Male urethritis with and without discharge: relation to microbiological findings and polymorphonuclear counts

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ABSTRACT

Objective We studied the relation between the presence or absence of urethral discharge, urethral pathogens, and polymorhonuclear (PMN) counts on Gram stained urethral smears in men with symptomatic urethritis.

Methods The study population was composed of 630 sexually active heterosexual men (aged 18-45 years) who had urethral symptoms and signs (discharge, dysuria or urethral discomfort). Participants were divided into two groups: the first (*n*=320) was comprised of men with urethral discharge confirmed on examination, while the other (*n*=310) was composed of patients with urethral symptoms but without discharge. Urethral swabs for Gram stained smears and microbiological analyses (*N. gonorrhoeae*, *C. trachomatis*, *T. vaginalis* and *U. urealyticum*) were taken from all study participants. Polymorphonuclear leukocytes (PMN) on Gram-stained urethral smears were counted in 5 oil immersion x1000 PMN per high power fields (phpf). Urethritis was defined as the presence of ≥5 PMN/hpf.

Results *N. gonorrhoeae* was isolated only in men with urethritis accompanied by discharge. The prevalence of *T. vaginalis*, *C. trachomatis* and *U. urealyticum* was significantly higher (F=8.854, *P*<0.01) in urethral swabs of urethritis patients with discharge compared to patients with no discharge. The most common urethral pathogen in both groups of patients was *T. vaginalis* (31.56% and 26.45%, respectively). One or more microorganisms were isolated in 258 (81%) subjects with urethritis with discharge, and in 166 (53.5%) urethritis patients without discharge. There was a positive correlation between the significant number of PMN in Gram stained urethral smears and positive microbiological findings in men with urethritis both with and without urethral discharge (Spearman's coefficients ρ=0.986 and ρ=0.993, respectively; *P*<0.01).

Conclusions The study found a relatively high prevalence of *T. vaginalis* among our men with urethritis irrespective of the presence or absence of urethral discharge, and showed that taking into account both discharge found on examination, and relevant PMN counts on Gram stained urethral smears fails to detect only 4.2% of oligosymptomatic urethritis patients who are infected with one of the strict urethral pathogens.

KEY WORDS

urethritis, discharge, men, polymorphonuclear leukocytes, sexually transmitted infections

Introduction

Microbial urethritis is one of the most common sexually transmitted infections (STI) in men. Its prevalence and rising incidence worldwide makes it a subject of intense research (1-3). Urethritis is usually classified as gonococcal and non-gonococcal (NGU) depending on the presence or absence of *Neisseria gonorrhoeae*. Though *Chlamydia trachomatis* accounts for up to 50% of cases of NGU and *Mycoplasma genitalium* and *Trichomonas vaginalis* are known to cause a smaller proportion, the cause of many cases of NGU remains unknown. *Ureaplasma urealyticum*, *Gardnerella vaginalis*, *Haemophilus species*, and *Streptococcus spp* have been associated with NGU but their causal role is unproved (4,5).

The most remarkable sign of male urethritis is mucopurulent or purulent urethral discharge (6). Sometimes the discharge, and even other signs and symptoms of urethral infection (dysuria, urethral discomfort, etc.) may be absent or very mild (7,8). In these cases, urethral inflammation may be confirmed by Gram stain of urethral secretions demonstrating ≥5 polymorphonuclear leukocytes (PMN) per oil immersion field. The Gram stain is the preferred rapid diagnostic test for evaluating urethritis (9). Several recent reports suggested that PMN counts on Gram stained urethral smears may not be sensitive enough in cases of *C. trachomatis*, and even *N. gonorrhoeae* infections (10,11).

The main objective of the study was to determine the relation between the presence or absence of urethral discharge, urethral pathogens, and PMN counts on Gram stained urethral smears in men with symptomatic urethritis.

Patients and methods

The study population was composed of 630 sexually active heterosexual men (aged 18-45 years) attending the Service for Sexually Transmitted Infections at the Institute of Dermatovenereology, Belgrade, from September 2004 to May 2006 who had urethral symptoms and signs (discharge, dysuria or urethral discomfort). The study was approved by the Institutional Review Board, and all participants gave an informed oral consent. We excluded men who had male sexual partners, those receiving antibiotics within the preceding month, who had HIV infection, or a current episode of genital herpes.

Urethral swabs for Gram stained urethral smears and microbiological analyses were taken from all study participants. Infection with *N. gonorrhoeae* was confirmed by finding intracellular Gram-negative diplococci and by culture on the modified chocolate agar under microaerophilic conditions (12). *Trichomonas vaginalis* was detected in a wet mount of urethral smear by adding 2-3 drops of saline (13). Infection with *C. trachomatis* was detected by direct immunofluorescence (Chlamydia Direct IF Identification, BioMérieux, Marcey L'étoile, France) (14). *Ureaplasma urealyticum* was identified by the Mycoplasma IST test (BioMérieux, Marcey L'étoile, France) (15). Polymorphonuclear leukocytes on Gram-stained urethral smear were counted in 5 oil immersion x1000 PMN per high power fields (phpf). Urethritis was defined as the presence of ≥5 PMN/hpf (11).

For the purpose of analysis, all patients were divided into two groups. The first (n=320) was comprised of men with clinically confirmed urethral discharge, while the other (n=310) was composed of patients with urethral symptoms but without discharge. Data were analysed on SPSS for Windows, Version 9.0 (Chicago, IL, USA). The significance of relationship involving clinical characteristics, urethral PMN count distribution and urethral pathogens was assessed by parametric tests (χ^2 test and analysis of variance for proportions), whereas the relation between PMN counts and urethral pathogens in patients with and without discharge was assessed by Spearman rank correlation.

Results

Urethral pathogen distribution in men with urethritis with and without urethral discharge is given in Table 1. *N. gonorrhoeae* was isolated only in men with ure-

Table 1. Urethral pathogen distribution across the subject groups

Urethral pathogen	**Patients with discharge (n =320)**		**Patients without discharge (n=310)**	
	n	%	*n*	%
Neisseriae gonorrhoeae	56	17.50	0	0
Trichomonas vaginalis	101	31.56	82	26.45
Chlamydia trachomatis	82	25.62	45	14.51
Ureaplasma urealyticum	77	24.06	58	18.70

F=8.854; P<0.01

Table 2. Correlation between urethral pathogen isolation and PMN counts in urethral smears in urethritis patients with and without discharge, and sensitivity, specificity, negative and positive predictive values for PMN counts.

PMN count phpf	Microbiological results (urethritis with discharge)			Microbiological results (urethritis without discharge)		
	positive	negative	total	positive	negative	total
≥5	254	32	286	119	9	128
<5	4	30	34	47	135	182
total	258	62	320	166	144	310
SN		98%			72%	
SP		48%			94%	
PPV		89%			93%	
NPV		88%			74%	

PMN, polymorphonuclear leukocytes; phpf, per high power field; SN, sensitivity; SP, specificity; PPV, positive predictive value; NPV, negative predictive value; ρ=0.986, P*<0.01; ρ=0.993;* P*<0.01; all of the pts had ureaplasma isolated; 29 pts had ureaplasma isolated.*

thritis accompanied by discharge (17.5%; n=56). The prevalence of *T. vaginalis*, *C. trachomatis* and *U. urealyticum* was significantly higher (F=8.854, *P*<0.01) in urethral swabs of urethritis patients with discharge. The most common urethral pathogen in both groups of patients was *T. vaginalis* (31.56% and 26.45%, respectively).

One or more of microorganisms were isolated in 258 (81%) subjects with urethritis with discharge, and in 166 (53.5%) urethritis patients without discharge. Urethritis caused by a single pathogen is the most common in both groups of patients (*n*=142; 55%, and *n*=128; 77%, respectively). Urethritis with simultaneous isolation of two pathogens was the most common occurrence, and more frequently found in patients with discharge. *N. gonorrhoeae* and *C. trachomatis* were found together in 11% of urethritis patients with discharge (not shown). Of note, in patients without discharge, there was not a single coinfection with *T. vaginalis* and *C. trachomatis*, but only *U. urealyticum* was found together with either of the former.

We found a positive correlation between the significant number of PMN in Gram stained urethral smears and positive microbiological findings in men with urethritis both with and without urethral discharge (Spearman's coefficients ρ=0.986 and ρ=0.993, respectively; *P*<0.01) (Table 2). In urethritis with discharge, only 1.5% of patients with identified urethral pathogen had <5 PMN phpf in their urethral smears explaining a relatively high sensitivity and positive predictive value (PPV) of the screening method in this group of patients – 98% and 89%, repectively (Table 2). On the other hand, in those patients without urethral discharge and with negative microbiological findings, ≥5 PMN phpf were found in only 6.2% giving the test in this setting reasonably high specificity and PPV (94 and 93%).

Discussion

The most prevalent urethral pathogen in our patients was *T. vaginalis*, both in those with (31.56%) and without (26.45%) urethral discharge. According to the World Health Organization (16), in Africa, trichomoniasis affects around 170 million people each year, whereas in Europe and USA the prevalence within high-risk populations ranges from 10-25% (17-19). Since *T. vaginalis* may be a cause of male infertility (reduces the motility of sperm cells) (13,16), and asymptomatic trichomoniasis may spread rapidly, it is important to diagnose and treat the infection appropriately (17).

C. trachomatis is the most common cause of nongonococcal urethritis. As a function of different detection methods (culture, direct immunofluorescence test, nucleic acid amplification tests, PCR) (20), its prevalence in symptomatic urethritis ranges from 18 to 31% (19,21), and in asymptomatic forms from 5 to 40.5% (7,22,23). Prevalence of *C. trachomatis* in our urethritis patients with and without discharge (25.62 and 14.51%) is similar to published prevalence rates. Iser et al. (24) found that the presence of urethral discharge on history or examination, and a history of previous NGU symptoms were statistically associated with the detection of chlamydia. A similar study (11) confirmed, on multivariate analysis, that the strongest associations with chlamydia infection were age, dysuria, and PMN per hpf. All of our patients were symptomatic but the presence of urethral discharge was associated with a doubled prevalence of *C. trachomatis* infection.

We isolated *N. gonorrhoeae* only in urethritis patients with discharge (17.50%). In a recent French survey, *N. gonorrhoeae* was found to be the second most common cause of male urethritis (13%) just after *C. trachomatis* (18%) (1). All of our patients had clinical

signs and symptoms of urethritis. In a series of 2626 men attending a STD clinic for routine evaluation, 990 were found positive for *C. trachomatis* and/or *N. gonorrhoeae* (11). Of them, 13 and 5%, respectively, were both asymptomatic and without urethral discharge.

U. urealyticum was detected in both groups of patients. It belongs to the normal flora of the genital tract, and the role it plays in nongonococcal male urethritis is not yet known (4,24). In roughly half of our uretritides where *U. urealyticum* was isolated, it was associated with other pathogens. It is speculated that coinfections trigger genital mycoplasmas to express their pathogenic potential (25).

Coinfection with two urethral pathogens were found in around 20% patients in both groups. The prevalence of *C. trachomatis* and *N. gonorrhoeae* coinfection in our patients with two agents detected concurrently was lower (10.81%) than those reported by other authors (25-43%) (26-28), but this may be a consequence of a lower sensitivity of DIF compared to amplification methods used to detect *C. trachomatis* in these studies. In urethritis patients without discharge, *C. trachomatis* and *T. vaginalis* occurred only with *U. urealyticum*, but never together. It is possible that, as being strict urethral pathogens, concommitant infection with chlamydia and trichomonas induces a strong inflammatory reaction clinically presenting as urethritis with discharge.

In our series of patients (Table 2), a relevant PMN count (≥5 PMN phpf) on Gram stained urethral smears strongly correlated with microbiological findings in both patients groups. Though a number of recent studies (10,11,24) showed that a proportion of men infected with *C. trachomatis* and even *N. gonorrhoeae* may have <5 PMN phpf on their uretheral smears, our results support the usefulness of the screening method in areas where more reliable and expensive diagnostic methods are not available. All of our patients with discharge in whom strict urethral pathogens were isolated had ≥5 PMN phpf in their Gram stained urethral smears (Table 2). Haddow et al. (10) confirmed that discharge was significantly associated with higher PMN count ($P<0.001$) and was associated with chlamydia infection. Probably those 6 and 11% of urethritis patients without discharge with discordant microbiological and PMN count findings represent recent sexual contacts with infected partners where epidemiologic treatment is justified.

The study disclosed a relatively high prevalence of *T. vaginalis* among our men with urethritis irrespective of the presence or absence of urethral discharge, and showed that taking into account both discharge found on examination, and relevant PMN counts on Gram stained urethral smears fails to detect only 4.2% of oligosymptomatic urethritis patients who are infected with one of the strict urethral pathogens. Thus in countries with limited diagnostic resources, Gram stained urethral smears are still a useful tool for therapeutic decision making in male urethritis.

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