Antimicrobial resistance in pharyngeal Neisseria gonorrhoeae infection: A cross-sectional study in England

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Public Health England
Background – increasing *Neisseria gonorrhoeae* AMR

2005: Recommendation of ceftriaxone OR cefixime as first line therapy

Data source: GRASP
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<table>
<thead>
<tr>
<th>Year</th>
<th>Ceftriaxone (&gt;0.125)</th>
<th>Azithromycin (&gt;0.5)</th>
<th>Cefixime (&gt;0.125)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2005</td>
<td>0%</td>
<td>0%</td>
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<td>0%</td>
</tr>
<tr>
<td>2008</td>
<td>2%</td>
<td>4%</td>
<td>0%</td>
</tr>
<tr>
<td>2009</td>
<td>2%</td>
<td>4%</td>
<td>0%</td>
</tr>
<tr>
<td>2010</td>
<td>2%</td>
<td>4%</td>
<td>0%</td>
</tr>
<tr>
<td>2011</td>
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<tr>
<td>2017</td>
<td>6%</td>
<td>8%</td>
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</tr>
</tbody>
</table>

Data source: GRASP

Antimicrobial resistance in pharyngeal *Neisseria gonorrhoeae* infection: A cross-sectional study in England
Background – why is site of infection important?

- Gonorrhoea is concentrated among specific population groups, especially gay, bisexual and other men who have sex with men (MSM). 67% of diagnoses are made among MSM.

- Genital gonorrhoea is most commonly diagnosed but is also common in the rectum and pharynx.

- Pharyngeal infections disproportionally effect MSM, with 48% of diagnoses in this group in the pharynx.

- Pharyngeal infection is often asymptomatic and thought to be more difficult to treat compared to other infection sites.
Objectives

To investigate the association between site of infection and reduced susceptibility to antimicrobials in MSM and heterosexual men and women
Methods – antimicrobials considered

We used data collected in GRASP from 2012 to 2017.

We look at the association between resistance or reduced susceptibility to three antimicrobials and site of infection.

<table>
<thead>
<tr>
<th>Antimicrobial</th>
<th>Resistance threshold (minimum inhibitory concentration (MIC))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azithromycin</td>
<td>MIC &gt;0.5 mg/L</td>
</tr>
<tr>
<td>Cefixime</td>
<td>MIC &gt;0.125 mg/L</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>MIC ≥ 0.015 mg/L</td>
</tr>
</tbody>
</table>

In samples collected from the pharynx and urethra from men who have sex with men and heterosexual men and women.
Methods – Statistical methods

Bivariate analysis was used to test for an association between antimicrobial resistance and:

**Factors associated with infection:**
- Site of infection
- Number of infection sites at time of gonorrhoea diagnosis
- The presence of symptoms

**Demographic factors:**
- Age group
- Ethnicity

**Behavioural factors:**
- HIV status
- Number of sexual partners
- Concurrent STI at the time of gonorrhoea diagnosis
- Previous gonorrhoea diagnosis

A multivariable logistic regression was used to adjust for factors with a significant association between site of infection and AMR.
Results: samples by site of infection and sexual orientation

2012-2017
8,437 samples submitted to GRASP

4,910
Genital or pharyngeal samples

3,038 MSM

77% Genital

24% Pharyngeal

1,761 Heterosexual

1,548 Males

77% Genital

24% Pharyngeal

168 Females

77% Genital

24% Pharyngeal
Results: Patient characteristics

Demographic Factors:
- Age Group: 20-24
- Age Group: 25-34
- Ethnicity: White
- Ethnicity: Black or Black British
- Diagnosed with HIV

Behavioural factors:
- More than one sexual partner in last 3 months
- Previous gonorrhoea infection

Factors associated with infection:
- Symptomatic infection
- More than one infection site

An analysis of the link between anti-retroviral therapy and syphilis in men who have sex with men in England 2008-2016
## Bivariate results: Odds of AMR by site of infection in three antimicrobials

**MSM:**

<table>
<thead>
<tr>
<th>Antimicrobial</th>
<th>Sample site</th>
<th>Odds Ratio</th>
<th>(95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azithromycin</td>
<td>Urethra</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pharynx</td>
<td>1.82</td>
<td>(1.29, 2.58)</td>
<td>0.001</td>
</tr>
<tr>
<td>Cefixime</td>
<td>Urethra</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pharynx</td>
<td>1.12</td>
<td>(0.67, 1.84)</td>
<td>0.671</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>Urethra</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pharynx</td>
<td>1.28</td>
<td>(1.07, 1.52)</td>
<td>0.006</td>
</tr>
</tbody>
</table>

**Heterosexuals:**

<table>
<thead>
<tr>
<th>Antimicrobial</th>
<th>Sample site</th>
<th>Odds Ratio</th>
<th>(95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azithromycin</td>
<td>Urethra</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pharynx</td>
<td>3.78</td>
<td>(1.72, 8.30)</td>
<td>0.001</td>
</tr>
<tr>
<td>Cefixime</td>
<td>Urethra</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pharynx</td>
<td>1.40</td>
<td>(0.59, 3.30)</td>
<td>0.443</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>Urethra</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pharynx</td>
<td>2.08</td>
<td>(1.29, 3.35)</td>
<td>0.003</td>
</tr>
</tbody>
</table>
Multivariable results: Association between AMR and site of infection in MSM

Azithromycin*

Ceftriaxone†

Cefixime ‡

* Azithromycin adjusted for year of infection
† Ceftriaxone adjusted for year of infection
‡ Cefixime adjusted for previous gonorrhoea infection, presence of symptoms and HIV status
Multivariable results: Association between AMR and site of infection in heterosexuals

- Azithromycin*: P = 0.002
- Ceftriaxone†: P = 0.085
- Cefixime ‡: P = 0.282

*Azithromycin adjusted for total sexual partners
† Ceftriaxone adjusted for year of infection
‡ Cefixime adjusted for previous gonorrhoea infection, presence of symptoms and HIV status
Limitations of the analysis

➢ As the GRASP programme only selects one sample per person we were not able to look at differences in MIC within individuals.

➢ The prioritisation of samples meant that isolates were retrieved from fewer pharyngeal samples compared to the other infection sites.
Conclusions and summary

➢ Pharyngeal infections were significantly associated with azithromycin resistance among both MSM and heterosexuals, compared to genital infections.

➢ Pharyngeal infections were significantly associated reduced susceptibility to ceftriaxone among MSM and not in heterosexuals, compared to genital infections.

➢ Our results show that in both MSM and heterosexual’s, pharyngeal infections are more likely to harbour resistance to azithromycin and in MSM, reduced susceptibility to ceftriaxone, compared to genital infections.

These results highlight the importance of extra-genital tests, antimicrobial susceptibility testing, and test of cure, especially among MSM, to reduce treatment failure and onward transmission of resistant strains.
Acknowledgments

We gratefully acknowledge all clinics who report to GUMCAD and laboratories involved in the GRASP programme, as well as all involved in testing samples and preparing the samples.

Thank you!

Questions?