Growth and Growth Hormone Therapy in Children with CKD ADC 2016

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Nationwide Children’s/the Ohio State University College of Medicine
Overview

Background

• Growth in Patients with CKD
• Causes of Growth Failure in CKD

Growth Assessment and Evaluation for Growth Hormone Treatment in Children with CKD

Growth Hormone Therapy in Children with CKD: Benefits, Risks

Guidelines for Evaluating the Growth Response to rhGH Therapy

Growth: the Paramount Concern!
1. Growth is one of the MOST important issues that children with CKD confront!
What Concerns Children and Parents About Living with CKD*?

- General health
- CRF/dialysis/transplant
- Other Treatment
- Growth
- Appearance
- Coming to hospital
- School and friends
- Effect on family
- Future health
- Future prospects
- Future (general)

Social Outcome Following Renal Transplantation is Greatly Influenced by Adult Height

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year of transplantation</td>
<td>.04</td>
</tr>
<tr>
<td>Higher educational level achieved</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Higher rate of paid employment</td>
<td>.02</td>
</tr>
<tr>
<td>Greater likelihood of marriage</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Greater likelihood of independent living</td>
<td>.0003</td>
</tr>
</tbody>
</table>

Mean adult height SDS score: 

$-1.56 \pm 1.55$

Height satisfaction correlated significantly with height SDS score ($r = 0.42; P = .006$)

Quality of life correlated significantly with height satisfaction ($r = 0.41; P = .008$)

Growth Patterns in Patients with CKD

Growth in Patients with CKD
Growth Failure in Children with CKD is Associated with Poorer Survival

Height in 2,306 patients with CKD – NAPRTCS
At initiation of dialysis - 1992-2001

Furth S, Pediatrics 2002
Growth Failure in Children on Dialysis is Associated with Poorer Survival

1,112 patients < 18 yo ESRD – USRDS Tanner Stage I to IV, ht data Jan-Dec 1990
2. The factors that can lead to poor growth in children with CKD include important modifiable and non-modifiable issues!
Variables That **Can** Contribute to Growth Failure in CKD*

- **Age of onset of CKD**
- **Primary renal disease**
- **Calorie deficiency and abnormal protein metabolism**
- **Metabolic acidosis**
- **Renal osteodystrophy (CKD – Mineral Bone Disorder)**
- **Delayed puberty**

**Other comorbidities**
- Urinary sodium loss
- Urine concentrating defect
- Glucocorticoid therapy

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*Growth hormone indicated for CRI patients only, i.e., patients with GFR<75 mL/min/1.73m².*
Patient AC

AC - boy born at 39 weeks gestation

- Birth weight: 3030 g
- Birth length: 47 cm
- Prune belly syndrome (renal dysplasia)

He was polyuric and required calcitriol, NaHCO$_3$, sodium polystyrene sulfonate, and Sim PM 60/40 formula.
Patient AC: Growth Chart 0-36 months
## Patient AC: Growth and Renal Status

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>Wt (kg)</th>
<th>Wt SDS</th>
<th>Ht (cm)</th>
<th>Ht SDS</th>
<th>Wt/Ht %tile</th>
<th>Cr (mg)</th>
<th>GFR (mL/min/1.73 m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth</td>
<td>3.03</td>
<td>-0.87</td>
<td>47</td>
<td>-1.11</td>
<td>74</td>
<td>1.9</td>
<td>11.1</td>
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<tr>
<td>0.5</td>
<td>5.4</td>
<td>-3.57</td>
<td>58.5</td>
<td>-4.26</td>
<td>42</td>
<td>1.5</td>
<td>17.5</td>
</tr>
<tr>
<td>0.9</td>
<td>8.84</td>
<td>-1.27</td>
<td>71</td>
<td>-1.42</td>
<td>53</td>
<td>1.0</td>
<td>31.9</td>
</tr>
<tr>
<td>1.9</td>
<td>11.2</td>
<td>-0.99</td>
<td>82</td>
<td>-1.16</td>
<td>43</td>
<td>1.0</td>
<td>45</td>
</tr>
<tr>
<td>2.9</td>
<td>12.9</td>
<td>-0.92</td>
<td>87.1</td>
<td>-2.06</td>
<td>60</td>
<td>1.1</td>
<td>43.5</td>
</tr>
<tr>
<td>3.7</td>
<td>15</td>
<td>-0.36</td>
<td>94.6</td>
<td>-1.38</td>
<td>73</td>
<td>1.3</td>
<td>40</td>
</tr>
<tr>
<td>4.5</td>
<td>16.9</td>
<td>-0.13</td>
<td>100.5</td>
<td>-1.09</td>
<td>79</td>
<td>1.4</td>
<td>39.5</td>
</tr>
</tbody>
</table>
Patient AC: Growth Chart 2-9 yrs

Midparental height
What Do We Know About Growth Failure in CKD?

Growth Failure May Occur at Any Level of CKD (GFR)
Growth Does Not Typically Improve with Dialysis
Growth Failure is Related to Multiple Factors:

**Non-Modifiable**
- Younger age at onset of renal disease
- More significant uremia
- Tubulo-interstitial disorders
- Glucocorticoid therapy

**Modifiable**
- Excessive water and sodium loss
- Calorie deficiency and abnormal protein metabolism
- Metabolic acidosis
- Renal osteodystrophy (CKD-MBD)
- Gonadotropin abnormalities
What Else Have We Learned About Growth Failure in CKD?

Growth Hormone Therapy Improves Growth in Children with CKD

Breakthrough!  
CKD is a Growth Hormone/IGF-1 Resistance State
Physiology of the GH/IGF-I Axis

Normal Physiology

GH – Growth Hormone
ALS – Acid Labile Subunit
IGFBP – Insulin-like Growth Factor 1 (IGF-1) Binding Protein

CKD Physiology

Janjua H. Adv Chronic Kid Dis 2011
Key GH-IGF-1 Pathophysiologic Points

1. GH and IGF-I levels are not reduced in patients with CKD
   [increased pulses of GH release and reduced renal GH clearance]

2. CKD = reduced responsiveness to endogenous GH and IGF-I
   • GH resistance reflects
   • Defect in post-receptor GH activated JAK2 STAT pathway
     [leads to blunted IGF-1 response to GH]
   • Decreased density of GH receptors in tissues [bone]
     [as indicated by decreased levels of GHBP]
   • IGF-I resistance related to increased circulating IGFBP-1,2,4,6 = up to 50% reduction in bioavailable IGF-I

3. Increased IGFBP-3 proteolysis leads to reduction in IGF-I circulating in IGF-I/ALS/IGFBP-3 complex—therefore reduced IGF-I receptor activation and reduced feedback to the hypothalamus and pituitary
Multiple Factors Cause GH Resistance in CKD

Table 1 Factors contributing to growth hormone resistance in CKD

- Serum concentration of GH increased, metabolic clearance decreased, Haffner et al., J Clin Invest 93, 1163–71.
- Resistance to GH and IGF-I Mak and Pak, Kidney Intern, 50, 40–6, 1996.

Mehls O 2008
GH-IGF-1 Axis in Children with CKD: CKiD

26 - short stature – no rGH Rx
206 - normal height – no rGH Rx.
34 [18 short, 16 normal Ht on rGH RX]
3. The modifiable factors that can lead to poor growth in children with CKD must be addressed in a determined manner!
# Modifiable Factors Associated with Growth Failure in CKD: Treatment Aspects

<table>
<thead>
<tr>
<th>Modifiable Factor</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Malnutrition (Cachexia)</td>
<td>Provision of 100-120% RDA calories - Kari</td>
</tr>
<tr>
<td>2. Salt and Water Wasting</td>
<td>Supplemental Na/H2O</td>
</tr>
<tr>
<td>3. Acidosis</td>
<td>Alkali – McSherry</td>
</tr>
<tr>
<td>4. Anemia</td>
<td>Improved growth associated with Hb&gt;11 - Boehm</td>
</tr>
<tr>
<td>5. CKD-Mineral Bone Disorder (Renal Osteodystrophy)</td>
<td>Better growth with Rx – Chesney</td>
</tr>
<tr>
<td>6. Gonadotropic Hormone Abnormalities</td>
<td>?</td>
</tr>
<tr>
<td>7. GH/IGF-1 Resistance</td>
<td>Distinct Benefit from rhGH Rx – Fine, Mehls</td>
</tr>
</tbody>
</table>
Nutrition and Growth in CKD

- 101 infants (1986-1998); 1 and 5 year survival - 87 and 78%
- **Supplemental feeding** as soon as growth was subnormal; 81 started enteral feeds at ages 0 to 4.5 years.
- 46% gastrostomy
- 22% Nissen

- **Mortality highest in yr 1**
- **Length in normal range by 1 year of age**
- **Weight gain better than height gain**

Growth in Children on Dialysis (NAPRTCS)

EXHIBIT 5.3
MEAN CHANGE FROM BASELINE (30 day) IN STANDARDIZED SCORE

Change in Height Z Score

AGE
- 0-1 years
- 2-5 years
- 6-12 years
- ≥13 years

Dialysis Visit Month

Nationwide Children’s
When your child needs a hospital, everything matters.™
The Ohio State University
Growth in Children After Transplantation NAPRTCS

EXHIBIT 6.3
CHANGE FROM BASELINE IN STANDARDIZED SCORE (MEAN ± SE)
BY AGE AT TRANSPLANT
(Index transplants with functioning graft)

Change in Height Z Score

Change in Weight Z Score

Years from Transplant
Growth in Children After Transplantation NAPRTCS

EXHIBIT 6.4
FINAL ADULT STANDARDIZED HEIGHT SCORE
BY YEAR OF TRANSPLANT

Transplant Year

Height Z Score

Growth in Children After Transplantation NAPRTCS

EXHIBIT 6.5
STANDARDIZED SCORES (MEAN ± SE) AT TRANSPLANT
BY YEAR OF TRANSPLANT
(Index transplants)
4. CKD is a state of GH and IGF-1 resistance – in some children recombinant GH will be necessary to achieve good growth.
Algorithm for Evaluation and Treatment of Growth Retardation in Children with CKD: Overview

Short stature or declining height velocity in CKD 2-5

Assess and treat poor growth

IF GROWTH VELOCITY IMPROVED?

YES

Continue therapy

NO

Start GH therapy

Monitor GH therapy

IS GROWTH ADEQUATE?

YES

Continue GH therapy

NO

Assess and correct: Dose, metabolic status, nutrition, compliance

Is Growth Adequate?

YES

Discontinue GH therapy if necessary*

NO

Consider consult

Reinitiate GH therapy if reason for discontinuation resolved

Evaluation of Growth in Children with CKD

A candidate for treatment of growth retardation should have:
- CRI (CKD) with GFR<75 mL/min/1.73m²
- Height SDS<-1.88 (3rd Percentile) or Ht Velocity SDS<-2

First, a practitioner should assess and optimally treat modifiable factors that may contribute to poor growth:
- Acidosis
- Insufficient nutrition/fluids
- Salt-wasting
- Renal osteodystrophy (CKD-MBD)
- Hypothyroidism

Determine whether the growth velocity improves following these treatments

Growth Calculator: www.nutropin.com
## Assessment for GH Treatment

<table>
<thead>
<tr>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recalculate height SDS, height velocity SDS and height velocity</td>
</tr>
<tr>
<td>Determine pubertal stage</td>
</tr>
<tr>
<td>Analyze bone age</td>
</tr>
<tr>
<td>Hip and knee X-rays</td>
</tr>
<tr>
<td>Baseline fundoscopic exam</td>
</tr>
<tr>
<td>Labs</td>
</tr>
<tr>
<td>• Baseline chemistries</td>
</tr>
<tr>
<td>• PTH</td>
</tr>
<tr>
<td>• Thyroid status</td>
</tr>
</tbody>
</table>

*PTH = parathyroid hormone

Growth Hormone Therapy in CKD

- Evaluation
- Authorization/Insurance approval
- GH Dose:
  - 0.35 mg/kg/wk;
  - divided into daily SC injections
- Patient education
Considerations for GH Administration in CKD

- Usually recommended to administer in the evening
- Hemodialysis patients should receive their injections at bedtime or at least 3 to 4 hours after treatment to avoid the possibility of hematoma formation from heparin use.
- Chronic cyclic peritoneal dialysis patients should receive injections in the morning after dialysis.
- Chronic ambulatory peritoneal dialysis patients should receive their injections in the evening, at the time of the overnight exchange.
### Growth Hormone Therapy in CKD: Ongoing

<table>
<thead>
<tr>
<th>Monitoring growth response/safety - every 3-4 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Height, weight, height velocity</td>
</tr>
<tr>
<td>• Pubertal stage</td>
</tr>
<tr>
<td>• Fundoscopic exam</td>
</tr>
<tr>
<td>• Bone age, hip and knee X-rays (every year)</td>
</tr>
<tr>
<td>• OFC* (until 3 years of age)</td>
</tr>
<tr>
<td>• Nutritional intake</td>
</tr>
<tr>
<td>• Labs (chemistries, PTH)</td>
</tr>
</tbody>
</table>

### Adjusting GH doses as needed

### Encouraging compliance/measuring IGF-1 levels

### Consider pubertal dosing if growth response lags during puberty
- 125-200 % of standard dose
- If limited time until epiphyseal closure
- If IGF-1 response is not large (large = > 3-4 times normal)

### Effect of rhGH Rx on Height SDS in Children with CKD: A Meta-Analysis

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment n</th>
<th>Control n</th>
<th>WMD (95% CI Random)</th>
<th>Weight %</th>
<th>WMD (95% CI Random)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maxwell 1998</td>
<td>4</td>
<td>3</td>
<td>3.4</td>
<td>3.4</td>
<td>0.60 (-0.81, 2.01)</td>
</tr>
<tr>
<td>Pubertal</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maxwell 1998</td>
<td>9</td>
<td>6</td>
<td>6.7</td>
<td>6.7</td>
<td>0.90 (-0.08, 1.88)</td>
</tr>
<tr>
<td>Prepubertal</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Guest 1998</td>
<td>41</td>
<td>44</td>
<td>19.7</td>
<td>19.7</td>
<td>0.30 (-0.21, 0.81)</td>
</tr>
<tr>
<td>Fine 1994</td>
<td>55</td>
<td>27</td>
<td>24.4</td>
<td>24.4</td>
<td>1.10 (0.66, 1.54)</td>
</tr>
<tr>
<td>Powell 1997</td>
<td>30</td>
<td>14</td>
<td>45.8</td>
<td>45.8</td>
<td>0.80 (0.56, 1.04)</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>139</td>
<td>94</td>
<td>100</td>
<td>100</td>
<td>0.77 (0.51, 1.04)</td>
</tr>
</tbody>
</table>

Improved Growth After rhGH Treatment in Children with CKD

Children with CKD who receive rhGH therapy have better growth rates than placebo-treated children.

Children with Poor Growth Treated with GH Experience Significant Height Prepubertal Gains

Children with CKD who receive GH therapy show a significant improvement in prepubertal height gain.

GH Treatment Provides Significant Height Gains in Children with CKD During Puberty

It is important to initiate GH therapy early in children with CKD

Adapted from Haffner NEJM. 2004;343:923-930.
Children with CKD Who Receive GH Rx Have Better Final Adult Height Than Those Who Do Not

**rhGH effectively improves Final Height in CKD RTx patients, without affecting kidney function**
GH Therapy Works Better in Children with CKD 2-4 Compared to Those on Dialysis

First Year Height Velocity in CKD: Assure Appropriate Growth Response

Height Velocity During Year 1 of Growth Hormone Treatment and Pretreatment Height Velocity: *Prepubertal Naïve Patients with Chronic Kidney Disease*

Year 1 Height Mean Velocity ± 1 SD in ISS Males and CKD Males

- ISS
- CKD

Year 1 Height Velocity (cm/yr)

Age at Baseline

Mean Height Velocity + 1*SD
Mean Height Velocity
Mean Height Velocity – 1 *SD
Predicting Response to GH Rx in Children with CKD

Results: Annualized height velocity (cm/year) during first year of GH Rx best predicted by:

- age at start
- weight SDS
- underlying renal disorder (hereditary kidney disorder)
- GFR (at baseline)
- GH dosage

Model explained 37% of variability of growth response (SE = 1.6 cm)
Age = most important predictor of growth response (20.3% of variability) followed by weight SDS at start
Only 27.2% of variability of 2nd year response predicted by 1st year response and GFR

5. GH Treatment is Safe and Effective for children with CKD and children Post Renal Transplantation; careful monitoring for complications and appropriateness of growth response is necessary during GH treatment
Guidelines for Growth Hormone Therapy Discontinuation

GH therapy should be discontinued in when:

- Achieved 50th percentile for height for age based on mid-parental height
- Closed epiphyses
- Active neoplasia
- Slipped femoral epiphyses
- Intracranial hypertension
- Noncompliance
- Severe hyperparathyroidism (PTH>800 pg/mL – Stage V; >400 pg/mL – Stage II-IV)
- At the time of renal transplantation

If height velocity remains <2 cm/year over baseline and reason for discontinuation is resolved, GH therapy re-initiation should be considered.

Safety: Incidence of Adverse Events in Children with CKD Treated with rhGH

## Targeted Events by Indication

<table>
<thead>
<tr>
<th>Results</th>
<th>NCGS</th>
<th>CRI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number</strong></td>
<td>54,996</td>
<td>1778</td>
</tr>
<tr>
<td>Adverse Events</td>
<td>6.2</td>
<td>10.9</td>
</tr>
<tr>
<td>Serious AE</td>
<td>2.4</td>
<td>6.5</td>
</tr>
<tr>
<td>Deaths</td>
<td>0.3</td>
<td>1.2</td>
</tr>
<tr>
<td>Malignancy*</td>
<td>0.1</td>
<td>0.0</td>
</tr>
<tr>
<td>IC Tumor Recurrence</td>
<td>0.3</td>
<td>0.1</td>
</tr>
<tr>
<td>Leukemia*†</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>2nd Neoplasm</td>
<td>0.1</td>
<td>0.1</td>
</tr>
<tr>
<td>Adrenal Insufficiency†</td>
<td>0.0</td>
<td>0.2</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>0.1</td>
<td>0.2</td>
</tr>
<tr>
<td>Intracranial Hypertension</td>
<td>0.1</td>
<td>0.3</td>
</tr>
<tr>
<td>SCFE</td>
<td>0.1</td>
<td>0.3</td>
</tr>
<tr>
<td>Scoliosis</td>
<td>0.4</td>
<td>0.2</td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>0.0</td>
<td>0.0</td>
</tr>
</tbody>
</table>

Data are expressed as percentage.  *New onset, no risk factors. †Based on fewer than 15 reports.

3/300 post-renal Tx
1/17 post-liver Tx
All 4 on concomitant immunosuppressives

Adapted from Bell et al. *J Clin Endocrinol Metab.* 2010;95:167-177.
Safety: Infants with CKD Treated with rhGH

RCT – open label – 16 infants
29 adverse events:
9 in the rhGH group
20 in the untreated group,
*no adverse effects with rhGH Rx
Safety: Post Transplant Lymphoproliferative Disorder in Patients Treated with rhGH

**PTLD Rates According to rhGH Use During CKD (n = 1647)**

<table>
<thead>
<tr>
<th></th>
<th>No PTLD</th>
<th>PTLD</th>
<th>Fisher Exact p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All cases</td>
<td>1606 (97.5%)</td>
<td>41 (2.5%)</td>
<td>0.009</td>
</tr>
<tr>
<td>No rhGH pre-Tx</td>
<td>1217 (98.1%)</td>
<td>23 (1.9%)</td>
<td></td>
</tr>
<tr>
<td>rhGH pretransplant</td>
<td>389 (95.6%)</td>
<td>18 (4.4%)</td>
<td></td>
</tr>
</tbody>
</table>

- Groups not equal for age, era or post-Tx meds.
- The hazard ratio for PTLD development post-transplant, adjusted for transplant era and age at transplant, was just borderline higher with rhGH use (ratio = 1.88, 95% CI = 1.00–3.55, p = 0.05).
- No data on length of therapy, co-morbidities or specifics of immunosuppression.

Dharnidharka V. Ped Transpl 2007
Major Barriers to GH Therapy in Children with CKD

Lack of urgency
- That rhGH treatment can be delayed
- Short stature perceived as a cosmetic issue

Evaluation and documentation
- Uncertainty - evaluation, rhGH dosing, monitoring
- Reimbursement worries – lack of appropriate support for reimbursement

Patient compliance
Patient RP

Boy born at 40 weeks of gestation

- Birth weight: 3370 g/Birth length: 47 cm
- Joubert’s syndrome with ARPKD

Polyuric and required NaHCO₃, calcitriol, anti-hypertensive agents, Epogen.

Required Synthroid for hypothyroidism.

Clinical course complicated by reactive airway disease, polyuria; several admissions for dehydration with gastroenteritis.

Delay in sitting and ability to walk noted during first year of life.

After repeated attempts to boost caloric intake, he remained near 3rd percentile for weight and below 3rd percentile for height.
## Patient RP: Growth and Renal Status

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>Wt (kg)</th>
<th>Wt SDS</th>
<th>Ht (cm)</th>
<th>Ht SDS</th>
<th>Wt/Ht SDS</th>
<th>Cr (mg)</th>
<th>GFR (mL/min/1.73 m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth</td>
<td>3.37</td>
<td>-0.71</td>
<td>47</td>
<td>-1.11</td>
<td>-0.25</td>
<td>1.9</td>
<td>11.1</td>
</tr>
<tr>
<td>2.8</td>
<td>10.6</td>
<td>-2.38</td>
<td>85.3</td>
<td>-2.23</td>
<td>-1.45</td>
<td>1.0</td>
<td>47</td>
</tr>
<tr>
<td>3.5</td>
<td>11.7</td>
<td>-2.22</td>
<td>89.5</td>
<td>-2.37</td>
<td>-1.25</td>
<td>0.9</td>
<td>57</td>
</tr>
<tr>
<td>4.0</td>
<td>11.9</td>
<td>-2.46</td>
<td>89.9</td>
<td>-2.98</td>
<td>-1.15</td>
<td>1.2</td>
<td>41</td>
</tr>
<tr>
<td>4.5</td>
<td>13.7</td>
<td>-1.94</td>
<td>96</td>
<td>-2.3</td>
<td>-0.79</td>
<td>1.2</td>
<td>44</td>
</tr>
<tr>
<td>5.0</td>
<td>15</td>
<td>-1.73</td>
<td>98.5</td>
<td>-2.38</td>
<td>-0.20</td>
<td>1.1</td>
<td>49</td>
</tr>
<tr>
<td>5.5</td>
<td>17.6</td>
<td>-0.94</td>
<td>105.8</td>
<td>-1.48</td>
<td>0.14</td>
<td>1.0</td>
<td>58</td>
</tr>
</tbody>
</table>

**GH Rx**

**Ht velocity SDS = 7.90!!!**
Patient RP: Growth Chart 2-20 yrs

DOB: 3/9/03
Weight: 3.37 kg
Height: 47 cm
3 Years/1 Month

3 Years/4 Months
4 Years/1 Month
On GH Rx

5 Years/7 Months

5 Years/11 Months
Take Home Messages: Growth is Important!

Growth is a Vital Sign

Poor growth deserves *our* attention

Use **Height SDS** *+/or* **Height Velocity** to monitor growth

Consider Mid Parental Height Projection

- \([\text{Mom’s ht (in)} + \text{Dad’s ht (in)}]/2\)
- Add 2.5 in male
- Subtract 2.5 in female

Use all available interventions to improve growth:

*Calories, fluid/Na, alkali, vitamin D, Growth Hormone*

*The earlier GH is used, the better the final adult height*
1. Growth is one of the MOST important medical issues that children with CKD confront!

2. The factors that can lead to poor growth in children with CKD include important modifiable and non-modifiable issues!

3. CKD is a state of GH and IGF-1 resistance – in some children recombinant GH will be necessary to achieve good growth.

4. Children with CKD who demonstrate growth failure should be evaluated and all modifiable factors addressed – if poor growth persists, GH therapy should be utilized.

5. GH Treatment is Safe and Effective for children with CKD and children Post Renal Transplantation; careful monitoring for complications and appropriateness of growth response is necessary during GH treatment.

6. Successfully optimizing growth in children with CKD really demonstrates your value as pediatric nephrologist!
References


References


References


Information for Patients and Families

National Kidney Foundation
  http://www.kidney.org/
MAGIC Foundation
  http://www.magicfoundation.org/www
American Association of Kidney Patients
  http://www.aakp.org/
Kidney & Urology Foundation of America
  http://www.kidneyurology.org/
Genentech’s Growth Hormone Site (including Stepping Stones, Understanding Growth in Kidney Disease, etc)
  www.nutropin.com
Algorithm for Evaluation and Treatment of Growth Retardation in Children with CKD
Algorithm for Evaluation and Treatment of Growth Retardation in Children with CRI

**Patient Selection**
GFR<75 mL/min/1.73m³
Ht SDS<-1.88 (3rd Percentile) or Ht Velocity SDS<-2

**Treat Contributors to Poor Growth**
Acidosis, Malnutrition, Salt-wasting, Osteodystrophy, Hypothyroidism

Is Growth Velocity Improved?

**YES**
Continue Current Therapy

Algorithm for Evaluation and Treatment of Growth Retardation in Children with CRI (Cont’d)

Is Growth Velocity Improved?

NO

Baseline Assessment for GH Therapy
- Recalculate Ht SDS, ht velocity SDS, and height velocity velocity
- Pubertal stage, Bone age, Hip and knee X-rays
- Funduscopic exam
- Chemistries, PTH, Thyroid studies

YES

Continue Current Therapy

Algorithm for Evaluation and Treatment of Growth Retardation in Children with CRI (Cont’d)

Start Growth Hormone Therapy
0.05 mg/kg/day SC (0.35 mg/kg/wk)

Monitor
Every 3-4 months
- Height, weight
- OFC (until 3 years of age)
- Pubertal stage
- Nutritional evaluation
- Funduscopic exam
- Chemistries, PTH
- Toxicity

Every year
- Bone age
- For symptoms
- Hip and knee X-rays

Algorithm for Evaluation and Treatment of Growth Retardation in Children with CRI (Cont’d)

Is Growth Adequate?
(Ht velocity 2 cm/yr>baseline)

Yes, Growth Adequate
- Continue GH Rx
- Adjust dose every 3-4 months based on weight

No, Growth Inadequate
- Assess & Correct
  - Dose for weight
  - Metabolic status
  - Nutrition
  - Compliance
- Consider Pediatric Endocrinology consult

Algorithm for Evaluation and Treatment of Growth Retardation in Children with CRI (Cont’d)

Discontinue GH Therapy for
Achieved ht goal based on mid-parental ht and/or 50th percentile for age;
Closed epiphyses; Active neoplasia;
Slipped femoral epiphyses;
Intracranial hypertension; Non-compliance;
Severe hyperparathyroidism (PTH>900 pg/mL – Stage V;
>400 pg/mL – Stage II-IV)

If height velocity<2 cm/yr, and reason for discontinuation resolved, consider reinitiation of GH therapy