University of Anbar
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Therapeutic I, 5th stage
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Urinary incontinence & BPH

1-*Urinary incontinence* (UI) is the complaint of involuntary leakage of urine. It occurs as a result of overfunctioning or underfunctioning of the urethra, bladder, or both.

Types and Pathophysiology

1- Urethral underactivity is known as **stress** UI (SUI) and occurs during activities such as **exercise, lifting, coughing, and sneezing**. The urethral sphincter no longer resists the flow of urine from the bladder during periods of physical activity.

2- Bladder overactivity is known as **urge UI** (UUI) and is associated with increased urinary **frequency and urgency**, with or without urge incontinence. The detrusor muscle is overactive and contracts inappropriately during the filling phase.

3-Urethral overactivity and/or bladder underactivity is known as **overflow incontinence.**

Common causes of urethral overactivity include **benign prostatic hyperplasia** ,**prostate cancer and**, in women, **cystocele formation**

4- Mixed incontinence includes the combination of **bladder overactivity** and **urethral underactivity.**

5-Functional incontinence is not caused by bladder- or urethra-specific factors but rather occurs in patients with conditions such as **cognitive or mobility deficits.**

Clinical presentation

Signs and symptoms of UI depend on the underlying pathophysiology.
Patients with **SUI** generally complain of **urine leakage** with physical activity, whereas those with **UUI** complain of **frequency**, **urgency**, **high-volume incontinence**, and **nocturnal incontinence.**

Diagnosis

A complete medical history, physical examination (ie, abdominal examination to exclude distended bladder, pelvic examination in women looking for evidence of prolapse or hormonal deficiency, and genital and prostate examination in men), and brief neurologic assessment of the perineum and lower extremities are recommended.

Treatment

NONPHARMACOLOGIC TREATMENT

is first-line treatment for UI , which include

1- Lifestyle modifications

2- Toilet scheduling regimens

3- Pelvic floor muscle rehabilitation

Goals of Treatment:

Restoration of continence, **reduction in the number of UI episodes**, and **prevention of complications.**

A: Bladder Overactivity: Urge Urinary Incontinence

OXYBUTYNIN

Oxybutynin immediate-release (IR) is the drug of first choice for UUI and the **"gold standard"** against which other drugs are compared.

Adverse effects due to:

Antimuscarinic effects (eg, dry mouth, constipation, vision impairment, confusion, cognitive dysfunction, and tachycardia)

α-adrenergic inhibition (eg, orthostatic hypotension),

histamine H_1 inhibition (eg, sedation and weight gain).

- Optimize tolerability of oxybutynin IR by initiating therapy with **low dose .**
- Oxybutynin transdermal system (TDS) has similar efficacy but is **better tolerated** than oxybutynin IR presumably because this route avoids first-pass metabolism in the liver, which generates the metabolite thought to cause adverse events, especially **dry mouth.**

Tolterodine

competitive muscarinic receptor antagonist, is considered first-line therapy in patients with **urinary frequency**, urgency, or urge incontinence.

It undergo hepatic metabolism , so **it has interactions** with fluoxetine, sertraline, fluvoxamine, macrolide antibiotics, azole antifungals, and grapefruit juice.

- most common adverse effects include dry mouth, dyspepsia, headache, constipation, and dry eyes.
- Fesoterodine fumarate is a prodrug for tolterodine and is considered an alternative first-line therapy.

Solifenacin succinate and darifenacin

are second-generation antimuscarinic agents. Both have been shown to improve quality-of-life domains. Drug interactions are possible if CYP 3A4 inhibitors are given with solifenacin.

Mirabegron

is a β3-adrenergic agonist alternative to anticholinergic/ antimuscarinic drugs for managing UUI. It has modest efficacy as compared with placebo.

- **Hypertension**, **nasopharyngitis**, **urinary tract infection**, and **headache** were the most common adverse effects reported.

B:Urethral Underactivity: Stress Urinary Incontinence

ESTROGENS :

Historically, **local and systemic** estrogens have been the mainstays of pharmacologic management of SUI.

Duloxetine

It is a dual inhibitor of serotonin and norepinephrine reuptake indicated for depression and painful diabetic neuropathy.

Duloxetine is thought to Facilitate the bladder- to-sympathetic reflex pathway, increasing **urethral and external Urethral sphincter muscle tone** during the storage phase.

2- ***Benign Prostatic Hyperplasia***

The precise pathophysiologic mechanisms that cause BPH are not clear. both **intraprostatic dihydrotestosterone** (DHT) and **type II 5α-reductase** are thought to be involved.

Obstructive signs and symptoms result when dynamic and/or static factors reduce bladder emptying. Patients experience urinary **Hesitancy** , **urine dribbles out** and the Bladder **feels full even after voiding.**

Irritative signs and symptoms are Common and result from long-standing Obstruction at the bladder neck. Patients experience **urinary frequency, urgency**, and **nocturia.**

Goals of Treatment: The goals are

1- To control symptoms

2- Prevent progression of complications

3- Delay need for surgical intervention.

Management options include watchful Waiting , drug therapy, and surgical intervention.

The choice depends on **severity of signs and symptoms** , which include

A: α-Adrenergic Antagonists

α-Adrenergic antagonists relax smooth muscle in the prostate and bladder neck , increasing urinary flow rates. **Ex : Prazosin, terazosin, doxazosin, and alfuzosin** .

Adverse effects include **first-dose syncope, orthostatic hypotension, and dizziness**.

Alfuzosin is less likely to cause cardiovascular adverse effects than other second-generation agents.

Tamsulosin and silodosin are third-generation α1-adrenergic antagonists, are **selective** for prostatic α1A-receptors. Therefore, they **do not cause** peripheral vascular smooth muscle relaxation and associated hypotension.

B: 5α-Reductase Inhibitors

5α-Reductase inhibitors interfere with the stimulatory effect of testosterone. These agents slow disease progression and decrease the risk of complications. **Ex :Dutasteride , finasteride**. Measure prostatic specific antigen (PSA) at baseline and again after 6 months of therapy. If PSA does not decrease by 50% after 6 months of therapy in a compliant patient, evaluate the patient for **prostate cancer.**

C: Phosphodiesterase Inhibitors

Increase in cyclic GMP by phosphodiesterase inhibitors (PI) may relax Smooth muscle in prostate and bladder neck. Its effectiveness may be result of **direct Relaxation of detrusor muscle of bladder.**

Ex:Tadalafil 5 mg daily improves voiding symptoms but does not increase urinary flow rate or reduce PVR urine volume.