IN PRACTICE

Symptoms of non-gonococcal urethritis in heterosexual men: a case control study

P Iser, TR H Read, S Tabrizi, C Bradshaw, D Lee, L Horvarth, S Garland, I Denham, C K Fairley

Methods: Case-control study of heterosexual men with non-gonococcal urethral symptoms (cases) and without urethral symptoms (controls) attending Melbourne Sexual Health Centre, Australia. Sexual behaviour and condom use were measured by questionnaire. First stream urine was tested for potential pathogens: Chlamydia trachomatis (ligase chain reaction), Mycoplasma genitalium (polymerase chain reaction, PCR), Ureaplasma urealyticum (culture and PCR), and Streptococcus spp, Gardnerella vaginalis, and Haemophilus species (culture). Urethral smears from cases were examined for polymorphonuclear leucocytes.

Results: 80 cases and 79 controls were recruited over 4 months in 2002–3. 49 cases (61%) had urethritis by microscopic criteria, 17 (21%) had Chlamydia trachomatis (adjusted odds ratio (OR) 27 (95% confidence interval (CI): 3.4 to 222)), five (6%) had Mycoplasma genitalium (OR 6.1 (95% CI: 0.6 to 61)), and 11 (14%) had Gardnerella vaginalis (OR 9.0 (95% CI: 1.6 to 52)). Other organisms were not significantly associated with urethral symptoms. The presence of urethritis on urethral smear did not predict the presence of Chlamydia trachomatis (OR 1.7 (95% CI: 0.5 to 5.4)). Urethral symptoms were significantly associated with unprotected vaginal sex with more than one casual partner (OR 9.3 (95% CI: 1.3 to 65)) and unprotected anal sex with a regular partner in the past month (OR 3.5 (95% CI: 1.0 to 13)).

Conclusion: Gardnerella vaginalis and unprotected anal sex may cause symptoms of non-gonococcal urethritis. Microscopy of the urethral smear to diagnose urethritis in this population does not help to identify which men with urethral symptoms require treatment for chlamydia.

Objective: To determine microbial and behavioural factors contributing to non-gonococcal urethral symptoms in men.

The cause of most cases of non-gonococcal urethritis (NGU) remains unknown. Chlamydia trachomatis accounts for 30–40% and Mycoplasma genitalium is now known to cause a smaller proportion, while other established causes are uncommon. Ureaplasma urealyticum, Gardnerella vaginalis, Haemophilus species, and Streptococcus spp have been associated with NGU but their causal role is unproved.

In Australian general practice men are often treated when they present with symptoms of NGU before laboratory confirmation of urethritis on urethral smear. It is therefore useful to establish the prevalence of urethral pathogens in all men with urethral symptoms regardless of the presence of urethritis on the urethral smear. We conducted a case-control study of men with symptoms of NGU and controls examining the prevalence of known and suspected pathogens and associations with sexual practices.
RESULTS

The 79 controls (mean age 30.2 years) were younger than the 80 cases (mean 35.8 years). Forty nine cases (61%) had 5 polymorphs/hpf or more and 19 (23%) had fewer than 1 polymorphs/hpf. Detection of Chlamydia trachomatis, Streptococci spp, and Gardnerella vaginalis was statistically associated with urethral symptoms in the crude and adjusted analysis (Table 1). When only cases with urethritis were included, both the crude and adjusted odds ratios remained essentially unchanged (data not shown). Mycoplasma genitalium was detected in five cases and one control, but this was not statistically significant.

Among cases the presence of 5 polymorphs/hpf or more in the urethral smear did not predict the presence of Chlamydia (OR 1.7 (95%CI: 0.5 to 5.4)) or any other organism (p = 0.15). The presence of urethral discharge on history or examination was statistically associated with the detection of chlamydia in cases, OR 3.9 (95% CI: 1.1 to 15) and 3.9 (95% CI: 1.2 to 14) respectively as was a history of previous NGU symptoms (OR 2.4 (95% CI 1.1 to 5.4). No other symptoms or signs were associated with the detection of other organisms (p>0.2).

The behavioural factors associated with NGU are shown in Table 1. In the adjusted analysis unprotected vaginal sex with a casual partner and unprotected anal sex with a regular partner were significantly associated with NGU, but more than one casual partner and unprotected anal sex with a regular partner were significantly associated with NGU, but more than one casual partner and unprotected anal sex with a regular partner and vaginal and oral sex with casual partners.

DISCUSSION

In this case-control study of heterosexual men with urethral symptoms, cases were more likely to have Chlamydia trachomatis, Gardnerella vaginalis, and any streptococci isolated from their urine and to report past urethral symptoms, unprotected vaginal sex with a casual partner, and unprotected anal sex with their regular partner. These results are particularly applicable to health services where most men with urethral symptoms are treated in primary care without access to on-site microscopy.

Gardnerella vaginalis was isolated from significantly more cases (14%) than controls (3%) indicating that organisms associated with bacterial vaginosis (BV) may cause urethral symptoms in men. G vaginalis has been isolated from men with urethritis, and NGU has also been associated with the presence of BV in female partners.

In this study unprotected anal sex with a regular partner was reported three times more commonly in cases than controls. It is possible that urethral irritation could result from exposure to rectal flora during anal sex.

Among men with urethral symptoms, urethritis by microscopic criteria did not predict the presence of Chlamydia trachomatis, whereas discharge was predictive. Several studies have also found that microscopic urethritis did not predict C trachomatis, while Horner et al found discharge to predict C trachomatis. The value of urethral symptoms over microscopy in predicting those likely to have C trachomatis, is supported by our finding that the prevalence of C trachomatis among urethritis negative cases (five of 31) was higher than among asymptomatic controls (one of 79; p = 0.002).

It is possible that our sample size, and the inclusion of cases without microscopic urethritis, prevented us from detecting weaker associations, such as those between individual organisms, microscopic urethritis, or certain behaviours. Ureaplasma urealyticum, Haemophilus influenzae, or any particular streptococcal species were not associated with urethral symptoms.

Acute urethral symptoms in a male population with a low prevalence of bacterial STIs may be due to other causes, including G vaginalis and anal sex. Our results support our practice of offering treatment for C trachomatis and partner notification to all men attending our clinic with symptoms of urethritis and a behavioural risk factor regardless of the presence of urethritis on their urethral smear.

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Table 1  Crude and adjusted odds ratios (OR) for organisms and behavioural risk factors

<table>
<thead>
<tr>
<th></th>
<th>Cases (%)</th>
<th>Controls (%)</th>
<th>Crude OR (95% CI)</th>
<th>Adjusted OR*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>80</td>
<td>79</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chlamydia trachomatis</td>
<td>17 (21.3)</td>
<td>1 (1.3)</td>
<td>2.10 (2.7 to 163)</td>
<td>27 (3.4 to 222)</td>
</tr>
<tr>
<td>Ureaplasma urealyticum (culture or PCR)</td>
<td>23 (28.8)</td>
<td>26 (32.9)</td>
<td>0.8 (0.4 to 1.6)</td>
<td>0.5 (0.3 to 1.4)</td>
</tr>
<tr>
<td>All streptococci</td>
<td>28 (35.0)</td>
<td>14 (17.7)</td>
<td>2.5 (1.2 to 5.2)</td>
<td>3.2 (1.1 to 9.6)</td>
</tr>
<tr>
<td>Group B Streptococcus</td>
<td>11 (13.8)</td>
<td>1 (1.3)</td>
<td>2.4 (0.8 to 7.1)</td>
<td>2.1 (0.5 to 11.4)</td>
</tr>
<tr>
<td>Haemophilus influenzae</td>
<td>2 (2.5)</td>
<td>0</td>
<td>p = 0.5</td>
<td></td>
</tr>
<tr>
<td>Gardnerella vaginalis</td>
<td>11 (13.8)</td>
<td>2 (2.5)</td>
<td>6.1 (1.3 to 29)</td>
<td>9.0 (1.6 to 52)</td>
</tr>
<tr>
<td>Mycoplasma genitalium</td>
<td>5 (6)</td>
<td>1 (1.3)</td>
<td>4.1 (0.5 to 37)</td>
<td>6.1 (0.6 to 61)</td>
</tr>
<tr>
<td>Previous similar symptoms†</td>
<td>36 (45)</td>
<td>19 (24)</td>
<td>2.5 (1.2 to 5.4)</td>
<td>2.4 (1.1 to 5.4)</td>
</tr>
<tr>
<td>Regular sexual partner</td>
<td>44 (57.1)</td>
<td>48 (64.0)</td>
<td>0.8 (0.4 to 1.4)</td>
<td></td>
</tr>
<tr>
<td>Vaginal sex</td>
<td>36 (47.4)</td>
<td>38 (51.4)</td>
<td>1.0 (0.5 to 1.9)</td>
<td></td>
</tr>
<tr>
<td>Oral sex</td>
<td>11 (14.5)</td>
<td>4 (5.5)</td>
<td>2.9 (0.9 to 9.6)</td>
<td>3.5 (1.0 to 13)</td>
</tr>
<tr>
<td>Anal sex</td>
<td>45 (58.4)</td>
<td>17 (23.3)</td>
<td>4.6 (2.3 to 9.4)</td>
<td>p = 0.05</td>
</tr>
<tr>
<td>Casual sexual partner (past month)</td>
<td>0</td>
<td>38 (50) 59 (68)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Vaginal sex</td>
<td>1 21 (28%)</td>
<td>12 (16)</td>
<td>1.9 (0.9 to 4.3)</td>
<td>2.1 (0.7 to 6.1)</td>
</tr>
<tr>
<td>Oral sex</td>
<td>1 16 (21%)</td>
<td>8 (11.1)</td>
<td>2.5 (1.0 to 6.3)</td>
<td>1.8 (0.5 to 6.1)</td>
</tr>
<tr>
<td>Anal sex</td>
<td>Any 3 (4.3)</td>
<td>1 (1.4)</td>
<td>3.1 (0.3 to 39)</td>
<td></td>
</tr>
</tbody>
</table>

*The first adjusted analysis included having a casual sexual partner in the previous month, past urethral symptoms, and the presence of other urethral organisms and a second adjusted analysis included anal sex with regular partner and vaginal and anal sex with casual partners.

†Refers to similar symptoms in a separate episode more than 1 month earlier.
CONTRIBUTORS
PI carried out the research project; TR and CF contributed to protocol design and wrote the paper with CB; ST and SG performed the PCR assays and contributed to the paper; ID and LH contributed to protocol design; and LH performed diagnostic microbiology; DL contributed to the paper.

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Ethical approval: The ethics committee of the Victorian Department of Human Services approved this study.

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