ED & LUTS-BPH
Making the link – bridging the gap

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GP, BACKWELL & NAILSEA MEDICAL GROUP

Case study

Mr S
53yr old
Not seen GP for few years
Presents with ED – third complaint of consultation

Case study

Overweight – BMI 32, Waist Circumference 105cm
No exercise, Poor diet
BP 164/100
Fasting glucose 6.4
Total Cholesterol 6.7, Qrisk 26%

PDE5 INHIBITOR OPTIONS
On demand: Short acting
On demand: Long acting
Daily dosing

Ageing society

UK population >50:
- 2010 21.5 million
- 2030 27.6 million

UK population > 60:
- 2010 10.3 million
- 2030 15.4 million
- 53,000 centenarians in 2030

Prevalence of ED increases with age
Prevalence of BPH increases with age

**2 conditions highly prevalent in men >50**

**ERECTILE DYSFUNCTION**
- Approximately 1/3 of men over 50 have moderate to severe LUTS
- 3.2 million men in UK
- Up to 24 million men in the EU

**LOWER URINARY TRACT SYMPTOMS**
- Prostate of the Nation Report – Prostate Action 2010
- Hutchison et al. EUR Urol 2006; 50: 555–562

Diseases associated with ED

<table>
<thead>
<tr>
<th>Disease</th>
<th>No ED</th>
<th>ED n=6,422</th>
</tr>
</thead>
<tbody>
<tr>
<td>HTN</td>
<td>18</td>
<td>25</td>
</tr>
<tr>
<td>CHD/angina</td>
<td>7</td>
<td>29</td>
</tr>
<tr>
<td>High cholesterol</td>
<td>16</td>
<td>25</td>
</tr>
<tr>
<td>Diabetes</td>
<td>14</td>
<td>21</td>
</tr>
<tr>
<td>Depression/anxiety</td>
<td>11</td>
<td>21</td>
</tr>
</tbody>
</table>

p < 0.0001

Atherosclerosis in Coronary Vessels

Atherosclerosis in Penile Arteries

**ED and CV Risk**

ED compared with subjects without ED have a significantly increased risk by:
- 44% for total CV events
- 62% for MI
- 38% for cerebrovascular events
- 25% for all-cause mortality
- 19% for CV mortality

Risk conferred by ED on events is of a magnitude similar to that of the risk conferred on events by established risk predictors such as hypertension and dyslipidaemia.

Consider multiplying CV risk (e.g. on QRisk) by 1.5 if patient also has ED
Diseases associated with LUTS/BPH

Correlation between severity of LUTS & ED

MSAM:
Multinational survey of the ageing male
N = 12,815 men aged 50-80 years

Risk Factors for LUTS & ED

LUTS and Male Sexual Dysfunction (MSAM-7)

LUTS / ED in UK Primary Care

UK Primary Care database – 333 practices
Study period: 2000 – 2007. Rising incidence of both conditions during the study

LUTS diagnosis preceded ED in 2/3 of men by a median of 4.8 years

Compared to men with no LUTS – odds ratios for ED (with 95% c.i.):
- Storage LUTS: 3.0 (2.6–3.4)
- Voiding LUTS: 2.6 (2.3–2.7)
- Mixed storage and voiding LUTS: 4.0 (3.4–4.8)
Tip of the iceberg......

Lifestyle Intervention – LUTS/BPH

“In older men, central obesity and higher physical activity associated with increased & decreased risks of incident LUTS, respectively.”

“Prevention of chronic urinary symptoms represents another potential health benefit of exercise in elderly men.”

“Statin use associated with 6.5 to 7 year delay in the onset of moderate / severe LUTS.”

The prostate: the ‘gateway to men’s health’......

Asking the LUTS patient about ED

DO WE ASK LUTS PATIENTS ABOUT ED?

- GP’s enquired about ED in <10%
- Offered no therapy for ED in >80%
- >90% of untreated ED patients would like treatment

WHY DON’T WE ASK?

- Lack of knowledge of the strong association
- Embarrassment (GP or patient)
- Respecting patient’s privacy
- Lack of confidence in assessing and treating ED
- Lack of time
- Cost of ED Rx
- Issues re prescribing LUTS meds that may worsen ED

Consensus statement

“Evidence suggests a strong link between erectile dysfunction and lower urinary tract symptoms in men that is independent of age. Co-diagnosis of these conditions is therefore important.”

Conclusions

Standardised difference in means in International Index of Erectile Function (IIEF) score after lifestyle intervention & cardiovascular risk factor reduction

Lifestyle changes alone

Lifestyle changes plus statins
Example questions:

"Many men with LUTS/waterworks symptoms etc also find that they have problems achieving or maintaining an erection – is that a problem for you?"

"Many men with erection difficulties also notice problems with their waterworks (or similar phrase) – has that been an issue for you?"

Treatments options for ED

Lifestyle measures & Psychosocial Counselling

PDE5 inhibitors
- On demand: Tadalafil (Cialis), Sildenafil (Viagra), Vardenafil (Levitra)
- Daily dosing: Cialis 5mg

Vacuum devices
- Intra-urethral, Intra-cavernosal & Topical Prostaglandins

Surgery

Alteration of modifiable risk factors
Sexual counselling and education
Oral agents
Vacuum therapies
Injection therapies
Surgical therapy
Hormone therapy
Injection therapies
Surgical therapy
Oral agents

A third of Men and Women have no set pattern of sexual timing

Men miss spontaneity

UKCLS01047a April 2012
Predicted Pharmacokinetic Modeling: 
Smg OD vs. Frequent 20-mg On-Demand Dosing

Historical Comparison (Long-Term Safety): Adverse Events at 24 Months

<table>
<thead>
<tr>
<th>Event Reported in ≥5% of Subjects in First Year of OD Open Extension Trial</th>
<th>24-Month Once-Daily*</th>
<th>24-Month On-Demand*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>5 (2.1%)</td>
<td>185 (15.8%)</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>9 (3.8%)</td>
<td>139 (11.8%)</td>
</tr>
<tr>
<td>Back Pain</td>
<td>12 (5.0%)</td>
<td>96 (8.2%)</td>
</tr>
<tr>
<td>Influenza</td>
<td>6 (2.5%)</td>
<td>37 (3.2%)</td>
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Discontinuation Due to Adverse Events
60 (6.7%) |
74 (6.3%)

Adapted from Wrishko et al. J. Sex. Med 2009

Case study
Men dislike ‘planning’ element of on demand PDE5 inhibitor

Very few currently offered daily dosing

Most are interested if they are offered

Case study
Mr S is treated with on demand PDE5 inhibitor

He doesn’t mention his LUTS

Asked opportunistically: ‘Many men with erection problems also have urinary problems – is that a problem for you?...’

Mixed storage and voiding symptoms

Embarrassed and bothered – relieved to be asked

NICE Guidelines 2010: LUTS in men

Sexual side effects of medical therapy for LUTS

ERECTILE DYSFUNCTION

COMBAT: ED 9% combination vs 7% dutasteride vs 5% tamsulosin

MTOPS: ED 5.3% combination vs 4.5% finasteride vs 3.5% doxazosin vs 3.3% placebo

EJACULATORY DYSFUNCTION

Meta analysis of 4 RCT’s, 4800 patients

EjD Combination vs Alpha-blocker monotherapy: 9.2% vs 2.7%, OR 3.75, p<0.0001

EjD Combination vs 5ARI monotherapy: 9.2% vs 3.5%, OR 2.76, p=0.02

GACCI MET AL. IMPACT OF MEDICAL TREATMENTS FOR MALE LUTS DUE TO BPH ON EJACULATORY FUNCTION. A SYSTEMATIC REVIEW & META-ANALYSIS. J SEX MED 2014 IN PRESS
PDE5 Inhibitors for LUTS-BPH

Total IPSS: Mean Change from Baseline

<table>
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<tr>
<th>Treatment</th>
<th>Baseline Mean (SD)</th>
<th>24 week endpoint Mean change (SD or LOCF)</th>
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<tr>
<td>Placebo</td>
<td>16.6 (6.0)</td>
<td>-3.6</td>
</tr>
<tr>
<td>Tadalafil</td>
<td>17.1 (6.1)</td>
<td>-5.6**</td>
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* p < .05, ** p < .01, Values for Week 5 are based on mIPSS


IIEF: Mean Change from Baseline

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<th>Domain</th>
<th>Baseline Mean (SD)</th>
<th>Week 4 Mean (SD)</th>
<th>Week 1 Mean (SD)</th>
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Please note, Tadalafil 2.5 mg OD is not licensed for the signs and symptoms of BPH.

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IPSS Total: Mean Change from baseline

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†IPSS = International Prostate Symptom Score.
IIEF-EF Total: Mean Change from Baseline

EAU Guidelines 2013: LUTS in men

Case study

LUTS assessed – diagnosed as secondary to BPH

Discussion re continued on demand plus addition of alpha blocker

Offered switch to daily dose of Tadalafil 5mg

Conclusions

Your ED patient probably also has LUTS
Your LUTS patient probably has ED

Think CV risk / T2 DM / Metabolic Syndrome in both sets of patients

Diagnosing ED in your LUTS patient might ‘save their life’

Medical treatment for LUTS has potential for adverse impact on sexual function

Once daily Tadalafil 5mg an option for the man with both LUTS & ED