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SPECIAL ARTICLE

Sodium Bicarbonate Vaginal Suppositories for Cytolytic Vaginitis Treatment

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ABSTRACT

Cytolytic vaginitis (CV) is a form of vaginal dysbiosis resulting from an overgrowth of *Lactobacilli*, which are the primary protective bacteria in the vagina. The symptoms closely resemble those of fungal vaginitis, including abnormal vaginal discharge, itching, dysuria, and dyspareunia. There is no accurate diagnostic method, but bed-side diagnosis requires microscopic examination and pH testing. The Royal Thai College of Obstetricians and Gynaecologists outlines the following diagnostic guidelines: vaginal acidity (pH < 4.5), absence of vaginal fungal hyphae, and a higher number of white blood cells than squamous epithelial cells. In contrast, cytolytic vaginosis is defined by a high concentration of *Lactobacilli* with predominant epithelial cells with cytolysis. Patients with either condition often experience similar symptoms and may have a history of various unsuccessful treatments. The recommended treatment includes vaginal douching with a sodium carbonate solution or the use of sodium bicarbonate suppositories. The vaginal douching can be difficult to follow, particularly for Thai women. The Unit of Infectious Diseases, Department of Obstetrics and Gynaecology, Faculty of Medicine Siriraj Hospital, has used 300 mg sodium bicarbonate tablets (Sodamint®) as vaginal suppositories to treat this condition. This article aims to demonstrate our treatment experience, potentially contributing to the development of further knowledge and research.

Keywords: cytolytic vaginitis, cytolytic vaginosis, sodium bicarbonate, treatment, suppository.

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Introduction

Cytolytic vaginosis, first described in 1961, affects approximately 5% of women with abnormal vaginal discharge. Diagnosing this condition can be a challenge as its symptoms resemble those of fungal vaginitis, and the microscopic features appear close to normal. The risk factors include pregnancy and being under 40 years of age. It is less common in women who engage in frequent sexual intercourse. Common symptoms include vaginal itching, increased vaginal discharge, dysuria, and dyspareunia. Some individuals experience symptoms that vary with their menstrual cycle, worsening during ovulation and improving before menstruation. Microscopically, a large number of *Lactobacilli* are typically observed, with white blood cells rarely present, though squamous epithelial cells can be found with cytolytic pictures. Some experts recommend performing fungal cultures to differentiate between conditions, though both can coexist[1].

Cytolytic vaginosis, lactobacillosis and leptothrix, all of which result from an increase in the number of *Lactobacilli*, have indistinguishably clear definition. Typically, *Lactobacilli* are beneficial bacteria that protect the vagina in women of all ethnicities. Studies from various countries published since 2017 have identified *L. crispatus* as the most common Lactobacillus species. In cases of cytolytic vaginosis, it was observed that there is an increased production of acid in the vagina, and women with this condition exhibit lower diversity of *Lactobacilli* compared to normal[2]. These three conditions overlap, thus some experts suggest that cytolytic vaginosis is characterized by an increase in number of *Lactobacilli* and cytolysis. In contrast, lactobacillosis and leptothrix do not involve cytolysis. Leptothrix has a distinctive microscopic appearance, which is long and coiled, and believed to be a type of *Lactobacilli*[3].

Diagnosis

Patients with lactobacillosis and leptothrix, are often asymptomatic. Although antibiotic treatment is sometimes recommended, its benefits remain unclear. Leptothrix is diagnosed by identifying long, non-branching filamentous *Lactobacilli* (> 60µm)[3]. In a study by Vieira-Baptista, of 3,620 slides of vaginal swab, 102 (102/3620, 2.8%) met the criteria for leptothrix. Among the symptomatic group, 45 individuals (45/1847, 2.4%) had leptothrix. Of them, only 12 cases are potentially linked to the symptoms. The most common symptoms, listed in order, were vaginal burning and itching, abnormal vaginal discharge, menstrual symptoms, and dyspareunia. The average age of patients was 38.8 ± 10.65 years. The only associated risk factor identified was having human immunodeficiency virus (HIV). Leptothrix was also found in conjunction with fungal vaginitis by nearly doubling the risk (odds ratio (OR) 1.90, 1.16-3.10-3.10)[4]. However, this study could not clearly establish the relationship between the disease and the abovementioned symptoms.

The Royal Thai College of Obstetricians and Gynaecologists has introduced a management guideline for women presenting with abnormal vaginal discharge[5]. This guideline suggests a diagnostic method based on pH levels and the ratio of white blood cell to squamous epithelial cells (Fig. 1). Unlike the diagnostic method for cytolytic vaginosis, treatment in this guideline is initiated when a woman has abnormal vaginal discharge, a higher number of white blood cells than squamous epithelial cells, and a pH level below 4.5. This condition is referred to as cytolytic vaginitis due to elevated white blood cell count. The rationale is that the disease progression resembles that of fungal vaginitis: initially, the number of squamous epithelial cells is higher, but as inflammation and cell lysis increase, more white blood cells migrate into the vagina, resulting in a higher white blood cell count[6].

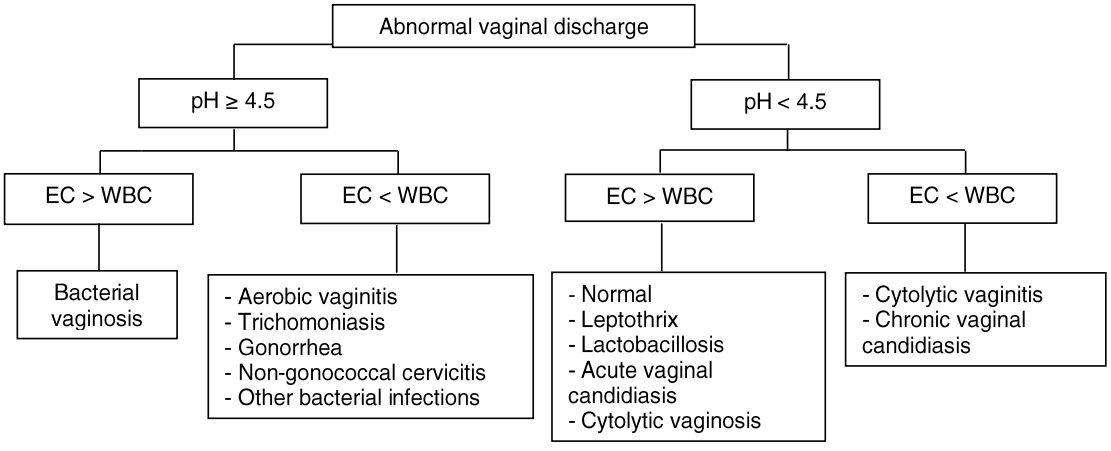

Fig. 1. Approach to abnormal vaginal discharge using vaginal pH and the ratio of epithelial cells to white blood cells.[5]

EC: epithelial cells, WBC: white blood cell

The prevalence of cytolytic vaginosis, lactobacillosis and leptothrix in Thai women has not been reported. One explanation is that the wet preparation of cytolytic vaginosis, lactobacillosis and leptothrix normally shows predominate squamous epithelial cells and share high similarity with the normal one. In contrast, microscopic finding of cytolytic vaginitis strikingly differs from that of normal vaginal discharge. Based on the unpublished data of the Siriraj Female STI Clinic, 49/186 (26.3%) of women presenting with abnormal vaginal discharge had vaginal pH < 4.5 and white blood cells ≥ 30/hpf. Of them, 20 had detected pseudohyphae in wet preparation. Therefore, 29/186 (15.6%) met the diagnostic criteria of cytolytic vaginitis. However, only a few of them agreed to try the novel treatment of Sodamint® and the treatment outcomes were shown in Table 1.

Treatment

Research on cytolytic vaginosis is limited. One study, conducted in Turkish women who underwent cervical Pap smears during 2015-2018, included 3,000 specimens. Those with ruptured squamous epithelium with bare nuclei; an increased number of *Lactobacilli*; few or no leukocytes; and no other significant bacteria were selected. Only patients with abnormal vaginal discharge and a pH ≤ 4.5 were selected, resulting in 53 patients (1.7%) being treated. The treatment involved mixing 1 tablespoon of sodium bicarbonate mixed with 4 liters of warm water, with patients sitting in the bathtub every other day for 10 days. All patients showed symptom improvement, with 43 patients (81%) improving at the start of treatment, and 10 (19%) showing improvement upon completing the treatment[7].

The treatment guidelines align with those for other types of vaginal dysbiosis, recommending treatment only when symptoms are present[3, 8]. The primary treatment method of cytolytic vaginosis and cytolytic vaginitis involves using a sodium carbonate solution for vaginal douching or sitting in a bath. This is typically recommended every morning for two weeks; however, some patients may require longer treatment or need to repeat the process whenever symptoms occur[3]. Other recommendations include avoiding tampons or vaginal cups; using antibiotics and fungicides only when necessary; exercising caution

when using probiotics; and avoiding excessive washing of the external genitalia[2]. The use of antibiotics is controversial, though clindamycin cream (2%) inserted into the vagina daily for 5 days or amoxicillin 500 mg taken orally three times a day for 7 days has been suggested[2]. The insertion of lactic acid products into the vagina is contraindicated, as it may increase the number of *Lactobacilli* and alter vaginal pH[9].

The use of vaginal suppositories to balance the vaginal environment is common, although its popularity varies across cultures. A study among female personnel working at Siriraj Hospital found that only 4.6% engaged in vaginal douching[10]. In contrast, various products are advertised in other countries as beneficial for promoting vaginal health. One study compared the effects of three products used for vaginal douching: water, sodium chloride, vinegar, and sodium benzoate (pH 3.0); citric acid, edetate disodium, water, sodium benzoate, sodium lauryl sulfate, trisodium phosphate, and povidone-iodine 0.3% (pH 3.5); and sodium bicarbonate and water (pH 9). The study found all three products could reduce *E.coli*, weaken the vaginal mucosa, and decrease the inflammatory effects of *Lactobacilli*. However, only sodium bicarbonate is effective at reducing the number of all types of *Lactobacilli* species, including *L. iners*, *L. crispatus, L. gasseri,* and *L. jensenii*[11]. This makes sodium bicarbonate a potential option for treating this condition.

In Thailand, sodium bicarbonate is available in two forms: as a solution and as an oral tablet (Sodamint®). It acts by reducing acidity in the bloodstream and stomach and alkalinizing the urine. This medication is inexpensive and readily available at all levels of medical facilities. The Royal Thai College of Obstetricians and Gynaecologists recommends treating abnormal vaginal discharge using sodium carbonate solution mixed with 1.5 liters of water for vaginal douching[8]. However, this method can be challenging for patients to perform by themselves. Additionally, based on our experience in caring for women with abnormal vaginal discharge, we found that many Thai women are reluctant or fearful of using such treatment methods. Since The Thai treatment guidelines also recommend the use of sodium bicarbonate tablet (Sodamint® 300 mg) as a vaginal suppository once or twice daily for 10-14 days, we have some experience of this treatment choice, and the series of patients is summarized in Table 1.

Table 1. Case series of women with cytolytic vaginitis at the Siriraj Female STD Clinic (n = 12).

Cases	Age (y)	BMI (kg/m²)	No. of child (ren)	Contraceptive methods	Last Pap result	Previous diagnosis	Polymerase chain reaction results						Cure
							NG	CT	TV	MG	MH	UU	UP	
1	21	20.2	0	Condom	NILM, Candida	-	neg	neg	neg	neg	pos	neg	pos	Yes
2	24	24.8	1	No	NILM	Bacterial vaginosis	-	-	-	-	-	-	-	Yes
3	29	21.3	1	Condom	NILM	Aerobic vaginitis	neg	pos	-	-	-	-	-	Yes
4	51	18.4	2	No	NILM	Bacterial vaginosis	neg	neg	-	-	-	-	-	Yes
5	29	26.0	0	Condom	NILM	Aerobic vaginitis	neg	neg	-	-	-	-	-	Yes
6	37	28.8	1	Pills	NILM, Candida	-	pos	neg	-	-	-	-	-	Yes
7	40	16.9	2	Pills	NILM	-	neg	neg	-	-	-	-	-	Yes
8	33	18.8	0	No	NILM	-	-	-	-	-	-	-	-	Yes
9	46	19.1	3	Sterilisation	NILM	Vaginal candidiasis	neg	neg	neg	neg	neg	neg	neg	No
10	42	29.6	1	Sterilisation	NILM	Aerobic vaginitis	neg	neg	neg	neg	neg	neg	neg	No
11	27	19.6	1	DMPA/Implant	ASCUS	Aerobic vaginitis	neg	pos	neg	pos	neg	pos	neg	No
12	23	26.1	1	No	NILM	Aerobic vaginitis	neg	pos	neg	neg	pos	neg	pos	No

BMI: body mass index, NILM: negative intraepithelial lesions or malignancy, ASCUS: atypical squamous cell of unknown significance, NG: N. gonorrhoeae, CT: *C. trachomatis*, TV: *T. vaginalis*, MG: *M. genitalium*, MH: *M. hominis*, UU: *U. urealyticum*, UP: *U.parvum*, DMPA: depot medroxyprogesterone acetate
Source: Unit of Infectious Diseases, Department of Obstetrics and Gynaecology, Faculty of Medicine Siriraj Hospital, Mahidol University

Initially, we started with Sodamint® vaginal suppositories administered in the morning and evening. However, two out of four patients reported discomfort, including burning, itching, and vaginal irritation. Since then, we adjusted the dosage to once daily for 10-14 days, followed by a two-week follow-up appointment for all patients. Out of 15 patients diagnosed with cytolytic vaginitis, 12 returned for the follow-up. A clinical cure was observed in 8 out of 12 patients (66.7%). Those who did not achieve a clinical cure were more likely to have child (ren), practice unprotected intercourse, and have a history of vaginal dysbiosis. No co-infections with vaginal candidiasis or trichomoniasis were found. Additionally, none of the patients reported severe adverse effects that required premature discontinuation of Sodamint®. After treatment, two out of 12 patients (16.7%) experienced a recurrence of symptoms and managed it by using the suppositories on an as-needed basis.

Other forms of sodium carbonate have been used to treat vaginitis caused by various factors. For instance, sodium bicarbonate gel has been used to treat fungal vaginitis. Studies have shown that this gel can reduce the growth of *C. glabrata*, *C. krusei*, *C. tropicalis*, *C. parapsilosis*, and *C. albicans*, with an optimal concentration of 5%. In vitro studies indicate that sodium bicarbonate can be used with Hela cells, which are a good model for vaginal epithelial cells, as it does not cause irritation[12]. Another study showed that using 5% sodium bicarbonate solution as a sitz bath once daily for 14 days, compared to a sitz bath with nystatin 500,000 units for the same duration, found no significant difference in the rate of symptom resolution or microscopic diagnosis. However, the group using nystatin experienced faster symptom relief. It is believed that reducing vaginal acidity can help limit fungal growth[13].

In general, various types of drugs can be administered vaginally, including hormonal medications, antibiotics, and antifungal agents. The benefits of this route of administration include localized action, no interference with gastrointestinal absorption or interactions with orally absorbed drugs, and ease of use[14]. Additionally, vaginal secretions from the fallopian tubes, uterus, Bartholin's gland, and Skene's gland enhance drug solubility[15]. Vaginal drug delivery also tends to have fewer side effects, reducing the risk of those associated with oral medications. This may help improve patient adherence[14]. In line with our case series, some studies showed that sodium bicarbonate in gel form causes irritation in the vulvovaginal area[12].

Conclusion

Cytolytic vaginosis or cytolytic vaginitis is a form of vaginal dysbiosis caused by an overgrowth of *Lactobacilli*. Treatment involves adjusting the *Lactobacilli* levels by reducing vaginal acidity; addressing risk factors that may contribute to the imbalance; and promoting overall vaginal health such as avoiding excessive genital cleansing, managing stress and correcting nutrient deficiencies. While sodium bicarbonate solution is readily available, it may be less suitable for use among Thai women. Sodium bicarbonate vaginal suppository offers an affordable, easily accessible, and convenient treatment option. Nonetheless, further research with a larger study population size and further prospective studies are needed.

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