Deflazacort Treatment in Duchenne Muscular Dystrophy

Parent Project Muscular Dystrophy
Chicago Roundtable
April 2004

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Why Steroids in DMD?

- Daflazacort
- Treatment protocol

Results:
- Mobility
- Pulmonary Function
- Scoliosos
- Heart
Why Steroids in DMD:?

Prednisone shown to change the course of DMD

- reduced weakness
- preserved motor function longer

but .....

- side effects common
What is Deflazacort?

Derivative of prednisone

Effect:

- anti-inflammatory
- immunosuppressive
Why Deflazacort?

Same benefits as prednisone but fewer side effects

Less:
- weight gain
- diabetogenic
- osteoporosis
- behaviour problems
Time to Start

Arbitrary, 5 – 7 years of age

When parents tell us:

- stairs are more difficult
- falling more
- difficulty getting up from floor
What Dose?

0.9 mgm / kgm / day

50 lb child ≈ 21 mg/day

Plus

- vitamin D 1000 units/day
- calcium supplements 750 mgm/day
Deflazacort Treatment of Duchenne Muscular Dystrophy:

Deflazacort Group #48 boys v.s. No Deflazacort Group #33 boys

Deflazacort Treatment of Duchenne Muscular Dystrophy:
No Deflazacort Group

- 33 boys
- age 9 – 19 years
- concerns about side effects:
  - weight gain
  - Behavior
  - not walking
  - other
- parental choice

Deflazacort Group

- 48 boys
- start age 6-8 years
- starting dose:
  
  0.9 mgm/kg/d

Deflazacort Treatment of Duchenne Muscular Dystrophy:
Our Findings Since ‘92

- normal weight gain
- some slowing of growth
- muscle strength preserved
- preserved pulmonary function
- delayed or prevented scoliosis
- preserved cardiac function

Deflazacort Treatment of Duchenne Muscular Dystrophy:
Our Findings Since ‘92 cont’d

- osteoporosis
- 30% cataracts
- some behaviour issues


Deflazacort Treatment of Duchenne Muscular Dystrophy:
Deflazacort Treatment of Duchenne Muscular Dystrophy:


Deflazacort Treatment of Duchenne Muscular Dystrophy:
Preserved Muscle Function
Walking

No deflazacort - 33 boys
- stop at 9.8 ± 1.8 years
Walking

- treated with deflazacort – 48 boys
- 15 stopped walking at 12.7 ± 2.9 years
- 33 still walking
- 12 of 33 are over 13 years:
  - 2 @ 13 years
  - 2 @ 16 years
  - 1 @ 14 years
  - 1 @ 17 years
  - 5 @ 15 years
  - 1 @ 18 years
<table>
<thead>
<tr>
<th>Naples</th>
<th>Toronto</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protocol-N</td>
<td>Protocol-T</td>
</tr>
<tr>
<td>4-8</td>
<td>Start (years)</td>
</tr>
<tr>
<td>0.6 mg/kg</td>
<td>Dose</td>
</tr>
<tr>
<td>20 days on 10 days off</td>
<td>Schedule</td>
</tr>
<tr>
<td>As needed for osteoporosis</td>
<td>Vitamin D Calcium</td>
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</table>
## Mobility - Up from floor

<table>
<thead>
<tr>
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<th>Toronto</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>32/37  (86)</td>
<td>24/32  (75)</td>
<td>5/30  (17)</td>
</tr>
<tr>
<td>12</td>
<td>8/26  (31)</td>
<td>11/23  (47)</td>
<td>0/30  (0)</td>
</tr>
<tr>
<td>15</td>
<td>0/12  (0)</td>
<td>3/13  (23)</td>
<td>0/30  (0)</td>
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</table>
# Mobility – Stair Climbing

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<tr>
<td>9</td>
<td>32/37 (86)</td>
<td>24/32 (100)</td>
<td>4/27 (15)</td>
</tr>
<tr>
<td>12</td>
<td>9/26 (35)</td>
<td>13/23 (56)</td>
<td>0/27 (0)</td>
</tr>
<tr>
<td>15</td>
<td>0/12 (0)</td>
<td>5/13 (38)</td>
<td>0/27 (0)</td>
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## Mobility — Walk 10 metres

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<tbody>
<tr>
<td>9</td>
<td>36/37 (97)</td>
<td>32/32 (100)</td>
<td>15/31 (48)</td>
</tr>
<tr>
<td>12</td>
<td>9/26 (35)</td>
<td>19/23 (83)</td>
<td>0/31 (0)</td>
</tr>
<tr>
<td>15</td>
<td>3/12 (25)</td>
<td>10/13 (77)</td>
<td>0/31 (0)</td>
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Arm Function

Feeding and self care extended for 5-6 years
Preserved Pulmonary Function
Impact of Deflazacort on Scoliosis
Criteria For Spine Surgery

- progressive curve (20 degrees +)
- pulmonary function (greater than 40%)
Spine Surgery in DMD

- no deflazacort
- 25/33 boys done at 13.75 years ± 3.6
- 8/33 not done
  - 3 spines straight at 20 years
  - 3 refused
  - 2 waiting - less than 13 years
Deflazacort treated:

- 24 boys older than 13-19 years
- 4/24 have had surgery
  - 2- compliance issues
  - 2- ages 14 and 17 years
Scoliosis - Boys 13yrs. & older

Naples: 30%*
Toronto: 16%*
Control: 90%*

*p<.0005
Dilemma

- natural history of scoliosis?
- adult spine surgeon?
- pulmonary function?
- osteoporosis?
Preserved Cardiac Function
## Cardiac Function

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<thead>
<tr>
<th></th>
<th>Control</th>
<th>Deflazacort</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>16 ± 2</td>
<td>14 ± 2</td>
<td>NS</td>
</tr>
<tr>
<td><strong>LVEF(&lt;45%)</strong></td>
<td>58%</td>
<td>5%</td>
<td>0.001</td>
</tr>
<tr>
<td><strong>% fractional shortening</strong></td>
<td>21 ± 8</td>
<td>33 ± 7</td>
<td>0.002</td>
</tr>
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</table>
Osteoporosis
Osteoporosis

- Bisphosphonates
- not approved for children
- side-effects?
- effective?
- growing bone?
Osteoporosis

Complications:

- adults on long-term steroids:
  - 25% fractures
- children?
  - spine fractures
- treatment
  - bisphosphonates in adults
  - ? in children
Osteoporosis

Preliminary Findings

Lumbar spine --- 6-10 % improvement

Total BMD --- not significantly increased
Summary

- alendronate
- well tolerated
- minimal side effects
- improved lumbar spine bone density
- not approved for children
1. More questions than answers
2. Most boys have osteoporosis
3. Probably worse with deflazacort
4. Risk of fractures, controversial
5. Can be treated, if indicated
6. More research needed
Incidence of Fractures

- Naples: 20%
- Toronto: 15%
- Control: 10%

Legend:
- Naples: Blue
- Toronto: Yellow
- Control: Grey
Benefits of deflazacort appear to outweigh side effects

**Major benefits:**
- prolonged ambulation
- improved pulmonary function
- improved upper extremity function
- delayed need for spine surgery
- preserved cardiac function
Cataracts

- 30%
- Small
- Eye sight normal
- No treatment needed
Behavioral Issues

- difficult to know
- 17 of 48
  - 8 on first visit
  - 5 at 6 weeks
  - 4 at 16 weeks
  - transient in 5
Conclusions (cont’d)

Side effects:
- weight
- height
- cataracts
- osteoporosis

Further studies needed:
optimum dose
Conclusions (cont’d)

- No hypertension
- No diabetes
- No renal stones
- No liver problems
- No increased fractures
For more information:

Articles:


Effects of Deflazacort on Left Ventricular Function in Patients With Duchenne Muscular Dystrophy: Silversides C. et al.

Steroid Treatment and the Development of Scoliosis in Males with Duchenne Muscular Dystrophy: Alman, B.A. et al.
Deflazacort Treatment in Duchenne Muscular Dystrophy

Thank You!

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