TOUGH CASES OF LOWER URINARY TRACT SYMPTOMS : LATEST THERAPEUTIC OPTIONS

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DISCLOSURE

The speaker has no conflict of interest to declare

OBJECTIVES

At the conclusion of this presentation, participants should be able to:

1) Outline the latest approach in the evaluation of complex cases of lower urinary tract symptoms

2) Discuss the various medical management options for lower urinary tract symptoms

3) Identify the pitfalls in the management complex lower urinary tract symptoms

LUTS – Lower Urinary Tract Symptoms

- One of the most common urological conditions seen in aging men
- BPH is one of the most common causes of LUTS in aging men
- Metabolic, cardiovascular, neurological disorders are associated with LUTS
- Bladder outlet obstruction vs bladder storage dysfunction
- Many new medical therapeutic options and many new surgical interventions

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LUTS – Update on evaluation

- Validated questionnaire to confirm your diagnosis
- To evaluate the severity of LUTS
- To evaluate disease progression over time
- International Prostate Symptom Score (IPSS) ; AUA symptom Index

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International Prostate Symptom Score (I-PSS)							
In the past month:	**Not at All**	**Less than 1 in 5 times**	**Less than Half the Time**	**About Half the Time**	**More than Half the Time**	**Almost Always**	**Your Score**
1. Incomplete Emptying How often have you had the sensation of not emptying your bladder?	0	1	2	3	4	5	
2. **Frequency** How often have you had to urinate less than every two hours?	0	1	2	3	4	5	
3. Intermittency How often have you found you stopped and started again several times when you urinated?	0	1	2	3	4	5	
4. Urgency How often have you found it difficult to postpone urination?	0	1	2	3	4	5	
5. Weak Stream How often have you had a weak urinary stream?	0	1	2	3	4	5	
6. Straining How often have you had to strain to start urination?	0	1	2	3	4	5	
	None	**1 time**	**2 times**	**3 times**	**4 times**	**5 times**	
7. Nocturia How many times did you typically get up at night to urinate?	0	1	2	3	4	5	
Total I-PSS Score							
Score:	1-7 Mild		8-19 Moderate		20-35 Severe		
		The first seven questions of the I-PSS are from the American Urological Association (AUA) Symptom Index					
Quality of Life Due to Urinary Symptoms							
	Delighted	**Pleased**	**Mostly Satisfied**	**Mixed**	**Mostly Dissatisfied**	**Unhappy**	**Terrible**
If you were to spend the rest of your life with your urinary condition just the way it is now, how would you feel about that?	**0**	**1**	**2**	**3**	**4**	**5**	**6**

LUTS – Update on evaluation

- Validated questionnaire to confirm your diagnosis
- To evaluate the severity of LUTS
- To evaluate disease progression over time
- International Prostate Symptom Score (IPSS) ; AUA symptom Index
- PSA – Not just for assessment for prostate cancer
- PSA – can indicate prostate volume
- PSA – can indicate BPH progression when LUTS worsen over time

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LUTS – Alpha Blockers

- Tamsulosin (Flomax®, Flomax-CR®) 0.4-0.8 mg
- Alfuzosin (Xatral®) 10 mg
- Silodosin (Rapaflo®) 8 mg
- Doxazosin and Terazosin are non-selective alpha-blockers for prostate
- Dizziness, hypotension, ejaculatory dysfunction, floppy iris syndrome

LUTS – 5-Alpha Reductase inhibitors

- Finasteride (Proscar®) 5 mg
- Dutasteride (Avodartl®) 0.5 mg
- 4-6 months before LUTS improvement
- ↓PSA by 50%
- Side effects on libido and ejaculatory function

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LUTS – Anticholinergics

- For storage symptoms to relax the bladder to improve compliance
- Oxybutynin
- Solifenacin (Vesicare®) 5-10 mg
- Tolterodine (Detrol®) 4 mg
- Fesoterodine (Toviaz®) 4-8 mg
- Darifenacin (Enablex®) 7.5-15 mg
- Trospium 20-60 mg
- Dry mouth, constipation, drowsiness,

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LUTS – beta agonist

- For storage symptoms to relax the bladder to improve compliance
- Mirabegron (Myrbetriq®) 25-50 mg
- Hypertension
- Much more tolerable than anticholinergics
- Cost issue

LUTS – PDE5-I

- Tadalafil (Cialis®) 5 mg QD
- Mechanism of action?
- Cost issue

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LUTS – Surgeries and minimally invasive procedures

- TURP
- Retropubic prostatectomy
- HoLEP, GreeLight vaporization
- TUIP – incision of prostate
- TUMT (microwave therapy)
- Urolift®
- Rezum® (Water vapor ablation)
- Aquablation® (Waterjet ablation)
- Prostatic artery embolization)

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CASE 1

Mr. P. is a 65 year-old previously healthy man with a family history of bladder and prostate cancers. He has a history of dyslipidemia and DM-II, both are well controlled with statin and metformin. He has been on alpha-blocker (tamsulosin CR) for the past five years for LUTS. However, over the past 6 months, he complains of worsening of LUTS with increased frequency, hesitancy and nocturia x 3.

His prostate exam revealed an enlarged, benign prostate. His urinalysis and urine culture were negative. His PSA this year was 3.7 (was 2.1 in 2018 and 2.8 in 2020). His IPSS symptom scores revealed significant bother by his LUTS.

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CASE 1

You suspect a progression of his BPH leading to his worsening LUTS. You added a 5-alpha reductase inhibitor (dutasteride) and will see him back in 6 months.

Six months later, his nocturia reduced to once a night with a significant reduction in his IPSS symptoms scores.

His repeat PSA is now 3.9 (from 3.7) and urinalysis remains negative. What is your next step of action?

1. Urology consultation
2. Keep current treatment with a follow-up in 1 yr
3. Repeat PSA
4. Stop tamsulosin and keep only dutasteride

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KEY MESSAGES – CASE 1

- BPH is one of the most common causes of LUTS in aging men
- LUTS due to BPH progresses with age
- Reevaluation of CV, renal and metabolic status along with a trial of life-style modification
- Medical management is effective in managing LUTS progression due to BPH progression
- Option: combining alpha-blocker with 5ARI
- Options: combining alpha-blocker with OAB meds (e.g. solifenacin 5 mg)
- Options: switching within same class of drug (e.g. tamsulosin → silodosin).

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KEY MESSAGES – CASE 1

- The use of 5ARI can reduced PSA level by ~50%.
- His PSA went from 2.1 → 2.5 → 3.7 → (5ARI) → 3.9
- He has a positive family history of prostate cancer
- This presentation warrants further evaluation to rule out prostate cancer
- Repeat PSA and DRE should be performed. If PSA remains high, a urological consultation should be arranged.
- PSA, DRE and prostate cancer risk assessment has been under-utilized in recent years

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PROSTATE CANCER SCREENING

- Controversial topic in Urology
- Prostate cancer is very common – 3rd leading cause of cancer-related death
- Prostate cancer is heterogeneous: from indolent to life-threatening
- "Over" diagnosis and treatment lead high risk of morbidity, mortality and costs.
- PSA screening should be offered to men with life expectancy > 10 yrs (up to age 70), starting age 50 (45 for high risk men)
- Pt's decision to have PSA done should be individualized after being counseled for the risks and benefits (shared decision-making model)

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CASE 2

Mr. J is a 55 year-old healthy man. He was diagnosed with LUTS and was placed on finasteride for the past year.
His LUTS, including weak stream, frequency and hesitancy all improved but he complained of decreased libido and erectile dysfunction for the past 3 months. He tried PDE5Is which helped only his ED but not the libido. His lab investigations including PSA, UA, serum total testosterone were all within normal limits.

1. Urology consultation
2. Testosterone supplement
3. Switch finasteride to dutasteride
4. Switch finasteride to an alpha-blocker

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CASE 2

Six months after discontinuing finasteride, his libido returned and his sexual function improved. However, he is suffering from LUTS with significant bother in his IPSS symptom scores. Otherwise, his lab evaluations were within normal limits.
He wants something to be done. Which of the following would you offer?

1. Urology consultation
2. Restart 5AR-I
3. Trial of saw palmetto
4. Trial of alpha-blocker

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CASE 2

He tried saw palmetto for 6 months with no significant benefits. He started taking tamsulosin and his LUTS were much improved 2 months after. However, he returned to your office with a new complain of “dry” ejaculation.

What would you recommend?

1. Urology consultation
2. Trial of pseudoephedrine
3. Tell him to get used to it
4. Switch to another alpha-blocker

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CASE 2

You switch his tamsulosin to alfuzosin and his ejaculation returned after 2 months.

He is once again a happy man!

KEY MESSAGES – CASE 2

- 5ARIs is associated with depression and sexual dysfunction
- Decreased in libido, ejaculatory dysfunction and erectile dysfunction
- Those with low or low-normal T levels are more prone to these sexual adverse events
- Takes a few months to develop these adverse events
- Switching drugs within same class has no benefits
- Possible improvement upon discontinuation for months. However, a subset of patients never regain their sexual function
- Trial of testosterone replacement have variable success in ameliorate these adverse events.

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KEY MESSAGES – CASE 2

- Alpha-blockers has no significant adverse events on erection and libido
- Anejaculation (not retrograde ejaculation) is very common with alpha-blockers
- Some aging men with infrequent sexual activity may not be bothered by it
- Some may believe it is less “messy” – but most younger patients who are sexually active are bothered by it
- Among the choices of prostate-selective alpha-blockers, alfuzosin has the lowest incidence of anejaculation. Hence switching to another alpha-blockers can be an options

KEY MESSAGES – CASE 2

- What if his anejaculation persists with other alpha-blockers??
- Does he have to live with his problems?
- Can any surgery help?
- Phytotherapies (e.g. saw palmetto, Af plum bark, stinging nettle) ?
- Phytotherapies are not recommended by current guidelines due to their lack of efficacy, inconsistent formulation, and potential drug interaction.
- One other option to manage his LUTS is to use tadalafil 5 mg QD. It may also improve his sexual function. Cost, however, is a major barrier.

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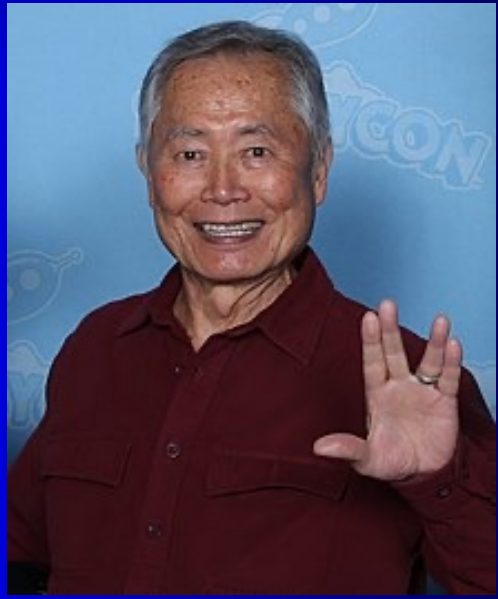
CASE 3

Mr. S is a 78 year-old man on medications for metabolic syndrome. He has been on flomax and dutasteride for over 5 years for LUTS. He recently complains of worsening of LUTS with increased frequency, urgency and nocturia x 3.
His physical exam including vitals signs, abdominal and DRE were normal.
His lab evaluation including urine culture, Cr, HbA1c were within normal limits.
You tried to double his flomax dosage for months with minimal benefits. What is your next step of management?



1. Urology consultation
2. Testosterone supplement
3. Switch to another alpha-blocker
4. Add an anti-cholinergic med

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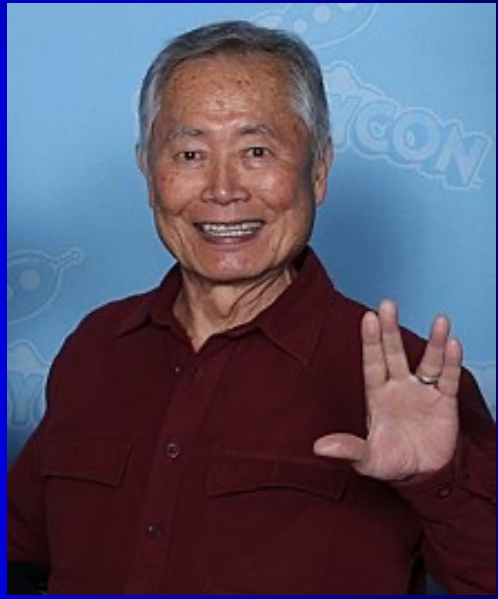
CASE 3

He was prescribed oxybutynin but he could not tolerate the side effects.
You changed his oxybutynin to solifenacin 5 mg. He experienced improved frequency and urgency.
The side effects were still bothersome but much more tolerable. He asks if he can increase his solifenacin to 10 mg. You would:



1. Suggest Urology consultation
2. Proceed with 10 mg solifenacin
3. Refuse to increase due to risk of retention
4. Change to another OAB med

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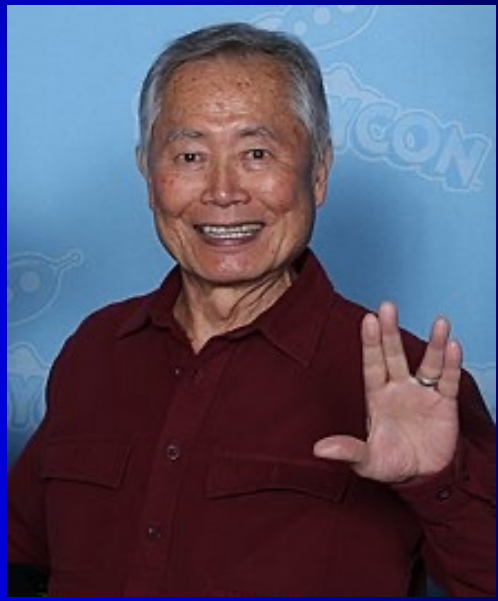
CASE 3

Though his LUTS improved significantly at 10 mg solifenacin, he cannot tolerate the side effects.
Six months after, he returns to your office with the same complaints of LUTS. His lab investigations were normal except his urinalysis showed microscopic hematuria.



You would:

1. Switch solifenacin to mirabegron
2. Repeat urinalysis
3. Obtain imaging study of abdo/pelvis
4. Consult urology

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KEY MESSAGES – CASE 3

- When dealing with worsening of LUTS, attempt should be made to distinguish voiding vs storage symptoms
- Worsening of voiding symptoms (hesitancy, weak stream, incomplete emptying, retention) suggest outlet obstruction (prostatic urethra, urethra, bladder outlet)
- Worsening of storage symptoms (urgency, frequency, nocturia) suggest bladder compliance or capacity issues
- Alpha-blockers and 5ARIs aim to relieve outlet obstruction, which, over time, can improve storage symptoms
- Worsening of voiding symptoms despite maximal medical therapy for outlet obstruciton (e.g. combo of alpha-blocker with 5ARIs) may require further evaluation for surgical intervention

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KEY MESSAGES – CASE 3

- In this case, his worsening of LUTS was mainly due to increased storage symptoms. Thus antimuscarinics or beta-3 agonists can be used
- Risk of retention is low in the absence of significant outlet obstruction or high post-void residual volume (>300 cc)
- While progression of BPH is a common cause of worsening of LUTS, assessment to rule out other causes should be performed
- The presence of microscopic hematuria requires further evaluations of the GU tract

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SUMMARY

- Many new options of medical and surgical therapies are available for the management of LUTS
- Clinicians should be aware of the latest development of clinical guidelines in the management of LUTS
- Many complex cases of LUTS can be evaluated and well managed at the primary care level
- Ruling out underlying hematuria, active infectious and inflammatory conditions, changes In cardiovascular and metabolic status is the key initial step of evaluation for most complex cases of LUTS
- Urological consultation should be considered in complex cases refractory to medical management or when further assessments of voiding mechanics are required

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