



Is overactive bladder independently associated with anxiety?

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Abstract

Introduction and hypothesis Although some psychiatric anxiety questionnaires include overactive bladder (OAB) questions, there are few controlled data to confirm such an association. We tested the association between OAB and anxiety using a control group of women with non-OAB lower urinary tract symptoms (LUTS).

Methods Patients referred to a urogynecology clinic for LUTS completed two questionnaires: the International Consultation on Incontinence Modular Questionnaire for Overactive Bladder (ICIQ-OAB), and the Generalized Anxiety Disorder 7-Item Scale (GAD-7). Based on ICIQ-OAB scores, patients were dichotomized as having OAB versus LUTS-other, and GAD-7 scores categorized patients as having anxiety. A 2-tailed Fisher's exact test was used to test the association between OAB and anxiety. Demographic variables were collected and significant confounders were included in a logistic regression analysis. Sample size calculation indicated a need for 100 subjects, but we recruited 105 subjects to account for incomplete questionnaires.

Results One hundred and five subjects were enrolled (one excluded owing to incomplete questionnaires). Sixty-five patients had OAB and 39 had LUTS-other. Of the OAB patients, 17 out of 65 (26.2%) had anxiety, compared with 3 out of 39 (7.7%) of the LUTS-other group ($p = 0.038$ by Fisher's exact test, with a slight drop to $p = 0.056$ in the regression analysis).

Conclusions There appears to be an association between OAB and anxiety and it may be of clinical importance to assess for anxiety in patients that present with OAB symptoms. The drop in statistical significance from $p = 0.038$ to a borderline significance of $p = 0.056$ in the regression analysis may be a reflection of the sample size.

Keywords Anxiety · Lower urinary tract symptoms · Overactive bladder

Introduction

Lower urinary tract symptoms (LUTS), including overactive bladder (OAB), have been shown to affect overall quality of life, but specific assessment of the relationship between OAB and anxiety is lacking. Some LUTS such as OAB may be specifically associated with anxiety compared with other LUTS such as stress incontinence. In fact, some psychiatric questionnaires aimed at

anxiety include questions regarding urinary frequency and urgency, in addition to other somatic symptoms such as muscular pains and aches, tinnitus, palpitations, difficulty swallowing, etc. However, when specifically considering OAB, it is difficult to ascertain whether urinary symptoms are the cause of anxiety or vice versa. Several studies have shown a correlation between stressful environments and more severe symptoms of OAB [1], in addition to those with OAB reporting a history of a traumatic event predating the development of symptoms [2–4]. Anger et al. [5], who studied the experiences of women suffering from OAB, called for a “chronic care model” as their study concluded that many women felt medical management was only partially effective and reported extremely low adherence rates to medications. This corresponds to Franco [6] who argued for a psychoneurogenic source of LUTS in both adults and children and further studies of corticotrophin-releasing factor (CRF) have found similar results. Current treatments for OAB are aimed at lifestyle

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modifications combined with behavioral therapy and pharmacotherapy [7]. However, an inclusion of psychopharmacotherapy in this treatment strategy may be warranted if there is a known correlation with OAB symptoms and anxiety.

Our primary objective was to determine the association between OAB and anxiety in a urogynecology clinic population. To help determine the presence of a direct association between OAB and anxiety, we used a control group of patients with other LUTS such as stress urinary incontinence (SUI), but without urinary urgency and frequency. It was hypothesized that validated questionnaire scores might show more anxiety in patients with symptoms of OAB. The relevance of such findings would be to help care providers to understand the pathophysiology of OAB and to highlight the importance of anxiety assessment in patients presenting with OAB symptoms. Furthermore, assessment of anxiety would therefore be important in determining the appropriate management plan for patients; that is, without this information a patient with OAB symptoms might be treated with antimuscarinic medication aimed at improving bladder capacity, but if anxiety is the actual precursor, the clinician may unknowingly neglect this opportunity for intervention.

Materials and methods

A prospectively planned cross-sectional study was performed in a tertiary level ambulatory urogynecology clinic. New patients referred for LUTS were invited to participate at the end of their clinic visit. Patients were excluded if they had a diagnosis of bladder pain syndrome/interstitial cystitis, pelvic organ prolapse greater than stage 2 (beyond the level of the hymen), were not fluent in English (since a translator may not be readily available), had cognitive impairment, or had a diagnosis of obsessive compulsive disorder. Patients were not excluded if they had prior or current pharmacological treatment for OAB, but this information was collected and presented with the results. Patients were given two questionnaires: the International Consultation on Incontinence Modular Questionnaire for Overactive Bladder (ICIQ-OAB; Appendix Table 2) and the Generalized Anxiety Disorder 7-Item Scale (GAD-7; Appendix Table 3). Various demographic data and potential confounding variables were considered a priori. These variables included the following: age, menopausal status, hormone replacement therapy (systemic and/or local), parity, health issues such as chronic pain syndromes, conditions that increase anxiety such as

hyperthyroidism, heart disease, asthma or chronic obstructive pulmonary disease, previous surgeries including urogynecological surgery for incontinence or prolapse, medications with lower urinary tract side effects such as anticholinergics or lithium, drugs that decrease anxiety such as beta-blockers or benzodiazepines, body mass index, and other urinary tract variables such as history of recurrent urinary tract infections, and post-void residual urine volume (by bladder scan or catheter). Potential psychiatric confounders were also considered such as depression as measured by the Patient Health Questionnaire (PHQ-9; Appendix Table 4; patients were considered to have depression if the score was greater than or equal to 18 out of a maximum score of 27), a pre-existing diagnosis of depression or anxiety (including the duration of any pre-existing anxiety disorder), and other potential modifying factors such as caffeine intake (self-reported number of cups of coffee or tea per day), total daily fluid intake (self-reported number of cups of liquid per day), level of education (as a proxy for socioeconomic status), marital/relationship status, current cigarette smoking, alcohol consumption, and recreational use of drugs or other stimulants. Most of the demographic data were extracted from the medical record, but the PHQ-9 for assessment of depression was administered together with the ICIQ-OAB and GAD-7 questionnaires.

Patients were divided into two groups: OAB (ICIQ-OAB greater than or equal to 28) or other LUTS (ICIQ-OAB score less than 28). Patients were then categorized as having anxiety if the GAD-7 score was greater than or equal to 14. These cut-off points were chosen to capture patients with significantly bothersome symptoms yet avoiding over-diagnosis; for example, this would correspond to an average bothersomeness level of at least 5 out of 10 on the sub-sections of the ICIQ-OAB scale, and symptoms on average occurring at least “more than half the days” on the GAD-7 scoring.

The sample size was estimated based on the prevalence of anxiety in the general population of 5% or less. The hypothesis was that at least 25% of OAB patients would have anxiety. Using a two-tailed Chi-squared test, alpha of 0.05, and power of 80%, we required 50 OAB subjects and 50 subjects with other LUTS. It was therefore decided that a total of 100 subjects would be required. This was increased to 105 to account for the possibility of incomplete questionnaires. Fisher’s exact test was used to look for a difference between OAB and non-OAB patients, comparing the proportion in each group that were categorized as having anxiety according to a GAD-7 score

greater than or equal to 14 out of a maximum score of 21. A two-tailed Fisher's exact test was used, with statistical significance considered to be a p value less than 0.05. Demographic variables were analyzed with descriptive statistics and differences between OAB versus non-OAB patients were tested for using a two-tailed Student's t test for continuous variables and a two-tailed Fisher's exact test for data that were not normally distributed. Potential confounders were tested using univariate analyses and any variables with a p value less than 0.05 were included in a logistic regression analysis to assess for a direct association between anxiety and OAB. We obtained approval from our hospital Research Ethics Board (Approval # 17-0146-E).

Results

Study subjects were recruited between July and September 2017. One hundred and five subjects were enrolled as planned, but one patient was excluded owing to incomplete questionnaires, leaving 104 subjects to be analyzed. Based on ICIQ-OAB scores greater than or equal to 28, a total of 65 study subjects were categorized as having OAB and 39 were categorized as LUTS-other (typically SUI). Of the OAB patients, 17 out of 65 (26.2%) were categorized as having anxiety compared with 3 out of 39 (7.7%) of the LUTS-other group ($p=0.038$ by Fisher's exact test). Of the potential cofounders (Table 1), only post-secondary education significantly differed between OAB patients (51 out of 65 = 78.5%) and LUTS-other patients (37 out of 39 = 94.9%; $p=0.03$ by Fisher's exact test). When including post-secondary education into the regression analysis, the significance level for the association between OAB and anxiety dropped to $p=0.056$. There were no significant differences in other variables that were collected, including hormone replacement therapy, medical conditions, surgical history, medications, body mass index, urinary tract infections, duration of pre-existing anxiety, alcohol consumption, and recreational drug use.

Of the 17 OAB group subjects that were classified as having anxiety according to their GAD-7 score, 10 of these had a pre-existing diagnosis of anxiety. Of the 3 control group subjects that were classified as having anxiety, only 1 had a pre-existing diagnosis of anxiety. There were 7 other subjects in the OAB group that had a pre-existing diagnosis of anxiety, but were not classified as having anxiety by their GAD-7 score (i.e., presumably their anxiety was mild or under control). Similarly, there were 5 other subjects in

the control group that had a pre-existing diagnosis of anxiety, but was not classified as having anxiety by the GAD-7 score. Three of the OAB group subjects were currently taking medication for OAB, but there were none in the control group ($p=0.29$ by Fisher's exact test). Nine of the 65 OAB subjects (13.8%) and 3 of the 39 control subjects (7.7%) were taking antidepressant medications (particularly serotonin-norepinephrine or serotonin reuptake inhibitors; $p=0.53$ by Fisher's exact test).

Discussion

Women who suffer from symptoms of OAB are thought to experience higher rates of anxiety than the general population. Our study has shown a link between women with symptoms of OAB and a current or previous history of anxiety. Knowledge of this association may change how we target our current therapy and treatment options for OAB. Current regimens often fail because of non-compliance, adverse side effects, or failure to improve symptoms. Anger et al. [5], who studied the experiences of women suffering from OAB, concluded that many women felt that medical management was only partially effective and reported extremely low adherence rates to medications. This calls for further exploration into the efficacy of currently used management options.

The theory that symptoms of OAB are linked to an abnormal psychological state has been previously studied. Corticotropin-releasing factor (CRF), which has anxiogenic properties, is released from the brain in stress-induced situations and acts through receptors not unlike those in the pelvic viscera, which may explain the connection between anxiety states and urinary pathology [6, 8]. The correlation between stress and worsening of OAB symptoms has led clinicians to believe that controlling psychological symptoms may be a target for future treatment goals [9, 10].

Current treatments for OAB mainly consist of lifestyle modifications and medications targeted at the muscarinic system. Anti-muscarinics bind directly to the receptors on the detrusor muscle, blocking acetylcholine from attaching and, therefore, preventing afferent nerve activity and stopping detrusor contractions. Along with this inhibition come side effect, which include dry mouth, cognitive impairment, constipation, and increased heart rate [8]. Once lifestyle changes have been exhausted, patients are started on this class of medications that many find hard to tolerate and even harder to adhere to. As the success rates for the medical management of OAB are quite

Table 1 Demographic data and potential confounding variables

	OAB (<i>n</i> = 65)	Control (<i>n</i> = 39)	<i>p</i> value
Mean age	53	51.5	0.6*
Mean parity	1.6	1.8	0.53*
Post-menopausal	30/65 (46.2%)	17/39 (43.6%)	0.84**
Smoker	4/65 (6.2%)	1/39 (2.6%)	0.65**
Coffee/tea (mean cups/day)	1.5	1.7	0.4*
Total fluids (mean cups/day)	6.7	7.3	0.34*
Post-void residual (mean mL)	19	34	0.08*
Depression (PHQ-9) ^a	4/65 (6.2%)	0/39 (0%)	0.29**
Married/partner	43/65 (66.2%)	27/39 (69.2%)	0.83**
Post-secondary education	51/65 (78.5%)	37/39 (94.9%)	0.03**
Pre-existing anxiety diagnosis	17/65 (26.2%)	6/39 (15.4%)	0.23**

OAB overactive bladder, PHQ Patient Health Questionnaire

*Student's *t* test

**Fisher's exact test

^a PHQ-9 score greater than or equal to 18

low, the search for more effective treatment targets is needed. Anxiolytic medications have been used to treat anxiety for decades and have proven efficacy with a tolerable side effect profile. If further research is aimed at changing treatment and management plans for OAB, a study using psychopharmacotherapy as a first- or second-line option may be warranted.

One weakness of our cross-sectional study design involves the inability to accurately judge the relationship between anxiety and OAB. Although we were able to establish an association with the data collected, we were unable to judge a cause and effect relationship between the OAB symptoms and the anxiety symptoms. Such a study would involve more in-depth questionnaire analyses in addition to prospectively following a cohort of patients with either anxiety or OAB to see if they develop the other affliction over time. Our study identified a confounding factor of post-secondary education, and when this was included in a regression analysis the statistical significance fell slightly to $p = 0.056$. This may be a reflection of the sample size and a larger study would be required.

Women suffering from OAB symptoms live with a debilitating condition that greatly affects their quality of life. The treatments are difficult to endure and seldom relieve their symptoms. Whether living with increased anxiety because of an overactive bladder, or if we note that those who have baseline anxiety exhibit OAB symptoms, the connection is still unclear. What is clear is that the two are related. Adding to the current management of OAB calls for further investigation into the underlying cause of OAB and treatments for those causes. If adequate treatment of anxiety, whether with

psychopharmacotherapy, behavioral therapy, or group therapy, is a common and well-known practice in psychiatry, then the expansion of these approaches into urogynecology may be warranted as either initial therapy or concurrent treatment. More research is needed to aid effective treatment of overactive bladder. Identifying women suffering from related psychiatric illness may move us one step forward in the direction of adding another therapeutic tool to current management options.

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Compliance with ethical standards

Conflicts of interest None.

Appendix 1: International Consultation on Incontinence Modular Questionnaire for Overactive Bladder (ICIQ-OAB)

Many people experience urinary symptoms some of the time. We are trying to find out how many people experience urinary symptoms, and how much they bother them. We would be grateful if you could answer the following questions, thinking about how you have been, on average, over the PAST FOUR WEEKS.

Appendix 3: The Patient Health Questionnaire (PHQ-9)

Over the last 2 weeks, how often have you been bothered by any of the following problems?

Table 4 The Patient Health Questionnaire (PHQ-9)

(Circle your answer)	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself – or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching TV	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed. Or the opposite—being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead, or of hurting yourself in some way	0	1	2	3

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