Anabolic Steroids in Critical Care: Oxandrolone

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Presentation Objectives

- Background to Anabolic-Androgenic Steroids (AAS)
- Background on Oxandrolone
- Literature Review
- Health Canada’s Position
- Prescribing Issues
- A ‘How to’ Guide to Obtain for Patient Use
- Suggested Uses for Oxandrolone
Background: AAS

- Common ICU associated conditions
  - Lean body mass loss
  - Anemia
  - Deconditioning
  - Impaired immune system
  - Lethargy
  - Decreased appetite
  - Impaired tissue healing and integrity
  - Impaired cellular metabolism
Background: How AAS Work

- AAS penetrate cell membrane of target cells
  - Easily as they are fat-soluble
  - Unlike peptide hormones
- ASS binds to Androgen Receptors in cytoplasm
Background: How AAS Work

Depending on the specific characteristics of AAS and the type of target cell, various effects are initiated:

- Increase synthesis of proteins
- Increase of rate and speed of transport of amino acids
- Block glucocorticoids
- Block development of fat-storage cells
- Increase BMR
### Background: Effects of AAS

<table>
<thead>
<tr>
<th>Anabolic Effects Of AAS</th>
<th>Androgenic Effects Of AAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Increase protein synthesis</td>
<td>• Change in primary and secondary sexual characteristics at puberty in males. Lifelong risk for females (AAS dependent)</td>
</tr>
<tr>
<td>• Increase amino acid transport through cell walls</td>
<td>• Increase CNS efficiency: alertness, motivation, and mood</td>
</tr>
<tr>
<td>• Increase appetite</td>
<td>• Increase aggressiveness</td>
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<tr>
<td>• Increase bone, tendon, ligament structural integrity</td>
<td>• Increase libido</td>
</tr>
<tr>
<td>• Anti-catabolic: reduce cortisol secretion, and sensitivity</td>
<td></td>
</tr>
<tr>
<td>• Promote IGF and HGH secretion</td>
<td></td>
</tr>
<tr>
<td>• Increase erythropoietin synthesis</td>
<td></td>
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<tr>
<td>• Retention of Nitrogen</td>
<td></td>
</tr>
<tr>
<td>• Promote lean body mass development and fat loss</td>
<td></td>
</tr>
</tbody>
</table>
Background: Adverse Effects of AAS

<table>
<thead>
<tr>
<th>Adverse Effects of AAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Effects are specific and variable to each AAS)</td>
</tr>
</tbody>
</table>

- Serum cholesterol changes (increase LDL, decrease HDL)
- HTN
- Hair loss (head)
- Virilization
- Liver damage
- LV structural changes
- Gynecomastia
- Testicular atrophy
- Acne
- Impaired sperm production
- Depression (Post Cycle)
- Sexual dysfunction (Post Cycle)
- Catabolism (Post Cycle)
Background: Families of AAS

- **Testosterone Derived Steroids**
  - Testosterone, Dianabol, Equipoise, Halotestin...

- **19-Nortestosterone Derived Steroids**
  - Nandrolone, Durabolan, Trenbolone, Parabolan...

- **Dihydrotestosterone Derived Steroids (DHT)**
  - Oxandrolone, Anadrol, Masteron, Primobolan, Winstrol...
# Background: Families of AAS

<table>
<thead>
<tr>
<th></th>
<th>Test</th>
<th>19-Nortest</th>
<th>DHT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anabolic Properties</strong></td>
<td>++++</td>
<td>+++</td>
<td>++++</td>
</tr>
<tr>
<td><strong>Androgenic Properties</strong></td>
<td>+++</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td><strong>Aromatization</strong></td>
<td>++++</td>
<td>++</td>
<td>0</td>
</tr>
<tr>
<td><strong>Virilizing Effects for Women</strong></td>
<td>++++</td>
<td>50/50</td>
<td>0</td>
</tr>
<tr>
<td><strong>Increase LDL, decrease HDL</strong></td>
<td>+++</td>
<td>+</td>
<td>0</td>
</tr>
<tr>
<td><strong>Aggression</strong></td>
<td>+++</td>
<td>+++</td>
<td>0</td>
</tr>
<tr>
<td><strong>Lipolysis</strong></td>
<td>++</td>
<td>++</td>
<td>++++</td>
</tr>
<tr>
<td><strong>Bone Density, Joints, Con. Tissue</strong></td>
<td>+++</td>
<td>+++++</td>
<td>+++</td>
</tr>
<tr>
<td><strong>Increase Metabolism</strong></td>
<td>+++</td>
<td>++++</td>
<td>+</td>
</tr>
<tr>
<td><strong>Erectile Dysfunction</strong></td>
<td>++</td>
<td>+++</td>
<td>+++</td>
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<tr>
<td><strong>Maintain Gains Post-Cycle</strong></td>
<td>++</td>
<td>++++</td>
<td>++++</td>
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<tr>
<td><strong>Increase Red Blood Cells</strong></td>
<td>++++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td><strong>Inhibition of HPTA</strong></td>
<td>+++</td>
<td>+++++</td>
<td>+</td>
</tr>
<tr>
<td><strong>Male Pattern Hair Loss</strong></td>
<td>++++</td>
<td>++</td>
<td>0</td>
</tr>
<tr>
<td><strong>Effects are Linear in Nature</strong></td>
<td>++++</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td><strong>Adverse Effects</strong></td>
<td>++++</td>
<td>+++</td>
<td>+</td>
</tr>
</tbody>
</table>
Background: Ideal AAS

- Highly anabolic
- Minimally androgenic
- Safe oral form
- Short acting (short half-life)
- Low adverse effect profile
- Long lasting results
Background: Oxandrolone

- **Anabolic/ Androgenic Ratio 500:25 (Test 100:100)**
- Alpha-alkylated compound: it is very mild on the liver
- Non-aromatizing: no estrogen as byproduct
- Non-virilizing: safe for women
- Mild on HPTA: minimally decreases endogenous testosterone in males
- Great fat loss agent
- Great anabolic agent
- Detection time ~ 3 weeks
Literature Review:

- 228 papers published in the last 20 years (1992-2012)
- 55 results for Burn/Trauma Patient Care
- 45 results for Turner Syndrome
- 24 results for Halting Weight Loss
- 22 results for AIDS Related Wasting
- 10 results for Cancer
- 9 results for Wound Healing
- 6 results for Hepatitis
- 4 results for Angioedema
- 4 results for Muscular Dystrophy
- 3 results for COPD
Severe Burns

- Most commonly used condition
- Halts catabolism related with major stress
- Non-age dependent
- Small doses counteracts the effects of cortisol
- Small doses (5mg-20mg per day) effective
- Minimal adverse effects
- Some evidence for improved tissue healing
- Lean muscle preservation
- Improved skin graft integrity in pediatric population
Literature Review: Strong Evidence

AIDS related wasting

- Strongest evidence for use
- Improves appetite
- Various doses studied (5mg-80mg/day)
- Halts muscle wasting immediately
- Starts rebuilding lean muscle mass after 1-2 weeks
- Strength gain
- No studies conducted on eventual outcome
- Effects long lasting even after cycle
- Minimal adverse effects even at high doses
Literature Review: Moderate Evidence

Polytrauma

- Evidence for halting catabolism associated with stress induced cortisol release
- Lean muscle mass preservation noted
- No benefit in Ventilator Days or LOS
- No evidence proven for improved long term outcome
Literature Review: Moderate Evidence

**Tissue healing**

- Strongest evidence from animal models
- Some evidence from burn patient care
- Improved wound healing in time and integrity
- Anecdotal evidence from athletes: highly effective for tendonitis and other tendon/ligamentous injuries
Literature Review: Moderate Evidence

Alcoholic Hepatitis Induced Malnourishment

- Moderate decrease of mortality when used in early/advanced liver disease
- Severe/End stage: no change in mortality/morbidity
- Low rate of adverse events despite alpha-alkylation
- Best effects noted with patients able to consume > 2500 kcal/day
COPD-Associated Weight Loss

- Strong evidence for restoration of lost lean muscle mass (similar pattern as liver disease)
- Minimally improvement in mortality
- Moderate improvement in morbidity
- No significant improvement in PFTs
- Well tolerated for long term use in low-moderate doses
- No gender related adverse effects noted
Literature Review: Weak Evidence

ALS

- No significant improvement in eventual outcome
- Some minor (non-statistically significant) improvement in lengthening ventilator free time period
Literature Review: Weak Evidence

Spinal Cord Injury

- Animal models only
- Minimal (non-statistically significant) improvement in motor and sensory function in rats
- No human trials
Literature Review: Weak Evidence

Duchenne MD

- High dose treatment yielded minimum slowing of muscle function deterioration when compared to placebo
- Increased benefits noted in children vs. teenagers and young adults
- No effect on outcome in general
- No improvement of muscle function
- No adverse effects noted
Health Canada’s Position

Special Access Program
- Allows practitioners to request medications that are not available for sale in Canada
  - IV Methadone
  - Pentobarbital
  - IV Rifampin
  - Oxandrolone
  - Nandrolone
  - Arsenic
  - Thalidomide
Prescribing

- You need a pharmacist to aid you in the process
- Exceedingly difficult to do it on your own
- Special Access Program FORM A needs to be filled out and submitted to Health Canada, along with extensive literature review
The ‘How to’ Guide

- Be informed about the medication/condition
- Have extensive reference list to back up your request
- Demonstrate that there are no available medications that are comparable and readily available
- Have patience
- Have time to do the paperwork
- Expect some hoops
Suggested Uses for Oxandrolone

- Burn patients
- AIDS related myopathy
- Any chronic condition that is accompanied by a wasting/catabolic element
  - COPD
  - Hepatitis
  - Malnourishment of any kind
- Any acutely ill AAS user/abuser
Questions? Comments? Suggestions?

Thank You for your attention!