



Article reuse guidelines:

sagepub.com/journals-permissions

DOI: 10.1177/09564624211004415

journals.sagepub.com/home/std

Can ceftriaxone be omitted in the treatment of nongonococcal pelvic inflammatory disease?

Dear Editor,

We read with interest the letter from Dabis regarding the decision by Watford Sexual Health to continue using doxycycline and metronidazole to treat non-gonococcal pelvic inflammatory disease (PID).¹ As Dabis has noted, this is not consistent with the British Association of Sexual Health and HIV guideline, which recommends that a single dose of intramuscular ceftriaxone be given in addition to doxycycline/metronidazole.² Dabis reports a retrospective study that suggests the omission of ceftriaxone did not affect patient outcomes. However, based on a number of factors, we would question whether this conclusion is valid.

Most importantly, clinical practice revolves around the principles of evidence-based medicine, where the best available evidence is used to guide clinical decision making. The report by Dabis is observational, retrospective, small (131 women) and has a high dropout rate between treatment and follow-up (48%), nor were the criteria for PID diagnosis or evaluation of cure standardised. The resultant findings are therefore at high risk of bias and, we would suggest, insufficient to justify a change in recommended practice. It remains possible that doxycycline/metronidazole alone may be as good as a cephalosporin-based regimen but, as outlined below, there are several reasons why this may not be the case.

Large randomised controlled trials have demonstrated that regimens which include a cephalosporin have high efficacy in PID.² A similar level of evidence is not available for doxycycline/metronidazole without a cephalosporin. This is reflected not just in the UK PID guidelines but also in those from the USA, Europe and Australia,^{3–5} none of which recommends doxycycline plus metronidazole in isolation. The Cochrane review on the treatment of PID to which Dabis refers⁶ does not include a comparison of doxycycline/metronidazole regimens with and without ceftriaxone, and is therefore not helpful in addressing this issue.

In addition to the empirical evidence from clinical trials, the inclusion of a cephalosporin is also supported by a need

to cover the relevant bacteria which cause PID. A wide variety of aerobic and anaerobic bacteria are associated with pelvic infection and ceftriaxone provides relevant broad spectrum activity, beyond just *Neisseria gonorrhoeae*.^{7,8} In contrast, the cover provided by doxycycline/metronidazole is limited.

Finally, Dabis suggests that two previous trials have found doxycycline/metronidazole to be not inferior when compared to other antibiotic regimens used in PID.^{9,10} However, this is of limited value since neither of the comparator regimens are a current standard of care and specifically do not include cephalosporin, limiting any conclusions about relative efficacy. A contemporaneous meta-analysis found the clinical and microbiological cure rate for doxycycline/metronidazole to be lower than alternative PID treatments.¹¹

We agree that further high-quality trials are needed to guide the optimal choice of therapy for women with PID. However, the current best evidence, based on the microbiology of pelvic infection and large clinical trials, is that treatment with doxycycline/metronidazole should be combined with ceftriaxone.

Declaration of conflicting interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Jonathan Ross is on the editorial board of International Journal of STD and AIDS.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

ORCID iD

James Ian McConville Ross  <https://orcid.org/0000-0002-4812-1528>

References

1. Dabis R. Clinical cure rate of pelvic inflammatory disease. Should ceftriaxone be part of the first line regimen? *Int J STD AIDS* 2020; 31(14): 1432–1433.
2. Ross J, Cole M, Evans C, et al. United Kingdom national guideline for the management of pelvic inflammatory disease

- (2019 Interim Update). British Association for Sexual Health and HIV, Vol. 117, p. 1–13, <https://www.bashhguidelines.org/media/1217/pid-update-2019.pdf> (2019, accessed February 15 2021).
3. Frieden TR, Harold Jaffe DW, Rasmussen SA, et al. Sexually transmitted diseases treatment guidelines, <https://www.cdc.gov/std/tg2015/tg-2015-print.pdf> (2015, accessed 20 February 2021).
 4. Ross J, Guaschino S, Cusini M, et al. European guideline for the management of pelvic inflammatory disease [Internet]. International Journal of STD and AIDS, Vol. 29, p. 108–114, <http://journals.sagepub.com/doi/10.1177/0956462417744099> (2017, accessed 20 February 2021).
 5. Australasian Society for HIV VH and SHM. PID - Pelvic inflammatory disease [Internet]. The Australasian STI Management Guidelines, <http://www.sti.guidelines.org.au/syndromes/pid-pelvic-inflammatory-disease> (2017, accessed 20 February 2021).
 6. Savaris RF, Fuhrich DG, Maissiat J, et al. Antibiotic therapy for pelvic inflammatory disease. *Cochrane database Syst Rev* 2020; 8: CD010285.
 7. Petrina MAB, Cosentino LA, Wiesenfeld HC, et al. Susceptibility of endometrial isolates recovered from women with clinical pelvic inflammatory disease or histological endometritis to antimicrobial agents. *Anaerobe* 2019; 56: 61–65.
 8. Wiesenfeld HC, Meyn LA, Darville T, et al. A randomized controlled trial of ceftriaxone and doxycycline, with or without metronidazole, for the treatment of acute pelvic inflammatory disease. *Clin Infect Dis* 2020. Epub ahead of print.
 9. Heinonen PK, Teisala K, Punnonen R, et al. Treating pelvic inflammatory disease with doxycycline and metronidazole or penicillin and metronidazole. *Sex Transm Infect* 1986; 62(4): 235–239.
 10. Witte EH, Peters AAW, Smit IBC, et al. A comparison of pefloxacin/metronidazole and doxycycline/metronidazole in the treatment of laparoscopically confirmed acute pelvic inflammatory disease. *Eur J Obstet Gynecol Reprod Biol* 1993; 50(2): 153–158.
 11. Walker CK, Kahn JG, Washington AE, et al. Pelvic inflammatory disease: metaanalysis of antimicrobial regimen efficacy. *J Infect Dis* 1993; 168(4): 969–978.

James Ian McConville Ross¹ 

Polly Morton Roads¹ and

Jonathan D C Ross²

¹*School of Medical Sciences, The University of Manchester, Manchester, UK*

²*Department of Sexual Health and HIV, Birmingham University Hospitals NHS Foundation Trust, Birmingham, UK*

Corresponding author:

James Ian McConville Ross, School of Medical Sciences, The University of Manchester, Oxford Road, Manchester M13 9PL, UK.

Email: jamie_i_m_ross@yahoo.co.uk