Effective Health Care Program

Breathing Conditions
Chronic Lung Disease

Use of Recombinant Human Growth Hormone for Pediatric Patients With Cystic Fibrosis

Key Clinical Issue

What are the benefits and harms of using recombinant human growth hormone (rhGH) to improve pulmonary and overall health outcomes for patients with cystic fibrosis (CF)?

Background Information

Patients with CF may experience growth retardation despite aggressive nutritional therapy. Low weight and short stature have been associated with increased morbidity and mortality, leading some investigators to propose that the growth-promoting and anabolic effects of rhGH may reduce disease symptoms and improve health outcomes. However, rhGH may exacerbate the existing risk of developing CF-related diabetes (CFRD) and gastrointestinal cancer.

While the effect of growth hormone on long-term outcomes (e.g., mortality risk and health-related quality of life [HRQoL]) is of greatest interest, current studies provide data only on intermediate outcomes. Therefore, the association between intermediate outcomes (pulmonary function, growth, exercise tolerance) and long-term outcomes in patients with CF was examined along with the evidence for rhGH effectiveness.

A note about this Clinician Guide

A systematic review of 79 clinical studies was conducted by independent researchers, funded by AHRQ, to synthesize the evidence on what is known and not known about this clinical issue.

This topic was nominated through a public process. The research questions and the results of the report were subject to expert input, peer review, and public comment.

The results of this review are summarized here for use in decisionmaking and in discussions with patients. The full report, with references for included and excluded studies, is available at http://www.effectivehealthcare.ahrq.gov/hgh.cfm.

Conclusions

Current evidence is inadequate for understanding the long-term outcomes and risks of using rhGH to improve pulmonary function and overall health in children with CF. Intermediate outcomes associated with mortality risk were mixed, and a modest decrease in annual hospitalizations was observed.

Important unknowns remain, including the characteristics of patients who are most likely to benefit and which dose and duration of treatment are optimal.

Clinical Bottom Line

Evidence Associating Intermediate Outcomes With Mortality Risk and HRQoL for Patients With CF*:

- Only one measure of pulmonary function, %FEV_1, is strongly associated with either mortality risk or some domains of HRQoL.
- Weight is associated with mortality risk, but its effect on HRQoL is not clear.

Evidence About Benefits:

- The data from current studies are insufficient to permit conclusions about mortality and HRQoL for patients with CF who were treated with rhGH.
- Patients treated with rhGH experienced 1.6 fewer hospitalizations per year (●●○).
- Effect on intermediate outcomes:
  - % FEV_1 was *not* significantly improved by rhGH treatment (●●○).
  - Weight, weight velocity, and BMI improved (●●○).
  - Percent ideal body weight improved (●○○).

Evidence About Harms:

- After the 6–12 month course of treatment typical in these studies, blood glucose was elevated (5.7 mg/dL over controls on average) (●●○), but evidence is insufficient to evaluate the long-term risks of either CFRD or cancer.
- Treatment with rhGH appeared to be well tolerated as study withdrawals were rare.

Additional Issues:

- Some studies have reported results for patient subgroups, including pubertal status and sex, but no conclusions about the role of these variables in response to rhGH treatment can be formed from current evidence.

* These findings are not based on studies of rhGH treatment.

BMI = body mass index; %FEV_1 = percent predicted forced expiratory volume in 1 second; weight velocity = the change in weight over time

Confidence Scale

High:	●●●	There are consistent results from good-quality studies. Further research is very unlikely to change the conclusions.
Moderate:	●●○	Findings are supported, but further research could change the conclusions.
Low:	●○○	There are very few studies, or existing studies are flawed.

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Outcomes Table

Health Outcomes (Number Treated, Control)	Effect Size Mean Difference*	95% CI
Hospitalizations per year† (64, 59)	-1.62	-1.98, -1.26
Pulmonary function		
$\%FEV_1$ (71, 48)	2.43%	-3.99, 8.85
Anthropometrics		
Weight† (100, 67)	1.48 kg	0.62, 2.33
Weight velocity† (40, 36)	2.15 kg/y	1.52, 2.78
Body mass index† (22, 18)	2.08 kg/m^2	1.20, 2.96
Percent ideal body weight† (23, 21)	12.57%	7.01, 18.12

* The mean difference is the difference between the mean values for treated and control groups for change from baseline.

† Statistically significant; the 95% confidence interval (CI) does not include zero.

Future Research

- Prospective cohort studies should be developed to assess important long-term health outcomes in patients who have received rhGH treatment to date.
- More evidence is needed to understand the impact of clinically important variables, including dose, duration of treatment, age, sex, baseline nutritional status, baseline clinical status, existing diabetes risk factors, concurrent medical therapies, and prior treatment.
- More definitive answers about what role, if any, rhGH has in the treatment of pediatric patients with CF will require a large, multicenter, randomized, placebo-controlled, double-blinded trial that includes prospective data collection for hospitalizations, mortality, bone fractures, and HRQoL.

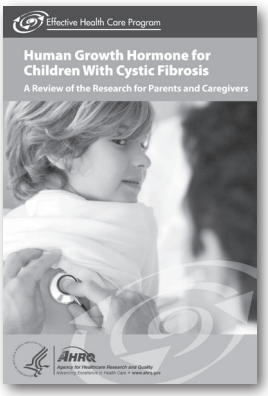
Source

The information in this guide is based on *Effectiveness of Recombinant Human Growth Hormone (rhGH) in the Treatment of Patients With Cystic Fibrosis*, Comparative Effectiveness Review No. 23, prepared by the University of Connecticut/Hartford Hospital Evidence-based Practice Center under Contract No. 290-2007-10067-I for the Agency for Healthcare Research and Quality, October 2010. AHRQ Pub. No. 11-EHC003-EF. Available at: http://www.effectivehealthcare.ahrq.gov/hgh.cfm. This guide was prepared by the John M. Eisenberg Center for Clinical Decisions and Communications Science at Baylor College of Medicine, Houston, TX.

What To Discuss With Caregivers

- That evidence about benefits and harms of rhGH treatment for patients with CF is limited.
- Whether the potential for fewer hospitalizations is relevant for the individual patient.
- Whether the risk of CFRD is relevant for the individual patient.
- Patient and caregiver values concerning rhGH administration (i.e., by injection).

Resource for Caregivers



Human Growth Hormone for Children With Cystic Fibrosis, A Review of the Research for Parents and Caregivers is a free companion to this clinician guide. It covers the state of the evidence for benefits and harms of adding this treatment.

Ordering Information

For electronic copies of *Human Growth Hormone for Children With Cystic Fibrosis, A Review of the Research for Parents and Caregivers* (AHRQ Pub. No. 11-EHC003-A), this clinician guide, and the full systematic review, visit www.effectivehealthcare.ahrq.gov. To order free print copies, call the AHRQ Publications Clearinghouse at 800-358-9295.

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