Tetracycline resistance in *Neisseria gonorrhoeae*

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Gonorrhoea

• sexually transmitted infection
  – *Neisseria gonorrhoeae*
  – increasing resistance to antibiotics

• syndromic management for discharge/urethritis
  – 3rd generation cephalosporin
  – doxycycline derivative of tetracycline
  – metronidazole (female)
Tetracyclines

- binds to bacterial ribosomes and prevents protein synthesis
- active against *N. gonorrhoeae* in absence of resistance mechanisms
Tetracycline Resistance

• low level resistance
  – chromosomally mediated

• high level resistance
  – plasmid mediated
    ➢ acquisition of the tetM plasmid

• 2 variants of tetM gene
  – Dutch
  – American
Aims

To determine:

• the MIC of *N. gonorrhoeae* isolates to tetracycline
• the presence of the tetM gene in tetracycline resistant isolates
Methodology

Ethics Number BE220/13

Specimen collection

- Pietermaritzburg
- Umlazi

Phenotypic Characterization

- Gram stain
- Oxidase test
- Carbohydrate utilization test
- MIC to tetracycline

Detection and Molecular Characterization of tetM gene

- Polymerase Chain Reaction
- Gel electrophoresis
Tetracycline Breakpoints for *N. gonorrhoeae*

- **EUCAST**
  - resistant $> 1 \text{mg/L}$
  - susceptible $\leq 0.5 \text{mg/L}$
Culture Results

1220 patients

319 (26%) positive
- 248 (78%) male
- 71 (22%) female

901 (74%) negative
- 258 (29%) male
- 643 (71%) female
Figure 1: Prevalence of *N. gonorrhoeae* stratified by age and gender
Table 1: Distribution of tetracycline MIC in *N. gonorrhoeae*

<table>
<thead>
<tr>
<th>MIC (mg/L)</th>
<th>PMB (n=264)</th>
<th>Umlazi (n=55)</th>
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<tbody>
<tr>
<td>8</td>
<td>4%</td>
<td>2%</td>
</tr>
<tr>
<td>16</td>
<td>96%</td>
<td>98%</td>
</tr>
<tr>
<td>≥32</td>
<td>96%</td>
<td>98%</td>
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</tbody>
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Figure 2: Gel electrophoresis of PCR products

1: molecular weigh marker 100bp, 2: American control, 3: Dutch control, 4: Negative control 5-20: *N. gonorrhoeae* clinical isolates
Figure 3: Distribution of \textit{tetM} variants amongst tetracycline resistant \textit{N.gonorrhoeae} isolates
Discussion and Conclusion

• previous studies in KZN
  – all high level tetracycline resistant strains
    ➢ harboured American variant

• new findings
  – Dutch *tetM* in KZN
  – high level resistance without *tetM*
    ➢ requires further exploration
• tetracycline should not be re-introduced for the treatment of gonorrhoea

• $tetM$ plasmid mediated: transferable between genera
  – ? utility for management of chlamydia infection as part of syndromic management
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