Growth and DMD – Endocrine aspects of care

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Where are we now?

Inactive

Reactive

Proactive
Objectives

- What is the endocrine system?
- Why is it important for DMD?
- Typical issues
- Topical issues – growth hormone
The endocrine system
The endocrine system and DMD

- GH
- LH, FSH
- TSH
- ACTH
- Calcium, vitamin D
- Insulin
- IGF-1
- Testosterone
- Thyroid hormone
- Cortisol

- Bone mineralization
- Growth
- Puberty
- Strength
“Typical” issues
Growth without steroids
Clinical effects of excess glucocorticoids

- Growth failure
- Increase body fat / weight gain
- Pubertal delay
- Bone demineralization
## Impact in DMD

<table>
<thead>
<tr>
<th>Growth failure</th>
<th>? QOL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increase body fat / weight gain</td>
<td>Decreased mobility, ? diabetes</td>
</tr>
<tr>
<td>Pubertal delay</td>
<td>Decreased muscle strength, osteoporosis</td>
</tr>
<tr>
<td>Bone demineralization</td>
<td>Fractures, pain, decreased mobility</td>
</tr>
</tbody>
</table>
Patient A

- 16-year-old boy with DMD (age 2)
- Deflazacort age 7 → prolonged ambulation
- Poor growth / absent puberty
- Fractures
- Parental concerns: Survival, quality of life, preservation of ambulation
## Initial endocrine tests

<table>
<thead>
<tr>
<th>Condition</th>
<th>Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Growth failure</td>
<td>IGF-1, IGFBP-3</td>
</tr>
<tr>
<td></td>
<td>Thyroid function tests</td>
</tr>
<tr>
<td>Increase body fat / weight gain</td>
<td>Fasting glucose, insulin</td>
</tr>
<tr>
<td>Pubertal delay</td>
<td>Testosterone, LH, FSH</td>
</tr>
<tr>
<td></td>
<td>Bone age xray</td>
</tr>
<tr>
<td>Bone demineralization</td>
<td>Vitamin D, calcium</td>
</tr>
<tr>
<td></td>
<td>DXA scan, spine xray</td>
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</tbody>
</table>
Growth hormone testing

- GH secretion pulsatile
  - random GH measurements not useful
- Provocative testing to test GH reserve
- “Fail” 2 tests = GHD
- Controversial...
- Many pitfalls...

[Diagram showing Pituitary gland and GH stimulus]
## Endocrine treatment options

<table>
<thead>
<tr>
<th>Condition</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Growth failure</td>
<td>? Growth hormone</td>
</tr>
<tr>
<td>Increase body fat / weight gain</td>
<td>Dietary modification, (exercise), (metformin)</td>
</tr>
<tr>
<td>Pubertal delay</td>
<td>Testosterone</td>
</tr>
<tr>
<td>Bone demineralization</td>
<td>Vitamin D, calcium, bisphosphonates, testosterone, (? GH)</td>
</tr>
</tbody>
</table>
Testosterone therapy
Growth hormone therapy
“Topical” issues
Quandaries & controversies

• **Growth hormone?**

• **Thyroid hormone supplementation?**

• **Treatment of weight gain / insulin resistance?**

• **Treatment of osteoporosis?**

• **Vitamin D dosing?**
Growth hormone ...

Potential benefits and concerns in DMD
Growth hormone – who to treat?

- FDA-approved uses
- Investigational uses

- Growth hormone deficiency
- Adults with GHD
- Intrauterine growth retardation
- Idiopathic short stature
- Etc…

- ? Glucocorticoid suppression of growth
Growth hormone – potential benefits
Growth hormone → non-growth effects in adults with GHD

- Loss of body fat
- Increased muscle mass and strength
- Increased bone density
- Improvement in quality of life
IGF-1 – animal studies of DMD mouse model (mdx mouse)

*IGF-1 treatment or overexpression in muscle:*

- Increased strength / decreased fatigue
- Increased muscle regeneration
- Decreased muscle death / damage
Growth hormone – potential benefits?

...or adverse consequences??

Cheater
Growth hormone – potential concerns

- “Scientific” literature
- ? Adverse effects
- Increased body size in DMD
- Cost
Growth hormone and DMD reports

Aged 13

Aged 18

Letter to the Editor: Benign Duchenne Muscular Dystrophy in a Patient With Growth Hormone Deficiency
Growth hormone inhibition studies

- Zatz 1986 – twins

*Other studies:*
- No consistent effect on GH secretion / growth
- No difference in muscle function
- Significant side effects
Growth hormone and DMD reports

- Few concerning case reports (n=3)
- Inconclusive GH inhibition studies
  - but –
- No long-term properly conducted trials
- 1 encouraging case report
- Studies of IGF-1 in dystrophic mdx mice
Growth hormone therapy – potential adverse effects (rare)

- Edema
- Intracranial hypertension
- Slipped capital femoral epiphyses
- Worsening of scoliosis
- Hyperglycemia
- Malignancy?
- Unknown long-term effects?
Growth hormone – potential concerns
GH in DMD – Patient 1
Patient 2

Before GH

After 1 year GH
Where are we now?

Inactive

↓

Reactive

↓

Proactive
Where are we going?

Inactive

↓

Reactive

↓

Proactive??
Conclusions

Endocrine care important in DMD

Monitor in a multidisciplinary setting

Individualized care

Optimize health and quality of life
Thank you!