

“Pills and Leaks”

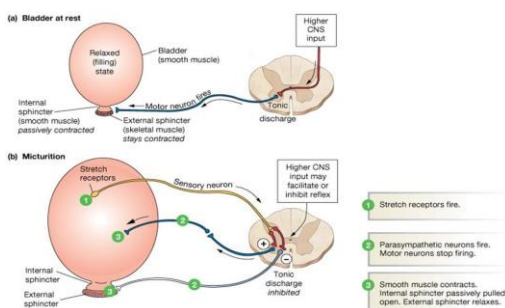


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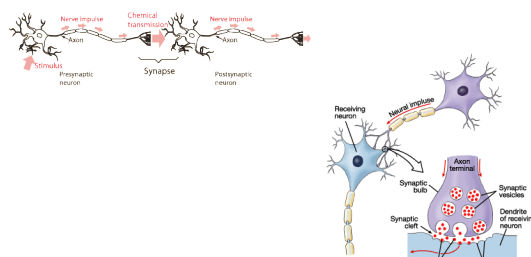
Assessment

- A good assessment is the key to successful treatment
- Treat the symptoms that bother the person the most – as this will increase their QOL
- Manage patient expectations

Functions of the bladder

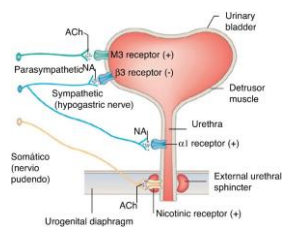


Neurotransmitters



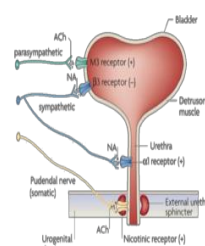
Role of Neurotransmitters in the Bladder

- Main neurotransmitter in storage phase - norepinephrine
- Activates adrenergic receptors in bladder muscle and internal sphincter (β_3 and α_1) – relax the bladder and close the internal sphincter



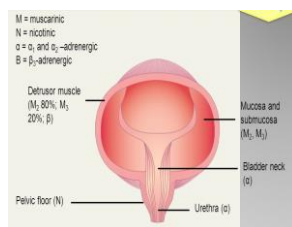
Role of Neurotransmitters in the Bladder

- Main neurotransmitter in voiding phase - acetylcholine
- Muscarinic receptor function mediated by acetylcholine – controls contraction of detrusor muscle and relaxation of internal sphincter muscle
- Purinergic receptors (P2X₃) are mediated by adenosine triphosphate (ATP) and sense bladder fullness for voiding



Muscarinic receptors

- Muscarinic receptors – subtypes M_2 and M_3 predominant
- M_3 important for normal bladder contractions
- M_2 may play more prominent role in certain disease states
- Binding of acetylcholine to M_3 on detrusor activates signalling → bladder contraction and voiding



Overactive bladder

- A problem with bladder storage function that causes a sudden urge to urinate.
- The urge may be difficult to suppress, and overactive bladder can lead to the involuntary loss of urine (incontinence).

Medication options – OAB

Antimuscarinic/Anticholinergic drugs first choice

- Choices:
- Darifenacin
- Fesoterodine fumarate
- Flavoxate Hydrochloride
- Oxybutinin Hydrochloride
- Propiverine Hydrochloride
- Solifenacin succinate
- Tolterodine tartrate
- Tropsium chloride

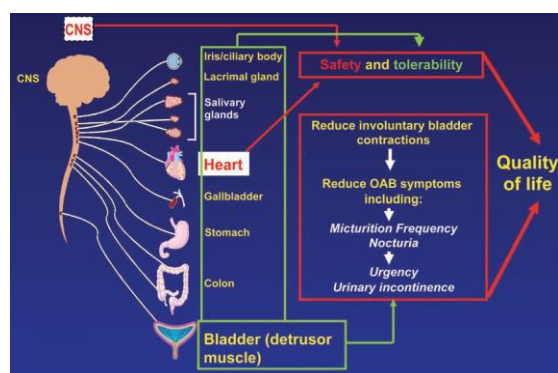
Mode of action

- Acetylcholine main neurotransmitter in bladder
- Drugs are competitive antagonists within smooth muscle
- Inhibiting micturition
- Some are M_3 selective – darifenacin
- Others are non-selective – oxybutynin, tolterodine

BETA₃ Adrenoceptor Agonists

- Mirabegron (Betmiga- MR) - potent and selective beta 3-adrenoceptor agonist → relaxation of bladder smooth muscle
- Side effects: GI disorders, ↑Blood pressure
- Mirabegron should be offered if 'antimuscarinics' do not work, if they are not suitable, or their side effects are unacceptable
- Combination therapy an option for anticholinergic-resistant neurogenic bladder

Side effects



Alternatives??

- **Atropine** – not used due to side effects
- **Flavoxate** - scarce clinical evidence of effectiveness
- **Propantheline** –non-selective –effects not well documented
- **Imipramine** – antidepressant with anticholinergic side effects – not recommended due to side effects especially cardiac)

How do you choose?

- Take into account pre-existing conditions
- Use of other anticholinergic medications
- Risk of adverse effects and common side effects
- Also consider
 - The likelihood of success
 - Frequency and route of administration
 - Some adverse effects may indicate treatment is starting to have an effect
 - May not see full benefit for 4 weeks

NICE (2013) Women's Incontinence and NICE (2010) LUTS in Men

- Do not use flavoxate, propantheline and imipramine for the treatment of UI or OAB
- Do not offer oxybutynin to frail older people
- First choice:
 - Oxybutynin (IR)
 - or Tolteradine (IR)
 - or Darifenacin (OD)
- Transdermal option
- Mibegron

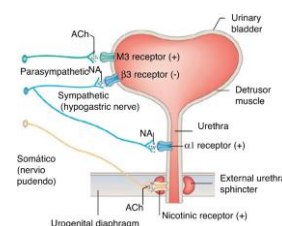
Stress incontinence

- Duloxetine – inhibits the reuptake of serotonin and norepinephrine – increases sphincter muscle activity during bladder filling/storage
- Moderate to severe stress incontinence

High withdrawal rates in studies

Therefore:

- **Not recommended** as first-line or second line treatment for women with predominant stress UI.
- Should only be offered if drug treatment is preferred, or surgery is not suitable.
- Counsel women about adverse effects. (NICE 2013)

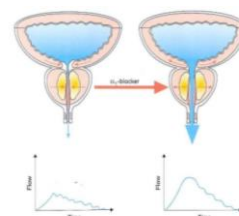


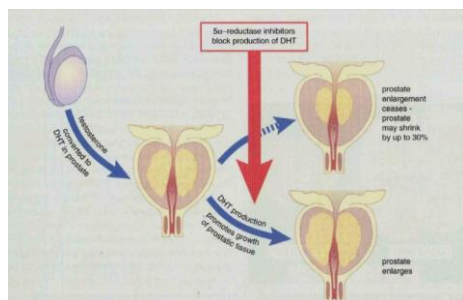
Bladder Outflow Resistance



Alpha-1a blocker

- The smooth-muscle tension is mediated by the alpha-1-adrenergic receptors.
- Alpha-1a receptor is most specifically concentrated in the bladder neck and prostate.
- Alpha-adrenergic receptor–blocking agents should decrease resistance along the bladder neck, prostate, and urethra by relaxing the smooth muscle and allowing passage of urine.





5-alpha reductase inhibitor

Men with LUTS who have prostates estimated to be larger than 30 g or a PSA level greater than 1.4 ng/ml

Alternative Therapies for BPH

- **Saw Palmetto** – a herbal remedy that comes from a type of palm tree.
- **Beta-sitosterol** - a mixture taken from different plants that contain cholesterol-like substances called sitosterols.
- **Pygeum** - from the bark of the African plum tree. Can cause stomach upset.
- **Rye Grass Pollen Extract** - from three types of grass pollen — rye, timothy, and corn.
- **Stinging Nettle** - sometimes used in combination with other natural BPH remedies, such as pygeum or saw palmetto. Side effects from nettle are usually mild, including upset stomach and skin rash

Nocturia

- Before treatment distinguish cause:
 - global polyuria
 - nocturnal polyuria or nocturnal urine overproduction
 - bladder storage problems, or decreased nocturnal bladder capacity (NBC)
 - mixed

Every patient of nocturia does not need treatment
Most people do not seek treatment for 1-2 times of nocturia

Nocturia

- Desmopressin – only available antidiuretic drug
- Treatment with desmopressin in the elderly requires careful monitoring of serum sodium concentration
- Diuretics given during the late afternoon or early evening may help to decrease third spacing of fluid and reduce nocturnal polyuria
- Treat associated OAB with anticholinergic medications

Considerations for all patients

- Polypharmacy/polymedicine
- Side effects
- Cautions

Patient information

- What is the medication for
- Frequency and route
- How long will it take to work
- Potential side effects
- How long will I take these for
- Monitoring/review requirements



THANK YOU FOR LISTENING

ANY QUESTIONS?