Growth hormone in adults

Clinical effectiveness and cost-effectiveness of growth hormone in adults in relation to impact on quality of life: a systematic review and economic evaluation

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Executive summary

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Executive summary

Background

The Society for Endocrinology estimates that the prevalence rate of adults with growth hormone deficiency (GHD) is approximately 2 in 10,000 of the adult population, with adult-onset GHD accounting for approximately 1 in 10,000. This prevalence rate equates to approximately 4200 patients with adult-onset GHD in England and Wales. The incidence rate of adult-onset GHD, based on the incidence of pituitary tumours, is suggested to be 1 per 100,000 annually.

Objectives

This review considers the clinical effectiveness and cost-effectiveness of growth hormone (GH) therapy in adults with either adult-onset or childhood-onset GHD, using impact on quality of life (QoL) as the outcome measure.

Methods

A systematic review of the literature and an economic evaluation were undertaken.

Data sources

The main electronic databases were searched, with English language limits, for the periods up to May 2001. The journal *Clinical Endocrinology* was handsearched from 1993 to August 2000. Bibliographies of related papers were assessed for relevant studies, and experts were contacted for advice and peer review, as well as to identify additional published and unpublished references. Manufacturer submissions to the National Institute for Clinical Excellence were reviewed.

Study selection

Studies were included if they fulfilled the following criteria, which were applied independently by two reviewers, with any disagreements resolved through discussion.

- Intervention was biosynthetic human GH (somatropin).
- Participants were adults diagnosed with GHD, including those who were continuing GH treatment from childhood.
- Outcomes were QoL measures.
- Designs were systematic reviews of randomised controlled trials (RCTs), or individual RCTs, that assessed the effects of GH compared with placebo. Economic evaluations of somatropin in adults had to include a comparator (or placebo) and assess both the costs and consequences (outcomes).

Data extraction and quality assessment

Data extraction and quality assessment were undertaken independently by two reviewers, with any disagreements resolved through discussion. The quality of RCTs was assessed using the Jadad criteria. The internal validity of economic evaluations was assessed using the *BMJ* checklist, and external validity by a series of relevant questions.

Data synthesis

The clinical effectiveness and cost-effectiveness of GH in adults were synthesised through a narrative review with full tabulation of results of all included studies. Meta-analyses were carried out using Cochrane Review Manager software, if practical and appropriate. For the economic evaluation, a cost model was constructed using the best available evidence to determine costs in a UK setting.

Results

Number and quality of studies

In total, 17 RCTs met the inclusion criteria of the review. These RCTs were of variable quality, with most trials having a Jadad quality score of 2/5 or 3/5. The outcome measure of interest was QoL, which was reported using a variety of measurement scales. These were mostly generic, such as the Nottingham Health Profile (NHP), and Hamilton Depression Scale.

No reliable economic evaluations of GH in adults were found.

Summary of benefits

The evidence suggests that GH may improve QoL, although most change scores were modest and only a few were statistically significant. The interpretation of these change scores in terms of meaningfulness to

patients is difficult. The analysis of the individual dimensions of the NHP from individual trials demonstrated statistically significant improvements in the GH replacement group, compared with the control group, for pain, emotional reactions and sleep. Meta-analysis showed a statistically significant difference in favour of GH on the NHP social isolation dimension.

Costs and cost-effectiveness

GH replacement in adults was found to cost £3424 annually at the average maintenance GH dose. Sensitivity analyses showed that the cost of GH therapy in adults is sensitive to GH dose, cost of GH and length of treatment. Further economic modelling was limited by the lack of a suitable effectiveness measure, and cost per unit of effect or cost per quality-adjusted life-year could not be estimated.

Conclusions

Implications

Fewer than half the adults with GHD are currently receiving GH therapy. Some may not be in clinical need; however, due to variation in prescribing policy, others who could potentially benefit are not being prescribed GH replacement therapy. Extending the use of GH to all those with severe GHD would have a budgetary impact. However, not all patients offered GH replacement therapy are likely to accept treatment.

Trials of GH therapy in adults with GHD have not shown consistent benefit on QoL. GH may have beneficial effects on other factors (such as bone mineral density and cardiac function) that may indirectly affect QoL, but these factors were not examined in this review.

Research recommendations

Further research is needed to develop methods to interpret the meaning of changes in QoL scores, and these methods can then be applied in well-designed trials (e.g. to determine optimal dosing strategies) and economic evaluations.

Publication

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