

Changes in antimicrobial resistance and antibiotics consumptions using Ceftriaxone monotherapy versus dual therapy with azithromycin for treatment of gonorrhoea in Melbourne, Australia

Authors:

Chow EPF^{1,2,3}, Stevens K⁴, De Petra V^{1,4}, Aguirre I¹, Ierano C⁵, Chen MY^{1,2}, Bradshaw CS^{1,2,3}, Sherry NL⁴, Ong JJ^{1,2}, Williamson DA^{6,7,8}, Howden BP^{4,9}, Fairley CK^{1,2}

¹Melbourne Sexual Health Centre, Alfred Health, Melbourne, Victoria, Australia, ²Central Clinical School, Faculty of Medicine, Nursing and Health Sciences, Monash University, Melbourne, Victoria, Australia, ³Centre for Epidemiology and Biostatistics, Melbourne School of Population and Global Health, The University of Melbourne, Melbourne, Victoria, Australia, ⁴Microbiological Diagnostic Unit Public Health Laboratory, Department of Microbiology and Immunology, University of Melbourne, at the Peter Doherty Institute for Infection and Immunity, Melbourne, Victoria, Australia, ⁵National Centre for Antimicrobial Stewardship, Department of Infectious Diseases, University of Melbourne, Melbourne, Victoria, Australia, ⁶Victorian Infectious Disease Reference Laboratory, The Royal Melbourne Hospital, at The Peter Doherty Institute for Infection and Immunity, Melbourne, Victoria, Australia, ⁷Department of Infectious Diseases, University of Melbourne, at the Peter Doherty Institute for Infection and Immunity, Melbourne, Victoria, Australia, ⁸Walter and Eliza Hall Institute, Melbourne, Victoria, Australia, ⁹Centre for Pathogen Genomics, University of Melbourne, Melbourne, Victoria, Australia

Background:

Since the late 2020s, several countries have changed gonorrhoea treatment from ceftriaxone (0.5g IM)/azithromycin (1g po) dual therapy to ceftriaxone (1g IM) monotherapy as per the CDC guidelines. Dual therapy is still the first-line treatment in Australia. In August-2021, the Melbourne Sexual Health Centre (MSHC) in-house gonorrhoea treatment guidelines were changed from dual therapy to monotherapy. This study aimed to examine changes in antimicrobial susceptibility and antimicrobial consumption before and after the guideline update.

Methods:

We compared antimicrobial resistance (i.e. ceftriaxone, azithromycin, ciprofloxacin and tetracycline) and consumption between the dual therapy period (3-Aug-2020 to 08-Aug-2021) and monotherapy period (09-Aug-2021 to 26-Aug-2022) at MSHC.

Results:

2,223 *N. gonorrhoeae* isolates (890 in dual therapy and 1333 in monotherapy period) were included. Cases were predominantly males (92.3%, $n=2052$). Monthly use of ceftriaxone increased (mean 24.1 vs 55.5 defined daily doses [DDD]/1000 presentations; $p<0.0001$) and azithromycin decreased (mean 83.5 vs 24.0 DDD/1000 presentations; $p<0.0001$) from the dual therapy to monotherapy period. After changing from dual therapy to monotherapy, there was a significant increase in azithromycin resistance (0.8% vs 5.2%; $p<0.0001$), ciprofloxacin resistance (49.6% vs 73.4%; $p<0.0001$) and tetracycline resistance (47.6% vs 62.1%; $p<0.0001$). However, there was a reduction in decreased susceptibility to ceftriaxone (1.1% vs 0%; $p<0.0001$). Multivariable analyses showed that while the switch to monotherapy

was not significantly associated with azithromycin resistance (aOR=1.02; 95%CI: 0.21-4.97); the re-opening of Australia's international borders (i.e. 15-Dec-2021) was significantly associated with azithromycin resistance (aOR=8.21; 95%CI: 1.99-33.80).

Conclusion:

Following switching from dual therapy to ceftriaxone monotherapy, we saw a reduction in gonococcal strains with decreased susceptibility to ceftriaxone. While there was also a rise in azithromycin resistance, this was significantly associated with reopening of Australia's borders, possibly reflecting importation of AMR. Future genomic work should assess the lineages of *N. gonorrhoeae* currently circulating in our setting.

Disclosure of Interest Statement:

EPFC, DAW and JJO are each supported by an Australian National Health and Medical Research Council (NHMRC) Emerging Leadership Investigator Grant (GNT1172873, GNT1174555, GNT1193955, respectively). CKF and CSB are each supported by an Australian NHMRC Leadership Investigator Grant (GNT1172900 and GNT1173361, respectively).