Letters to the Editor

Chlamydia trachomatis in infertile women undergoing uterine instrumentation: Screen or treat

Dear Sir,

We read with interest ‘Chlamydia trachomatis in infertile women undergoing uterine instrumentation: Screen or treat’ (Land et al., 2002), proposing that prophylactic antibiotics should be given to all infertile women undergoing uterine instrumentation instead of screening for C. trachomatis and treating positive cases only. Universal screening was not considered by the authors to be cost-effective in view of the low incidence of detection of C. trachomatis in the endocervix of infertile women. Possible reactivation of C. trachomatis infection may also follow uterine instrumentation as a result of persistent micro-organisms in the upper genital tract despite adequate treatment. We would like to point out some of the problems that may arise from adopting the universal prophylaxis approach.

It is obvious that criteria for selective screening are not useful in infertility, as the majority of infertile women are >25 years old and the couples usually have stable monogamous relationships for several years prior to seeking infertility treatment. Therefore, all women presenting for infertility investigation should be screened for C. trachomatis (Royal College of Obstetricians and Gynaecologists, 1998). The cost-effectiveness of universal screening for C. trachomatis depends on the prevalence of asymptomatic infection. The threshold prevalence of C. trachomatis, over which universal screening is shown to be cost effective, varied from 3.1–10.0% (Sellors et al., 1992; Gene and Mardh, 1996; Marazzo et al., 1997; Howell et al., 1998; Paavonen et al., 1998). The variation in the threshold prevalence rate can be explained by the very wide range of direct and indirect costs used in the economic models (McIntosh et al., 1999). These studies mainly addressed the cost implications associated with prevention of infectious pelvic inflammatory episodes.

The prevalence of C. trachomatis in infertile women, which is much lower than other clinical settings (Macmillan et al., 2000), is 1.3% (95% CI 0.2–4.7%) (Eggert-Kruse et al., 1997) and 1.9% (95% CI 0.5–4.8%) (Macmillan and Templeton, 1999) using ligase chain reaction (LCR). The upper range of the prevalence in infertile women is still within the threshold prevalence rate (3.1–10.0%) for which universal screening is cost effective, even after taking into consideration unpublished data (J.A.Land et al., 2002) using polymerase chain reaction (PCR).

Other advantages of the screen and treat approach that cannot be offered by the universal prophylaxis approach include screening for other sexually transmitted diseases in the women and treatment of sexual partners when chlamydial infection is detected. These steps help to reduce the spread of sexually transmitted diseases in the community. Recurrent chlamydial infections are a common problem even after completion of adequate and appropriate antibiotic therapy and are usually thought to be a consequence of reinfection. Re-screening of women for chlamydial infection a few months after treatment has been recommended as a routine prevention strategy (Whittington et al., 2001). The universal prophylaxis approach would not be able to detect these recurrent infections. The risk of pelvic infection was mostly confined to patients with existing tubal damage and anaerobic bacteria were isolated more commonly than C. trachomatis (Forsey et al., 1990). It is unlikely that these infections after hysterosalpingography can be prevented by the universal prophylaxis approach, which may also contribute further to the development of persistent infection and resistance to antibiotics.

Efficient inhibition of chlamydial growth by tetracycline or azithromycin was readily shown in the conventional in-vitro system used for susceptibility testing in which antibiotics are usually added 48 h after the infectious agent or are sometimes added simultaneously. This did not reflect the situation in vivo for chlamydial infection. During natural infections, chlamydia sp. are usually exposed to antibiotics long after an infection has been well established. Using an in-vitro cell culture model with a longer incubation period of 20 days, prolonged treatment of ciprofloxacin/ofloxacin (Dreses-Werringloer et al., 2000) and azithromycin (Dreses-Werringloer et al., 2001) not only failed to eradicate chlamydia from host cells but also induced a persistent state, although these antibiotics were efficient in the usual susceptibility testing. The emergence of multiple drug-resistant C. trachomatis has been recently reported (Somani et al., 2000).

In conclusion, the screen and treat approach remains the most cost-effective way to prevent the development of infectious morbidity following uterine instrumentation. Routine antibiotic prophylaxis may be associated with an increased risk of persistent infection and development of multiple drug resistant chlamydia.

References


© European Society of Human Reproduction and Embryology
Dear Sir,

In the ‘screen or treat’ debate Dr Ng and colleagues make a plea for a chlamydia screening policy, opposing our proposal for routine antibiotic prophylaxis in subfertile women undergoing uterine instrumentation.

Their standpoint is based on the presumption that all persisting chlamydia infections can be identified in cervical samples, and that selective treatment of only positive cases will suffice. Since evidence exists that viable chlamydia can be obtained from the upper genital tract in patients with negative test results from the cervix, cervical screening must be considered inadequate in identifying all patients at risk. Sampling from the upper genital tract can however only be performed by invasive means, and it remains to be established whether all patients develop serum antibodies. Therefore, at this moment there is no test available that can identify by simple means all patients with viable, persisting chlamydia.

It is generally agreed that antibiotic prophylaxis is indicated in procedures with a high risk for microbial contamination (e.g. intestinal surgery), as well as in procedures following which infections are rare, but may have disastrous consequences (e.g. orthopaedic operations and uterine instrumentation). In these cases the benefits of antibiotics are considered to outweigh their possible detriments, i.e. unwanted drug effects and increased antibiotic resistance. Randomized controlled trials (RCT) are the most powerful tools available for evaluating preoperative antibiotic prophylaxis policies and to prove efficacy. Appropriate evaluation of antibiotic prophylaxis for uterine instrumentation by RCT is hampered by the fact that postoperative infections are infrequent (but disastrous) and remain asymptomatic in the majority of patients.

Reports from the literature indicate that antibiotics may not efficiently eliminate chlamydia from all host cells in vitro (Dreses-Werringloer et al., 2001), in macaques (Patton et al., 1997) and in humans (Bragina et al., 2001). In patients with persisting chlamydia infections atypical small intracellular inclusions have been found, suggesting that antibiotics may modulate the micro-organism and render it less susceptible to antibiotics. These observations deserve further exploration, since they question the principles and efficacy of treatment of acute as well as chronic chlamydial infections.

Thus, until an adequate non-invasive screening test has been developed to identify all patients with viable chlamydia in their genital tracts, clinical guidelines concerning precautions in subfertile women undergoing uterine instrumentation can only be based on theoretical arguments.

References


Jolande A.Land
Department of Obstetrics and Gynaecology, Academisch Ziekenhuis Maastricht, P.O. Box 5800, 6202 AZ Maastricht, The Netherlands
E-mail: jlan@sryn.azm.nl