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PHARMACOLOGICAL MANAGEMENT OF OVERACTIVE BLADDER

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ABSTRACT

Patients' quality of life is greatly impacted by overactive bladder (OAB), a chronic urological condition marked by urgency, frequency, nocturia, and urge incontinence. Overactive Bladder occurs due to fragile hip diaphragm, injury to nerve fibers, UTI, excise weight, and postmenopausal condition. The bladder contracts leading to a strong desire to urinate, although bladder is not completely filled. These symptoms occur due to detrusor muscle overactivity or bladder hyperactivity, leading to involuntary contractions of the bladder during the filling phase. Some individuals with OAB may experience difficulty in initiating urination, asymptom called hesitancy.

Keywords: Overactive bladder; Urination; (PEO); Urine; Nocturia; Miragebron.

1. INTRODUCTION

This ailment is characterized by an uncontrolled need for urination, where frequency of urination is generally increased with or without urinary incontinence and nocturia. It causes poor sleep and interferes with the normal daily schedules and may also lead to anxiety and depression. In US, 16% of men and 16.9% of women were suffering from Overactive Bladder and the prevalence rate was increased with increase in patient's age (> 40 years); other factors like family history and hygiene also contributes to this. The distribution of dry and wet Overactive Bladder in females was 7.6% and 9.3% respectively. It was 13.6% and 2.6% in males[1].

Overactive Bladder occurs due to fragile hip diaphragm, injury to nerve fibers, UTI, excise weight, and postmenopausal condition. The bladder contracts leading to a strong desire to urinate, although bladder is not completely filled[2].

2. Clinical presentation of overactive bladder (OAB)

These symptoms occur due to detrusor muscle overactivity or bladder hyperactivity, leading to involuntary contractions of the bladder during the filling phase. The severity of OAB symptoms can vary among individuals, but the condition typically presents with the following hallmark symptoms:

Urgency

Urgency is the most prominent and defining symptom of OAB. It refers to the sudden, strong need for urination that cannot be suppressed and often occurs even when the bladder is not full. It is important to differentiate urgency from incontinence, as some individuals may feel the urge without actually experiencing leakage of urine, while others may have urgency combined with incontinence[3].

Frequency

Frequency in context to OAB refers to the need to urinate more than eight times during the day, and may also include nighttime urination (nocturia). This occurs as the bladder contracts more often than normal, leading to

a frequent need to empty it. The individuals with OAB feel the need to urinate multiple times within a short period, often resulting in interrupted daily activities[4].

Nocturia

Nocturia is the need to wake up at least once or twice during the night to urinate. It is a common symptom in individuals with OAB and is often associated with disrupted sleep. Nocturia can significantly impact quality of life, leading to fatigue, poor sleep, and impaired daytime functioning[5]. It may occur due to bladder hyperactivity during the night, or it may be influenced by other factor such as fluid intake or underlying medical conditions.

Accidental urine leakage

It is the most common feature of OAB. Several forms of incontinence can occur in OAB:

Urgency incontinence: The sudden and strong urgetourinate is so intense that it results in leakage of urine before the individual can reach a toilet. This is a hallmark of OAB[6].

Daytime incontinence: In some cases, individuals may experience urine leakage during the day due to uncontrolled bladder contractions, despite the presence of urgency.

Nocturnal enuresis: Some individuals with OAB experience leakage during sleep, especially if they have nocturia and are unable to wake up in time to void.

Hesitancy and delayed voiding

Some individuals with OAB may experience difficulty in initiating urination, asymptom called hesitancy. This occurs because of impaired coordination between the detrusor muscle and the urethral sphincters, which can delaythe start of urination. It is more commonly associated with bladder outlet obstruction, but can also be present in OAB due to altered neurogenic regulation of the bladder and urethra[7].

Sensation of incomplete bladder emptying

Individuals with OAB may report the sensation that their bladder is not fully emptied after urination. This sensation of incomplete emptying can lead to repeated voiding, further contributing to the sense of urgency and frequency. This symptom may overlap with other conditions such as bladder outlet obstruction or urinary tract infections (UTIs), so careful evaluation is necessary.

Urinary retention (less Common)

In some cases, OAB can be associated with urinary retention, particularly in neurogenic bladder or when there is bladder under activity. Individuals may feel as though they are unable to completely evacuate their bladder, which causes a combination of urgency and retention[8]. This may result in an increased frequency of urination, as the bladder is unable to store urine efficiently.

Associated symptoms

Pelvic pain: Although less common, some individuals with OAB may experience pelvic discomfort or pain. This could be due to the frequent bladder contractions or an underlying condition such as interstitial cystitis.

Urgency associated with physical activities: Some individuals may experience urgency when engaged in activities like lifting, exercising, or coughing. This can further impair daily activities and reduce quality of life[9].

Influence on daily routine

The clinical presentation of OAB considerably influences individual's daily routine. The OAB signals that causes an uncontrolled desire for urination and even leakage can lead to social embarrassment, anxiety, and avoidance of certain activities. Individuals with confidence, reduced self-esteem, and social isolation due to the unpredictable nature of symptoms. Additionally, nocturia and urgency in continence may result in sleep disturbances, leading today time fatigue and a reduced ability to focus on daily tasks[10].

3. Causes of overactive bladder (OAB)

Causes of OAB varies with its types and it depends on several factors associated with structure, physiology or neurons-related, or can be environmentally linked. The ultimate cause is the

uncontrolled behavior of bladder due to improper functioning of detrusor muscle and the associated nerves. Presence of disease and lifestyles can further contribute to OAB. The actual cause of OAB is still not completely understood. In order to treat OAB effectively, the timely and proper diagnosis and its causative factor must be known[11,12].

Neurological causes of OAB

It is mainly caused due to neurological disturbances**.** Bladder contraction and dilation is caused by the cortex and the micturition center of brain, any damage to this area causes the OAB symptoms. Strokes, multiple sclerosis and Parkinson's affect brain or spinal cord region and impair the nerve[13]

communication that controls the activity of detrusor muscles. Pelvic nerve injury and damage to sacral spinal cord also leads to OAB. Aging and enlarged prostate also contribute to OAB symptoms.

Diabetic neuropathy

In patients suffering from diabetes mellitus, maintenance of high blood sugar level for longer duration leads to nerve damage and can cause OAB[14].

Autonomic dysfunction

Disorders that affect the autonomic nervous system, such as autonomic neuropathy, can also impair bladder function. The autonomic nerves are responsible for regulating bladder contraction and relaxation.

Musculo skeletal and structural uses

OAB may be caused by structural and anatomical abnormalities in the urethra, pelvic floor muscles and bladder. OAB symptoms are mostly influenced by the relationship between pelvic floor support and bladder muscle tone[15]. Pelvic floor injuries in women who have given birth vaginally might result in weak pelvic muscles and problems controlling their bladder. Atrophy of pelvic floor muscles and tissues can result from hormonal changes after menopause, especially decreasing estrogen levels, which lowers bladder support and raises the risk of OAB. Urgency and incontinence can result from strain on the bladder that can cause a medical condition where uterus or bladder falls into the vaginal canal.

Bladder outlet obstruction

It can occur due to enlarged prostate in men (benign prostatic hyperplasia, BPH). This obstruction increases the pressure in the bladder, which can lead to bladder over activity and OAB symptoms. The bladder may contract involuntarily as a compensatory mechanism to overcome the obstruction, resulting in symptoms of urgency and frequency[16].

Bladder cancer or tumors

Bladder tumors, whether benign or malignant, can irritate the bladder and lead to symptoms similar to OAB. Tumors can cause inflammation of the bladder wall, increase bladder sensitivity, and result in urgency and frequency[17].

Inflammatory causes

While OAB symptoms caused by UTIs typically go away after treatment, but recurrent or chronic

UTIs can lead to long-term bladder dysfunction. Urinary tract infections (UTIs) can irritate the bladder lining, causing urgency, frequency, and occasionally incontinence. An underlying reason in some patients is 'Interstitial cystitis' an inflammatory bladder wall disorder that produces pain, urgency, and frequency. It frequently coexists with OAB. Chronic bladder irritation or inflammation, sometimes brought on by food, beverages, or medications, is known as irritable bladder syndrome. It causes hypersensitivity with increased urgency, frequency, and discomfort.

Hormonal and age-related factors

It is one of the biggest risk factors for OAB since with aging the detrusor muscle becomes more irritable and the bladder's ability to hold urine tends to decline, which increases contractions and causes OAB symptoms. According to Wllsworth (2009), age-related alterations in the neural system may also cause older persons to lose neurological control over their bladder. Hormonal changes, reduced estrogen levels can modify the urethral function, pelvic floor muscles, and bladder lining, making the bladder more prone to over activity. Females after menopause and males suffering from decline in testosterone levels, enlarged prostate frequently suffer from OAB[18].

Behavioral and lifestyle factors

OAB is more common in obese people, since increase in fat in abdominal region creates pressure on bladder and affect its normal functioning. Obesity also leads to sleep apnea and diabetes that is another leading cause of OAB. Certain drugs, caffeine and alcohols that irritates mucosal lining of bladder, increases the urine production as well as OAB symptoms.

Psychological factors

Psychological triggers like stress and anxiety leads to the development of OAB symptoms-such as increased muscle spasms, bladder sensitivity, increase in frequency and urgency of urination.

4. Pathophysiology of OAB

OAB occurs due to any abnormality in the pathophysiology of urination, which a complex network between the brain, neurons, and bladder muscles. Any event in this complex network that impairs functioning of associated neurons, bladder muscles, emptying, and storage of bladder is expressed as OAB symptoms (e.g. urgency, frequency, and nocturia)[19].

Overactivity of detrusor muscles

During bladder filling in OAB, the detrusor muscle, which is incharge of urinating, contracts reflexively, creating urgency even at modest levels. Abnormal signaling within bladder nerves produces detrusor overactivity; neurogenic causes include diabetic neuropathy, multiple sclerosis, and stroke. Because a stiff bladder cause premature contractions, reduced bladder compliance, increases urgency even more.

Hyperactivity of bladder and sensory dysfunction

Normal bladder filling can seem uncomfortable or critical due to hypersensitivity of bladder sensory fibers. Involuntary voiding is caused by increased sensory activity brought on by inflammation or nerve injury. Through neuro plastic alterations,

chronic irritation causes central sensitization in the brain and spinal cord, intensifying urgency.

Decrease in supraspinal and cortical control

Involuntary bladder contractions are typically suppressed by higher brain regions like the frontal cortex and the pontine micturition center (PMC). Multiple sclerosis, Parkinson's disease, and stroke all cause damage to these regions, which impairs inhibition and coordination and results and urgency.

Altered functioning of ANS

Detrusor over activity is encouraged in OAB due to a disruption in this equilibrium caused by excessive parasympathetic drive or autonomic dysfunction (such as in diabetes, Parkinson's disease, or spinal injury).

Approaches for treatment of OAB

The ultimate aim of OAB treatment is to get relief from its symptoms including urinary urgency, incontinence and its frequency. The various treatment approaches includes:

5. Drugs used for the treatment of OAB

Drugs that are used to treat overactive bladder are Tolterodine tartrate, Oxybutynin chloride, Solifenacin succinate, Darifenacin, Fesoterodine fumarate and Mirabegron. Oxybutynin chloride is non- selective antagonist of muscarinic receptor and has numerous adverse effects like blurry eye-vision, dryness of mouth, constipation moreover sometimes decline in cognition, so patient discontinuation rate are very high. Solifenacin succinate, Darifenacin, Fesoterodine fumarate is M2 and M3 selective antimuscarinic drugs[20].

5.1 Marketed formulation of Mirabegron

Mirabegron is available as extended-release tablets in 25mg and 50mg dose. In US, mirabegron formulations are marketed as Detrol tablets, Ditropan XL tablets, Vesicar tablets, Toviaz tablets and Myrbetriq SR tablets. In India, mirabegron isavailable under the brand names of Vesibeta, Miratas, Mirakem and Miranix (USFDA).

5.2 Advantages of Mirabegron

In contrast to anticholinergics, β3-adrenergic agonists reduce urgency by relaxing the detrusor muscle during bladder filling.

Generally well tolerated: In the majority of trials, adverse events (TEAEs) like headaches, UTIs, and hypertension happen at rates comparable to placebo.

No signs of cognitive impairment in older persons and have shown similar efficacy and tolerability to younger adults.

Advantages of combination therapy: Compared to monotherapy, adding mirabegron to solifenacin improves symptom control without significantly increasing side effects.

Reduced events of constipation, dryness of mouth, cognitive risks which is crucial for elderly or fragile individuals.

5.3 Disadvantage of Mirabegron

Cost and availability: It is more expensive and the only β3 agonist accessible in some countries.

Limited safety data is available for average high-risk patient (FDA data).

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