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Trend Analysis of Sexually Transmitted Infection Treatments in Korea

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Purpose: The revision of the 2023 Guidelines for the Treatment of Sexually Transmitted Infections (STIs) has been released. Hence, it is necessary to analyze the current status of STI treatments in Korea.

Materials and Methods: A questionnaire was distributed to urologists and gynecologists from December 2022 to January 2023 through an online survey program. Three hundred and forty-one urologists and 302 gynecologists responded to the questionnaire.

Results: For *Neisseria gonorrhea* treatment, ceftriaxone 500 mg and 100 mg of doxycycline twice daily for seven days were most preferred by urologists (22.58%). The treatment most preferred by gynecologists (15.23%) was 500 mg of ceftriaxone and 1 g of azithromycin in a single dose. Both urologists and gynecologists generally treat *Chlamydia trachomatis* according to the treatment guidelines. For treating *Mycoplasma genitalium*, 29.03% of urologists preferred administering azithromycin at 500 mg once daily, followed by 250 mg for four days. In contrast, 33.11% of gynecologists preferred doxycycline 100 mg twice daily for seven days.

Conclusions: Most urologists and gynecologists followed the treatments recommended in the 2nd edition of the STI treatment guidelines, revised in 2016. As many treatment regimens have changed because of the recent increase in antibiotic-resistant STIs, there is a need to encourage them to follow the new treatment guidelines.

Keywords: Guideline; Sexually transmitted infections; Questionnaire; Trends

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INTRODUCTION

The Korean Association of Urogenital Infection and Inflammation (KAUTII) published treatment guidelines and is operating a surveillance system to prevent resistance to the antibiotics used to treat sexually transmitted infections (STIs) in collaboration with the Korea Disease Control and Prevention Agency (KDCA) [1]. The revision of the 2023 Guidelines for Treatment of STIs (3rd edition) has been released, and regular updates will be implemented in the future [2]. Updates to the guidelines are made through collaboration with various academic societies, including the Korean Association of Obstetricians and Gynecologists, the Korean Society of Obstetrics and Gynecology, and the Korean College of Obstetrics and Gynecology, as well as the KAUTII. Therefore, the current treatments of STIs by urologists and gynecologists in Korea need to be examined.

MATERIALS AND METHODS

A questionnaire titled "Analysis of antimicrobial agents for treatment of STIs and current status of treatment" was distributed to urologists and gynecologists from December 2022 to January 2023 to assess the current situation of sexually transmitted infection treatments in Korea. The questionnaire was distributed using an online survey program. The questions in the questionnaire consisted of nine questions:

1. Are you aware of the Korean STI guidelines (jointly published by the KAUTII and the KDCA)?
2. When male urethritis or female cervicitis/vaginitis is suspected, what sample do you use for polymerase chain reaction (PCR) testing?
3. Do you take additional samples from the pharynx when gonococcal urethritis is suspected?
4. What medications do you use to treat *Neisseria gonorrhea* (*N. gonorrhea*)?
5. What medications do you use to treat *Chlamydia trachomatis* (*C. trachomatis*)?
6. What medications do you use to treat *Mycoplasma genitalium* (*M. genitalium*)?
7. Do you provide treatment if asymptomatic *Ureaplasma urealyticum* (*U. urealyticum*) is diagnosed through a PCR test?
8. Do you provide treatment if asymptomatic *Ureaplasma parvum* (*U. parvum*) or *Mycoplasma hominis* (*M. hominis*) is diagnosed using a PCR test?
9. If you have been diagnosed and treated for a sexually transmitted infection by PCR, when is a follow-up PCR test performed?

Three hundred and forty-one at urology (305 at primary medical institutions, 30 at secondary medical institutions, and six at tertiary medical institutions), 302 at obstetrics and gynecology (219 at primary medical institutions, 74 at secondary medical institutions, 37 at tertiary medical institutions, and two at other institutions) responded. Ethical approval was not applicable because this study did not involve humans or animals.

RESULTS

When urethritis is suspected in men, urologists use urine as a specimen for multiplex real-time PCR analysis rather than a urethral swab in approximately 98% of cases. When cervicitis/vaginitis is suspected in women, gynecologists mainly use vaginal and cervical swabs rather than urine as a specimen for PCR testing. In addition, in Korea, female patients do not directly collect vaginal swabs using a swab kit and send them to a laboratory, as in other countries.

For *N. gonorrhea* treatment, a single 500 mg dose of ceftriaxone and 100 mg of doxycycline twice a day for seven days (22.58%) was most preferred by urologists, followed by a single 500 mg dose of ceftriaxone and a single administration of 1 g azithromycin (12.32%). In contrast, a single dose of ceftriaxone at 1 g or a single dose of ceftriaxone at 500 mg each showed a low preference of approximately 5%. For gynecologists, a single 500 mg dose of ceftriaxone and a single 1 g dose of azithromycin was preferred the most (15.23%), followed by a single 1 g dose of ceftriaxone and 100 mg of doxycycline twice a day for seven days (12.91%). Unlike urologists, a single 1 g dose of ceftriaxone and a single 500 mg dose of ceftriaxone also showed high preferences of approximately 10% (Table 1).

In the case of preferred *C. trachomatis* treatments, more than 90% of urologists and gynecologists preferred doxycycline or azithromycin; 55.43% of the urologists preferred doxycycline at 100 mg twice a day for seven days, and 51.32% of the gynecologists preferred a single 1 g dose of azithromycin. Doxycycline is currently the first-line treatment, and azithromycin is recommended as an alternative treatment for *C. trachomatis*. Therefore, urologists and gynecologists generally treat *C. trachomatis* according to the treatment guidelines (Table 2).

In the case of *M. genitalium*, 29.03% of the urologists responded that they administered 500 mg of azithromycin once a day and 250 mg once daily for four days. Of the urologists, 23.75% responded that they use doxycycline at 100 mg twice daily for seven days. Only 12.61% of the urologists preferred using 100 mg of doxycycline twice daily for seven days and 500 mg of azithromycin once daily, followed by 250 mg once daily for four days. In contrast, 33.11% of the gynecologists preferred doxycycline at 100 mg twice daily for seven days, and 26.49% preferred administering a single 1 g dose of azithromycin (Table 3).

When asymptomatic *U. urealyticum* is diagnosed using a PCR test, urologists and gynecologists currently prescribe antibiotics in 70-80% of the cases. In addition, when asymptomatic *U. parvum* or *M. hominis* is diagnosed by a

Table 1. *Neisseria gonorrhea* treatment preferences of urologists and gynecologists

Answer choices (question: what regimen do you use to treat *Neisseria gonorrhea*?)	Urologists		Gynecologists	
	%	n	%	n
Ceftriaxone 250 mg in a single dose+azithromycin 1 g in a single dose	4.69	16	7.95	24
Ceftriaxone 500 mg in a single dose+azithromycin 1 g in a single dose	12.32	42	15.23	46
Ceftriaxone 1 g in a single dose+azithromycin 1 g in a single dose	11.73	40	8.61	26
Spectinomycin 2 g in a single dose+azithromycin 1 g in a single dose	1.17	4	2.98	9
Ceftriaxone 250 mg in a single dose	0.59	2	3.64	11
Ceftriaxone 500 mg in a single dose	5.28	18	10.93	33
Ceftriaxone 1 g in a single dose	5.28	18	9.93	30
Azithromycin 1 g in a single dose	5.87	20	4.30	13
Spectinomycin 2 g in a single dose	0.29	1	2.98	9
Ceftriaxone 250 mg in a single dose+doxycycline 100 mg twice a day for seven days	8.50	29	4.97	15
Ceftriaxone 500 mg in a single dose+doxycycline 100 mg twice a day for seven days	22.58	77	8.61	26
Ceftriaxone 1 g in a single dose+doxycycline 100 mg twice a day for seven days	9.38	32	12.91	39
Fluoroquinolone	1.17	4	0.66	2
Cephalosporin	7.04	24	4.30	13
Others	4.11	14	1.99	6

Table 2. *Chlamydia trachomatis* treatment preferences of urologists and gynecologists

Answer choices (question: what regimen do you use to treat *Chlamydia trachomatis*?)	Urologists		Gynecologists	
	%	n	%	n
Azithromycin 1 g in a single dose	36.07	123	51.32	155
Doxycycline 100 mg twice a day for seven days	55.43	189	46.69	141
Minocycline 100 mg twice a day for seven days	3.81	13	0.99	3
Fluoroquinolone	3.23	11	0.00	0
Cephalosporin	0.29	1	0.33	1
Others	1.17	4	0.66	2

Table 3. *Mycoplasma genitalium* treatment preferences of urologists and gynecologists

Answer choices (question: what regimen do you use to treat *Mycoplasma genitalium*?)	Urologists		Gynecologists	
	%	n	%	n
Azithromycin 1 g in a single dose	10.56	36	26.49	80
Azithromycin 500 mg once a day, followed by 250 mg once a day for four days	29.03	99	11.26	34
Azithromycin 1 g once a day, followed by 500 mg once a day for three days	4.69	16	5.30	16
Doxycycline 100 mg twice a day for seven days	23.75	81	33.11	100
Minocycline 100 mg twice a day for seven days	2.35	8	0.33	1
Moxifloxacin 400 mg once daily for 10-14 days	1.17	4	2.65	8
Doxycycline 100 mg twice a day for seven days+azithromycin 500 mg once a day, followed by 250 mg once a day for four days	12.61	43	6.95	21
Doxycycline 100 mg twice a day for seven days+azithromycin 1 g once a day, followed by 500 mg once a day for three days	7.33	25	6.62	20
Doxycycline 100 mg twice a day for seven days+moxifloxacin 400 mg once a day for seven days	2.35	8	3.97	12
Minocycline 100 mg twice a day for seven days+azithromycin 500 mg once a day, followed by 250 mg once a day for four days	1.17	4	0.00	0
Minocycline 100 mg twice a day for seven days+azithromycin 1 g once a day, followed by 500 mg once a day for three days	0.59	2	0.99	3
Minocycline 100 mg twice a day for seven days+moxifloxacin 400 mg once a day for seven days	0.00	0	0.00	0
Fluoroquinolone	2.35	8	0.33	1
Cephalosporin	0.00	0	0.33	1
Others	2.05	7	1.66	5

PCR test, more than 40% of urologists and gynecologists prescribe antibiotics.

DISCUSSION

A questionnaire on antibacterial agents and STI treatment was distributed to analyze the STI treatment trends of domestic doctors. Currently, the primary treatment for *N. gonorrhea* recommended in the 2nd edition of the STI treatment guidelines revised in 2016 is a single 500 mg dose of ceftriaxone and a single 1 g dose of azithromycin. Azithromycin was added to the recommended treatment

regimen in 2016 for the treatment of *N. gonorrhea* with increased resistance to ceftriaxone [1]. On the other hand, resistance to azithromycin has been increasing worldwide, including in Korea [3-7]. A randomized controlled trial reported that a 1 g dose of azithromycin may be insufficient for treating *N. gonorrhea* [8]. In addition, low-dose ceftriaxone may be adequate for treating most *N. gonorrhea* infections, but a higher dose of ceftriaxone is more effective against isolates with increased minimum inhibitory concentrations (MICs) [9]. Although ceftriaxone-resistant isolates showed an MIC>0.125 mg/L have not been reported in Korea [10], they have already been confirmed in the United Kingdom and worldwide [4,11-13]. Therefore, the recommendations were revised in the 3rd edition of the STI treatment guidelines in 2023 as follows: a single 500 mg or 1 g dose of ceftriaxone is recommended for treating *N. gonorrhea* infections of the genitals or rectum. The recommended dose of ceftriaxone was increased to 1 g for adults weighing 100 kg or more to treat *N. gonorrhea* with reduced susceptibility successfully [14].

In addition, according to the 2nd edition of the STI treatment guidelines in 2016, combination therapy of ceftriaxone and azithromycin may be used until *N. gonorrhoeae* is clinically confirmed to be the sole infection by PCR testing [1]. On the other hand, caution is advised when using azithromycin to treat *N. gonorrhoeae* because it may increase the resistance in other strains, such as *M. genitalium* [14].

In cases of suspected gonococcal urethritis or gonococcal cervicitis/vaginitis, the rate of additional specimen collection from the pharynx was less than 3% in urologists and gynecologists. Active sample collection may not occur in practice because the awareness and importance of pharyngeal gonococcal infections have only emerged recently. In addition, education on sample collection should be provided because most physicians are unfamiliar with collecting pharyngeal samples. Furthermore, pharyngeal samples are not currently covered by health insurance in Korea. Hence, there is an urgent need for coordination with the Health Insurance Review and Assessment Service of Korea.

In the case of the preferred treatment of *C. trachomatis*, most physicians treat these infections according to medical guidelines. *M. genitalium* is currently an important STI, and a co-infection rate of 3 to 15% with *C. trachomatis* has been reported [15,16]. As increased resistance to azithromycin in *M. genitalium* has continuously been reported [17], doxycycline 100 mg twice a day for seven days is recommended for treating *C. trachomatis* infections of the genitals, pharynx, and rectum.

The primary treatment recommended for *M. genitalium* in the 2nd edition of the STI treatments guidelines is azithromycin at 500 mg once a day, followed by 250 mg once a day for six days to complete a seven-day course of therapy [1]. In the case of treatment failure from a 1 g dose of azithromycin or macrolide-resistant infections, however, 1.5 g of azithromycin therapy is also likely to fail. The two-stage therapy concept was developed from reports of low cure rates with azithromycin monotherapy for high-burden infections. In this regimen, patients were treated with doxycycline while awaiting the results of macrolide resistance testing, which lowered the burden of *M. genitalium*. Azithromycin at 1 g was administered, followed by 500 mg for three days [18-20].

U. urealyticum was recently reported to act as a pathogen, but it only causes symptoms when the number of bacteria is very high. Therefore, it is necessary to determine if the patient has had sexual contact and whether there are symptoms. No treatment is required if asymptomatic *U. urealyticum* is diagnosed because most cases do not cause disease. *U. parvum* or *M. hominis* are not considered true STIs, and they do not require treatment. On the other hand, treatment should be considered if an association when pregnancy-related complications are suspected. Considering the current increase in antibiotic resistance, physicians' awareness regarding this point must be improved [21].

In the case of follow-up PCR testing, 74% of the gynecologists perform the test after three weeks or later. On the other hand, only 40% of the urologists performed the test after three weeks, 28% after two weeks, and 22% after one week. Currently, post-treatment PCR follow-up testing can be covered by health insurance, and it is recommended after three weeks when the false-positive effect disappears to prevent unnecessary additional treatment. Therefore, providing education on the timing of post-treatment PCR follow-up testing is important.

CONCLUSIONS

Most urologists and gynecologists appeared to follow the treatments recommended in the 2nd edition of the STI treatment guidelines, revised in 2016. On the other hand, there were several changes in the 3rd edition of the STI treatment guidelines, including treatment guidelines for *N. gonorrhea*, *M. genitalium*, and *C. trachomatis*. The guidelines were also changed according to the domestic insurance policy for prescribing azithromycin and the macrolide resistance status in Korea. As many treatment regimens have changed because of the recent increase in antibiotic-resistant STIs, there is a need to encourage them to follow the new treatment guidelines.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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AUTHOR CONTRIBUTIONS

S.J.L. and J.B.C. participated in the conceptualization. B.K.H. and S.B. participated in data curation. S.P. and J.B.C. participated in the formal analysis. S.P. and J.B.C. participated in visualization and writing-original draft. S.J.L. and J.B.C. participated in writing, reviewing, and editing.

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