Update to the 2015 BASHH UK National Guideline on the management of non-gonococcal urethritis

November 2018

The 2015 guideline and its 2017 update have been further updated following consideration of:

- The BASHH *M. genitalium* (Mgen) guideline, which recommends doxycycline 100mg bd for 7 days followed by azithromycin 1 g then 500mg od for 2 days as first line treatment for Mgen. Prior treatment with doxycycline reduces the Mgen load and risk of azithromycin selecting and/or inducing macrolide resistance
- The recent addendum to the BASHH chlamydia guideline which no longer recommends azithromycin 1g for treatment of uncomplicated chlamydia infection at any site, regardless of the gender of the infected individual. Doxycycline 100mg bd for 7 days is now recommended as first line treatment. Individuals who are allergic to, or intolerant of tetracyclines, and pregnant women should be treated with azithromycin 1g orally as a single dose followed by 500mg od for 2 days

Background

Up to 25% of uncomplicated cases of non-gonococcal urethritis (NGU) are caused by infection with *Mycoplasma genitalium* (Mgen).[1] This organism is likely to be implicated in an even higher proportion of cases of recurrent or persistent NGU.[1] However, many men with Mgen infection will not develop NGU.[2]

Optimal management of NGU requires testing for Mgen in addition to *C. trachomatis*, and providing appropriate antimicrobial therapy in the presence of a positive test (and carrying out a test-of-cure if necessary). The prevalence of pre-treatment macrolide resistance in Mgen in the United Kingdom is almost certainly >40%, which is probably due to the widespread use of azithromycin 1g to treat STIs and the limited availability of diagnostic tests for Mgen.[2,3]

Pending widespread availability of Mgen detection assays, the Clinical Effectiveness Group has considered the best available evidence and updated the NGU guideline so that treatment regimens are consistent with the revised chlamydia and the new Mgen guideline.

TREATMENT OF FIRST EPISODE NGU

Recommended

Doxycycline 100mg twice daily for 7 days

Alternatives

Azithromycin 1 g stat then 500mg once daily for the next 2 days (three days total treatment)*

NB Patients should be advised to abstain from sexual intercourse until 14 days after the start of treatment, and until symptoms have resolved. This is likely to reduce the risk of selecting/inducing macrolide resistance if exposed to Mgen or *Neisseria gonorrhoeae* which would make these infections more difficult to treat.*

or

Ofloxacin 200mg twice daily, or 400mg once daily, for 7 days

*While there are no data on the utility of this regimen in treating NGU caused by Mgen without pre-existing macrolide resistance mutations, it will be at least as effective as 500mgs then 250mgs once daily for the next four days for which there is moderate but conflicting data, and probably more so.[2,4-8] Azithromycin has a long half life (68 hours) with sub-MIC levels persisting for 2-4 weeks and probably longer intracellularly[9,10]; the higher the total dose the longer the persistence of sub-MIC levels. BASHH took the pragmatic approach of increasing the total dose from 1.5 g but not to 2.5 g total used by Read et al[8] which would be associated with a longer duration of intracellular sub-MIC levels (see BASHH Mgen guideline) and recommending no sexual intercourse with a new partner for 2 weeks after commencing therapy.

TREATMENT OF RECURRENT OR PERSISTENT NGU

If treated with doxycycline regimen first line:

Recommended

Azithromycin 1 g stat then 500 mg once daily for the next 2 days, plus metronidazole 400mg twice daily for five days

Azithromycin should be started within 2 weeks of finishing doxycycline. This is not necessary if the person has tested Mgen-negative.

NB patients should be advised to abstain from sexual intercourse until 14 days after the start of treatment and until symptoms have resolved.* (see above)

If treated with azithromycin regimen first line:

Recommended

Moxifloxacin 400mg once daily for 10 days, plus metronidazole 400mg twice daily for five days

Alternative

Doxycycline 100mg twice daily for 7 days, plus metronidazole 400mg twice daily for five days**

**In the event of non-availability of Mgen detection assays, it may be reasonable to try this regimen before using moxifloxacin.[2]

EPIDEMIOLOGICAL TREATMENT

In the absence of Mgen testing, it is reasonable to provide epidemiological treatment to the partners of men with NGU using the same antimicrobial regimen that resulted in cure in the index case.

These recommendations are subject to change in light of new available evidence. We recommend that clinicians appraise and share data regarding NGU causes, treatment and outcomes to develop the evidence base in the UK.

References

1. Horner P, Blee K, O'Mahony C, Muir P, Evans C, Radcliffe K. 2015 UK National Guideline on the management of non-gonococcal urethritis. *Int J STD AIDS* 2016; **27**(2): 85-96.
2. Horner P, Martin D. *Mycoplasma genitalium* Infection in Men. *The Journal of infectious diseases* 2017;216(suppl_2):S396-S405.
3. Jensen JS, Cusini M, Gomberg M, Moi H. 2016 European guideline on *Mycoplasma genitalium* infections. *Journal of the European Academy of Dermatology and Venereology* 2016; **30**(10): 1650-6.
4. Anagrius C, Loré B, Jensen JS. Treatment of *Mycoplasma genitalium*. Observations from a Swedish STD Clinic. *PLoS ONE* 2013; **8**(4): e61481.
5. Gesink D, Racey CS, Seah C, et al. *Mycoplasma genitalium* in Toronto, Ontario: Estimates of prevalence and macrolide resistance. *Canadian Family Physician* 2016; **62**(2): e96-e101.
6. Read TR, Fairley CK, Tabrizi SN, et al. Azithromycin 1.5g Over 5 Days Compared to 1g Single Dose in Urethral *Mycoplasma genitalium*: Impact on Treatment Outcome and Resistance. *Clinical infectious diseases* 2016; **64**(3): 250-6.
7. Horner P, Ingle S, Garrett F, et al. Which azithromycin regimen should be used for treating *Mycoplasma genitalium*? – A meta-analysis. *Sexually Transmitted Infections*. 2018; **94**(1): 14-20.
8. Read TRH, Fairley CK, Murray GL et al. Outcomes of resistance-guided sequential treatment of *Mycoplasma genitalium* infections: a prospective evaluation. *Clin Infect Dis* 2018: doi: 10.1093/cid/ciy477
9. Crokaert F, Hubloux A, Cauchie P. A Phase I Determination of Azithromycin in Plasma during a 6-Week Period in Normal Volunteers after a Standard Dose of 500mg Once Daily for 3 Days. *Clin Drug Investig* 1998; **16**: 161-6.
10. Horner P, Saunders J. Should azithromycin 1 g be abandoned as a treatment for bacterial STIs? The case for and against. *Sex Transm Infect* 2017;93:85-7.