Take Home Messages: Androgens

Landon Trost, MD
Assistant Professor of Urology
Mayo Clinic, Rochester, MN

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Overview – Androgens

- **Plenaries: 6**
  - The role of testosterone in sexual function – Luiz Otavio Torres
  - The history of testosterone therapy – Abraham Morgentaler
  - Actual candidates for low testosterone therapy – William Conners
  - Neuroendocrine in HSDD – James Simon
  - Testosterone alternatives – Mohit Khera
  - Endocrine aspects of transgender care – Charles Moser

- **Podiums: 9**

- **Posters: 21**
Association Studies
#15 – Male Non-standard Shift Workers Are Predisposed to Depression and HG Symptoms

- Lindgren M, et al:

Men Completing Questionnaires
Shift work, PHQ-9, qADAM
(n=2,066)

Non-Standard Shift Workers
(n=590)

Standard Shift Workers
(n=1,476)

Demographics
Hormone Levels
Depressive & Hypogonadal Symptoms
#15 – Male Non-standard Shift Workers Are Predisposed to Depression and HG Symptoms

<table>
<thead>
<tr>
<th>PHQ-9 Question</th>
<th>Shift Workers (mean±SD)</th>
<th>Non-Shift Workers (mean±SD)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Little interest or pleasure</td>
<td>0.64 ± 0.83</td>
<td>0.50 ± 0.77</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Feeling tired / low energy</td>
<td>1.12 ± 0.98</td>
<td>0.94 ±0.94</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Poor appetite / overeating</td>
<td>0.73 ± 0.95</td>
<td>0.55 ± 0.85</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Trouble concentrating</td>
<td>0.62 ± 0.89</td>
<td>0.51 ± 0.84</td>
<td>0.002</td>
</tr>
</tbody>
</table>

- Positive correlation between number of non-standard shifts and PHQ-9 score ($\rho=0.125$, $p=0.002$)
#15 – Male Non-standard Shift Workers Are Predisposed to Depression and HG Symptoms

<table>
<thead>
<tr>
<th>qADAM Question</th>
<th>Shift Workers (mean±SD)</th>
<th>Non-Shift Workers (mean±SD)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy level</td>
<td>2.96 ± 0.99</td>
<td>3.15 ± 0.98</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Enjoyment of life</td>
<td>3.50 ± 0.87</td>
<td>3.63 ± 0.91</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Happiness level</td>
<td>3.51 ± 0.88</td>
<td>3.62 ± 0.90</td>
<td>0.006</td>
</tr>
<tr>
<td>Fall asleep after dinner</td>
<td>3.91 ± 1.24</td>
<td>4.23 ± 1.11</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Height lost</td>
<td>4.85 ± 0.52</td>
<td>4.78 ± 0.66</td>
<td>0.033</td>
</tr>
<tr>
<td>Total qADAM Score</td>
<td>38.70 ± 4.61</td>
<td>39.12 ± 4.68</td>
<td>0.041</td>
</tr>
</tbody>
</table>

- Depressive and HG symptoms worsen with number of non-standard shifts per week
- Most impacted symptoms relate to fatigue
#23 – Prevalence of T Deficiency in Men Treated with CCH for PD

- Krakowsky Y, et al:
  - Evaluated rate of low T (TT<350, FT<10)
  - Mean age 54
  - Outcomes contrast to other studies

- Percentage of T Deficient Men, TT<350 ng/dL: 62%
- Percentage of T Deficient Men, FT<10: 86%
#24 – Serum Concentrations of SHBG Vary Widely in Younger and Older Men: Clinical Data from a Men’s Health Practice

• Krakowsky Y, et al:
#24 – Serum Concentrations of SHBG Vary Widely in Younger and Older Men: Clinical Data from a Men’s Health Practice

55 and older (n=465)
#24 – Serum Concentrations of SHBG Vary Widely in Younger and Older Men: Clinical Data from a Men’s Health Practice

<table>
<thead>
<tr>
<th>Cohort</th>
<th>% with SHBG &gt;50 nmol/L</th>
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</thead>
<tbody>
<tr>
<td>All ages</td>
<td>13.3%</td>
</tr>
<tr>
<td>&lt;55 yo</td>
<td>8.2%</td>
</tr>
<tr>
<td>≥55 yo</td>
<td>19.6%</td>
</tr>
</tbody>
</table>
#48 – Feelings of Depression Are Associated with Sexual Dysfunction and Hypogonadal Symptoms

• Murri M, et al:

Men presenting between July 2014 – February 2015

(n=451)

Mild to Moderate Depressive Sx
PHQ-9 <15
(n=308)

Moderate to Severe Depressive Sx
PHQ-9 ≥15
(n=141)

Comparison of Depressive Symptoms (PHQ-9)
Hypogonadal Symptoms (ADAM, qADAM)
Sexual Dysfunction (IIEF)
#48 – Feelings of Depression Are Associated with Sexual Dysfunction and Hypogonadal Symptoms

![Chart showing total IIEF score comparison between depressed and not depressed groups.](chart.png)

- **Depressed (PHQ-9 ≥15)**
  - Total IIEF Score: 55
  - p < 0.01

- **Not Depressed (PHQ-9 < 15)**
  - Total IIEF Score: 65

Feelings of Depression Are Associated with Sexual Dysfunction and Hypogonadal Symptoms.
#48 – Feelings of Depression Are Associated with Sexual Dysfunction and Hypogonadal Symptoms

Depressed (PHQ-9 ≥15)  Not Depressed (PHQ-9 < 15)

ADAM Score

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#140 – Does Neoadjuvant Androgen Deprivation Therapy Impact Erectile Function Recovery Post-radical Prostatectomy?

- **Jenkins L, et al:**
  - Retrospective analysis 1089 men post-prostatectomy
  - Neoadjuvant ADT
  - 43 (ADT+), 1046 (ADT-)

- **Results**
  - ADT significantly worsened EF
  - Equivalent to nerve sparing score
  - Age, baseline fx more important

<table>
<thead>
<tr>
<th>Factor</th>
<th>ADT+</th>
<th>ADT-</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good EF (EFD ≥ 24)</td>
<td>19%</td>
<td>41%</td>
<td>0.45</td>
</tr>
<tr>
<td>Severe ED (EFD ≤ 10)</td>
<td>44%</td>
<td>24%</td>
<td>1.96</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Factor</th>
<th>Beta</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>-0.18</td>
</tr>
<tr>
<td>Baseline EF</td>
<td>0.31</td>
</tr>
<tr>
<td>Number Vascular Comorbidities</td>
<td>-0.07</td>
</tr>
<tr>
<td>Nerves Sparing Score</td>
<td>-0.10</td>
</tr>
<tr>
<td>ADT Group</td>
<td>-0.08</td>
</tr>
</tbody>
</table>
Safety of Androgens
#17 – Safety of TTh in Patients on Active Surveillance for Prostate Cancer

- Jenkins L, et al:
  - Prospective data on TTh in AS patients
  - Gl ≤7, PSA≤10
  - N=24, mean age 65, 17% Gl 7, min 6 mo f/u
  - 33% (8/24) had ≥ 1 pt increase in PSA
  - 4% (1/24) stopped d/t anxiety
  - 8% (2/24) pts upgraded (G6 to 7)

- Conclusions – Fails to demonstrate increased risks with TTh in monitored setting; conversion to active treatment similar to non TTh cohorts
#231 – TTh Is Not Associated with Clinical Worsening of LUTS

- Gupta N, et al:
  - HG men randomized to oral T vs topical 1.62% x 12 mo
  - IPSS and QOL evaluated – clinical significance 3 points

- Results:

<table>
<thead>
<tr>
<th></th>
<th>Baseline IPSS</th>
<th>Change in IPSS</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral</td>
<td>5.56</td>
<td>+1.02</td>
<td>0.002</td>
</tr>
<tr>
<td>Topical 1.62%</td>
<td>4.64</td>
<td>+2.32</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Efficacy Studies
#16 – Long-term TTh Improves Urinary and Sexual Function in HG Men – Results from a Propensity-matched Subgroup of a Controlled Registry Study

• Saad F, et al:
  • Registry maintained of HG men electing and not electing TTh
  • 82 men matched from TTh+ and TTh – for:
    • Age, waist circumference, BMI
  • Followed up to 8 years
  • Outcomes IPSS, IIEF-EF, post-void volume, AMS
IIEF-EF (maximum score: 30)

Testosterone Control

NS
p<0.0001
Post-Voiding Bladder Volume (ml)

- **Testosterone** line shows a steady increase over 8 years.
- **Control** line shows a steady decrease over 8 years.

NS: Not Significant
AMS (maximum score: 85)

Testosterone Control
AMS (maximum score: 85)

AMS (maximum score: 85)

AMS (maximum score: 85)

AMS (maximum score: 85)

AMS (maximum score: 85)

AMS (maximum score: 85)

AMS (maximum score: 85)

AMS (maximum score: 85)

p<0.0001
#130 – Long-term TTh Improves Glycemic Control in HG Men – Results from a Propensitymatched Subgroup of a Controlled Registry Study

Fasting Glucose
#130 – Long-term TTh Improves Glycemic Control in HG Men – Results from a Propensitymatched Subgroup of a Controlled Registry Study

HbA1c
#132 – Long-term TTh Leads to Sustained Weight Loss in HG Men – Results from a Propensity-matched Subgroup of a Controlled Registry Study

Weight Loss

- 18.9 kg difference after 8 yrs
#21 – Cessation of PDE5i Use in Men with ED Following TTh

- Lin J, et al:

  Hypogonadal Men on PDE5i (n=80)
  - Continued PDE5i (n=67)
  - Discontinued PDE5i (n=13)

  Follow up every 3-6 months
  - Erectile Function → Sexual Health Inventory for Men (SHIM) score
  - Hormones → T, Free T (FT)
#21 – Cessation of PDE5i Use in Men with ED Following TTh

- 16.3% stopped PDE5i therapy – mean f/u 25-30 mo
- Men with less severe ED more likely to d/c PDE5i
#173 – Effect of T 2% Solution on Ejaculatory Function as Measured by Perineal U/S in HG Men

• Bach PV, et al:
  • N=7 w/ EjD (excluded PE), 50 yo, TT 221
  • 16 weeks T 2% - TT 300-1050

• Results:
  • # of bulbocavernous muscle contractions – 7.8 to 11
  • Time to ejaculation – 481 sec to 303
  • No change in force of ejaculate or # of emissions
New Concepts and Technology
#134 – Improvements in Psychosexual Function Among Hypogonadal Men Enrolled in the Steady Trial of a Novel, Subcutaneous Auto-injector for Testosterone Replacement

• Wang C, et al:
  • IM T administered via new auto-injector
  • Psychosexual daily questionnaire
  • Phase III, double blind, multicenter trial
  • N=137, 12 wk treatment
  • 91% achieved TT 300-1100
    • Primary endpoint
    • Improved sexual function in all PDQ domains
Distribution of 14C-Enclomiphene and 14C-Zuclomiphene Following Oral Administration to Mice

- Fontenot G, et al:
  - Zuclomiphene had longer half-life
  - No difference in male/female distribution
  - Zuclomiphene accumulated in eye, gallbladder, brain, lung, fat, adrenals, kidneys, and reproductive tissues

- Clinical question
  - Similar distribution in humans?
  - Adverse effects with zuclomiphene accumulation?
Other
#36 – Estradiol As a Metric of Male Sexual Health

- Stout, T, et al:
  - Obj - evaluate role of E2 in libido, mood, and sexual fx
  - Retrospective, eugonadal, HG, on TTh
#36 – Estradiol As a Metric of Male Sexual Health

- Stout, T, et al:
  - N=?
  - ? Optimal range for E2

<table>
<thead>
<tr>
<th></th>
<th>TTh Alone</th>
<th>TTh + Anastrozole</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estradiol (ng/dl)</td>
<td>5.6 ± 3.7</td>
<td>3.7 ± 2.4</td>
<td>0.03</td>
</tr>
<tr>
<td>ADAM</td>
<td>2.7 ± 3.0</td>
<td>2.3 ± 3.0</td>
<td>0.53</td>
</tr>
<tr>
<td>IIEF Sexual Desire</td>
<td>7.2 ± 2.6</td>
<td>7.5 ± 2.9</td>
<td>0.62</td>
</tr>
<tr>
<td>IIEF Intercourse Satisfaction</td>
<td>9.9 ± 4.4</td>
<td>10.3 ± 4.8</td>
<td>0.63</td>
</tr>
<tr>
<td>IIEF Overall Satisfaction</td>
<td>7.2 ± 2.8</td>
<td>7.7 ± 2.8</td>
<td>0.83</td>
</tr>
<tr>
<td>PHQ-9</td>
<td>6.6 ± 4.9</td>
<td>6.5 ± 4.3</td>
<td>0.96</td>
</tr>
</tbody>
</table>
#155 – Vasectomy Does Not Affect Insulin Like Growth Factor 3 Levels As a Marker of Leydig Cell Function

- Helo S, et al:
  - Does Leydig cell fx change post-vasectomy
  - Evaluated changes in insulin-like GF3 as surrogate
    - Not affected by gonadotropins, minimal diurnal variation

- N=26, mean age 39, BMI 30, 12 week f/u

- Results – no change in ILGF3, TT, fT, LH, FSH, Estradiol, SHBG

- Clinical implication – vasectomy does not affect gonadal function
#135 – Testosterone for Sale: An Unsafe Internet Alternative

- Herati A, et al:
  - Google search for “Testosterone Replacement” and 5 largest cities in US; other searches including body building to purchase
  - 112 websites reviewed
    - 37% physician managed (none sold online)
    - 83% of non-physician managed permitted purchase w/o T assessment
      - 36% discussed AE’s, 8% discussed contraindications
  - Demonstrated ease of purchasing online w/o physician oversight
#139 – Gaps in Patient Knowledge About the Risks and Benefits Associated with Testosterone Replacement Therapy

- Gilbert K, et al:
  - Evaluated pt knowledge on risks / benefits of TTh
    - Surveys, N=97, median age 41-50
    - Common perceived low T symptoms:
      - ED, libido, energy, strength
    - Perceived benefits
      - Sexual fx, energy, generally feeling better
    - Perceived risks
      - 50% unsure, 21% prostate ca, 17% infertility, 16% MI, 14% reduced testicular size, all others ≤10%
Thank You