Overactive Bladder Significantly Affects Quality of Life

Paul Abrams, MD; C.J. Kelleher, MD, MRCOG; Lindsey A. Kerr, MD; and Rebecca G. Rogers, MD

Presentation Summary

Overactive bladder (OAB), with symptoms of frequency, urgency, and urge incontinence, substantially affects the lives of millions of people. The symptoms associated with OAB can significantly affect the social, psychological, occupational, domestic, physical, and sexual aspects of those who suffer from it. Unfortunately, many sufferers are reluctant to discuss their condition with their healthcare provider or family members. As a result, OAB remains underreported, despite increased awareness and improved diagnosis and treatment. Health-related quality of life can be measured objectively, and several instruments have been developed, validated, and used in research. Currently, there are 2 major types of quality-of-life questionnaires: generic and disease specific. Although these questionnaires have been helpful and are widely used, the goal is to establish a single questionnaire that is acceptable throughout the world for use by urologists, gynecologists, urogynecologists, geriatricians, and epidemiologists.

Overactive bladder (OAB) is a major cause of suffering in many patients, requiring long-term therapy to maintain symptom relief. Although OAB can affect anyone at any age, the prevalence tends to increase with advancing age.[1] The symptoms are associated with significant social, psychological, occupational, domestic, and physical stigmas. Patients who suffer from OAB focus on and may be preoccupied with such concerns as locating the closest bathroom, looking for aisle seating, and estimating the amount of time until their next work break. Furthermore, OAB affects daily activities, such as travel, physical activity, relationships, sexual function, and nocturnal bladder control, which can affect sleep.

© Advanced Medical Communications, Inc.

Impact of OAB

It is estimated that at least 17 million Americans are affected by OAB; however, the prevalence is difficult to estimate because few surveys have measured symptoms of urgency and frequency with or without urge incontinence.[2] OAB is characterized by symptoms of urgency (a sudden, strong desire to urinate), frequency (urinating more than 8 times in 24 hours), or urge incontinence (sudden and involuntary loss of urine), alone or in combination. Both urinary inconti-

Petitioner - Avation Medical, Inc.
Ex. 1010, p. 580

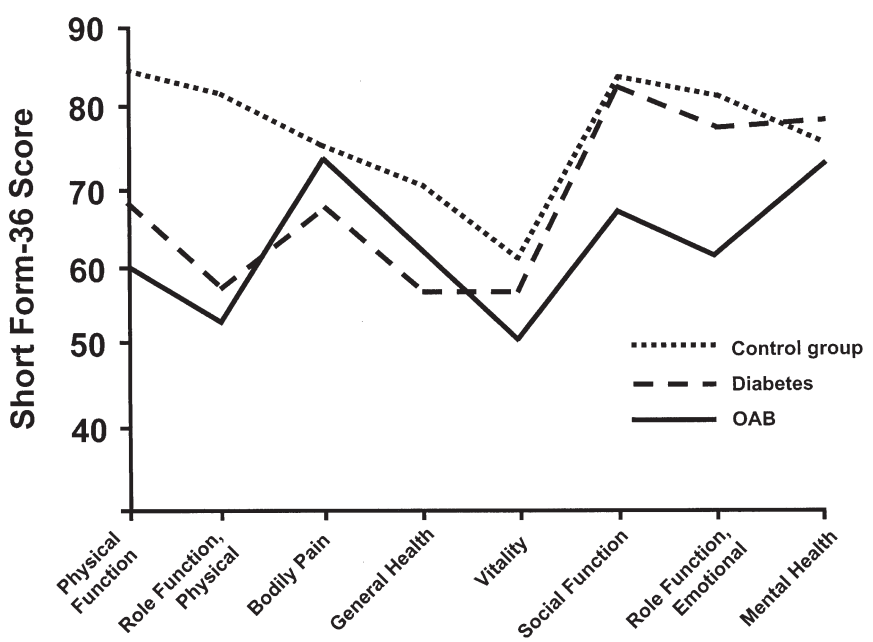
nence and urgency/frequency have been shown to affect a patient's physical, social, and emotional well-being. Unfortunately, many people do not seek medical help because they mistakenly believe that bladder control problems are an inevitable part of aging and that there is no treatment available or they are too embarrassed to discuss their problem with their healthcare provider. Of those sufferers who seek medical attention, it is estimated that 30% receive no assessment of their symptoms and approximately 80% are not treated.[2]

In a European survey conducted by SIFO Research and Consulting AB,[1] it was found that OAB adversely affected the lives of the majority of respondents with symptoms of OAB (65% to 67%). In addition, 60% found the symptoms bothersome enough to consult a medical practitioner. Interestingly, frequency and urgency were almost as common as urge incontinence as a reason for seeking help. Most important, only half the respondents with OAB said they were likely to discuss the problem with their healthcare provider again, providing additional evidence that although many people find the symptoms troubling, the disease remains vastly underreported.

Patient's Perception

Studies have shown that patients with OAB have a significantly poorer quality of life than age-matched populations. For instance, using the patient-administered Short Form 36 (SF-36) quality-of-life questionnaire, patients who suffer from OAB were found to have a lower quality of life in the social and functional domains than patients with diabetes (Figure 1).[3,4] Many people

Figure 1. Comparison of Quality-of-Life Scores in Patients with OAB, Diabetes, and Normal Subjects



Source: Abrams P, Wein AJ. *The Overactive Bladder: A Widespread But Treatable Condition.* Stockhom, Sweden: Erik Sparre Medical AB; 1998. Reprinted with permission.

Petitioner - Avation Medical, Inc.
Ex. 1010, p. 581

with OAB tend to stop pursuing many of the social and physical activities they have enjoyed for much of their lives, enduring OAB and its symptoms in silence because they are too embarrassed to talk about it or are unaware that it can be treated.

The most common reactions to urinary incontinence are embarrassment, frustration, anxiety, annoyance, depression, and fear of odor. To cope with symptoms of OAB, many sufferers develop elaborate behaviors (coping mechanisms) aimed at hiding and managing urine loss, such as:

- Limiting daily travel to places and routes where they know the locations of all restrooms
- Reducing fluid intake
- Avoiding sexual intimacy
- Wearing adult incontinence pads or diapers
- Preferring to drive themselves everywhere, so they can control bathroom stops
- Carrying extra clothes and diapers everywhere they go, in the event of a wetting accident
- Wearing dark, often baggy clothing to hide wet spots and/or conceal adult diapers
- Sitting on the aisle at the theater and on planes to have easier access to the bathroom
- Sitting closest to the door for easier access to the bathroom.

Table 1. Selected Quotations Related to Quality-of-Life Issues

Feelings
- "I have lost control over my bodily functions, and I resent it."
- "I'm just wet, and I feel like a child."
- "You're scared to stand next to people. You're afraid the urine smell is there."
- "There are times when I just sit and cry because I get so frustrated with it."

Activities
- "I no longer plan activities, unless I know I will have access to a restroom."
- "I keep sending my resumes out, and I keep thinking I'm gonna blow the interview because I have to go to the bathroom."
- "My boss asked people if I was doing drugs in the bathroom."
- "I was a big runner and tennis player. That's difficult to do any more."

Relationships
- "This problem overshadows my sex life."
- "I don't want to be away from my house. My son says, 'You're becoming a hermit.'"

Source: Adapted and reprinted with permission from Brown JS, Subak LL, Gras J, et al. Urge incontinence: The patient's perspective. *J Women's Health* 1998;7:1263-1269.

Quality-of-Life Issues Affecting Women

In a series of focus groups composed of women of diverse ages and racial and ethnic backgrounds who suffered from urge incontinence, it was shown that the effects of incontinence on quality of life correlated with frequency, nocturia, and pad use.[5] It was also shown that 24% of respondents worried about bathroom availability, 14% about loss of control, 11% about anxiety, and 10% about sleep disturbances. Compared with older women (≥70 years), those younger than 70 years of age were more likely to report feelings of unattractiveness and low self-esteem (12% vs 2%; $P < 0.007$), as well as adverse effects on dating and sexual activity (45% vs 0%; $P < 0.02$). Table 1 lists several comments of the focus group participants.

In a study conducted by Lam and colleagues,[6] the reduction in social contacts and activities in 511 women (30 to 59 years of age) with stress, urge, mixed, or nonspecific urinary incontinence was evaluated using a study-specific questionnaire. Across all types of incontinence, 99 women (19.4%) reported avoiding at least 1 social activity, and 32 women (6.3%) avoided more than 1 type of social activity. Five women (1%) abstained from work, 14 (2.7%) from visiting friends, 18 (3.5%) from going to the movies, 80 (15.7%) from sports, and 16 (3.1%) from shopping. Although urinary incontinence does not appear to be a socially disabling condition, it may have a substantial impact on the everyday lives of women.

According to research presented by Roe and colleagues,[7] those who suffer

Petitioner - Avation Medical, Inc.
Ex. 1010, p. 582

from urinary incontinence are more likely to need assistance with their activities of daily living. When compared with those respondents who were continent, people suffering from incontinence were significantly more likely to need help with cooking, housework, shopping, or their laundry. It was also shown that respondents who were incontinent were significantly more likely to need help with personal care, such as dressing, feeding, bathing, or going to the toilet, than respondents who were continent.

In a questionnaire surveying the prevalence of urinary incontinence and its influence on quality of life, it was shown that women with urinary incontinence reported a poorer quality of life compared with continent women ($P < 0.01$).[8] Women with urge incontinence and women with mixed incontinence reported a poorer quality of life than women with stress incontinence ($P < 0.05$). Only 6% of the women surveyed had sought medical attention for urinary incontinence.

Quality-of-Life Issues Affecting Men

There are few studies that address the impact of incontinence on quality of life in men. According to Lenderking and colleagues,[9] incontinence causes greater impairment in physical functioning in men than in women. In a self-assessment questionnaire addressing quality of life in 50 men (mean age, 67 years), it was shown that 26% of men with moderate-to-severe incontinence had severely limited their physical activities.[10]

In a random sample that included 1883 men (≥30 years of age), the consequences of incontinence were examined, in addition to its prevalence.[11] Thirty-six percent of incontinent respondents believed that the disorder had affected their lifestyle a great deal or fair amount, and only 23% believed there had been no effect. Only 30% to 45% of the respondents felt very confident in major activities of social life; however, activities were curtailed to a greater degree in men and the elderly compared with women and younger individuals. The general activity restrictions imposed by incontinence included drinking less when going out (35%), making a conscious effort to locate a public restroom (33%), going out less (15%), and restricting certain activities, such as lifting (10%).

Seeking Medical Attention

The Special Committee on Aging in the United States has identified urinary incontinence as one of the top 4 important health-related quality-of-life problems affecting senior citizens (others include Alzheimer's disease, loss of vision, and osteoporosis and fractures). Nevertheless, many sufferers have a misconception that urinary incontinence is an effect of aging, which has a negative impact on their decision to seek treatment.[12] In a survey conducted to examine the occurrence, attitudes, and knowledge about urinary incontinence among women 55 years of age and older, respondents were not likely to seek help if they perceived urinary incontinence to be an inevitable outcome of advancing age and believed that no beneficial therapies were available. Instead, they were more likely to try to adjust their lifestyles to compensate. Although attempts to compensate for mild urinary incontinence may have little impact on lifestyle, quality of life and general health may be impaired when an individual limits social and/or recreational activities because of more severe urinary incontinence.

As a result of this study,[12] it has been suggested that education on lower urinary tract health be provided to both the general public and to healthcare providers. Public education should focus on the fact that the occurrence of frequency, urgency, and urge incontinence is not a normal part of aging and that effective treatment methods are available. Furthermore, healthcare providers should be taught how to make basic

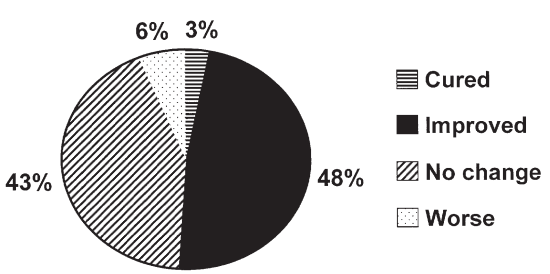
Petitioner - Avation Medical, Inc.
Ex. 1010, p. 583

continence assessments and informed of the available treatment options.

In its role as an advocacy group for those with incontinence, the National Association for Continence (NAFC), reported results of a member survey.[13] There was a 1.9% rate of return from detailed questionnaires mailed to 98,000 subscribers. Most respondents were covered by health insurance (Medicare, 61.3%; managed care organizations, 25%; Medicaid, 5.7%; no insurance, 2.4%). Consumer satisfaction with treatment of incontinence was very low, with 64% reporting that they were not satisfied with treatment. Dissatisfaction corresponded to overall general health and type of incontinence, with those who had good health or less severe incontinence tending to be more satisfied with treatment outcomes. Those with stress or mixed incontinence were more satisfied with treatment than those with urge incontinence. It was shown that younger respondents (36 to 45 years of age) were as dissatisfied and unhappy with their treatment outcomes as those 65 years of age and older.[13]

The majority of respondents (51%) rated conservative and behavioral treatment, such as pelvic muscle exercises, bladder retraining, and diet modification, as being most helpful; 43% of respondents observed no change in outcome from their most helpful treatment; and only 3% reported being cured (Figure 2). These figures probably underrepresent the actual percentage of patients who benefit from treatment because those who elected to participate in the NAFC and respond to the survey are likely to be those who remained incontinent. Nevertheless, this survey indicates that there is a gap in the expectations patients have of current therapies and suggests that improved communications are needed regarding treatment options and anticipated outcomes between patients and healthcare providers.

Figure 2. Consumer Response to Outcome of Therapies (Behavioral and Pharmacotherapeutic) for Urinary Incontinence



Source: Verdell L ed. *Consumer Focus "99: A Survey.* Spartanburg, South Carolina: National Association for Continence; 1999. Reprinted with permission from the National Association for Continence and the Alliance for Aging Research.

Compliance With Therapy

Although behavioral therapy has been shown to be highly effective (80% cure rate) in patients with OAB,[14] noncompliance outside the clinical trial setting limits its long-term efficacy. Some patients will comply better with pharmacotherapy than behavioral modifications, unless they experience adverse effects or a complicated regimen is prescribed. In addition, if the prescribed therapy comes from a specialist and the patient receives long-term management from his or her primary care physician, acceptance of the plan of therapy by the primary care physician is another often overlooked factor that influences compliance. Importantly, if patients perceive an improvement in their quality of life as a result of therapy, they are more likely to comply.

Overactive bladder is a chronic condition that often requires long-term therapy. However, there is a lack of outcome data on the management of patients over extended periods of time, as well as limited information on long-term compliance with therapy for OAB. Most compliance data come from clinical trials, which do not provide an accurate assessment of adherence in the everyday world.

Petitioner - Avation Medical, Inc.
Ex. 1010, p. 584

Oxybutynin is an effective agent for managing the symptoms of OAB; however, dry mouth occurs in about 50% of patients, contributing to an overall discontinuation rate up to 27% of patients in clinical trials.[15] A study of 348 women with OAB from the United Kingdom suggests that compliance rates with oxybutynin in clinical practice are even lower.[16] A total of 73.6% of women with a mean age of 50.7 years responded to a survey at 6 and 12 months after referral to a specialist for urinary symptoms. Most patients (83.5%) had been prescribed oxybutynin. At 6 months, even though only 5.5% of respondents reported complete resolution of all their urinary symptoms, a dismal 18.2% remained on therapy. The occurrence of side effects was reported as the reason for discontinuation of therapy by 39.8% of women. Lack of efficacy did not seem to play a major role, because 71.9% of women considered drug therapy to be effective.

A follow-up study was conducted to evaluate whether commencing oxybutynin therapy at a lower dose with written instructions for gradually increasing the dose would result in improved compliance (C.J. Kelleher, unpublished data). Ninety-six women with OAB were randomly prescribed oxybutynin, 2.5 mg twice daily or 5 mg at bedtime, with instructions to increase the dose to 5 mg 3 times daily over 6 weeks. Of the 96 women enrolled, 66 responded to a questionnaire 2 years later. Similar to the previous study, a high percentage of women (66.7%) were no longer taking oxybutynin, of whom 63.6% had discontinued therapy after 2 months. Of those who stopped therapy, 43.2% reported that it was due to side effects. Thus, lower dosage and slow titration did not substantially improve compliance.

In clinical trials, tolterodine 2 mg twice daily has been demonstrated to have a lower rate of dry mouth and discontinuation because of dry mouth than oxybutynin 5 mg 3 times daily,[17,18] which may result in improved compliance. However, long-term studies are needed to determine whether this improved tolerability results in better compliance.

Evaluating Sexual Functioning

It should be no surprise that incontinence or the fear of leaking urine would interfere with sexual function; however, studies evaluating the burden of OAB on sexual quality of life are scarce. Of the studies that have evaluated the impact of OAB on sexual functioning, only 1 incorporated the use of validated questionnaires to determine quality-of-life measures.

It should be no surprise that incontinence or the fear of leaking urine would interfere with sexual function; however, studies evaluating the burden of OAB on sexual quality of life are scarce.

There are some problems with using general rather than condition-specific questionnaires, however. For example, Weber and colleagues[19] compared sexual function in women with and without uterovaginal prolapse and urinary incontinence. Using multivariate analysis, increasing age was the only significant factor predictive of poorer sexual function. The general questionnaire used in this study may not have been sensitive enough to detect differences in function in this specific population.

In an effort to have a specific, validated, and reliable questionnaire to evaluate sexual functioning in this population, Rogers and Kammerer have developed the Pelvic Organ Prolapse/Incontinence Sexual Questionnaire (PISQ®; R. Rogers, unpublished data). This questionnaire consists of 31 questions in 3 domains: behavioral-emotive, physical, and part-

Petitioner - Avation Medical, Inc.
Ex. 1010, p. 585

ner related. The PISQ has been shown to have high internal consistency, test and retest reliability, and a good correlation with the Sexual History Form-12 (SHF-12), another questionnaire often used in urogynecologic research. In clinical studies, the PISQ has been able to distinguish between patients with and without sexual dysfunction (R. Rogers, unpublished data).

The PISQ was applied to 139 sexually active women. Patients provided information regarding pelvic organ prolapse or urinary incontinence; self-reports were not confirmed by physical examination. There were significant differences in PISQ scores among women with incontinence compared with those without incontinence. Specifically, although the desired frequency of intercourse was similar between patients with and without incontinence, the actual frequency of intercourse was significantly less among patients with incontinence than among those without incontinence. Patients with incontinence or prolapse reported having previous loss of urine with intercourse and restricting sexual activity for fear of losing urine during it. Additionally, patients with incontinence reported significantly more dyspareunia and vaginal dryness, regardless of their use of hormone replacement therapy compared with patients without incontinence or prolapse. These results support a relationship between OAB and poor sexual functioning (Table 2).

Table 2. Differences in Sexual Function

	UI/POP n = 83 (%)	No UI/POP n = 56 (%)	*P*
Frequency			
Desired (>monthly)	96	100	0.98
Actual (>monthly)	71	95	0.04
Loss of urine with sex	45	14	<0.001
Dyspareunia	42	24	0.03
Restrict sexual activity	27	4	0.005
Vaginal dryness	70	46	0.002

Source: R. Rogers, unpublished observations.
UI = urinary incontinence; POP = pelvic organ prolapse.

Assessing Quality of Life

Evaluation of the severity of OAB normally involves a record of urinary symptom scores, a bladder diary, and, in select cases, objective urodynamic data. Although these are essential clinical measures, they provide little information regarding the impact on a patient's life. Many other factors play a role in OAB, so it is important to include an evaluation of quality of life in clinical trials. In measuring the quality of life associated with OAB, it is vital to examine both severity and duration as well as to establish the correct diagnosis. In developing any definitive instrument to assess quality of life in both men and women, an in-depth interview with the patient should be conducted, with discussion of such areas as sleep, emotional, sexual, and social functioning. Within emotional functioning, self-esteem, anxiety over hygiene (ie, odor) and having incontinent episodes, sadness, health preoccupation, and helplessness all appear to be important issues for those who suffer from OAB.

Within social functioning, it is essential to assess work loss, socializing, and activity avoidance. In addition, the use of the word "bother" may be more appropriate than that of "problem" in quality-of-life evaluations, because patients may find symptoms bothersome but may not consider them problematic, in that they are not associated with serious illness or mortality.

Quality of life can be measured objectively, and several instruments for such measurement have been developed, validated, and used extensively. Currently, there are 2 major types of quality-of-life questionnaires: generic and disease specific.

Generic quality-of-life questionnaires (eg, Medical Outcome Study

Petitioner - Avation Medical, Inc.
Ex. 1010, p. 586

Short Forms 36 and 20 [MOS SF-36, SF-20], European Quality of Life Scale [Euro-QoL], and Sickness Impact Profile) offer some advantages because they are reliable, validated, readily available, and useful in assessing a broad range of populations and ages in many different disease states. However, the problem with using generic questionnaires is that results are often insensitive to the specific condition measured and therefore fail to address many of the issues relevant to the disease. As a result disease-specific instruments are more beneficial in evaluating the impact of a specific lower urinary tract symptom on quality of life and are more sensitive than their generic counterparts in detecting changes as a result of treatment. The Incontinence Impact Questionnaire, the Urinary Distress Inventory, the York Incontinence Perception Scale, the Incontinence Quality of Life Index, and the King's Health Questionnaire (KHQ) are several instruments that have been developed specifically for urinary incontinence. With the exception of the KHQ, the disadvantage in using a disease-specific questionnaire to evaluate quality of life is that other health dimensions, including psychological aspects, are not assessed, and comparisons with other diseases cannot be made.

The King's Health Questionnaire

The KHQ is a short, patient-completed, condition-specific, validated quality-of-life and symptom-impact short-form questionnaire.[20] Symptom-impact and quality-of-life measures are divided and can be presented either as domain scores, total scores, or individual scores across the questionnaire. The questionnaire has been shown to be sensitive and responsive to clinical changes in lower urinary tract symptoms. Although the KHQ was initially designed and validated for use among women, recent studies also have also proved it to be a valid and reliable instrument for evaluating quality of life in men with urinary incontinence. There is good correlation between the KHQ and generic questionnaires, including the SF-36. There are 8 validated cultural adaptations of the questionnaire available in 26 languages, including German, Spanish, Swedish, Greek, Italian, and Japanese.

The KHQ was originally tested in 293 women who were referred for evaluation of urinary incontinence.[20] The results of this analysis show that symptoms are significantly more bothersome in patients with OAB than in patients with stress incontinence. This may be the result, in part, of the greater predictability of leakage because of stress incontinence than urge incontinence, making adaptive measures more successful in women with stress incontinence. When combined-domain scores were evaluated, women with OAB also had significantly greater quality-of-life impairment compared with women with normal urodynamic function or women with stress incontinence (Figure 3).

The KHQ has also been used to assess responses to clinical changes in a recent naturalistic study comparing the effects of 10 weeks of tolterodine or oxybutynin therapy on OAB symptoms in 378 patients (67% women) older than 50 years of age.[21] A total of 294 patients completed both generic instruments (SF-36 and the Euro-QoL) and the KHQ until study completion. In a subset analysis performed by C.J. Kelleher, mean scores for the KHQ, corrected for comorbidity, were significantly higher in younger women than in older women, with the higher scores indicating greater impairment. The less significant effect on quality of life in older women may be a result of adaptive changes they have made over time, or possibly it is because younger women have a more active lifestyle and thus perceive symptoms as more bothersome. Women who received either tolterodine or oxybutynin therapy during the study showed significant

Petitioner - Avation Medical, Inc.
Ex. 1010, p. 587

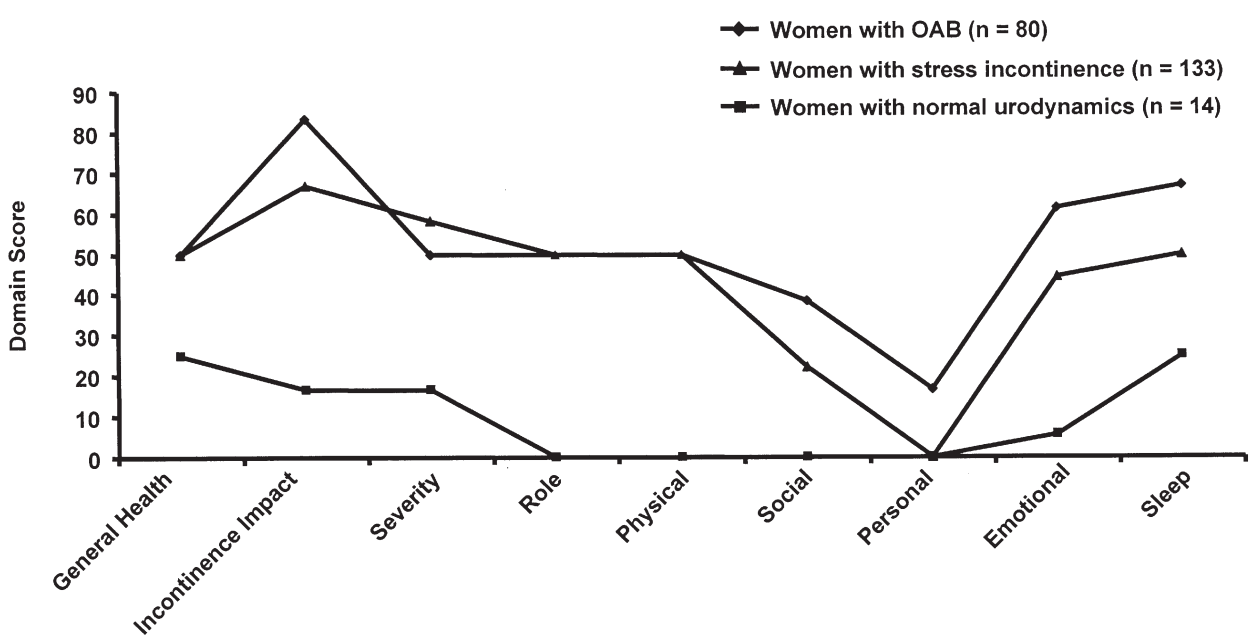
improvements from baseline in all domains other than health perceptions and interpersonal relationships.[21] However, effects on interpersonal relationships are difficult to evaluate with the KHQ for 2 reasons: the number of questions is limited, and questions regarding interpersonal relationships exclude patients who are not having interpersonal relationships at study initiation. There was no significant difference in mean scores obtained from the SF-36 or the EuroQoL questionnaire during the 10-week course of treatment; however, when it was measured with the KHQ, quality of life improved significantly.

Directions for Future Study

Overactive bladder can result in social seclusion and psychological stress and limit the day-to-day activities of those who suffer from it. There are currently many different types of questionnaires that healthcare providers can use to further their understanding of the impact of OAB on their patients' day-to-day lives. However, there is a need to develop a short, concise questionnaire that can be used universally in clinical trials and studies. It also may be necessary to adapt a validated disease-specific questionnaire for use in specific patient groups.

As Roe and colleagues[7] point out in their study, people from ethnic minority groups are underrepresented; therefore, future research on prevalence estimates of urinary incontinence should also target ethnic minorities, using stratified sampling techniques as well as questionnaires that contain appropriate language.

Figure 3. Domain Scores of the King's Health Questionnaire by Urodynamic Diagnosis



Source: Kelleher CJ, Cardozo LD, Khuller V, Salvatore S. A new questionnaire to assess the quality of life in urinary incontinent women. *Br J Obstet Gynaecol* 1997;104:1374-1379. Adapted with permission from C.J. Kelleher and the *British Journal of Obstetrics and Gynaecology*.

Petitioner - Avation Medical, Inc.
Ex. 1010, p. 588

In the National Overactive BLadder Evaluation (NOBLE) Program, the individual burden of OAB in the United States will be researched by estimating the population prevalence of OAB and its symptoms (urgency, frequency, and urge incontinence), assessing the extent to which OAB interferes with functioning, and determining how OAB influences overall health. A longitudinal cohort also will be identified to measure the natural history of the disease. These results will be used as supportive information in future estimates of the economic burden of OAB to society.

In addition, results from the NOBLE Program will be used to develop a bladder health questionnaire that can be used by primary care physicians to screen individuals with bladder health problems and to validate a computer-assisted telephone interview used to screen people with OAB symptoms. Furthermore, the development of a simple bladder health questionnaire will also provide patients with terminology for their symptoms and a better understanding of their condition, facilitating open communication between patient and physician. The goal of the program is to allow patients to feel comfortable discussing OAB with their healthcare provider. An OAB-specific quality-of-life instrument is also being developed and validated.

Conclusion

Appreciation of the specific impact of OAB on the quality of life is critical to understanding the need for appropriate health services. Many sufferers of OAB seek to manage their symptoms by adjusting to the problem instead of seeking treatment. Although many elderly people with urinary incontinence initially may manage their condition with adaptive measures, medical attention is needed before it becomes troublesome; for example, severe restriction of fluid intake may lead to more serious consequences, such as dehydration or concentrated urine that leads to urinary tract infections.

It has been shown that approximately half of all OAB sufferers would welcome some form of treatment; however, they are reluctant to seek help. Of those who discuss their symptoms with their primary care physicians, 30% do not receive treatment and 80% are not examined.[2] Dismissing incontinence and its related symptoms not only has a negative impact on the quality of life of those who suffer, but it also puts a considerable financial burden on society, resulting from a failure to properly diagnose and treat OAB.

··· REFERENCES ···

1. Milsom I. The prevalence of overactive bladder. Presented at the 14th Congress of the European Association of Gynecology and Obstetrics, September 1999, Grenada, Spain.

2. Wein AJ, Rovner ES. The overactive bladder: An overview for primary care health providers. *Int J Fertil* 1999;44:56-66.

3. Kobelt-Nguyen G, Johanesson M, Mattiasson A, et al. Correlations between symptoms of urge incontinence and scores of a generic quality of life instrument (SF36) and health status measurements (Euro-Qol) and between changes in symptoms and QoL scores. Presented at the 27th Annual Meeting of the International Continence Society, September 23-26, 1997, Yokohama, Japan. Abstract.

4. Komaroff AL, Fagioli LR, Doolittle TH, et al. Health status in patients with chronic fatigue syndrome and in general population and disease comparison groups. *Am J Med* 1996;101:281-290.

5. Brown JS, Subak LL, Gras J, et al. Urge incontinence: The patient's perspective. *J Women's Health* 1998;7:1263-1269.

6. Lam GW, Foldspang A, Elving LB, Mommsen S. Social context, social abstention, and problem recognition correlated with adult female urinary incontinence. *Dan Med Bull* 1992;39:565-570.

7. Roe B, Doll H, Wilson K. Help seeking behaviour and health and social services utilisation by people suffering from urinary incontinence. *Int J Nurs Stud* 1999; 36:245-253.

Petitioner - Avation Medical, Inc.
Ex. 1010, p. 589

8. Simeonova Z, Milsom I, Kullendorff AM, Molander U, Bengtson C. The prevalence of urinary incontinence and its influence on the quality of life in women from an urban Swedish population. *Acta Obstet Gynecol Scand* 1999;78:546-551.
9. Lenderking WR, Nackley JF, Anderson RB, Testa MA. A review of the quality-of-life aspects of urinary urge incontinence. *Pharmacoeconomics* 1996;9:11-23.
10. Herr HW. Quality of life of incontinent men after radical prostatectomy. *J Urol* 1994;151:652-654.
11. Brocklehurst JC. Urinary incontinence in the community: Analysis of a MORI poll. *BMJ* 1993;306:832-824.
12. Keller SL. Urinary incontinence: Occurrence, knowledge, and attitudes among women aged 55 and older in a rural midwestern setting. *J Wound Ostomy Continence Nurs* 1999;26:30-38.
13. Verdell L, ed. *Consumer Focus '99: A Survey*. Spartanburg, South Carolina: National Association for Continence; 1999.
14. Frewen WK. The management of urgency and frequency of micturition. *Br J Urol* 1980;52:367-369.
15. Yarker Y, Goa KL, Fitton A. Oxybutynin: A review of its pharmacodynamics and pharmacokinetic properties, and its therapeutic use in detrusor instability. *Drugs Aging* 1995;6:243-262.
16. Kelleher CJ, Cardozo LD, Khuller V, Salvatore S. A medium term analysis of the subjective efficacy of treatment for women with detrusor instability and low bladder compliance. *Br J Obstet Gynaecol* 1997;104:988-993.
17. Abrams P, Freeman R, Anderström C, Mattiasson A. Tolterodine, a new antimuscarinic agent: As effective but better tolerated than oxybutynin in patients with an overactive bladder. *Br J Urol* 1998;81:801-810.
18. Appell RA. Clinical efficacy and safety of tolterodine in the treatment of overactive bladder: A pooled analysis. *Urology* 1997;50(suppl 6A):90-96.
19. Weber AM, Walters MD, Schover LR, Mitchinson A. Sexual function in women with uterovaginal prolapse and urinary incontinence. *Obstet Gynecol* 1995;85:483-487.
20. Kelleher CJ, Cardozo LD, Khuller V, Salvatore S. A new questionnaire to assess the quality of life of urinary incontinent women. *Br J Obstet Gynaecol* 1997; 104:1374-1379.
21. Kobelt G, Kirchberger I, Malone-Lee J. Quality-of-life aspects of the overactive bladder and the effect of treatment with tolterodine. *Br J Urol Int* 1999;83:583-590.
22. Abrams P, Wein AJ. *The Overactive Bladder: A Widespread but Treatable Condition*. Stockholm, Sweden: Erik Sparre Medical AB; 1998.

Petitioner - Avation Medical, Inc.
Ex. 1010, p. 590

View publication stats