Pharmacology in Urinary Incontinence
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An understanding of the neurological control and the involved neurotransmitters are important when studying the pharmacology in urinary incontinence. The bladder and urethra are controlled by the parasympathetic (S2-4), sympathetic (T10-L2) and somatic (S2-4) nerves. For the parasympathetic efferent system, the neurotransmitters include acetylcholine in the detrusor neuromuscular junction and nitric oxide in the smooth muscle urethral sphincter. The receptors on the detrusor muscle are mainly M2 (75%) and M3 (25%). For the sympathetic efferent system, the neurotransmitter is noradrenaline and the receptors are α1 at smooth muscle urethral sphincter and β3 at the detrusor muscle. For the somatic efferent system, the neurotransmitter is acetylcholine and the receptor is nicotinic at the striated muscles of urethral sphincter and pelvic floor. Neurotransmitters involved in the spinal cord and brain include acetylcholine, noradrenaline, glutamate and serotonin. Since the neurotransmitters and receptors are not specific to a tissue or organ, disturbance of the bladder control is a common side effect for many drug treatments.

The mainstay treatment for OAB/DO is anti-muscarinic agents. They act as competitive inhibitors by blocking the M3 and M2 receptors responsible for detrusor contraction. M2 and M3 receptors are also found in the urothelium and suburothelium and anti-muscarinic agents may also play a role in suppressing the afferent pathway for DO. Anti-muscarinic agents can be divided into two groups: tertiary and quaternary amines. Tertiary amines (e.g. oxybutynin, tolterodine, solifenacin and darifenacin) are easily absorbed from the gastrointestinal tract and also readily cross the blood brain barrier which may cause cognitive impairment. They are usually metabolized by cytochrome P450 system in the liver and so have many drug-drug interactions. Quaternary amine (e.g. Trospium) are poorly absorbed from the gastrointestinal tract but would not cross blood brain barrier and so would not cause CNS side effects. They are excreted unchanged by the kidney and so very few drug interaction problems. Local treatment by intravesical instillation is an effective way to eliminate the systemic side effects but convenience and acceptability is a problem.

Other drugs used for treating OAB/DO include: calcium channel blockers, potassium channel openers, β3-agonists, purinergic receptor blockers, tricyclic antidepressant, baclofen, opioids, gabapentin, prostaglandin inhibitors, botulinum toxin injection, capsaicin and resiniferatoxin instillation.

Drug treatment for stress incontinence aims at increasing the urethral sphincter closure pressure and include: α1-adrenergic agonists, β-blockers, β2-agonists, tricyclic antidepressants and selective serotonin and noradrenaline reuptake inhibitors.

Drug treatment for voiding dysfunctions aims at reducing the outflow resistance (α1-blockers, skeletal muscle relaxants and botulinum toxin injection into urethral sphincter) and increasing the detrusor contractility (muscarinic receptor agonists and cholinesterase inhibitors).