Doxycycline Prophylaxis for Prevention of Bacterial STDs: The Cons

Olusegun O. Soge, PhD
Assistant Professor
Global Health and Medicine (Infectious Diseases)
University of Washington

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Key Questions

- Do we have comprehensive data on the safety, efficacy, acceptability, and risks of doxycycline prophylaxis?
- What is the impact of doxycycline prophylaxis on individual- and population-level tetracycline resistance?
- What is the impact of doxycycline prophylaxis on gut microbiome and resistome?
- Do the benefits of doxycycline prophylaxis outweigh the risks and unintended consequences?
Position statement on doxycycline prophylaxis for prevention of bacterial STDs

- No position statement from CDC
- Not endorsed by the British Association for Sexual Health and HIV (BASHH) and Public Health England (PHE)
- “Any potential benefits will be outweighed by the considerable potential to select resistance in STI pathogens and other bacterial species.”
- “Further studies are required to measure the wider impact of prophylactic doxycycline on antimicrobial resistance (AMR) at an individual and population level.”

MRSA is the leading cause of healthcare-associated infections.

Treatment failures of last resort drugs for gonorrhea have been reported from 10 countries.

Antimicrobial resistance is a global problem.

AMR infections cause 8 million hospital days and $30 billion cost to U.S. health care system per year.

No new major antibiotics have been discovered for 25 years.

The major reason for resistance development is inappropriate use of antimicrobial drugs.

1.2 million infections and $96 million cost are caused by resistant *Streptococcus pneumoniae* in the U.S. per year.

Multi-drug resistant tuberculosis strains caused 450,000 infections worldwide in 2012.

The WHO predicts a post-antibiotic era.

Source: http://2014.igem.org/Team:LMU-Munich/Project/Problem
Neisseria gonorrhoeae — Prevalence of Tetracycline, Penicillin, or Fluoroquinolone Resistance or Elevated Cefixime, Ceftriaxone, or Azithromycin Minimum Inhibitory Concentrations (MICs)†, by Year — Gonococcal Isolate Surveillance Project (GISP), 2000–2017

Gonococcal tetracycline resistance, Seattle, WA, 2007-2016
Neisseria gonorrhoeae high-level tetracycline resistance

- 97-100% high-level tetracycline resistance in several countries including Kenya, South Africa, WHO South-East Asia Region (Bhutan, India, Sri Lanka and Thailand)
Emergence of azithromycin resistance in Treponema pallidum due to antibiotic selection

- Use of azithromycin led to rapid increase in azithromycin resistance in *T. pallidum*

Fig: Proportion of *T. pallidum* strains harboring the 23S rRNA mutation that confers resistance to macrolide

- Possible risk of emergence of tetracycline resistance in *T. pallidum* due to doxycycline prophylaxis
Tetracycline resistance in *Chlamydia*

- Antibiotic selective pressure promotes selection of tetracycline resistance in *Chlamydia suis*
- *In vitro* horizontal transfer of tetracycline resistance among *Chlamydia* spp. including *C. trachomatis*
Selection of tetracycline resistance and cross resistance to other classes of antibiotics

- Genetic linkage between genes conferring resistance to tetracycline and macrolides
- Co-selection of resistance to multiple classes of antibiotics encoded on high-level tetracycline resistance plasmids
- Selection, induction, and expansion of tetracycline resistance in *S. aureus*, MRSA, commensal *Neisseria* spp., and other bacteria
- Strong association between clinical use of tetracycline, doxycycline, and minocycline and *in vitro* resistance of *S. aureus*
Impact on the gut microbiome and resistome

- Alteration of gut microbiome
- Decrease diversity of gut flora
- Change in predominant species
- Expansion of reservoir of tetracycline resistance genes
- Enrichment of antibiotic resistome
Summary: Is doxycycline prophylaxis ready for prime time?

- No comprehensive data on the safety, efficacy, acceptability, adherence, and risks of doxycycline prophylaxis among diverse populations
- No data on population-wide benefits of doxycycline prophylaxis and antibiotic resistance
- No data on gut microbiome and resistome
- No scientific evidence suggesting that the benefits of doxycycline prophylaxis outweigh the significant risks and unintended consequences