

Wyoming Drug Utilization Review

Pharmacotherapy of Overactive Bladder

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When storage of urine and bladder filling cause inappropriate bladder muscle contractions, this is termed bladder overactivity or urge urinary incontinence (UUI).¹ More specifically, an overactive detrusor muscle results in contractions that occur while the bladder is filling. Overactive bladder occurs in the absence of another disease and is defined as: a symptom syndrome involving the need to urinate without delay; with frequent nocturnal and diurnal urinations; with or without urinary leakage.

Overactive bladder is usually idiopathic. Risk factors for UUI include: “normal aging, neurologic disease (including stroke, Parkinson’s disease, multiple sclerosis, and spinal cord injury) and bladder outlet obstruction (e.g. due to benign prostatic hyperplasia (BPH) or prostate cancer).”¹

Symptoms including urinary urgency and frequency are used to diagnose overactive bladder.¹ Urgency is the need to micturate immediately. A patient who urinates over eight times per day has urinary frequency. Urinary frequency and urgency can both contribute to incontinence. Patients with overactive bladder often experience enuresis and nocturia. These nocturnal symptoms can result in sleep loss. A great volume of urine can be lost during nocturnal incontinence episodes.¹

Several nonprescription treatment modalities with varying degrees of efficacy are available for treating overactive bladder.²⁻⁴ These include nonpharmacologic treatments such as timed

voiding, Kegel exercises, and biofeedback¹; the supplement chondroitin⁴. There are currently no over-the-counter medications that are FDA-approved for treatment of overactive bladder.² Diphenhydramine has been used to treat urinary incontinence but it is not FDA-approved for this indication and it should be avoided in patients with narrow-angle glaucoma, peptic ulcer, or urinary tract obstruction.⁵ This medication should only be used after thorough evaluation by a physician.⁵ NSAIDs have also been used to treat overactive bladder but there is little data supporting the efficacy of this treatment.⁶ This lack of OTC products probably exists because effective medications used to treat overactive bladder require diagnosis of the type of urinary incontinence⁵ and regular monitoring by a physician for efficacy and adverse effects⁷ such as urinary tract infection¹. Guidelines and literature reviews state that nonpharmacologic methods should be used prior to and in conjunction with antimuscarinics when treating urge incontinence. The efficacy of most recommended lifestyle changes has not been well-studied.

Antimuscarinics: Several antimuscarinic agents are approved by the FDA for the treatment of overactive bladder.⁸⁻¹⁰ These drugs include: oxybutynin, tolterodine, trospium, solifenacin, darifenacin, and fesoterodine. This class of drugs is considered first line therapy in the treatment of overactive bladder with oxybutynin and tolterodine the preferred agents. All of these medications have similar efficacy and adverse effect (AE) profiles with differences in the rates of AEs.⁸⁻¹⁰ Trospium is the only quaternary amine among the antimuscarinics used to treat overactive bladder; this characteristic decreases the risk of cognitive side effects.¹¹ Trospium is also the only drug in this class that is not significantly metabolized, therefore the risk for drug interactions is decreased with this medication.¹² However, trospium does interact with other medications that are eliminated via active tubular secretion and thus it should be used cautiously with these drugs.¹² At recommended starting doses, there is a reduced incidence of adverse effects with the long-acting formulations within this class compared to the short-acting counterparts.¹⁰ The newer medications are more selective for receptors in the bladder detrusor muscle.⁸ Patients may be advised to exercise, drink plenty of

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Cautious Use of Antibiotics

The Centers for Disease Control and Prevention (CDC) has published guidelines for the cautious use of antibiotics in pediatrics¹ and adults². These guidelines are available at the following websites:

<http://www.cdc.gov/getsmart/campaign-materials/pediatric-treatment.html>

<http://www.cdc.gov/getsmart/campaign-materials/adult-treatment.html>

In general, the CDC does not recommend routine prescribing of antibiotics for most cases of upper respiratory infections, including pharyngitis, rhinosinusitis, bronchitis, and otitis media (with the exception of acute otitis media).

A 2007 Cochrane review³ studied the evidence regarding delayed prescribing of antibiotics (providing the prescription, but advising to wait 48 hours before filling). There was no difference in most clinical outcomes for immediate, delayed and avoidance of antibiotics with the exception of those patients with acute otitis media, in which immediate antibiotics was more effective. For sore throat, the data appears mixed. In one study, immediate antibiotics were more effective and in another, there was no difference between the delayed antibiotic group and no antibiotic group in terms of symptom resolution. The review concluded that this strategy had little advantage over avoiding antibiotics in cases where it is safe to do so.

In 2009, Wyoming Medicaid spent \$1.36 million dollars on oral outpatient antibiotics. The table below provides details of utilization. The percentage of recipients with a respiratory infection, including the diagnoses listed above,

is estimated based on those who received an outpatient oral antibiotic and had a related diagnosis dated within the same week. It is not possible to exactly match prescription claims to diagnosis, however, this is thought to be a reasonable approximation. Insufficient data was available to make assumptions about those aged 60+ as most of this population received medications through Medicare Part D.

This information suggests that a significant portion of antibiotic prescribing may fall outside of the CDC's cautious antibiotic prescribing guidelines. The CDC's Get Smart: Know When Antibiotics Work website, www.cdc.gov/getsmart/, has a wealth of information on the topics of appropriate antibiotic use and antibiotic resistance, including printable handouts that can be used to educate patients.

Wyoming EqualityCare asks for your cooperation in the judicious prescribing of antibiotics so that our clients can receive the best treatment possible without the threat of antibiotic resistance or unnecessary utilization of medication.

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Wyoming Medicaid Antibiotic Utilization 1/1/09 - 12/31/09				
Age (decades)	Recipient Count	Rx Count	Total Dollars	% with URI diagnosis
000-9	15240	33498	\$849,491.99	54%
010-19	7383	13631	\$240,493.03	41%
020-29	3153	6311	\$102,734.03	32%
030-39	1642	3613	\$55,430.51	33%
040-49	831	2051	\$52,085.94	29%
050-59	622	1562	\$38,076.91	31%
060-69	261	680	\$17,799.28	insufficient data
070-79	6	13	\$84.31	insufficient data
080-89	9	25	\$385.05	insufficient data
090-99	7	12	\$173.37	insufficient data
Total	29154	61396	\$1,356,754.42	47%

fluids, eat more fiber and take a stool softener to reduce constipation while on these medications.¹² Major drug interactions include potent CYP3A4 inhibitors, which can increase levels of the antimuscarinics (except tiroprium) and therefore lower antimuscarinic doses should be used. Patients on antimuscarinics should be monitored for overactive bladder symptoms, and anticholinergic adverse effects. Antimuscarinics are contraindicated in patients with untreated narrow angle glaucoma, and bladder or gastrointestinal retention. Caution should be used in renal or hepatic impairment (except tiroprium), QT prolongation, and avoiding heat prostration with strenuous activity.¹²

Clinical guidelines do not state when to move to another treatment modality precisely, however clinical trials used to approve and compare these medications usually ran for twelve weeks¹⁰ therefore, this should be sufficient time to see efficacy and a decision to use an alternative treatment modality could be made at that time. According to a meta-analysis comparing placebo-controlled trials for efficacy, mean change in incontinence episodes per day ranged between -0.11 to -1.52 and mean change in urgency episodes per day ranged between -0.12 to -1.88.¹⁰ Therefore, realistic expectations of these medications should be communicated to patients.

No other agents are FDA-approved to treat overactive bladder, however, other agents can be tried if antimuscarinics are not effective despite minimal evidence supporting their use. The decision of which second line agent to move to is based upon comorbidities; TCAs are used for patients who are also depressed; topical estrogens are used for postmenopausal women with urethritis or vaginitis; alpha₁-blockers for men with BPH.¹ If these agents fail, guidelines recommend a thorough evaluation by a specialist and moving to a treatment modality based upon the underlying cause of overactive bladder symptoms including neurostimulation, sacral blockage, botulinum toxin, bladder augmentation or urinary diversion.¹³

Overactive bladder is a common, debilitating syndrome that can be partially managed with nonpharmacologic and pharmacologic treatment modalities.¹ The choice of therapy should depend upon patient age, concurrent medications, comorbidities, and ability to adhere to the prescription. If an agent fails to provide symptom relief that is noticeable to the patient within twelve weeks, another agent may be added on to therapy or switching to another agent should be considered. A thorough evaluation of the underlying causes of the symptoms should guide the choice of alternative treatment modalities.^{10,11}

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