Emergence of TetM-mediated tetracycline resistance in rural South Africa

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Sir,

Sexually transmitted infections (STIs) caused by antibiotic-resistant *Neisseria gonorrhoeae* are a major therapeutic problem in many parts of the world. Effective therapy against this pathogen has barely stayed ahead of the acquisition of resistance mechanisms and studies continue to document the increase in antimicrobial resistance of *N. gonorrhoeae* to a variety of antibiotics.1,2

The high prevalence of mixed infections, compounded by the imprecision of an aetiological diagnosis in developing countries, underscores the feasibility of the syndromic approach in the management of STIs. In 1995, South Africa implemented a modified version of the WHO’s syndromic management protocol for the treatment of STIs. Doxycycline is the recommended drug for the treatment of *Chlamydia trachomatis*. However, since the differentiation between gonorrhoea and chlamydial infection is not made, patients with gonorrhoea are exposed to doxycycline as part of the syndromic management of genital discharge.

In Southern Africa, plasmid-mediated high-level resistance to tetracycline of *N. gonorrhoeae* (MIC ≥ 16 mg/L) was first described in 1995 among 11 isolates obtained from Namibia and Botswana.3 These isolates all carried the American type of *tetM* gene. This was followed by a report from Bloemfontein, South Africa, where the prevalence was reported to have increased from 2% (3/145) in 1994 to 18.5% (12/65) in 1995.4 The resistance patterns of this organism vary geographically and the presence of high-level tetracycline-resistant organisms has not been described in the province of KwaZuluNatal.

The Africa Centre for Population Studies and Reproductive Health is situated in the rural district of Hlabisa in KwaZuluNatal. A direct spinoff of this centre has been the establishment of an STD clinic for the area. During STD prevalence and antimicrobial surveillance studies at this clinic in 1999, high-level resistance to tetracycline was observed. This study was therefore carried out to determine whether this was TetM mediated, and which variant of the gene was involved.

Urethral and cervical specimens were collected from patients presenting with genital discharge to the KwaZuluNatal, Kwamatshe STD clinic, in the rural Hlabisa district, KwaZuluNatal, between March and December 1999. These specimens were inoculated on to New York City agar plates for the isolation of *N. gonorrhoeae*. MICs of tetracycline were determined using the agar dilution method and breakpoint criteria as defined by the NCCLS.5

Selection of potential tetracycline-resistant *N. gonorrhoeae* strains was performed by screening for growth on GC agar (supplemented with 1% yeast autolysate and 5% lysed horse blood) containing 10 mg/L tetracycline. PCR detection and characterization of the *tetM* gene was performed on strains of *N. gonorrhoeae* that grew on the tetracycline-containing plate, by means of a one-step PCR.6 PCR products were electrophoresed in a 1% agarose gel containing ethidium bromide and visualized by UV fluorescence.

Two-hundred and four strains of *N. gonorrhoeae* were collected during the study period. One-hundred and thirty-six strains (67%) had MICs ≥ 16 mg/L of tetracycline. All these strains grew on the 10 mg/L tetracycline-containing plate and were found to carry the American variant of the *tetM* gene, as revealed by the production of a 778 bp PCR product. The Dutch *tetM* gene was not found among these isolates.

In addition to the use of doxycycline as part of syndromic management, tetracycline derivatives, being relatively cheap, are widely used for the empirical treatment of respiratory and skin and soft tissue infections (P. Moodley et al., unpublished results).6 The emergence of TetM-mediated tetracycline resistance in this area was sudden and is mediated by a single variant of the *tetM* gene. Whether this is a result of the spread of a single strain or by transfer of the resistance plasmid within the gonococcal population needs further investigation.

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References


