The contribution of *Mycoplasma genitalium* to the aetiology of sexually acquired infectious proctitis in men who have sex with men

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**Background (1)**

- Rectal infections with pathogens increase the risk for HIV acquisition\(^1\)
- Unprotected receptive anal sex confers a high risk for HIV acquisition\(^2\)
- Previous studies have described the spectrum of pathogens responsible for proctitis in MSM\(^3,4,5\)


**Background (2)**

- *Mycoplasma genitalium* causes urethritis in men and genital tract infection in women
- Previous studies identified *M. genitalium* in the rectum of MSM
- Prevalence rates between 1.6 % and 5.0%,\(^1,4\)

1. Francis S et al. *Sexually Transmitted Diseases* 2008; 35(9):797-800

**Aims**

- Prospective study of MSM presenting with symptomatic proctitis
- Determine the prevalence of rectal *M. genitalium*
- Compare these between HIV positive and HIV negative men
- Compare the load of *M. genitalium* in men with symptomatic rectal infection to men with asymptomatic rectal infection

**Methods (1)**

- From 1\(^{st}\) May 2012 all MSM with clinical proctitis at MSHC tested for rectal:
  - *Mycoplasma genitalium*
  - Gonorrhoea, Chlamydia, HSV
- Diagnosis of proctitis: clinical based on the presence of rectal pain and/or discharge
Methods (2)

- Between May 2012 and August 2013 measured prevalence of rectal *M. genitalium* in consecutive MSM with symptomatic proctitis
- Measured organism load in men with *M. genitalium*-associated symptomatic proctitis
- Compared this in a separate group of men with asymptomatic rectal *M. genitalium* infection

Methods (3)

- Asymptomatic sexual contacts of men with urethral *M. genitalium*
- Selected into the study from the beginning of the study period in consecutive order of presentation
- One case of asymptomatic rectal *M. genitalium* infection for each case of *M. genitalium* associated symptomatic proctitis

Methods (4)

- *Chlamydia trachomatis* using SDA
- Genotyping for LGV on chlamydia positive samples using an in-house OMP-1 DNA sequencing method
- *Neisseria gonorrhoeae* using culture
- HSV using an in-house herpes multiplex PCR

Methods (5)

- Syphilis serological testing using RPR and EIA
- *Treponema pallidium* by PCR using TaqMan real-time PCR assay
- *M. genitalium* using qPCR targeting a 517bp region of the 16S rRNA gene
- HIV by immunoassay (Murex UK)
  

Statistical analysis (1)

- Sample size 150 men (95% CI prevalence of 6-10%)
- Prevalence of each rectal pathogen
- Difference in prevalence between HIV positive and HIV negative men
- Chi square test to compare proportions

Statistical analysis (2)

- Log transformed rectal *M. genitalium* load
- Linear regression to determine if load differed between men with symptomatic and asymptomatic rectal infection
- Ethical approval for the study was obtained from the Alfred HREC (522/14)
Results (1)

- 154 men with proctitis
- 48 (31%) HIV positive
- 106 (69%) HIV negative
- Median age 38 years (range: 22-58 years)
- Median CD4 count: 475 cells/μL
- 81% on ART and 97% on ARV - HIV VL < 50 copies/ml
- Clinical presentation men broadly similar in both groups

Results (3)

- 9/12 (75%) men with external anal ulceration had HSV detected:
  - 5/9 (56%) HIV positive
  - 4/9 (44%) HIV negative
  - 3 men with anal ulcers not associated with HSV were T. pallidum PCR positive

Aetiology of proctitis by HIV status in MSM

<table>
<thead>
<tr>
<th>Pathogens detected</th>
<th>HIV positive</th>
<th>HIV negative</th>
<th>Unadjusted Odds Ratio (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlamydia trachomatis</td>
<td>10 (21; 36)</td>
<td>20 (19; 28)</td>
<td>1.13 (0.48 - 2.64)</td>
<td>p=0.77</td>
</tr>
<tr>
<td>Neisseria gonorrhoeae</td>
<td>14 (29; 42)</td>
<td>24 (31; 51)</td>
<td>1.41 (0.65 - 3.04)</td>
<td>p=0.43</td>
</tr>
<tr>
<td>HSV</td>
<td>9 (19; 30)</td>
<td>18 (17; 24)</td>
<td>1.20 (0.47 - 2.73)</td>
<td>p=0.76</td>
</tr>
<tr>
<td>HSV-1</td>
<td>2 (4; 10)</td>
<td>14 (13; 19)</td>
<td>0.29 (0.06 - 1.31)</td>
<td>p=0.9</td>
</tr>
<tr>
<td>HSV-2</td>
<td>7 (15; 25)</td>
<td>4 (4; 8)</td>
<td>4.35 (1.21 - 14.67)</td>
<td>p=0.02</td>
</tr>
<tr>
<td>LGV</td>
<td>4 (8; 16)</td>
<td>1 (1; 3)</td>
<td>9.5 (1.03 - 87.83)</td>
<td>p=0.02</td>
</tr>
<tr>
<td>Two or more pathogens</td>
<td>9 (19; 36)</td>
<td>8 (7; 12)</td>
<td>2.83 (1.01 - 7.86)</td>
<td>p=0.03</td>
</tr>
</tbody>
</table>

Mycoplasma genitalium associated proctitis

<table>
<thead>
<tr>
<th>Pathogens detected</th>
<th>HIV positive</th>
<th>HIV negative</th>
<th>Odds Ratio (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mycoplasma genitalium</td>
<td>10 (21; 36)</td>
<td>8 (8; 13)</td>
<td>3.22 (1.18 - 8.78)</td>
<td>p=0.02</td>
</tr>
</tbody>
</table>

Discussion (1)

- First prospective cohort study of MSM with symptomatic proctitis systematically tested for rectal M. genitalium
- First study showing quantitative data of M. genitalium load in the rectum and its association with symptomatic proctitis
- Relative prevalence of pathogens seen in HIV positive men differed from that seen in HIV negative men
- Significantly higher prevalence among HIV positive men of M. genitalium, HSV 2, LGV and multiple pathogens
Discussion (2)

- M. genitalium present in 12% of MSM presenting with proctitis
- HIV positive status strongly associated with M. genitalium proctitis
- 21% of HIV positive men compared with 8% of HIV negative men with proctitis infected with M. genitalium
- Significantly higher rectal M. genitalium loads in men with symptomatic proctitis than men with asymptomatic rectal infection

Discussion (3)

- Other studies1-5 examined the prevalence of rectal M. genitalium among MSM
- None included men specifically selected because of the presence of symptomatic proctitis

Discussion (4)

- Higher rates of rectal M. genitalium among HIV positive compared to HIV negative MSM:
  - 21% versus 8% (p=0.02)
  - 11% versus 4% (p=0.005)1
  - 14% versus 2% (p=0.001)2
  - 19% versus 5% (p=0.02)3

Discussion (5)

- Overall rate of rectal M. genitalium in our study is higher than in these previous studies
- Selected MSM with symptomatic proctitis
- Inclusion of HIV positive men, where sexual risk behaviours have contributed to higher rates of bacterial sexually transmitted infections

Discussion (6)

- In-vitro studies demonstrated that M. genitalium can establish long term infection in human endocervical cells1
- Studies in females demonstrated presence of HIV susceptible cells in the mucosa of cervix with M. genitalium infection1
- HIV negative men with rectal mucosal inflammation severe enough to cause symptomatic proctitis and mucosal ulceration may also have increased susceptibility to HIV

Rectal Infection with M. genitalium

<table>
<thead>
<tr>
<th>Authors</th>
<th>Population</th>
<th>Rectal M. genitalium prevalence (%95%CI)</th>
<th>Rectal symptoms and signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Francis 2008</td>
<td>500 consecutive rectal MSM samples</td>
<td>27(5.4,3.6-7.7)</td>
<td>Not significantly associated with proctitis Associated with HIV (AOR:3.2)</td>
</tr>
<tr>
<td>Bradshaw 2009</td>
<td>cross sectional study 521 Australian MSM attending SOPV</td>
<td>8/497(1.6, 0.8-3.0)</td>
<td>All asymptomatic</td>
</tr>
<tr>
<td>Soni 2009</td>
<td>438 MSM attending STD clinic</td>
<td>19/412(4.6, 2.6-6.6)</td>
<td>Not significantly associated with proctitis Associated with HIV (AOR:7.6)</td>
</tr>
<tr>
<td>Renton 2013</td>
<td>retrospective analysis of 1778 MSM rectal samples</td>
<td>65/1778(3.7, 2.8-4.5)</td>
<td>Unavailable</td>
</tr>
<tr>
<td>Zheng 2014</td>
<td>405 MSM attending STD clinic</td>
<td>22/405(5.4,3.5-7.7)</td>
<td>Unavailable Associated with HIV (OR:4.49)</td>
</tr>
</tbody>
</table>
Discussion (7)

- Previous study demonstrated that symptomatic gonococcal proctitis was associated with higher loads of *N. gonorrhoeae* than seen with asymptomatic rectal gonorrhoea.
- Organism load significantly higher in men with symptomatic rectal *M. genitalium* compared to men with asymptomatic rectal infection


Strengths and Limitations

- Conducted prospectively and consecutive MSM tested for *M. genitalium* and other rectal pathogens
- Diagnosis of proctitis was based on clinical criteria and not evaluated by rectal biopsy
- Gonorrhoea testing using culture which is less sensitive than NAAT for rectal infections


Conclusion

- *Mycoplasma genitalium*:
  - Important rectal pathogen among MSM
  - Cause of symptomatic proctitis
  - Testing should be undertaken in MSM presenting proctitis

Acknowledgments

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