Eurosurveillance
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Eurosurveillance, Volume 8, Issue 14, 01 April 2004

Articles

Citation style for this article: Simms I, French P, Fenton KA. Azithromycin failures in the treatment of syphilis in the United States. Euro Surveill. 2004;8(14):pii=2432. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=2432

Azithromycin failures in the treatment of syphilis in the United States

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Since the late 1990s there has been a dramatic change in the incidence of infectious syphilis in many western industrialised countries and outbreaks have been seen in major cities in Europe, North America and Australia (1-6). Syphilis has been increasing in the United States since 2000 and San Francisco has one of the highest rates of primary and secondary syphilis in the US. The San Francisco Department of Public Health (SFDPH) investigated several clinical failures in syphilis patients treated with azithromycin (7). Single oral dose azithromycin therapy is more convenient to administer than intramuscular benzathine penicillin (CDC's recommended treatment for syphilis) and facilitates the management of cases and their sexual contacts (8).

Between September 2002 and July 2003, 8 cases of treatment failure were seen involving single dose azithromycin therapy. All the patients were men who have sex with men, and had a median patient age of 34 years (range 23 to 39). Five of the men were HIV seropositive. Each symptomatic patient was treated with 2 g of azithromycin. Of the two patients with penile ulcers, one ulcer was positive by dark field microscopy after 5 days, and the other was positive by dark-field microscopy after 5 weeks. A patient with an oral ulcer was positive by dark field microscopy after 18 days. Five patients who were seronegative contacts of the cases received a dose of 1 g of azithromycin, but all either seroconverted or developed early syphilis after treatment. Subsequently, all patients were treated successfully with either penicillin or doxycycline. Resistance to erythromycin has been reported in *Treponema pallidum* (9) and investigators at the University of Washington are collaborating with SFDPH and others to investigate the molecular mechanism that confers azithromycin resistance.

It is disappointing that these azithromycin treatment failures of early syphilis have been reported. Azithromycin as a single oral dose has good efficacy against a number of sexually transmitted infections including *Chlamydia trachomatis* and chancroid (8). The availability of an effective single dose oral therapy might improve syphilis control by allowing treatment to be given in non-clinic and outreach settings. Indeed, this therapy was recently used in an attempt to control an epidemic of syphilis in Vancouver by widespread availability of single dose azithromycin amongst people at high risk of having syphilis (6). This intervention appeared to be unsuccessful and it is possible that treatment failure may have played a part in this lack of success. The evidence base for the use of azithromycin in the treatment of syphilis remains poor. Animal studies show good activity against *Treponema pallidum* (10) and uncontrolled open studies of longer courses of azithromycin appear to show efficacy in early disease (11). But poor transplacental (12) and cerebrospinal fluid (13) penetration of azithromycin is likely to limit its usefulness in pregnancy and late syphilis respectively, and to date, only small randomised studies suggest it is efficacious in early syphilis (8). Many clinicians will consider that until more evidence is available, macrolides (including azithromycin) remain fourth line agents for syphilis after penicillin, tetracyclines (such as doxycycline) and cephalosporins (such as ceftriaxone) (14).

References:

1. Fenton K, Nicoll A, Kinghorn G. Resurgence of syphilis in England: time for more radical and nationally co-ordinated approaches. *Sex Transm Inf* 2001;**77**:309-10.
2. Van der Meijden W, van der Snoek E, Haks K, van de Laar M. Outbreak of syphilis in Rotterdam, the Netherlands, *Eurosurveillance Weekly* 2002; **6**(13): 28/03/2002. (http://www.eurosurveillance.org/ew/2002/020328.asp)
3. Halsos AM, Edgardh K. An outbreak of syphilis in Oslo. Int J STD AIDS 2002;13:370-2.
4. De Schrijver K. Syphilis outbreak in Antewerp, Belgium. *Eurosurveillance Weekly* 2001 **5**(19): 10/02/2001. (http://www.eurosurveillance.org/ew/2001/010510.asp)
5. Axelsen N, Smith E, Koch-Hansen GH. Syphilis cases increasing in Denmark, 2000-01. *Eurosurveillance Weekly* 2002 **6**(35):29/08/2002. (http://www.eurosurveillance.org/ew/2002/020829.asp)
6. Reckart MC, Patrick DM, Jolly A, Maks S, Maginley J et al. Heterosexual outbreak of infectious syphilis: epidemiological and ethnographical analysis and implications for control. *Sex Transm Infect* 2002;**78**:S164-9.
7. CDC. Azithromycin treatment failures in syphilis infections--San Francisco, California, 2002-2003. *MMWR Morb Mortal Wkly Rep* 2004; **53**(9):197-8. (http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5309a4.htm)
8. CDC. Sexually transmitted disease treatment guidelines 2002. *MMWR Recomm Rep* 2002;**51**(RR06):1-80. (http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5106a1.htm)
9. Stapleton JT. Stamm LV, Bassford PJ. Potential for development of antibiotic resistance in pathogenic treponemes. *Rev Infect Dis* 1985; **7 suppl 2**:S314-7.
10. Lukhart SA, Fohn M J, Baker-Zander SA. Efficacy of azithromycin for therapy of active syphilis in the rabbit model. *J Antimicrob Chemother* 1990;**25 Suppl A**:91-9.
11. Mashkilleyson AL, Gomberg MA, Mashkilleyson N, Kutin SA. Treatment of syphilis with azithromycin. *Int J STD AIDS* 1996;**7 Suppl 1**:13-5.

12. Heikkinen T, Laine K, Neuvonen PJ, Ekblad U. The transplacental transfer of the macrolide antibiotics erythromycin, roxithromycin and azithromycin. *BJOG* 2000;**107**:770-5.
13. Jururatanasirikul S, Hortiwakul R, Tantisarasart T, Phuenpathom N, Tussanasunthornwong S. The distribution of azithromycin into brain tissue, cerebrospinal fluid, and aqueous humor of the eye. *J Antimicrob Chemother* 1996;**40**:825-6.
14. Hook EW, Martin DH, Stephens J, Smith BS, Smith K. A randomised, comparative pilot study of azithromycin versus benzathine penicillin G for treatment of early syphilis. *Sex Trans Dis* 2002;**29**: 486-90.

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