Comorbidities Associated With Overactive Bladder

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Presentation Summary

Overactive bladder (OAB), defined as symptoms of frequency, urgency, and urge incontinence, that occur singly or in any combination in the absence of local pathologic or metabolic factors, is a highly prevalent disorder with an unknown etiology. Few risk factors for OAB have been elucidated through epidemiologic studies, and even less is known about the contribution of OAB to other morbidities. An overview is provided of the impact of OAB on other problems now known to coexist with OAB including falls and fractures, urinary tract and skin infections, sleep disturbances, and depression.

Overactive bladder (OAB) is a disorder of involuntary contractions of the detrusor muscles of the bladder characterized by symptoms of frequency, urgency, and urge or reflex incontinence that occur singly or in any combination. Although OAB is considered a highly prevalent disorder, its etiology remains unknown. Symptoms of OAB can have a profound effect on an individual's quality of life, causing his or her withdrawal from social life and physical activities.[1,2] OAB is expensive; in 1995, the total societal costs of incontinence alone for individuals 65 years of age or older was $26 billion.[3] In addition, many patients are often too embarrassed to seek professional treatment and choose instead to restrict activities of daily living, which contributes to difficulties in understanding the disease.

Several risk factors for OAB have been described, including advanced age, diabetes, and urinary tract infections (UTIs).[4] Not only are urinary incontinence and OAB conditions that can impair an individual's overall quality of life, but their presence can create additional health-related problems for the patient. For example, the cost of illness in OAB is heightened by comorbid conditions, including UTIs and skin infections.[3]

Increases in Falls and Fractures in Patients With OAB

Older men and women are plagued with a number of health problems, including cardiovascular disease, degenerative disease of the central nervous system, diabetes, and lower urinary tract symptoms. Women particularly are affected by osteoporosis and other conditions that may result from estrogen depletion. Some of these health problems contribute to falls and subsequent fractures that lead to marked morbidity and mortality. Hip fractures, in particular, are highly prevalent and costly among the

elderly.[5] Experiencing a fall, even without a corresponding fracture, can instill fear in elderly patients and cause them to restrict their activities of daily living, thereby adversely affecting their quality of life. Falls occur in 1 of 3 people 65 years of age and older, and hip fractures resulting from falls lead to the greatest number of health problems and death.[6] As a result, reducing the risk for falls is a primary goal for improving quality of life and reducing economic costs among the elderly.

Studies assessing the relationship between falls and fractures and urinary incontinence have yielded varying results. Some studies[7,8] have identified urinary urgency and incontinence as predictors of recurrent falls and fractures among the elderly, whereas other studies[9,10] have found no association between urinary urgency or incontinence and falls or fractures. A large, population-based survey of more than 10,000 women from 7 birth cohorts found a significant, independent correlation between urinary incontinence, a history of urinary incontinence, and UTIs and fractures after 30 years of age.[11] Another study determined that the odds ratio of hip fracture in urinary-incontinent elderly women was twice that of the general population.[12] The variability in the results of these studies can be explained by their failure to classify results according to the severity and type of incontinence.

A recent study sought to explore the relationship between OAB and the risk for falls and fractures among community-dwelling elderly women.[13] This prospective cohort study was conducted in more than 6000 women currently enrolled in an ongoing osteoporosis fracture cohort study. Unlike previous studies, it distinguished between stress and urge incontinence and identified episodes that occurred at least weekly as a clinically important frequency of incontinence. In a mean follow-up period of 3 years, 11,869 falls and 514 fractures occurred.

Using multivariate analysis, incontinence was independently associated with falls and fractures; women with weekly urge incontinence had a 26% greater risk of sustaining a fall and a 34% increased risk of fracture after adjusting for other causes (eg, age, frailty, poor overall health, and previous fall or fracture). More frequent incontinence was associated with increased risk, and women with daily urge incontinence had increased risks of 35% and 45% of sustaining falls and fractures, respectively. Previous studies have demonstrated that urge incontinence is associated with frequency/urgency and nocturia, suggesting that any OAB symptom, not just urge incontinence, has the potential to increase the risk of falls and fractures among elderly women.[4,14] These results support the need for early diagnosis and intervention in OAB to reduce the risk of falls and fractures and associated morbidity and mortality among elderly people.

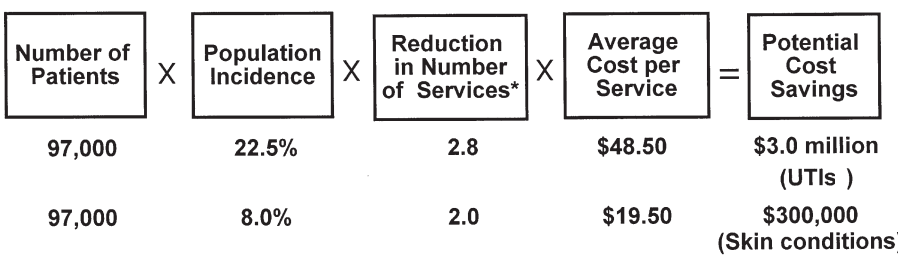
Urinary Tract and Skin Infections

Wagner and Hu[3] previously identified UTIs and skin infections as factors that increase the cost of OAB. Recent analyses suggest a potential reduction in healthcare costs if patients receive treatment for OAB.[15] A 5% random sampling of the 1996-1997 California Medicaid Program (Medi-Cal) claims data showed that 22.5% and 8% of the OAB population received treatment for UTIs and skin infections, respectively. After OAB was diagnosed, the number of services received for UTIs and skin infection decreased 40% to 60%, respectively, and was associated with potential cost savings (Figure).[15] Assuming a 22.5% population incidence rate for UTIs at an average cost of $48.50, a potential cost savings of $3 million per year would be realized through the reduction of UTIs after the diagnosis of OAB in 97,000 patients. Assuming a popu-

lation incidence rate of 8%, the corresponding cost savings for a reduction in skin conditions would be $300,000 per year. Other data derived from the Medi-Cal claims database show that patients who received and continued pharmacotherapy for OAB required 2.8 and 2.0 fewer services for UTIs and skin infections, respectively, compared with those in whom therapy was discontinued. These reductions in services translate to corresponding potential cost savings of $15.30 and $1.56 per patient over a 6-month period (or $2.55 and $0.26 per member per month), respectively.

Using information derived from Illinois Medicaid claims data, the calculated cost savings of reductions in medications and services for UTIs and skin infections are approximately $200 for a 2-year period during which a patient remains on pharmacotherapy for OAB (Table).[16] However, these figures do not account for pad or prescription costs, suggesting the total costs are actually higher. These data strongly support an association between compliance with pharma-

Figure. Costs Related to UTIs and Skin Infections in a Managed Care Population



Source: Based on analysis from the Medi-Cal database, which demonstrates the potential cost savings associated with a reduction in UTIs and skin infections after the diagnosis of OAB.
*Difference in number of services before and after diagnosis: UTIs—6.6 services before diagnosis compared with 3.8 after diagnosis; skin conditions—3.3 services before diagnosis compared with 1.3 after diagnosis
UTIs = urinary tract infections.

Table. Lower Costs Associated With UTIs and Skin Infections When Patients Remain on Therapy for OAB

Total Cost Comparison (1.5 years) — With and Without Drug Treatment for OAB

Group*	Total UTI Rx Costs	Total Skin Rx Costs	Total UTI Med Services Costs	Total Skin Med Services Costs	Total Payments per Patient
1	$ 19,341	$ 753	$ 47,101	$ 742	$ 124
2	$ 4485	$ 478	$ 30,511	$ 621	$ 141
3	$ 43,481	$ 3304	$ 58,802	$ 8388	$ 323

Source: Based on an analysis from Illinois Medicaid claims (data on file, Pharmacia Corporation).
*Groups: Group 1 maintained on Rx/pads (at least 3 scripts); group 2 Pads/no Rx; and group 3 Rx/no pads.
UTI = urinary tract infection; Rx = drug.

cotherapy for OAB and overall cost savings based on fewer services needed for associated comorbidities.

Sleep Disturbances and OAB

Nocturia (getting out of bed to urinate at least 2 times during the night) and nocturnal enuresis (urinary incontinence while sleeping at night) are common manifestations of OAB.[2,17-19] Not surprisingly, nocturia correlates with poor health, reduced quality of life, and disturbed sleep.[2,17,20] Among nursing home residents, nocturia is the most frequent cause of disturbed sleep, affecting 70% of cognitively intact nursing home residents at least 3 times per week.[20] Even young patients with OAB are adversely affected by nocturia. In an epidemiologic study of women aged 20 to 59 years with urge incontinence, multiple nighttime awakenings for nocturia correlated with poor health.[17] People with nocturia report a lack of energy and chronic fatigue as a result of many awakenings and the loss of a good night's sleep. Comments regarding nocturia made in a focus group of women with urge incontinence included such observations as "I'm up every hour. It's ridiculous that I can't sleep 2 to 3 hours straight!" and "Being awake every 2 hours all night long takes away my energy."[2]

Although no studies have evaluated the economic costs related to nocturia and related sleep disturbances, it is highly likely that these conditions are associated with substantial indirect and intangible costs (ie, impaired productivity at work or activities of daily living). As a result, it is important to determine whether reducing the symptoms of OAB leads to improved sleep and related quality of life. Recent clinical trials[16] have shown that pharmacologic treatment of OAB significantly reduces the number of episodes of nocturia. Diokno and colleagues[21] reported the results of a study in which tolterodine reduced the incidence of nocturia in patients with 2 or more episodes per night. In this single-blind, open-label trial of 389 patients with OAB, patients who received tolterodine for 16 weeks had a 30% reduction in nocturia. Additional studies are needed to determine whether this reduction affects the quality of life and economic burden.

The extent to which OAB contributes to sleep disturbances remains unclear. Many people, particularly the elderly, report sleep problems, including difficulty falling and staying asleep, excessive daytime somnolence, inability to fall asleep at the right time, and abnormal movements and behaviors during sleep.[22,23] In many cases, it is unclear whether nocturia, or other factors, is causing the patient to awaken at night. Additionally, although nocturnal enuresis coexists with urodynamically proven detrusor instability in some patients, OAB is not documented in all enuretics.[18]

Several differences exist in the sleep architecture among younger adults compared with elderly adults that may explain disturbed sleep among the latter. The main difference is that elderly people have markedly reduced slow-wave, or deep sleep. Consequently, they tend to have more awakenings during the night than younger adults and to wake up earlier in the morning. Among the elderly, periodic leg movements also are common during sleep and can cause brief arousals, which lead to increased sleep fragmentation and disturbance of sleep. Dementia and psychiatric disorders, such as anxiety and depression, also affect sleep architecture.

Neural control of micturition stems from 3 areas of the brain: the cerebral, pontine, and spinal micturition centers. The pontine micturition center lies very close to the rapid eye movement-generating neurons in the pons, so damage in this area of the brain, possibly as a result of a stroke or other neurologic disorder, can lead to an inappropriate, dysfunctional associa-

tion between micturition and sleep. The etiology of nocturnal enuresis in this type of situation is not OAB.

Because of the many factors that can disturb sleep, particularly among the elderly, it is difficult to determine a definitive causal relationship between OAB and sleep disturbances. Currently, clinicians could benefit from additional data derived from clinical studies that assess the relationship between nocturia, incontinence, and sleep. Such studies should incorporate valid laboratory sleep investigations (ie, overnight polysomnography and cystomanometry) and autonomic function tests to rule out autonomic dysfunction of the micturition centers as a cause of urinary incontinence.

Depression

A recent study[24] has suggested that there is a strong association between depression and urge incontinence. A total of 115 incontinent patients (36 with stress, 44 with urge, and 35 with mixed incontinence based on video urodynamics) who presented to an incontinence clinic were queried about a history of depression and completed a Beck Depression Inventory. Urge incontinence was further classified as being idiopathic or neuropathic, depending on whether neurologic findings were absent or present. The results were compared with those of 80 continent controls. Depression was highly prevalent among those with idiopathic urge incontinence, occurring in 60%. In contrast, depression was noted in only 14% of patients with stress incontinence and 42% of patients with mixed incontinence. Of all patients with incontinence, only those with idiopathic urge incontinence were significantly more likely than controls to have an elevated Beck Depression Inventory score or a history of depression. That patients with stress incontinence were no more likely to be depressed than continent controls suggests the relationship between depression and urge incontinence is not merely a likelihood. These authors propose that OAB and depression share a common neuropharmacologic basis probably related to reduced serotonergic functioning.

Conclusion

Recent studies have suggested strong associations between OAB and other morbidities, including falls and fractures, UTIs and skin infections, sleep disturbances, and depression. Such relationships also may be associated with increased morbidity, mortality, impaired quality of life, and increased economic costs. That multivariate analyses among patients with falls and fractures have shown OAB to be a risk factor among the elderly is justification for early diagnosis and treatment of OAB to help reduce associated fall- and fracture-related morbidity and mortality. Recent analyses suggest a potential reduction in healthcare costs for UTIs and skin infections and a reduction in the number of nocturia episodes if patients receive treatment for OAB. Although no studies have evaluated the economic costs associated with nocturia and related sleep disturbances, it is highly likely that these conditions would be linked to the economic costs related to impaired productivity.

Plausible explanations can be suggested for some of these findings. For example, it is reasonable to hypothesize that urine leakage and its subsequent prolonged contact with skin could lead to skin irritation and infections. Other associations between OAB and comorbidities are more difficult to explain in the absence of more detailed study. The relationship between OAB and other illnesses is just beginning to be elucidated. Further research is warranted to obtain additional information pertaining to the presence of OAB as a risk factor for other disease, including a study that determines the impact of effective pharmacotherapy for OAB on morbidity, quality of life, and

healthcare costs. Currently, intervention trials are the most appropriate means to gather such information.

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