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Mini Review

Clinical Practice Guidelines for the Diagnosis and Treatment of *Ureaplasma Urealyticum* Infections are Needed

Zhonghua Liu[1], Jun Wang[2], Changtai Zhu[3]*

[1]Shanghai Key Laboratory of Tuberculosis, Tongji University School of Medicine, China

[2]Department of Obstetrics and Gynecology, Shanghai Jiao Tong University, China

[3]Department of Laboratory Medicine, Shanghai Jiao Tong University, China

***Corresponding author:** Changtai Zhu, Department of Laboratory Medicine, Shanghai Key Laboratory of Tuberculosis, Shanghai Pulmonary Hospital, Tongji University School of Medicine, No. 507 Zhengmin Rd, Shanghai 200433, China

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Abstract

As genital mycoplasmal opportunists, *Ureaplasma urealyticum* (UU) can cause various infectious diseases. At present, as far as the diagnosis and treatment of UU infections are concerned, there are many problems in the clinical practice as follows: i) although there are a great many clinical and pathological reports on UU infections, the available data that can help clinicians make decisions are limited; ii) lacks of epidemiological data worldwide; iii) the test kits for UU is not homogeneous, so reliable quality controls should be carried out in future; and iv) due to lack of evidence-based medicine and guidelines for the management of UU infections, some clinicians adopt agents based on empirical therapy rather than antimicrobial susceptibility test, which not only caused the failures of treatment, but also lead to drug abuse. Considering that currently confused situations occur in the management of UU infections and there is a considerable part of subjects with UU have underwent unnecessary or improper treatments, clinical practice guidelines for the diagnosis and treatment of UU infections should be drafted as soon as possible.

Keywords: *Ureaplasma urealyticum*; Infectious diseases; Clinical practice; Guidelines; Sexually transmitted diseases

Introduction

Ureaplasma urealyticum (UU) together with *Ureaplasma parvum*, which are classified as *Ureaplasma* species, are the smallest free-living organisms. Due to lack of cell wall, UU has nonsusceptibility to beta-lactams antimicrobial agents. As genital mycoplasmal opportunists, UU can cause various infections in susceptible persons. However, there had great difference in the prevalence rate of UU in different populations and regions. According to the report from Iran [1], UU positive rate was 9.14% (32/350) in pregnant women. In Northern Greece [2], 16.13% of asymptomatic women were confirmed to have UU mostly in reproductive ages. UU was present in 68.9% (111/161) in with vaginal discharge syndrome in Cuba [3]. A study from Italy showed a prevalence of 1856 positive patients for genital mycoplasmas (18.6 %) and among positive cultures, 89 % of isolates were UU [4]. In China, the overall positive incidence of genital mycoplasmas was 62.16% and the most common pattern was UU monoinfection (46.52%) [5]. It is not clear what the causes of the difference of UU prevalence rates in different regions are.

The relationship between human diseases and UU

According to the previous reports, the human diseases related to UU could be summarized as following: i) urogenital tract infections including non-gonococcal urethritis, prostatitis, orchitis, epididymitis, pelvic inflammation, cervicitis, adnexitis, cervicitis,etc.; ii) infertility; iii) perinatal infectious diseases, premature rupture of the amniotic fluid, chorioamnionitis, abortion, endometritis, premature birth, stillbirth, postpartum fever, low birth weight and bacteremia; and iv) neonatal respiratory system disease include neonatal pneumonia, and neonatal pulmonary hypoplasia [6-8].

Identification and antimicrobial susceptibility test of UU

UU testing methods mainly include: culture method (liquid broth culture and solid medium culture), immunological methods based on antigen and antibody identification, and molecular biology methods (PCR, fluorescence quantitative PCR and biological chip technology, etc.) [9-12].

As UU growth is slower in solid medium culture, liquid broth culture method is commonly used in clinical practice

[13-16]. The principle is based on that the UU strain contains urease, which can produce alkaline by decomposing urea of the broth, and then makes the color of the broth change. In addition, as a rapid test tool, the fluorescence quantitative PCR is also often used for UU identification [13,17].

However, for research purposes, the serum typing were identified by immunology methods and molecular testing tools based on the difference of the multi-band antigen gene, intergenic spacer region of 16 S-23 S rRNA, and urease gene [6,18,19].

Currently, the testing methods of UU resistance mainly include: micro-broth dilution method, agar dilution method, direct broth method and E-test method, etc.. However, the commercial kits by using micro-broth dilution method can test the sensitivities of quinolones, tetracyclines, and macrolides against UU, have been often used in clinical practice [13,20].

Treatment for UU infections

At present, the antimicrobial agents including levofloxacin, doxycycline, josamycin, ofloxacin, erythromycin, tetracycline,

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ciprofloxacin, azithromycin, clarithromycin and pristinamycin can be used for the clinical treatment of UU infections [2,3,13,21]. But, with the widespread use of antimicrobials, some clinical UU isolates have shown high resistance to some agents (especially to quinolones and macrolides) to varying degrees [1-3,21-24]. Thus, the clinical treatment for UU infections is becoming more and more difficult in some regions. In addition, some Chinese herbals have been reported to have the properties of killing or inhibiting UU in vitro, which can be used as an alternative therapy [25,26].

Problems and confusions in the diagnosis and treatment of UU infections

At present, as far as the diagnosis and treatment of UU infections are concerned, there are many problems in the clinical practice as follows: i) although there are a great many clinical and pathological reports on UU infections, the available data to help clinicians making decisions are limited; ii) lacks of epidemiological data worldwide; iii) the test kits for UU is not homogeneous, so reliable quality controls should be carried out in future; and iv) due to lack of evidence-based medicine and guidelines for the management of UU infections, some clinicians adopt agents based on empirical therapy rather than antimicrobial susceptibility test, which not only caused the failures of treatment, but also lead to drug abuse.

Urgent need to guidelines for UU infection

In the clinical practice, the clinicians had some confusions and vague understandings about the clinical significance of presence of UU in different persons and species and lack of a scientific interpretation of test results, which are summarized as follows.

- How to determine whether UU colonization or infection?
- What significance is UU quantitative or count?
- What conditions do clinicians need to intervene UU?
- When should clinicians stop treatment?
- How to treat some special UU infections such as prostatitis and adnexitis?

At present, only in China, there are more than 4 million people who have been received treatment related to UU infections and the total expenditure is about 2 billion dollars each year according to our preliminary estimates. The subjects are mainly from Department of Obstetrics and Gynecology, Department of Dermatology, and Department of Urology Surgery. To be sure, there is a considerable part of subjects who are only carriers of UU have received unnecessary treatment. The improper therapy not only causes economic losses but also increases the risk of adverse drug reactions. Presently, the improper therapy involving UU commonly occurs in some for-profit hospitals in China, which are run by commercial companies and enterprises rather than charities [27]. Therefore in China the health administrative departments should carry out the strict examination and the effective management to these hospitals in the future. Both UU and Chlamydia are considered Sexually Transmitted Diseases (STD), but in the guidelines to deal with STD did not mention the treatment of mycoplasma species including UU [28, 29].

Considering there has an urgent need to improve and standardize the diagnosis and treatment of UU infections, clinical practice guidelines for the diagnosis and treatment of UU infections should be drafted as soon as possible.

Conclusion

Due to lack of clinical practice guidelines, some diagnosis and therapy of UU is problematic, which not only caused the failures of treatment, but also lead to drug abuse. Considering that currently confused situations occur in the management of UU infections, clinical practice guidelines for the diagnosis and treatment of UU infections should be drafted as soon as possible.

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