Take Home Messages: Erectile Dysfunction

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

ISSM – 16th World Meeting on Sexual Medicine
October 12th, 2014
Overview – ED Well Represented

• Prosthetic Surgery Symposium
• Plenary Sessions: 6
• Workshops: 8
• Moderated Poster / Podium Sessions: 15
  • Basic Science: 14
  • Clinical Evaluation / Epidemiology: 17
  • Medical / Surgical Management: 12
ED Basic Science
#116 - Estrogen Mediates Metabolic Syndrome-induced Erectile Dysfunction: A Study in the Rabbit

• Vignozzi, et al:
  • Compared high-fat (MetS) rabbits to regular diet
  • Evaluated association of hormones

• Results / Conclusions:
  • Estradiol, rather than low T impairs endothelium-dependent relaxation in MetS
  • Estradiol, rather than T, regulates PDE5 expression in MetS
  • Partially restored by Tamoxifen

• Clinically relevant – T supplementation in MetS
#170 – Peripheral effects of opiate agonists in isolated corpus cavernosum

- Rodriguez RL, et al:
  - Isolated rat CC strips – treated with opiates; assessed molecular mechanisms

- Results / Conclusions:
  - Opioid receptors present in CC
  - Activation of opioid receptors results in relaxation of CC and increased ICP
  - Possibly NO, cGMP independent pathway
  - Dependent on potassium channels

- Clinical implications for priapism and narcotics
#169 – Efficacy of pioglitazone on erectile function recovery in a rat model of post-prostatectomy ED

- Aliperti L, et al:
  - Thiazolinedione (TZD), DM drug used to increase insulin sensitivity
  - Protective of vascular smooth muscle, antifibrotic

- Results / Conclusions:
  - Improves erectile responses
  - Increases eNOS / nNOS / smooth muscle

- Clinical role unclear; new mechanism
#002 – Cell Stretching – The Putative Mechanism of Penile Traction; An In-vitro Cellular Analysis

- De Young, L, et al:
  - Compared expression of TGF-B1, IL-6, MMPs, TIMPs
  - Control vs mechanically stretched cultured myofibroblasts

- Results / Conclusions:
  - Mechanical stretching decreased TIMP1, TIMP2, and increased MMP12, 13
  - Clinically – May account for benefits on plaques in PD with mechanical traction
#003 – Hemolysis Contributes to PDE5 Dysregulation and Priapism in Sickle Cell Bone Marrow Transplanted Mice

- Matsui H, et al:
  - Induced chronic hemolysis - rat model of SCD
  - Treated with PDE5i to assess for impact

- Results
  - Hemolysis induced ROS, NO/PDE5 dysregulation, priapism
  - PDE5i improves priapism by restoring NO/PDE5 balance and reducing ROS

- Clinically validates use of PDE5s for treatment of priapism
Clinical Evaluation / Epidemiology of ED
#159 – Long-term erectile function outcomes in patients submitted to either TURP or HoLEP

- Capogrosso P, et al:
  - Reviewed 201 pts undergoing TURP vs HoLEP
  - IIEF / IPSS scores
  - 5 year f/u

- Results:
  - 7% improvement over 5 years
  - TURP / HoLEP similar

<table>
<thead>
<tr>
<th>Predictors</th>
<th>TURP p value (OR)</th>
<th>HoLEP p value (OR)</th>
<th>Overall p value (OR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCI</td>
<td>0.09 (0.63)</td>
<td>0.66 (0.85)</td>
<td>0.16 (0.75)</td>
</tr>
<tr>
<td>Age @ FU</td>
<td>0.38 (0.96)</td>
<td>0.00 (0.83)</td>
<td>0.001 (0.90)</td>
</tr>
<tr>
<td>BMI</td>
<td>0.66 (1.03)</td>
<td>0.19 (1.15)</td>
<td>0.24 (1.06)</td>
</tr>
<tr>
<td>EF pre OP</td>
<td>0.001 (0.90)</td>
<td>0.001 (0.87)</td>
<td>0.00 (0.89)</td>
</tr>
<tr>
<td>IPSS pre OP</td>
<td>0.98 (0.99)</td>
<td>0.61 (1.02)</td>
<td>0.79 (1.00)</td>
</tr>
<tr>
<td>Prostate Vol.</td>
<td>0.92 (1.00)</td>
<td>0.70 (1.00)</td>
<td>0.94 (1.00)</td>
</tr>
<tr>
<td>Adenoma Vol.</td>
<td>0.72 (0.98)</td>
<td>0.91 (1.00)</td>
<td>0.96 (1.00)</td>
</tr>
</tbody>
</table>
#182 – Long-term Treatment with T Undecanoate Improves Metabolic Control and EF in HG Men with DM2

- Saad F, et al:
  - Reported long-term outcomes of T replacement in HG+DM
  - T<350 baseline

- Results:
  - Sustained, progressive benefits with BMI, EF, BP, DM, Waist circumference
  - 21 kg weight loss
  - Results atypical with BP, Lipids
#182 – Long-term Treatment with T Undecanoate Improves Metabolic Control and EF in HG Men with DM2
#182 – Long-term Treatment with T Undecanoate Improves Metabolic Control and EF in HG Men with DM2
#027– Sexual Function Recovery in Kidney Transplant Donors and Receptors After a Year of Follow-up

- Magana-Rodriguez J, et al:
  - Evaluated sexual function in male renal donors
  - IIEF pre-op and monthly x 1 yr

Results / Conclusions:
- 52 recipients, 42 donors
- Pre-op recipients worse baseline EF
- Returns to baseline within 3-6 mo

<table>
<thead>
<tr>
<th></th>
<th>Donor</th>
<th>Recipient</th>
<th>P=</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>61.5 (12.2)</td>
<td>35.33 (22.04)</td>
<td>0.02</td>
</tr>
<tr>
<td>1 Month</td>
<td>32.21 (16.15)</td>
<td>37.3 (24.87)</td>
<td>0.67</td>
</tr>
<tr>
<td>3 Months</td>
<td>57.75 (14.93)</td>
<td>47.67 (21.4)</td>
<td>0.38</td>
</tr>
<tr>
<td>6 Months</td>
<td>56.75 (12.5)</td>
<td>61.00 (21.4)</td>
<td>0.66</td>
</tr>
<tr>
<td>12 Months</td>
<td>45.75 (25.47)</td>
<td>61.78 (15.54)</td>
<td>0.18</td>
</tr>
</tbody>
</table>
Medical Management of ED
#055 – Empirical vs Risk-based Approach to Intracavernosal Injection Therapy: A Prospective Study

- Segal R, et al:
  - Attempted to incorporate risk-based treatment strategy for selecting ICI / dose
  - Primary outcome EDITS at 3 and 6 mo

**Empiric Approach**
- PGE1 10 mcg regardless of etiology.
- Self-titration regimen of PGE1.

**Risk-based Approach**
- Neurogenic ED → bimix
- Organic ED - 1-2 risk factors → trimix (30/1/10)
- if organic ED with ≥ 3 risk factors, duration of ED >2yrs → super trimix (30/2/40)
- Post RP with normal pre-operative EF, NS, within one year → bimix
- Post RP with impaired pre-operative EF, non-NS, >1 year → trimix
- if post-pelvic irradiation, androgen deprivation → trimix
#055 – Empirical vs Risk-based Approach to Intracavernosal Injection Therapy: A Prospective Study

- No significant difference in any outcome measure
#059 – Frequency of Intracavernosal Injections Improves Erectile Function Recovery Following Radical Prostatectomy

• Nelson C, et al:
  • Evaluated men post RP < 6 mo
  • Excluded poor ICI responders and excellent PDE5 responders

• Results:
  • Mean 1.6 ICI / week; Mean 22 mo f/u
  • ICI / week significant on multivariate analysis
  • 16% improvement in PDE5i response per 1 injection weekly
  • 11% improvement in spontaneous erectile function per 1 injection weekly
#153 – Detection of a Tadalafil Analogue as an Adulterant in a Dietary Supplement for Erectile Dysfunction

- Ulloa J, et al:
  - Evaluated a dietary supplement commonly used in Argentina for EF
  - Performed spectroscopic analysis and compared to known PDE5i’s

- Results:
  - Structure similar to tadalafil
  - Untested - unknown AE’s
  - Supports role for increased regulation of supplement market
Surgical Management of ED
#046 – Key Factors and Influencers Impacting the Penile Implant Decision

- Nelson C, et al:
  - 1 - Evaluated men attending AMS seminar (n=257)
  - 2 – Evaluated men recommended to have an IPP by urologist
    - 31 elected to have surgery
    - 30 elected to not have surgery
  - Outcomes – Differences between groups via telephone survey
#046 – Key Factors and Influencers Impacting the Penile Implant Decision

- Results:

  **Implanters (n=31)**
  - 36% Urologist
  - 23% Spouse/Partner
  - 10% PCP
  - 4% Friends/Family
  - 5% Myself

  **Non-Implanters (n=30)**
  - 29% Urologist
  - 27% Spouse/Partner
  - 29% Myself
  - 5% Friends/Family
  - 4% PCP
#046 – Key Factors and Influencers Impacting the Penile Implant Decision

**Results:**

- Factors increasing the likelihood for having the procedure:
  - Increased certainty that it is the best option for my ED
  - Spouse/partner on board with procedure
  - Stronger recommendation by my physician
#047 – MRI Analysis of Architectural Changes of the Retropubic Space and Relevant Structures Post Radical Prostatectomy: Implications for Penile Prosthesis Reservoir Placement

- Sullivan JF, et al:
  - Evaluated MRIs pre- and post- RP
  - Assessed distances from pubic symphysis, inguinal ring, iliac vessels, bladder
#047 – MRI Analysis of Architectural Changes of the Retropubic Space and Relevant Structures Post Radical Prostatectomy: Implications for Penile Prosthesis Reservoir Placement

• Results:
  • N=22; No significant difference pre- vs post-op
  • 10cm³ = 1 mm decrease to bladder
  • Variably increased signal intensity in space of Retzius (similar to ligament); worse with open vs robotic

<table>
<thead>
<tr>
<th>Measurements</th>
<th>Pre RP</th>
<th>Post RP</th>
</tr>
</thead>
<tbody>
<tr>
<td>External Inguinal Ring to External Iliac Vein</td>
<td>3.00 (1.94-3.83)</td>
<td>2.95 (1.94-3.76)</td>
</tr>
<tr>
<td>External Inguinal Ring to Bladder</td>
<td>2.62 (1.47-3.92)</td>
<td>2.75 (2.10-4.10)</td>
</tr>
<tr>
<td>Superior Pubic Symphysis (midline) to Bladder</td>
<td>1.05 (0.56-1.82)</td>
<td>1.09 (0.69-1.62)</td>
</tr>
</tbody>
</table>
#106 – Maximal Penile Length and Girth Restoration Combined with Penile Prosthesis Implantation Without Grafting: “The Modified Sliding Technique”

- Kuehhas FE, et al:
  - N=143; undergoing modified “sliding technique” without grafting and with IPP placement
- Results:
  - Hematomas in majority
  - 5% glanular partial numbness – resolved
  - Mean 3.1 cm length gain
  - All able to resume sexual intercourse
#045 – Improved Infection Outcomes after Mulcahy Salvage Procedure and Replacement of Infected IPP with Malleable Prosthesis

• Gross M, et al:
  • Evaluated series of 57 salvage IPPs d/t infection
  • Patients underwent malleable placement at time of washout

• Results:
  • Mean time to salvage 2 mo
  • 28% of patients subsequently had malleable replaced with IPP
  • 93% rate of successful salvage

<table>
<thead>
<tr>
<th>Surgical History</th>
<th>N</th>
<th>Salvage rate %</th>
</tr>
</thead>
<tbody>
<tr>
<td>First time IPP</td>
<td>39</td>
<td>92.3%</td>
</tr>
<tr>
<td>Previous IPP Surgeries</td>
<td>18</td>
<td>94.5%</td>
</tr>
<tr>
<td>Total</td>
<td>57</td>
<td>93%</td>
</tr>
</tbody>
</table>
Martinez D, et al:

- N=9, CaSO4 + Vanc + Tobramycin placed at time of infected device removal (20-30cc)
- Reimplanted 6-18 wks later
- Mean 1 cm loss of prosthesis length
#044 - ”Just the Tip”: Closed Suction Drain Cultures After Penile Implant Surgery with Prolonged Drains

- Martinez D, et al:
  - N=12
  - 72 hour drainage
  - Cultured tip and 1 cm distal to penile skin surface of removed tubing

- Results:
  - No hematomas
  - 0% of tips infected
  - 1/12 of 1cm proximal to skin surface with bacterial growth
Other ED Therapies
Initial Clinical Experience of Linear Focused, Low Intensity Shockwave for Treatment of ED Patients with Different Severity Symptoms

N, et al: Applied low intensity shock-wave therapy (~80 bar; ESWL = 450 bar)

900 shock waves at each location
14,400 waves/wk session x 4 wks
N=81, mean ED x 5 yrs
85% using PDE5i’s at baseline
57% non-responders at baseline
comes: IIEF at baseline, 1, 3 mo
placebo group
Initial Clinical Experience of Linear Focused, Low Intensity Shockwave for Treatment of ED Patients with Different Severity Symptoms
Safety and Efficient Duration of Linear Focused Shockwave Treatment for Erectile Dysfunction – A 12 Month Follow-up Pilot Study

Yaman Y, et al:
Pilot study of Renova shockwave system
N=20
300 shocks / min, 4 areas, 900 shocks per area
1x / weekly x 4 weeks
Outcomes: SEP, IIEF, GAQ at baseline, 1, 3, 6, 12 mo
Safety and Efficient Duration of Linear Focused Shockwave Treatment for Erectile Dysfunction – A 12 Month Follow-up Pilot Study

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>6 months</th>
<th>12 months</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Success (N)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>90% (18)</td>
<td>75% (15)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T-EF score</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11.4±3.2</td>
<td>20.7±2.6</td>
<td>18.7±2.6</td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td>P-Q 2 % success</td>
<td>50</td>
<td>90</td>
<td>90</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>P-Q 3 % success</td>
<td>5</td>
<td>55</td>
<td>40</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Q- Q1 %success</td>
<td>90</td>
<td></td>
<td>80</td>
<td></td>
</tr>
<tr>
<td>Q- Q2 %success</td>
<td>60</td>
<td></td>
<td>45</td>
<td></td>
</tr>
<tr>
<td>E5i response</td>
<td>80%</td>
<td></td>
<td>100%</td>
<td></td>
</tr>
</tbody>
</table>
Thank You