Azithromycin treatment failure in women diagnosed with genital chlamydia

Hocking JS,1 Vodstrcil L,1 Huston W,2 Timms P,3 Chen M,4 Bradshaw C,4 Worthington K,4 Lawrence A,2 McIver R,5 Phillips S,6 Tabrizi SN.7,8


Acknowledgements

• Professor Christopher Fairley
  — Melbourne Sexual Health Centre

• Dr Anna McNulty
  — Sydney Sexual Health Centre

• National Health and Medical Research Council No. 1023239

Melbourne School of Population and Global Health

High repeat infection rates among women

• 18% to 57% in adolescents in the USA1,2
• 10% per year in general population sample in the Netherlands3
• 22.3% per year (Australia) to 29.9% per year (UK) in general practice4,5
  — Median time to repeat infection 4.6 months4

What does repeat infection mean?

• Re-infection due to unprotected sexual contact with an infected partner
• Treatment failure as a result of:
  — Non-compliance with treatment
  — Poor absorption of the drug
  — Reduced antimicrobial susceptibility or antimicrobial resistance
• Persistence due to host factors such as immune response

Evidence to support azithromycin treatment failure?

• 2 studies of women in whom re-infection had been ruled out found azithromycin failure of ~8%.1,2
• RCT reported an azithromycin failure for chlamydia of 23% - significantly higher than 5.2% observed for doxycycline.3
• Failure for rectal chlamydia infection from 6% to 21%.4,6

Meta-analysis comparing azithromycin with doxycycline for urogenital chlamydia

Doxycycline 3% greater efficacy than azithromycin
3% (95%CI: 1.0%, 5.0%)

Kong et al. CID 2014;59:193-205.
Aim

• To estimate the proportion of women infected with chlamydia who experience failure after treatment with 1 gram azithromycin.

Methods – study design

• Cohort study of women diagnosed positive for urogenital chlamydia attending Melbourne Sexual Health Centre or Sydney Sexual Health Centre between Oct 2012 and Dec 2014.

• Participants – eligibility criteria
  – Age ≥16
  – NAAT positive for chlamydia
  – Adequate English for informed consent
  – Able to attend clinic in person at day 7

• Treated with 1 gram azithromycin

• Women followed up weekly through mail for 56 days OR until a repeat infection diagnosed

Outcome definition

Study endpoint

• Test of cure conducted in real time on swabs collected at day 28, 42 or 56.

• If PCR+, then study endpoint reached, otherwise followed up until day 56.

Methods – follow up and testing schedule

Melbourne School of Population and Global Health

**Methods - analysis**

- Proportions and 95%CI calculated using exact binomial methods
- Kaplan Meier used to investigate time till repeat positivity
- Cox regression used to investigate factors associated with repeat infection.

**Results (1)**

- 305 women recruited – response rate = 66%
- 241 (79%) were retained till study endpoint
- 2,373 weeks of follow-up
- Median age 23 years (IQR=21-26yrs)
- A total of 36 repeat infections were detected
  - 14.9% (95%CI: 10.7%, 20.1%)
- Incidence of repeat infection
  - 1.5 per 100 weeks (95%CI: 1.1, 2.1)

- 305 women recruited
- 241 (79%) retained till study endpoint
- 2,373 weeks of follow-up
- Median age: 23 years (IQR=21-26yrs)
- 36 repeat infections detected
  - 14.9% (95%CI: 10.7%, 20.1%)
- Incidence: 1.5 per 100 weeks (95%CI: 1.1, 2.1)

**Results (2)**

- Treatment failure: 12 cases (5.0% (95%CI: 2.6%, 8.5%)) based on sex behaviour and genovar
- Further laboratory analysis in process
**Discussion**

- About 15% of women will present with a repeat positive chlamydia diagnosis within 12 weeks following treatment
  - Most repeat infections will occur within 9 weeks
- Repeat infection is associated with organism load
- At this stage, an estimated 1 in 20 women with chlamydia treated with 1 gram azithromycin will fail treatment – consistent with other studies.\(^1,2\)
  - No evidence of MIC shift.
  - Likely to be less than that observed for rectal chlamydia infection.\(^3\)

---