to increase compliance with treatment.

Growth hormone can be obtained by the patient via FP10 or delivered direct by a homecare delivery company arranged by the family through the Home Care support service in consultation with the GP practice / PCT.

Duration of GH Therapy

This is determined by:

1. Age of diagnosis of GH deficiency + age at puberty of skeletal fusion.
2. Response to GH treatment. Height improvement in severe GH deficiency is impressive and further confirms the diagnosis. In less severe GH insufficiency, (which overlaps with normal variant short stature), the response may be more equivocal and the cost benefit of continued therapy has to be examined at regular intervals.
3. It is appropriate to continue growth hormone therapy until peak bone mass has been achieved, which may be later than and not necessarily contemporaneous with cessation of growth in stature.

Frequency of injection of GH plays an important role in determining initial growth acceleration and ultimately final height. It is generally accepted that the correct dosing frequency is daily subcutaneous injections of r-hGH.

GH Side Effects

In general side effects of r-hGH are uncommon. Transient skin reactions and loss or increase of adipose tissue at injection sites can occur, particularly if the injection site is not rotated. In adult practice, r-hGH can lead to fluid retention and peripheral oedema but in children this is less of a problem. Fluid retention many play a role in the generation of raised intra-cranial pressure (benign intra-cranial hypertension). This may occur at the onset of GH therapy and is associated with severe headache and papilloedema. In such circumstances the therapy is discontinued for 2 – 3 weeks and then recommenced at a lower dose and gradually built back up.

Growth hormone is associated with insulin insensitivity and there is a rise in serum insulin concentrations although blood glucose and glycosylated haemoglobin concentrations usually remain with normal limits. Consequently, patients with diabetes mellitus taking r-hGH may need their diabetic therapy adjusted. Consideration also needs to be given to the possible unmasking of diabetes in patient groups with a family history of Type 2 diabetes mellitus.

The safety record is excellent. Antibody formation can be detected but is rarely of physiological relevance.

Neoplasia: Extensive surveys have **not** suggested an increased tumour or leukaemia risk with GH therapy, compared with similar patients who have not received GH therapy when replacement doses are physiological in confirmed GHD. Supra-physiological doses have not been used in this situation. What may be of more concern is the recent report from the UK that young adults treated with human pituitary GH up until 1985 had a higher mortality risk for colon cancer and non-Hodgkin lymphomas than the general population (Swerdlow AJ, Higgins, CD, Adlard P, Preece MA). Risk of cancer in patients treated with human pituitary growth hormone in the UK, 1959-85: a cohort study. Lancet 2002; 360: 273-7

Although this data raises concern **they do not provide firm evidence of an association.** Long-term surveillance of patients receiving GH therapy irrespective of diagnosis is continuing through National Cancer Registries.

Prader-Willi Syndrome: Prader-Willi Syndrone (PWS) is a rare genetic disorder with an incidence of approximately one in 10,000 births. In the first year of life it is characterised by Hypotonia and failure to thrive, but in later years if energy intake is not restricted, severe obesity results. Other components of this syndrome include short stature which is now generally accepted to be associated with GHD. As obesity is associated with reduced GH responses on testing, it was argued that the GH abnormality in PWS was not the primary problem. More detailed neuroendocrine studies, however, revealed that the majority of individuals with PWS have GHD. Randomised controlled studies of r-hGH in PWS have demonstrated an increase in short term linear growth analogous to that seen in patients with GHD. The r-hGH dosing schedule is similar to that used in GHD. Further data on final heights are now becoming available and are similar to those observed in GHD patients.

Although the value of increasing the stature of these individuals can be questioned, the effects of r-hGH treatment on body composition is perhaps of greater importance. Growth Hormone therapy leads to fat sparing and an increase in lean body mass. The latter is less obvious in PWS and is in contrast to the reports of increased muscle strength and agility. The observation of improved respiratory muscle function is of particular importance in these individuals.

To date the safety profile of growth hormone in PWS is similar to that observed in the GHD child. However, in severely obese PWS patients there appears to be a potential risk of sudden death associated with GH use (April 4, 2003. Addendum to the Pharmacia statement on recently reported cases of death in growth treated patients with PWS, January 7, 2003). For this reason, at present LCPEM does **not** currently advocate the treatment of severely obese patients with PWS.

Guidelines for Share Care Strategy

1. A patient with confirmed GH deficiency and in an otherwise stable condition does not require frequent hospital supervision and may be managed by the GP.
2. Biosynthetic GH has a good safety record and monitoring of response more frequently than every 3-6 months is not required. Dose adjustment may be required annually.
3. GH therapy is very expensive and continuation has to be justified by objective evidence of accelerated growth rate and improvement of predicted final height.
4. A minority of candidates for GH therapy have had, or continue to have complex health disorders requiring specialist management eg brain tumour in established

remission. The Specialist must discuss each case with the GP in order to agree on a treatment and share care strategy.

GP Responsibilities

1. Providing family with advice on the potential role of investigation and therapy for the child's growth problem.
2. Prescribing GH therapy for licensed indications when this is part of a shared care agreement.
3. Advice re GH usage, and safe storage and disposal of injection equipment and requirement for long distance travel.
4. Reporting adverse effects of therapy to Specialist or deputy.

Growth Specialist Responsibilities

1. Reviewing the patient's growth and general condition at 3 to 6 monthly intervals. Monitoring will include accurate height and weight measurements and bone age assessment as indicated, as well as determination of pubertal status. All patients require serum IGF-1 concentrations to be monitored at 4-6 monthly intervals in adults and yearly in children.
2. Reassessment of endocrinology and neuro-radiological imaging when required, especially for the assessment of puberty and the detection of an evolving endocrinopathy.
3. Reviewing GH dosage guided by height velocity, weight/surface area, pubertal stage and/or serum IGF-1 concentration.
4. Advising GP as to the continued justification for GH therapy.
5. Reviewing associated drug therapy.
6. Auditing patient's response to GH therapy compared to nationally agreed criteria.
7. Teaching and monitoring injection techniques.
8. Liaison with the GP.
9. Deciding on the timing of cessation of treatment and re-assessment.
10. Deciding on transition to adult service for replacement adult GH.
11. Monitoring of outcomes.

Availability of Support and Advice

Consultant Paediatric Endocrinologist

Dr Charles Buchanan,
King's College Hospital, Denmark Hill, London SE5 9RS
Secretary: 020 3299 3431

Endocrine Nurse Specialist

Miss Jenny Kalitsi
King's College Hospital, Denmark Hill, London SE5 9RS
Direct Line: 020 3299 1307

Patient Support Groups

The Child Growth Foundation: 2 Mayfield Avenue, Chiswick, London W4 1PW
Tel: 020 8994 7625

The Pituitary Foundation: (PitPat) of the Society for Endocrinology, 17/18 The Courtyard, Woodlands, Almondsbury, Bristol BS12 4NQ
Tel: 0117 927 3355

Medical Society Information

BSPED – www.bsped.org.uk

NICE – www.nice.org.uk