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Impact of sexually transmitted infections, lifetime sexual partner count and recreational drug use on lower urinary tract symptoms in men who have sex with men

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Abstract

Objective—Lower urinary tract symptoms (LUTS) in men are a source of considerable morbidity, distress and medical expense. We investigate the relationship of LUTS to urinary tract infection (UTI), prostatitis, sexually transmitted infection (STI), lifetime sexual partner count, and recreational drug use in a population of men who have sex with men (MSM).

Methods—We conducted a cross-sectional, internet-based survey of urinary quality of life outcomes in MSM. The main outcome was the International Prostate Symptom Score (IPSS) classified as none/mild (IPSS 0–7) or moderate/severe (8–35) or severe (20–35). Participants were also asked if they ever sought medical attention for urinary problems.

Results—The survey website was accessed by 2783 men, of whom 2348 (84.3%) completed the questionnaire. The median age was 39 (range 18–81). Age, depression, HIV infection, gonorrhea, syphilis, prostatitis, and prescription drug abuse were all associated with LUTS. Men who sought medical attention for LUTS were more likely to report older age, diabetes, depression, gonorrhea, UTI history, and prostatitis.

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Conclusion—Specific infectious conditions of the urinary tract and depressive symptoms are independent predictors of LUTS in MSM. While LUTS are often multi-factorial, a common unifying explanation for our finding could be the effects of local and systemic inflammation on the lower urinary tract.

Keywords

Lower Urinary Tract Symptoms; sexually transmitted infection; urinary tract infection

Introduction

Lower urinary tract symptoms (LUTS) in men are a source of considerable morbidity and distress. Billions of dollars are spent annually to treat this condition.[1] LUTS can be caused by bladder outlet obstruction secondary to benign prostatic hypertrophy (BPH). However, it is increasingly recognized that conditions affecting the urethra and bladder are also significant contributors to LUTS in men.[2]

Both LUTS and BPH have been associated with local and systemic inflammation. The inflammatory marker C-reactive protein has been shown to be elevated in men with LUTS[3], inflammatory tissue is common in BPH prostatic nodules[4], and inflammation has been shown to induce prostatic epithelial cell growth and proliferation via cytokine modulation in animal models.[5] A history of urinary tract infection (UTI) with either sexually or non-sexually transmitted pathogens has been linked to LUTS.[6–8] There is also evidence that recreational drugs such as ketamine elicit bladder inflammation and dysfunction.[9]

In this study we investigate the relationship of LUTS to UTI, prostatitis, sexually transmitted infection (STI), lifetime sexual partners, and recreational drug use in a population of men who have sex with men (MSM). MSM make up 4–5% of the male population of the United States.[10] MSM are of particular interest because this population has been reported to have elevated STI rates and has sexual practices that generally differ from the rest of the male population.[11] We hypothesized that MSM would have similar risk factors for LUTS as the general male population, and that a history of urinary tract inflammation and drug use would be associated with greater burden of urinary symptomatology.

Methods

Study Design and Cohort Description

Institutional Review Board approval was obtained prior to initiating the study. We conducted a cross-sectional, internet-based survey of urinary quality of life outcomes in MSM. The cohort was restricted to literate, internet-using MSM who were greater than 17 years of age. International sampling was achieved by distribution of a survey invitation to local, national and international lesbian, gay, bisexual and transgender community centers, organizations catering to MSM, and advertisements on Facebook® (www.facebook.com, Palo Alto, California, U.S.A.) aimed at self-identified MSM. Potential respondents were given the option of clicking on a link to the survey which was posted on the internet based survey site Survey Monkey® (www.surveymonkey.com, Palo Alto, CA, USA). Respondents

were informed that they would be asked questions regarding their sexual and urinary wellness and given the option to decline participation or stop the survey at any time. To maintain privacy, no personally identifying information was collected. Responses were collected from January 19, 2010 to May 19, 2010.

Description of Variables

Outcome Variables—The main outcome variable was the International Prostate Symptom Score (IPSS), an internationally validated metric of bothersome LUTS.[12,13] IPSS is graded on a scale of 0–35 and based on 7 Likert-style questions pertaining to urinary symptoms including: frequency, urgency, nocturia, intermittency, weak stream, straining, and incomplete emptying. Validated categorical severity scales distinguished lower urinary tract symptoms into none/mild (IPSS 0–7), moderate to severe (8–35) and severe (20–35).[14–16] Participants were asked if they ever sought medical attention for problems related to urination (yes/no).

Exposure Variables—Respondents reported their age, geographic location, and size of city, and race/ethnicity (African-American, Asian-American, Caucasian, Latin-American, Native American, other). Respondents were asked if they had, or had ever have been treated for, the following medical conditions: (coronary artery disease [yes/no], diabetes [yes/no], hyperlipidemia [yes/no] and depression [yes/no]). Respondents were asked if they were HIV-infected [yes/no/uncertain]. Individuals were asked if they had ever had Chlamydia [yes/no], gonorrhea [yes/no]), syphilis [yes/no], and genital herpes [yes/no]. We inquired about whether the respondent had ever had a urinary tract infection that required antibiotic treatment (excluding sexually transmitted diseases) or if they had been diagnosed with prostatitis or chronic pelvic pain [yes/no]. Participants were asked to report their number of lifetime sexual partners. Respondents were provided an extensive list of sexual practices (e.g. anal receptive and/or insertive intercourse, giving and receiving fellatio, sex with female partners, etc) and asked whether they include these acts in their sexual repertoire (data not shown). Respondents were asked if they used the following recreational drugs: methamphetamine, cocaine, ketamine, ecstasy, prescription pills. For each drug, participants were asked "how often do you use drugs to get high?" [never, rarely/about once per year, sometimes/several times a year, monthly, weekly, daily]. For ease of interpretation, the variable was made binary by grouping several times a year, monthly, and daily as a positive response to drug use and never, and rarely/about once per year as a negative response.

Statistical Analysis

Descriptive statistics were used to characterize the study population. We then used age-adjusted odds ratios and 95% confidence intervals to identify the independent predictors of 1) the presence of moderate to severe LUTS 2) the presence of severe LUTS and 3) whether the subjects had sought medical attention for urination problems. A so-called continuation ratio model was used to jointly compare moderate/severe to none/mild LUTS as well as severe to moderate LUTS. We tested the effects of each exposure overall and on each of the nested comparisons, and finally assessed the equality of the two nested effects. Variables associated with the outcome with a p-value   0.20 after multiple adjustment were retained in the final multiple logistic model. Goodness of fit was checked using Hosmer-Lemeshow and

le Cessie-van Houwelingen-Copas-Hosmer tests.[17] In the primary analysis, respondents with missing data were excluded, but a sensitivity analysis using multiple imputation of missing data was also conducted, without material change to the results. Statistical significance was set at $p < 0.05$ and all tests were 2-sided. STATA 11 (Statacorp, College Station, TX, USA) was used for all analysis.

Results

The survey website was accessed by 2783 men, of whom 2348 (84.3%) completed the questionnaire. Patient demographics, co-morbidities and infectious disease history, lifetime sexual partner history, and recreational drug use history are presented in table 1. The median age was 39 (Interquartile range 31–47; range 18–81). The majority (~75%) of the cohort were from the United States and 82% of the respondents were Caucasian. Having a history of or being currently treated for depression was common (39%). A history of gonorrhea and Chlamydia were reported by 19% and 12.6%, respectively.

Total IPSS scores stratified by age and categorized for the entire population are displayed in table 2. Moderate to severe LUTS were reported by 33% of the population. Seeking medical attention for LUTS was endorsed by 18% with a dramatic rise with aging.

In the continuation ratio model (table 3), age, depression, HIV infection, gonorrhea, syphilis, prostatitis, and prescription drug abuse were all associated with LUTS, based on the overall P-values. Age, diabetes, and depression were important in both nested comparisons. In the comparison of moderate/severe to none/mild LUTS, gonorrhea, UTI, prostatitis, lifetime number of partners, and prescription pill abuse were important; no other recreational drugs were important in either comparison. HIV infection was the only predictor that distinguished severe from moderate LUTS without also differentiating moderate/severe from none/mild. We were unable to detect any differences in the strength of the associations across the two nested comparisons.

In a separate analysis, we investigated the relationship between sexual activities and LUTS. None of the sexual activities about which we inquired were associated with significantly different risk of LUTS (data not shown).

Presented in table 4 are variables associated with men seeking medical attention for their urinary symptoms. Increasing age, history of diabetes, depression, gonorrhea, UTI history, and prostatitis all reached statistical significance in the multivariate model. Drug use, the number of sexual partners, HIV infection, chlamydia, syphilis, and herpes were not associated with help seeking behavior in the multivariate model.

Discussion

In this internet survey of predominantly Caucasian young and middle-aged MSM, we found that age, depression, HIV infection, gonorrhea, syphilis, prostatitis, and prescription drug were independently associated with LUTS by self-report. Help seeking behaviors for LUTS were more common in older men and in those with diabetes, depression, history of gonorrhea, UTI or prostatitis.

Our results corroborate previous studies indicating that a history of urinary tract inflammation from infections including HIV, gonorrhea, prostatitis, and non-sexually transmitted UTI increase the risk of subsequent moderate to severe LUTS.[7,18–21]

Despite their known inflammatory effects, Chlamydia and genital herpes infection were not independent predictors of LUTS in our sample. Chlamydia may have been under-reported because it is often clinically silent and/or associated with gonorrhea in men. Additionally, herpes typically produces lesions on the external genitalia and may not involve the urinary tract; this may explain why urinary symptoms were not significantly associated with these entities after multi-variate adjustment.

Others have demonstrated a link between infection and self-reported urinary bother.[7,18–21] Research from the Health Professionals Follow-up Study showed that self-report of a history of gonorrhea was associated with a 1.8-fold increased odds of moderate to severe LUTS.[18] In addition, self-report of prostatitis at a young age increased the odds of reporting moderate to severe LUTS by 1.6.

New evidence has suggested that systemic inflammation may also be a risk factor for subsequent LUTS.[3,23,24] St. Sauver and colleagues found that participants with higher levels of C-reactive protein were approximately two times more likely to have rapid progression of LUTS irritative symptoms and an almost 2.5 times more likely to have a rapid decrease in urinary flow rates.[3] However, men with elevated C-reactive protein levels were not more likely to experience increases in prostate v Men reporting a history of more than 6 sexual partners maybe at a slight increased risk of moderate/severe LUTS. In our study, the relationship was not strong. It was not present in the nested comparison of moderate to severe LUTS. In addition, the overall P value for number of lifetime partners was not significant. A possible explanation for the positive findings are an increased risk of contracting STIs associated with increased partner count. While we controlled for any history of each of the common STIs, the survey did not ascertain frequency of these infections. Thus adjustment may not have fully captured these effects. olume independent of LUTS or PSA level.

To our knowledge, this is the first large-scale examination of the association of recreational drug use with LUTS. Recreational drug use is associated with high risk sexual behaviors including unprotected intercourse with multiple partners, and thus may also reflect more frequent STIs.[25] In addition, some recreational drugs may have direct effects on bladder function; in particular, ketamine is a known lower urinary tract irritant that has been associated with a painful bladder syndrome of unclear etiology.[9] However – with the exception of abuse of prescription medication – recreational drug use did not appear to increase the risk of LUTS in our sample.

Depression may in part explain the link between prescription drug abuse and LUTS. In our study, both were independently associated with LUTS. Individuals being treated for depression may have greater access to prescription medications, and also be more prone to using them as recreational drugs. Unfortunately, we did not determine what type of prescription pills were used recreationally.

The relationship between depression and LUTS is of interest. While self-reported LUTS is to some extent subjective and thus potentially influenced by depression, there may also be a physiological link.[26] In particular, depression has been shown to elevate serum levels of the inflammatory cytokines including tumor necrosis factor alpha, C–reactive protein, and interleukin-6.[27] Of note, inflammatory pathways have also been implicated in the relationships between depression and myocardial infarction, diabetes, and malignancy.[28] Whether inflammatory pathways and/or psychological factors mediate the relationship between LUTS and depression merits further investigation. As these conditions are frequently seen together, an improved understanding of this relationship might aid clinicians in prevention and treatment of both disorders.

The likelihood of seeking medical attention for LUTS was, as might be expected, increased in men with conditions shown in our analysis to be independent associations of LUTS. It is noteworthy that 18% men reported having spoken to their healthcare provider about LUTS whereas 33% reported significant LUTS (IPSS > 8). Many men are embarrassed by urinary symptoms and/or believe that declines in urinary function are a necessary fact of aging; these men may be unlikely to report bothersome symptoms.[29] It is thus incumbent on providers to make efforts to screen patients with a history of these associated conditions for LUTS. Addressing these issues with patients may help to start a conversation that could lead to effective treatment and substantial enhancement of quality of life.

Several important limitations of this study warrant mention. Firstly, the cross-sectional nature of the dataset makes causal inferences problematic. In addition, non-response bias and volunteer bias may diminish the generalizability of our results to the general MSM population. In particular, MSM who do not read or use computers are almost surely under-represented, and the survey was available only in English. In addition, some researchers have raised the concern that internet survey sampling may over-estimate disease prevalence in younger cohorts.[30] However, it is important to note that we did find positive associations with age and depression, both established risk factors for LUTS. We did not determine whether the reported gonorrhea infection arose from the urethra, rectum or pharynx. Th ais may result in misclassification bias if someone reported an affirmative response for a gonorhea exposure that did not involve the urethra.

Future investigations should explore the temporal relationship between infectious exposure and LUTS. Confirmation of associations in a prospective longitudinal dataset would be informative.

Conclusion

Infectious conditions of the urinary tract and depressive symptoms are independent predictors of LUTS in men. While LUTS are multi-factorial, a common unifying explanation for our finding could be the effects of inflammation on the lower urinary tract.

Acknowledgments

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Table 1

Descriptive statistics of respondent demographic, comorbid and infectious disease history, lifetime sexual partner estimate and recreational drug use history.

	n	%
Age		
18–29	435	18.5
30–39	748	31.9
40–49	708	30.2
50–59	319	13.6
60–81	138	5.9
Geographic location		
Western US	427	18.3
Midwest US	331	14.2
Northeast US	407	17.4
Southern US	338	14.5
Southwest US	146	6.2
Northwest US	78	3.3
Canada	158	6.8
Europe	286	12.2
Australia	140	6.0
Other	27	1.2
City population		
<100, 000	732	31.3
100,000–1,000,000	860	36.8
>1,000,000	746	31.9
Race/Ethnicity		
African-American	68	2.9
Asian-American	66	2.8
Caucasion	1959	83.4
Latin-American	155	6.6
Native-American	31	1.3
***Other**	24	1.0
Co-morbid conditions		
Coronary Artery Disease	121	5.2
Diabetes	163	6.9
Hyperlipidemia	441	18.8
Depression	916	39.0
Lifetime history of infectious condition		
HIV-infection	331	14.1
Chlamydia	295	12.6
Gonorrhea	446	19.0
Syphilis	221	9.4

	n	%
Genital herpes	190	8.1
Urinary Tract Infection	531	22.7
Prostatitis	178	7.6
Estimated number of lifetime partners		
0 to 6	574	25.9
7 to 29	529	23.9
30 to 100	556	25.1
greater than 100	554	25
Do you use the following drugs more than 1 time per year to get high?		
Methamphetamine	104	4.98
Cocaine	119	5.72
Ketamine	39	1.88
Ecstasy	117	5.61
Prescription Pills	206	9.94

Table 2

Total IPSS stratified by age, distribution of categorized IPSS and percent of men who sought medical attention for LUTS by age

Total IPSS		(mean+/−SD)	
	Overall	6.6+/−6	
	18–29	4.6+/−4.4	
	30–39	5.9+/−5.2	
	40–49	7.2+/−6.3	
	50–59	8.3+/−6.8	
	60–81	10.4+/−7.7	
Categorized IPSS		n	%
	None-mild	1570	67
	Moderate	665	28
	Severe	113	5
Percent who sought medical attention for LUTS by age			
	Overall	422	18
	18–29	23	5
	30–39	93	12
	40–49	130	18
	50–59	103	32
	60–81	73	53

Table 3

Continuation ratio model comparing moderate/severe to none/mild LUTS as well as severe to moderate LUTS

	None/mild versus moderate/severe			Moderate versus severe			Overall P-value	P-value for equality
	OR	95% CI	P-value	OR	95% CI	P-value		
Age in 10 year increments*	1.26	1.15, 1.39	<0.001	1.57	1.24, 1.98	<0.001	<0.001	0.091
Diabetes	1.57	1.07, 2.29	0.021	0.93	0.438, 1.98	0.859	0.07	0.231
Depression	1.57	1.29, 1.93	<0.001	1.51	0.92, 2.46	0.102	<0.001	0.869
Lifetime history of infectious condition								
HIV-infection	1.21	0.89, 1.64	0.205	2.03	1.15, 3.59	0.015	0.005	0.867
Gonorrhea	1.43	1.08, 1.88	0.012	0.982	0.55, 1.77	0.958	0.041	0.262
Syphilis	1.4	0.97, 2.01	0.07	1.76	0.92, 3.38	0.087	0.044	0.542
Urinary Tract Infection	1.3	1.3, 1.65	0.029	1.07	0.63, 1.82	0.789	0.089	0.516
Prostatitis	1.57	1.09, 2.24	0.014	0.88	0.43, 1.80	0.735	0.045	0.159
Estimated number of lifetime partners								
0 to 6	Ref							
7 to 29	1.37	1.02, 1.82	0.033	0.76	0.36, 1.58	0.461	0.16	0.75
30 to 100	1.46	1.1, 1.93	0.009	0.85	0.44, 1.67	0.644		
greater than 100	1.22	0.91, 1.64	0.185	0.67	0.34, 1.3	0.233		
Do you use the following drugs more than 1 time per year to get high?								
Prescription Pills	1.69	1.21, 2.36	0.002	1.3	0.66, 2.59	0.451	0.007	0.507

Table 4

Age-adjusted bivariate and multivariate predictors associated with seeking medical attention for urinary problems

	Age-adjusted			Multiple variable		
	OR	95% CI	p-value	OR	95% CI	p-value
Age in 10 year increments[*]	1.95	1.76, 2.14	<0.001	1.74	1.56, 1.96	<0.001
Coronary Artery Disease	1.79	1.19, 2.71	0.006			
Diabetes	1.77	1.23, 2.54	0.002	1.91	1.27, 2.88	0.002
Hyperlipidemia	1.48	1.14, 1.91	0.003			
Depression	1.76	1.41, 2.20	<0.001	1.58	1.23, 2.04	<0.001
Lifetime history of infectious condition						
HIV-infection	1.02	0.89, 1.16	0.758			
Chlamydia	1.23	0.89, 1.69	0.193			
Gonorrhea	1.53	1.19, 1.98	0.001	1.53	1.12, 2.09	0.007
Syphilis	0.81	0.56, 1.16	0.26	0.65	0.42, 1.01	0.059
Genital herpes	1.49	1.05, 2.11	0.023			
Urinary Tract Infection	3.14	2.48, 3.97	<0.001	2.09	1.6, 2.75	<0.001
Prostatitis	6.03	4.29, 8.46	<0.001	4.59	3.16, 6.69	<0.001
Estimated number of lifetime partners						
0 to 6						
7 to 29	0.94	0.67, 1.35	0.743			
30 to 100	1.1	0.79, 1.53	0.543			
greater than 100	1.15	0.84, 1.58	0.374			
Do you use the following drugs more than 1 time per year to get high?						
Methamphetamine	0.74	0.41, 1.33	0.322			
Cocaine	0.8	0.44, 1.47	0.5			
Ketamine	1.04	0.42, 2.56	0.09			
Ecstasy	0.34	0.15, 0.75	0.008	0.34	0.15, 0.77	0.009
Prescription Pills	1.35	0.92, 1.99	0.115			

[*] Not adjusted for age