Thai Journal of Obstetrics and Gynaecology
September 2023, Vol. 31, No. 5, pp. 318-325.

SPECIAL ARTICLE

Bacterial Vaginosis: A Comprehensive Approach to Management in Reproductive-Aged Thai Women

Chenchit Chayachinda, M.D.*,
Kittipoom Chinhiran, M.D.**,
Payaow Aneklap, M.D.***,
Porntip Rachapromma, M.D.***,
Sunisa Sonwicha, M.D.*
Chanon Neungton, M.D.*

** Unit of Infectious Diseases, Department of Obstetrics and Gynaecology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand*
*** Bangrak STIs Center, Division of AIDS and STIs, Department of Disease Control, Ministry of Public Health, Bangkok, Thailand*
**** Department of Nursing, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand*

ABSTRACT

Bacterial vaginosis (BV) is the predominant condition of vaginal dysbiosis leading women to seek gynecologic care. Excessive genital cleansing, particularly through vaginal douching, appears to be a precipitating factor. BV does not induce any inflammatory response, with more than half of patients remaining asymptomatic. The chief complaints are an increased vaginal discharge volume and an altered odor. BV compromises the body's natural defense mechanisms, thereby increasing susceptibility to local and ascending infections. BV also heightens the risk of sexually transmitted infections, including pelvic inflammatory disease. For many years before 2022, our institution employed a metronidazole regimen of 1,200 mg daily, which demonstrated favorable efficacy. Metronidazole commonly leads to side effects such as nausea, vomiting, and a metallic taste. Unfortunately, many women discontinue the medication once their symptoms alleviate, as they often perceive BV as a vaginal imbalance rather than an infectious disease. In 2022, the Royal Thai College of Obstetricians and Gynaecologists introduced a recommended treatment guideline for BV that emphasized a balanced approach to medications and lifestyle modifications. Consequently, the primary antibiotic now used in Thailand is metronidazole, administered as a single 2 g dose or 800 mg daily for 7 days. At the Siriraj Female Sexually Transmitted Infections Clinic, we have utilized various metronidazole treatment regimens accompanied by comprehensive educational sessions and counseling. This article shows a comprehensive approach to management of BV in reproductive-aged Thai women, particularly based on Siriraj experience.

Keywords: bacterial vaginosis, Siriraj experience, treatment, vaginal dysbiosis, metronidazole.

Correspondence to: *Chenchit Chayachinda, M.D., Unit of Infectious Diseases, Department of Obstetrics and Gynaecology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand. E-mail: chenchit.cha@mahidol.ac.th*

Received: 19 June 2023, **Revised:** 25 August 2023, **Accepted:** 30 August 2023

Introduction

Disruption of the vaginal ecosystem leads to abnormal proliferation of the vaginal flora, characterized by an altered microbial ratio[1]. Bacterial vaginosis (BV) represents the predominant manifestation of vaginal dysbiosis, prompting women to seek gynecologic care[2]. BV arises from an overgrowth of anaerobic bacteria, notably *Gardnerella vaginalis*, resulting in an abundance of vaginal discharge with an unpleasant odor, commonly described as fishy. Notably, BV is not classified as a sexually transmitted infection (STI). Symptoms are often more pronounced during and after menstruation or sexual intercourse, with some individuals experiencing persistent and severe symptoms throughout the day. Nevertheless, nearly half of BV cases are asymptomatic. Dysbiosis weakens the vaginal environment and enhances vulnerability to various infections[3]. BV poses additional concerns in pregnant women, as it may heighten the risks of preterm labor or premature rupture of membranes[4].

The vagina serves as an elastic and muscular canal that links the external genitalia to the cervix. In prepubescent females, the predominant bacteria in the vagina are *E. coli*, diphtheroids, and coagulase-negative *Staphylococcus*[5]. Upon entering reproductive age, increased estrogen levels lead to the proliferation of mature squamous cells and enhanced glycogen accumulation within vaginal epithelial cells. Vaginal enzymes, such as alpha-amylase, degrade glycogen into maltose, maltotriose, and alpha-dextrins. Subsequently, *Lactobacilli's* lactase dehydrogenase hydrolyzes these compounds into lactic acid, which inhibits the growth of other bacteria. Lactic acid is believed to enter the cytoplasm and induce bacterial cell death. *Lactobacilli*, the primary protective bacteria in the vaginal ecosystem, produce both L- and D-lactic acid. However, D-lactic acid specifically contributes to maintaining vaginal balance[6]. Additionally, certain strains of *Lactobacilli*, notably *L. crispatus*, exhibit a higher capacity for hydrogen peroxide production, while *L. iners* produces comparatively low levels of hydrogen peroxide[7].

Both intrinsic and extrinsic factors can easily disrupt the stability of the vaginal ecosystem. Intrinsic factors encompass sex hormone levels and the presence of menstrual blood. Conditions that lead to decreased estrogen levels, such as menopause and breastfeeding, result in reduced quantities of *Lactobacilli* in the vagina. Additionally, the alkalinity of menstrual blood diminishes the activity of lactic acid, creating an environment conducive to the proliferation of other bacteria, thereby disrupting the protective role of *Lactobacilli*. Notably, *L. crispatus*, a beneficial strain of *Lactobacilli*, experiences a significant 100-fold decrease during menstruation, whereas *L. iners* and other anaerobic bacteria exhibit increased abundance[8]. Extrinsic factors encompass birth control methods that cause abnormal bleeding patterns, which can interfere with *Lactobacillus* function like the interaction of menstrual blood. Furthermore, certain risk behaviors, such as vaginal douching, excessive genital cleansing, and intercourse, directly reduce *Lactobacilli* in the vaginal ecosystem.

The Nugent scoring system is considered the gold standard diagnostic method for BV[9]. However, due to the expertise required by examiners, clinical diagnosis methods such as Amsel's criteria have gained popularity. The criteria necessitate the presence of at least three out of four indicators. They are a thin grayish-white homogenous discharge, pH > 4.5, clue cells (vaginal squamous epithelial cells with adherent bacteria), and a positive whiff test (characterized by a fishy odor upon adding 10% KOH)[10]. Nonetheless, a limitation of this method is its inability to be used in cases involving blood or amniotic fluid contamination. To address the limitation, the Royal Thai College of Obstetricians

and Gynaecologists recommends utilizing clue cells as a standalone diagnostic tool for BV, focusing on determining the proportion of clue cells present. An inclusion threshold of at least 20% clue cells achieves a sensitivity and a specificity of 87.1% and 55.8%, respectively, for diagnosing BV[11].

In line with the guidelines provided by the Center for Disease Control and Prevention, the International Union against Sexually Transmitted Infections and the World Health Organization[12, 13], the Royal Thai College of Obstetricians and Gynaecologists has issued treatment recommendations for reproductive-aged women presenting with abnormal vaginal discharge based on the available medications in Thailand[14]. The recommended regimens for BV treatment are follows:

- Metronidazole: 400 - 500 mg orally, twice a day for 7 days,
- Metronidazole: 2 g orally as a single dose,
- Metronidazole: 750 mg vaginal suppositories for 7 days,
- Tinidazole: 2 g orally as a single dose, or
- Clindamycin: 300 mg orally, twice a day for 7 days

Medical personnel should inquire about patients' experiences and comfort with vaginal suppositories, as they may not be suitable for individuals who have never engaged in penetrative sexual intercourse. Premature discontinuation of the regimen is a common issue[15], resulting in the improper disposal of residual drugs into the environment. Therefore, the single-dose regimen is often favored as the initial choice. However, being cautious of potential immediate vomiting following drug intake is crucial. One suggested approach is to slowly consume tablets, ingesting one or two at a time but ensuring that all tablets are swallowed within 5 minutes. As importantly, alcohol-containing food or drink should be withheld until 24 hours following last metronidazole tablet/ suppository or 72 hours until last tinidazole tablet.

It is crucial to ensure that all patients have a comprehensive understanding of the nature of the disease, its underlying causes, appropriate treatment, and self-care measures to prevent recurrence. The key messages to convey are as follows: "BV is not a sexually transmitted disease but rather a disruption in the vaginal ecosystem," "Recurrence is very common if lifestyle modifications are not followed", and "BV can result in many severe diseases, particularly ascending infections." Additionally, it is essential to provide clear explanations regarding proper drug administration and potential side effects. These explanations can be delivered through individualized one-on-one counseling sessions or online platforms. At the Siriraj Female Sexually Transmitted Infections (STI) Clinic, easily comprehensible educational materials have been developed to aid patients in understanding the correct technique for suppository administration and optimal vaginal care (see Fig. 1).

1A) Proper vaginal suppository method

1B) Vaginal care

Source: Unit of Infectious Diseases, Department of Obstetrics and Gynaecology, Faculty of Medicine Siriraj Hospital, Mahidol University

Fig. 1. QR code for accessing information on the proper usage of vaginal suppositories and vaginal care

Advice regarding proper vaginal care can vary across countries, and no universally agreed-upon best method exists. However, it is generally acknowledged that vaginal douching can lead to complications[16]. In Thailand, 4.8% of asymptomatic reproductive-aged[17] women practice vaginal douching, and this prevalence doubles among those with BV[18]. Surveys indicate that up to 90% of Thai women engage in genital cleansing outside of shower time, with three-thirds doing so at least twice daily[17]. It is important to dispel common myths surrounding vaginal care, such as the belief that urine is unclean, the misconception that a woman's genitals should have no odor, and the notion that seminal fluid must be completely washed out after intercourse. Most Thai women rely on plain water for external genital cleansing[17], whereas women from other countries often prefer various cleansing products[19]. However, once abnormal vaginal discharge is experienced, it is advisable to reduce the habit of internal and external genital cleansing.

The Siriraj Female STI Clinic provides specific recommendations for genital care. First, gentle blotting with dry tissue paper should be performed after urination. Second, sanitary pads should not be used outside of the menstrual cycle. Third, direct spraying of water onto the genitals should be avoided. Fourth, in cases of vaginitis or abnormal vaginal discharge, activities involving water immersion, such as swimming, should be avoided. Finally, if currently engaging in vaginal douching, it is advised to discontinue this behavior.

Experience of treating women with BV at the Siriraj Female STI Clinic

The primary treatment approach for BV involves the use of simple antibiotics, such as metronidazole, in either the oral or vaginal form. Since 2020, the Clinic has implemented a treatment and response monitoring system for all BV patients. Specifically, patients were requested to return for a follow-up visit after 2 weeks. In cases where no treatment response was observed, an alternative regimen was prescribed, with a further follow-up appointment scheduled for the following 2 weeks.

Patient characteristics are detailed in Table 1. Data analysis revealed therapeutic efficacy rates ranging from 66.7% to 80% for all metronidazole regimens (Fig. 2). These findings align with previous studies conducted among Thai women, which reported cure rates ranging from 77.8% to 78.6% based on the Amsel criteria[18, 20]. It should be noted that a proportion of patients, approximately 10%, exhibited two Amsel criteria, indicating an abnormal condition or mild BV[21].

BV often involves the formation of anaerobic biofilms that exhibit poor response to treatment. One study demonstrated that using metronidazole vaginal suppositories is more effective and faster at destroying biofilms[22]. However, our findings indicate that the treatment efficacy of vaginal metronidazole suppositories in combination with miconazole did not differ from that of oral metronidazole[18].

Lactic acid, a weak acid produced by *Lactobacilli*, plays a role in maintaining vaginal balance and acts as a precursor for hydrogen peroxide formation[7]. While lactic acid has been utilized in BV treatment, its efficacy is inferior to that of metronidazole[23, 24]. Therefore, its use is recommended in cases with mild symptoms or when less than three Amsel criteria are met. It is more favorably utilized in combination with metronidazole. Additionally, lactic acid can serve as a long-term preventive measure against BV recurrence and is considered safe for pregnant women[21, 25].

Our observations indicated that lactic acid was well-tolerated by patients. Only 13.6% (3/22) of patients reported a mild burning sensation from the first day of use. One patient also noted a slightly bothersome vaginal discharge, which resolved by the end of the 7-day treatment period. Patients expressed increased satisfaction during

the second and third days of use, reporting improved comfort and reduced odor. However, the treatment efficacy results at the 2-week follow-up did not differ from those of the other groups.

Table 1. Patient characteristics and treatment outcomes by treatment regimen.

	Metronidazole 400mg BID, 7d (n = 33)	Metronidazole 400mg TID, 7d (n = 30)	Metronidazole 2g (n=31)	Metronidazole 2g + Lactic acid (n=22)	Dequalinium chloride (n=22)
Age (years)	32.4±10.1	33.4±10.3	32.6±7.5	33.1±10.8	31.3±10.1
Being parous	12 (36.4)	13 (43.3)	11 (35.5)	8 (36.4)	5 (22.7)
Being pregnant	8 (24.2)	2 (6.7)	2 (6.5)	3 (13.6)	4 (18.2)
Vaginal care					
Panty-liner outside period	18 (54.6)	17 (56.7)	18 (58.1)	13 (59.1)	14 (63.6)
Special genital soap	18 (54.6)	17 (56.7)	15 (48.4)	15 (68.2)	13 (59.1)
Douche	10 (30.3)	5 (16.7)	6 (19.4)	11 (50.0)	6 (27.3)
Tampon	4 (12.1)	0	1 (3.2)	3 (13.6)	3 (13.6)
History of STDs					
Genital warts	5 (15.2)	2 (6.7)	2 (6.5)	1 (4.6)	3 (13.6)
Gonorrhea	2 (6.1)	1 (3.3)	2 (6.5)	1 (4.6)	1 (4.6)
Herpes genitalis	1 (3.0)	2 (6.7)	1 (3.2)	0	0
Trichomoniasis	1 (3.0)	1 (3.3)	0	0	0
Diagnosis of BV (Amsel criteria)					
pH > 4.5	31 (93.9)	29 (96.7)	28 (90.3)	19 (86.4)	20 (90.9)
Whiff test	25 (75.8)	20 (66.7)	27 (87.1)	19 (86.4)	20 (90.9)
Homogeneous whitish discharge	27 (81.8)	28 (84.8)	26 (83.9)	17 (77.3)	14 (63.6)
Presence of clue cells	31 (93.9)	28 (84.8)	30 (96.8)	22 (100)	21 (95.5)
Percentage of clue cells	50 [30-80]	45 [20-70]	40[30-60]	60[50-80]	60[50-90]
Number of Amsel criteria					
3	13 (39.4)	12 (40.0)	12 (38.7)	10 (45.5)	10 (45.5)
4	20 (60.6)	16 (53.3)	19 (61.3)	12 (54.6)	12 (54.6)
At 2-week follow-up					
No symptom	19 (57.6)	22 (73.3)	23 (74.2)	12 (54.6)	8 (36.4)
pH > 4.5	10 (30.3)	12 (40.0)	10 (32.3)	11 (50.0)	7 (31.8)
Whiff test	3 (9.1)	2 (6.7)	3 (9.7)	4 (18.2)	3 (13.6)
Homogeneous whitish discharge	5 (15.2)	1 (3.3)	5 (16.1)	2 (9.1)	6 (27.2)
Presence of clue cells	12 (36.4)	11 (36.7)	12 (38.7)	9 (40.9)	13 (59.1)
Presence of pseudohyphae	8 (24.2)	9 (30.0)	10 (32.3)	8 (36.4)	2 (9.1)
Presence of cervicitis*	3 (9.1)	4 (12.1)	2 (6.5)	1 (4.6)	2 (9.1)
Recurrence at 2 months	1/18 (5.6)	2/30 (6.7)	2/30 (6.7)	1/5 (20.0)	0/2 (0)

Abbreviation: BV, bacterial vaginosis, *Cervicitis = leukocytes ≥30/high power field (under 400x microscope)

Source: Unit of Infectious Diseases, Department of Obstetrics and Gynaecology, Faculty of Medicine Siriraj Hospital, Mahidol University

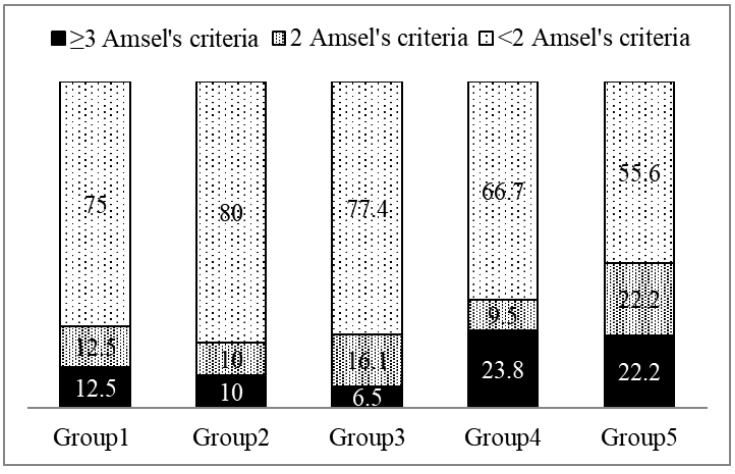

Fig. 2. Cure rates based on Amsel criteria at 2-week follow-up

Group 1 = Metronidazole 400mg BID, 7d (n = 33); Group 2 = Metronidazole 400 mg TID, 7d (n = 30); Group 3 = Metronidazole 2g (n = 31); Group 4 = Metronidazole 2g + Lactic acid (n = 22); Group 5 = Dequalinium chloride (n = 22)

Source: Unit of Infectious Diseases, Department of Obstetrics and Gynaecology, Faculty of Medicine Siriraj Hospital, Mahidol University

Dequalinium chloride is an antiseptic agent that can eradicate *G. vaginalis* biofilms[26], making it a potential treatment option for BV. However, our experience revealed an effectiveness rate of only 55.6%, with 22.2% of participants still exhibiting two Amsel criteria. Further studies are required to investigate the use of this drug. Our preliminary findings suggest that dequalinium chloride is an alternative treatment for patients who prefer to avoid antibiotics. Additionally, our previous report showed that its additional benefit was a non-inferior efficacy to clotrimazole in treating women with vaginal candidiasis[11]. As up to 36.4% of women with BV demonstrated vaginal candidiasis at the 2-week follow-up, dequalinium chloride may be advantageous. Nevertheless, close monitoring of treatment response is necessary, as antibiotics or antimycotics may eventually be needed.

Another non-antibiotic therapy for BV is *Lactobacillus* suppository since its deprivation is the mainstay pathophysiology. The only product in the Hospital's drug list is a combination of estriol 0.03 mg and 10^8 CFU of *Lactobacillus acidophilus*. Previous studies showed that, in terms of cure rate, it was superior to placebo and non-inferior to antibiotics[27, 28]. Using the combination as the first line BV treatment, we found that 10/20 (50.0%) women were symptom-free at 2-week follow-up but seven of them met at least three Amsel criteria. Out of the twenty patients, six met four Amsel criteria, seven met three, and five met two criteria at 2-week follow-up. Like dequalinium chloride, this product may be an option for those who prefer non-antibiotic treatment.

Currently, we have limited experience of using tinidazole and clindamycin. Tinidazole is a long-acting nitroimidazole antibiotic but is not included in the Hospital's drug list. Based on the data of 9 non-pregnant women with BV who came for 2-week follow-up, a 7-day-course of twice daily 300mg clindamycin showed lower cure rate by Amsel criteria than that in a previous study in Thailand[29], at 66.7% vs 94.3%. Moreover, we found one case of angioedema following clindamycin consumption.

Regarding symptom assessment, it was observed that the group receiving metronidazole 400 mg three times daily for 7 days displayed the fewest symptoms on the follow-up day (Table 1). However, this group expressed the highest level of dissatisfaction with the treatment approach. The regimen of metronidazole 400 mg three times daily for BV

treatment has been in use at Siriraj Hospital for over 20 years. At the moment, the Clinic maintains this regimen for cases that do not respond to the initial treatment, and it has shown a treatment efficacy rate of nearly 100%. For those who failed the regimen of 7-day metronidazole 1,200 mg, the 12-day course of dequalinium chloride was then prescribed and resulted in good treatment response.

When being assessed at two months, recurrence was rare. Three main causes of BV recurrence were residual infection, resistance to treatment, or re-infection[25]. The first two causes are unlikely since the follow-up until being cured was performed in all cases. This underlines the importance of education session about vaginal health care and follow-up for all women with BV. Nonetheless, longer term follow-up and further studies are required in order to demonstrate the sole effect of lifestyle modification on BV recurrence.

Beside treatment outcomes, the new diagnoses which were disclosed at 2-week follow-up were as important. Up to 36.4% of women initially being diagnosed with BV were positive for pseudohyphae, a marker of vaginal candidiasis, under light microscope. We chose to treat all of them regardless of symptoms and asked them to return for evaluation until the finding became negative. In contrast, although presence of leukocytes ≥ 30/high power field (under 400x magnification) yields diagnostic accuracy of chlamydial cervicitis at 21.8%[30], we did not initiate treatment. Further information is required to guide clinicians' decision.

Conclusion

Vaginal dysbiosis is a challenge for obstetricians and gynecologists because of its potential severe consequences. The main precipitating factor is the patient's genital care practice which needs to be discussed, investigated and modified in conjunction with drug treatment. The choices of treatment regimens are at the moment vast. The prescriptions should be based on to the experience of the healthcare personnel and the acceptance of the patients. This article shows that higher-dose drug use may not improve the patient's recovery rate. Guidelines for treating this group of patients still have room for further development to provide patients with the best possible care.

Potential conflicts of interest

The authors declare no conflicts of interest.

References

1. Chayachinda C, Chinhiran K, Kittiyaowamarn R, Chaithongwongwatthana S, Teeratakulpisarn N. The Thai 2022 sexually transmitted infections treatment guideline: Abnormal vaginal discharge. Thai J Obstet Gynaecol 2022:222-33.
2. Chayachinda C, Thamkhantho M, Chalermchockcharoenkit A, Neungton C, Thipmontree W. Characteristics of clients at the Siriraj female STD clinic during 2011-2015. Siriraj Med Bull 2018;11:182-9.
3. Ravel J, Moreno I, Simón C. Bacterial vaginosis and its association with infertility, endometritis, and pelvic inflammatory disease. Am J Obstet Gynecol 2021;224:251-7.
4. Tachawatcharapunya S, Chayachinda C, Parkpinyo N. The prevalence of bacterial vaginosis in asymptomatic pregnant women during early third trimester and the pregnancy complications. Thai J Obstet Gynaecol 2017;25:96-103.
5. Smith SB, Ravel J. The vaginal microbiota, host defence and reproductive physiology. J Physiol 2017;595:451-63.
6. Witkin SS, Mendes-Soares H, Linhares IM, Jayaram A, Ledger WJ, Forney LJ. Influence of vaginal bacteria and D- and L-lactic acid isomers on vaginal extracellular matrix metalloproteinase inducer: implications for protection against upper genital tract infections. mBio 2013;4:e00460-13.
7. Aroutcheva A, Gariti D, Simon M, Shott S, Faro J, Simoes J, et al. Defense factors of vaginal lactobacilli. Am J Obstet Gynecol 2001;185:375-9.
8. Srinivasan S, Liu C, Mitchell CM, Fiedler TL, Thomas KK, Agnew KJ, et al. Temporal variability of human vaginal bacteria and relationship with bacterial vaginosis. PLoS One. 2010;5:e10197.
9. Nugent RP, Krohn MA, Hillier SL. Reliability of diagnosing bacterial vaginosis is improved by a standardized method of gram stain interpretation. J Clin Microbiol 1991;29:297-301.
10. Amsel R, Totten P, Spiegel C, Chen K, Eschenbach

D, Holmes K. Nonspecific vaginitis. Diagnostic criteria and microbial and epidemiologic associations. Am J Med 1983;74:14-22.
11. Chayachinda C, Baukaew L, Thamkhantho M, Bangpichet A, Sodsee S, Pharkjaksu S. Clue cell as a single diagnostic tool for bacterial vaginosis during pregnancy. J Med Assoc Thai 2020;103:353-8.
12. Workowski K, Bachmann L, Chan P, Johnston C, Muzny C, Park I, et al. Sexually transmitted infections treatment guidelines 2021. MMWR Recomm Rep 2021;70:1-187.
13. Sherrard J, Wilson J, Donders G, Mendling W, Jensen J. 2018 European (IUSTI/WHO) International Union against Sexually Transmitted Infections (IUSTI) World Health Organization (WHO) guideline on the management of vaginal discharge. International Journal of STD & AIDs 2018;29:1258-72.
14. Royal Thai College of Obstetrics and Gynaecologists. Management of abnormal vaginal discharge in reproductive-aged women. Siriraj Med Bull 2023;16:187-29.
15. Kardas P, Devine S, Golembesky A, Roberts C. A systematic review and meta-analysis of misuse of antibiotic therapies in the community. Int J Antimicrob Agents 2005;26:106-13.
16. Aslan E, Bechelaghem N. To 'douche' or not to 'douche': hygiene habits may have detrimental effects on vaginal microbiota. J Obstet Gynaecol 2018;38: 678-81.
17. Hosiriphon K, Chayachinda C, Keawpoonsub K, Taibowornpitak K, Tuangrattanasirikun D. A survey of daily genital care practices among reproductive-aged female personnel at Siriraj Hospital. Siriraj Med J 2023;75:259-65.
18. Thamkhantho M, Chayachinda C, Lertaroonchai C. Vaginal suppository of metronidazole (750mg) plus miconazole nitrate (200mg) versus oral metronidazole (2g) for bacterial vaginosis: A randomized controlled trial. Siriraj Med J 2021;73:644-51.
19. Crann S, Cunningham S, Albert A, Money D, O'Doherty K. Vaginal health and hygiene practices and product use in Canada: a national cross-sectional survey. BMC Womens Health 2018;18:52.
20. Chaithongwongwatthana S, Limpongsanurak S, Sitthi-Amorn C. Single hydrogen peroxide vaginal douching versus single-dose oral metronidazole for the treatment of bacterial vaginosis: a randomized controlled trial. J Med Assoc Thai 2003;86 Suppl 2:S379-84.
21. Mendling W, Shazly M, Zhang L. The role of lactic acid in the management of bacterial vaginosis: a systematic literature review. Future Pharmacology 2022;2:198-213.
22. Armstrong E, Hemmerling A, Miller S, Burke K, Newmann S, Morris S, et al. Metronidazole treatment rapidly reduces genital inflammation through effects on bacterial vaginosis-associated bacteria rather than lactobacilli. J Clin Invest 2022;132:e152930.
23. Decena D, Co J, Manalastas RJ, Palaypayon E, Padolina C, Sison J, et al. Metronidazole with Lactacyd vaginal gel in bacterial vaginosis. J Obstet Gynaecol Res 2006;32:243-51.
24. Andersch B, Forssman L, Lincoln K, Torstensson P. Treatment of bacterial vaginosis with an acid cream: a comparison between the effect of lactate-gel and metronidazole. Gynecol Obstet Invest 1986;21:19-25.
25. Faught B, Reyes S. Characterization and Treatment of Recurrent Bacterial Vaginosis. J Womens Health (Larchmt) 2019;28:1218-26.
26. Gaspar C, Rolo J, Cerca N, Palmeira-de-Oliveira R, Martinez-de-Oliveira J, Palmeira-de-Oliveira A. Dequalinium Chloride Effectively Disrupts Bacterial Vaginosis (BV) Gardnerella spp. Biofilms. Pathogens 2021;10:261.
27. Donders G, Van Bulck B, Van de Walle P, Kaiser R, Pohli G, Gonser S, et al. Effect of Lyophilized Lactobacilli and 0.03 mg estriol (Gynoflor®) on vaginitis and vaginosis with disrupted vaginal microflora: A multicenter, randomized, single-blind, active-controlled pilot study subject area: Further areas women's and children's health. Gynecol Obstet Invest 2010;70:264-72.
28. Parent D, Bossens M, Bayot D, Kirkpatrick C, Graf F, Wilkinson F, et al. Therapy of bacterial vaginosis using exogenously-applied Lactobacilli acidophili and a low dose of estriol: a placebo-controlled multicentric clinical trial. Arzneimittelforschung 1996;46:68-73.
29. Leetanaporn R, Chandeying V, Tungphaisal S. The efficacy of oral clindamycin in the treatment of bacterial vaginosis. Thai J Obstet Gynaecol 1994;6: 91-9.
30. Marrazzo JM, Handsfield HH, Whittington WL. Predicting chlamydial and gonococcal cervical infection: implications for management of cervicitis. Obstet Gynecol 2002;100:579-84.