



Original Research Article

Knowledge, awareness, approach and management of vulvo-vaginal infections with topical combination preparations: A cross-sectional, questionnaire based gynaecologists survey

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ABSTRACT

Background: Vulvo-vaginal infection (VVI) often results in abnormal vaginal discharge, soreness, redness and pain during urination. As per CDC 2017, vulvovaginitis is a second common infection. For management of VVI, both oral and topical preparations are available. But, there is scarcity of data on prevalent clinical practices in the management of VVI in India.

Materials and Methods: This cross-sectional, non-interventional, observational, multicentric, questionnaire based survey was conducted with 992 gynaecologists across India. A series of 10 multiple choice questions were prepared. The questionnaire was targeted on prevalent practices in topical management of patients with VVI. All the parameters were summarized using descriptive statistics.

Results: Majority of the gynaecologists (N=772/992, 78%) in the survey responded that they treat approximately 10 patients with VVI per week. About 54% of gynaecologists (N=532/992) consider pH of the topical preparation as an important parameter. Nearly, 82% of gynaecologists (N=818/992) prefer using a lower potency steroid like mometasone for application on genital areas instead of higher potency steroid like clobetasol. About 98% of gynaecologists were satisfied (67%; N=664/992) to very satisfied (31%; N=312/992) with the use of triple drug topical combination of nadifloxacin, terbinafine and mometasone in the management of VVI.

Conclusion: This survey concluded that VVI is commonly seen in gynaecological practice in India. Further more, triple drug topical combination of antibiotic, antifungal and steroid is generally preferred by gynaecologists in the management of VVI with satisfactory results.

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1. Introduction

Vulvo-vaginal infection (VVI) is symptomatic vaginitis (inflammation of the vagina and vulva) most often caused by bacterial vaginosis, candidiasis and trichomoniasis.^{1,2} Centers for Disease Control and Prevention (CDC) reported that around 75% of women are susceptible for at least one episode of VVC and 40%–45% will have two or more episodes.³ The symptoms include soreness, pain during urination, itching and abnormal vaginal discharge.⁴ Although most infections are mild in nature, some women

can develop severe infections involving redness, swelling and crack in mucosal wall of the vagina. It was reported that about 20% of women normally have Candida in their vagina without having any symptoms.⁵ According to a research conducted in urban population in India, candida accounted for 30% of vulvovaginal infections in reproductive age females while bacterial vaginosis was also quite prevalent at 17.3%.⁶ Another study by Aubyn et al. (2013) reported prevalence of bacterial vaginosis 28%, Candida infection 22% and co-infection of bacterial and candida 16%. A review of studies found that 20–30% of women with bacterial vaginosis are co-infected with Candida species while 60–80% of cases with bacterial

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vaginosis are co-infected with *T. vaginalis*. In such cases, therapeutic eradication of the dominant pathogen can lead to the sequential emergence of the second pathogen.⁷

Both oral and local therapies (antibacterial, antibiotic and antifungal agents) are available for the management of VVI. The main goal of VVI treatment is to get relief from symptoms and prevent the recurrence of infection. Topical combination preparations containing antibiotics, antifungals and steroids are available in India and are used in gynaecological practice in management of VVI. One such topical preparation is nadifloxacin, terbinafine and mometasone combination. Nadifloxacin, a topical fluoroquinolone antibiotic, is effective against both aerobic gram positive and gram negative, anaerobic bacteria and is well tolerated for the treatment of patients with bacterial skin infections.⁸ Terbinafine, is an allylamine antifungal agent that is safe and effective for the treatment of superficial and mycotic infections.⁹ Mometasone is a medium potency topical steroid.¹⁰

In India, data on use of such triple drug topical combination in management of VVI and gynaecologists' approach for such preparations is limited. Hence, the present questionnaire-based survey was conducted to assess approach of gynaecologists' for management of VVI and their perception towards use of topical combination preparations.

2. Materials and Methods

2.1. Study design

This was a cross-sectional, non-interventional, observational, questionnaire based survey conducted from August 28 to October 16, 2019. Gynaecologists from different regions of India who were willing to provide responses to the questionnaire were included in this survey (west: Mumbai, Pune, Ahmedabad, Jaipur; north: Delhi, Chandigarh, Lucknow; south: Chennai, Bangalore, Trivandrum; East: Kolkata, Guwahati, Patna; central: Indore, Hyderabad, Nagpur). As this survey did not collect any patient data, ethics committee permission was not sought.

2.2. Questionnaire

A series of 10 multiple choice questions were prepared to analyse gynaecologists' opinion on management of VVI. The questionnaire was targeted on cases of VVI, prevalent practices in topical management for VVI patients and the formulation factors affecting the clinical practice protocol. The questions pertained to the information regarding:

1. Importance of formulation parameters of topical preparations in management of VVI patients
2. Role and preference of topical corticosteroid, antifungals and antibacterials in management of VVI

The detailed questions are presented in Table 1. The responses for all the questions were collected through an online link provided to the personnel collecting the data from gynaecologists.

2.3. Statistical analysis

No formal sample size calculation was done. Descriptive statistics were used to assess the responses to the questions.

3. Results

3.1. Patient flow in practice

A total of 992 gynaecologists participated in this survey and responded to 10 questions. Majority of the gynaecologists (N=420/992, 42%) in the survey responded that they treat approximately 10 patients with VVI per week. 4% of gynaecologists (N=42/992) treat more than 20 cases per week.

3.2. Culture and sensitivity testing

About 69% of the gynaecologists (N=688/992) sometimes advise culture and sensitivity testing in patients with VVI. Overall, 23% of gynaecologists (N=227/992) always advise culture and sensitivity testing as shown in Figures 1 and 2.

3.3. Consideration of various parameters while prescribing

Around 54% of gynaecologists (N=532/992) consider efficacy of topical preparations which can work at acidic pH (vaginal pH) as an important parameter while treating patients with VVI whereas 44% of gynaecologists (N=436/992) consider it as a very important parameter (Figure 3). Likewise, pH of the topical preparation was also considered as an important parameter by 53% of gynaecologists (N=529/992) while 3% of gynaecologists (N=28/992) gave no importance to pH of topical preparations. According to 53% of gynaecologists (N=521/992) patients with VVI generally require topical management for a period of two weeks but 22% of gynaecologists (N=224/992) consider one week of prescription. About 42% (N=413/992) of gynaecologists responded that they frequently prescribe combination topical preparations in the management of VVI and 30.5% (N=306/992) sometimes prescribe as shown in Figure 4.

Nearly, 48% of gynaecologists believed (N=478/992) that broad spectrum activity of nadifloxacin against Gram positive, Gram negative aerobes and anaerobes is a very important feature while using it in management of suspected bacterial VVI (Figure 5).

Overall, 82.5% of gynaecologists (N=818/992) preferred using a lower potency steroid like mometasone for application on delicate genital areas instead of higher potency steroid like clobetasol. About 88% of gynaecologists

Table 1: Structure of questionnaire

S.No	Question	Response
1	How many cases of VVI do you see in your practice?	<input type="checkbox"/> 0-5 cases/wk <input type="checkbox"/> 6-10 cases/wk <input type="checkbox"/> 11-20 cases/wk <input type="checkbox"/> >20 cases /wk
2	Do you advice culture and sensitivity testing in patients of VVI?	<input type="checkbox"/> Always <input type="checkbox"/> Sometimes <input type="checkbox"/> Never
3	Do you consider efficacy of topical preparation, which works at acidic pH (Vaginal pH) as an important parameter while treating VVI?	<input type="checkbox"/> Very important <input type="checkbox"/> important <input type="checkbox"/> Not important
4	Do you feel pH of the topical preparation, should be considered as an important parameter while treating VVI?	<input type="checkbox"/> Very important <input type="checkbox"/> Important <input type="checkbox"/> Not important
5	Do you feel broad spectrum activity of nadifloxacin against Gram +ve, Gram -ve aerobes and anaerobes is an important feature while using it in suspected bacterial VVI?	<input type="checkbox"/> Very important <input type="checkbox"/> Important <input type="checkbox"/> Not important
6	Do you prefer fungicidal allylamines (terbinafine) instead of fungistatic azoles (clotrimazole/miconazole) in suspected fungal VVI?	<input type="checkbox"/> Yes <input type="checkbox"/> No
7	For how long generally do your VVI patients require the topical management?	<input type="checkbox"/> 1 wk <input type="checkbox"/> 2wks <input type="checkbox"/> 3wks <input type="checkbox"/> ≥4 wks
8	Do you prefer using a lower potency steroid (mometasone) compared to higher potency steroid (clobetasol) for application on genital areas?	<input type="checkbox"/> Yes <input type="checkbox"/> No
9	Do you prescribe combination topical preparations of antibiotics, antifungals & steroids in management of VVI?	<input type="checkbox"/> Always <input type="checkbox"/> Frequently <input type="checkbox"/> Sometimes <input type="checkbox"/> Never
10	How satisfied are you with the use of topical triple combination of nadifloxacin, terbinafine and mometasone in management of VVI?	<input type="checkbox"/> Very satisfied <input type="checkbox"/> Satisfied <input type="checkbox"/> Not satisfied

(N=872/992) preferred fungicidal allylamines (terbinafine) instead of fungistatic azoles (clotrimazole/miconazole) in suspected fungal VVI while 12% of gynaecologists (N=120/992) do not prefer fungicidal allylamines (Figure 6).

3.4. Satisfaction about combination topical preparation-

About 98% of gynaecologists were satisfied (67%; N=664/992) to very satisfied (31%; N=312/992) with the use of triple drug topical combination of nadifloxacin, terbinafine and mometasone in the management of VVI. Overall, in this survey more than 99% of gynaecologists were satisfied with the use of triple drug combination for management of VVI (Figure 5).

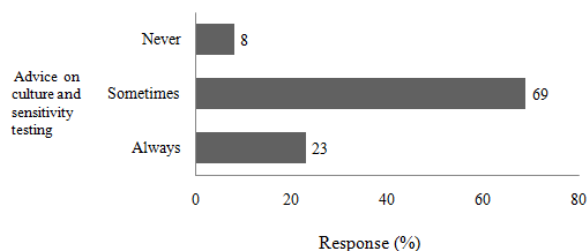


Fig. 2: Gynaecologists’ response on screening tests in patients with VVI

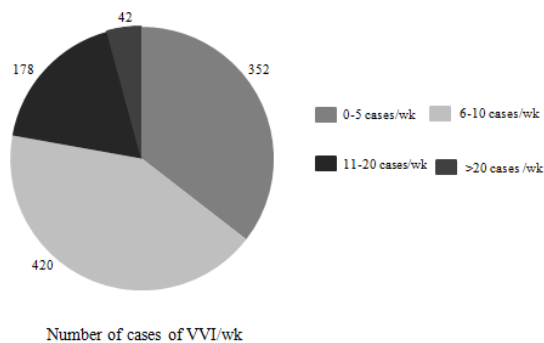


Fig. 1: Gynaecologists’ response for number of cases of VVI seen in their clinical practice

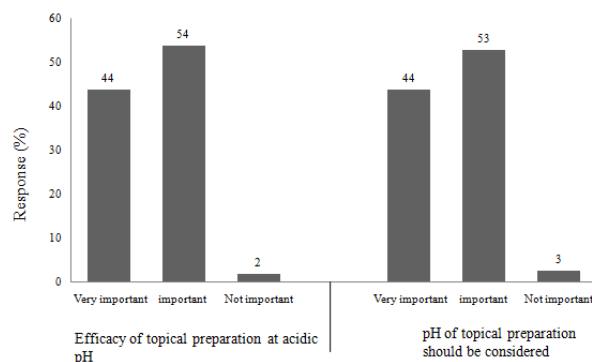


Fig. 3: Gynaecologists’ response for pH of topical preparation and pH of topical preparation

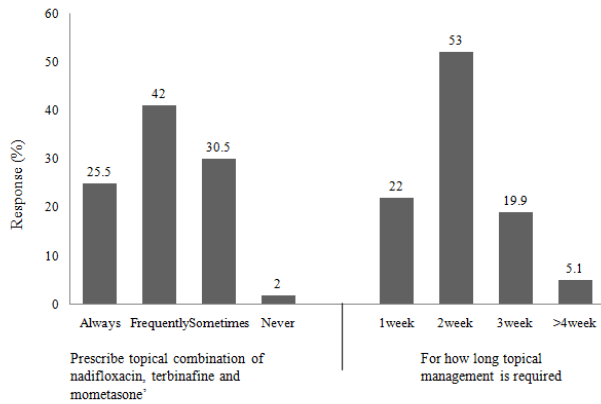


Fig. 4: Gynaecologists’ response for topical combination of nadifloxacin, terbinafine and mometasone and duration of treatment

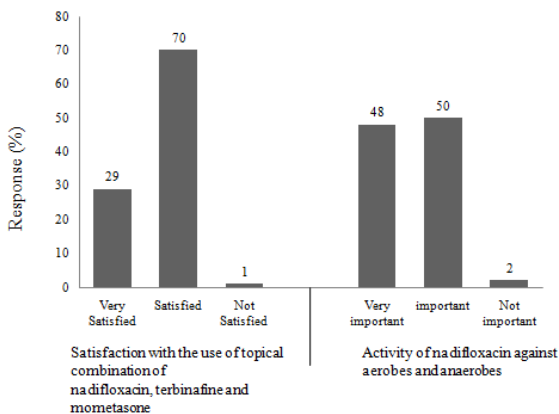


Fig. 5: Gynaecologists’ response on use of triple drug topical combination of nadifloxacin, terbinafine and mometasone and nadifloxacin and antimicrobial coverage of nadifloxacin

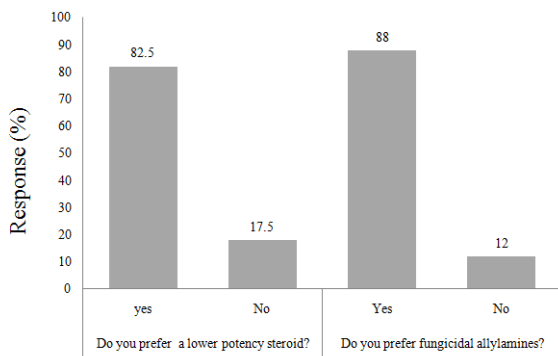


Fig. 6: Gynaecologists’ response on preference of steroids and allylamines antifungal

4. Discussion

This survey reported that VVI is common in India with 42% of gynaecologists observing 6 to 10 cases of VVI per week. 54% of gynaecologists considered efficacy of topical preparations which can work at acidic pH (vaginal pH) as an important parameter while deciding the management of VVI. Around 41% of gynaecologists frequently prescribed combination topical preparations for the management of VVI. Nearly half of the gynaecologists reported of recommending topical preparations for a period of two weeks in VVI patients. Overall, 99% of the gynaecologists were either very satisfied or satisfied with the results of triple drug topical combination of nadifloxacin, terbinafine and mometasone.

Microbial composition of the vagina varies with the vaginal pH. It was evident that Candida species appears more frequently at pH 4 and other infectious micro flora appears at higher vaginal pH.^{11,12} In India, VVI is mainly caused by Candida albicans, Candida tropicalis, Candida glabrata and Gardnerella vaginalis which grows at acidic pH.^{13–15} Vaginal pH should be frequently checked for early diagnosis of VVI.¹⁶ Topical preparations which are able to work at vaginal pH are recommended for VVI.¹⁷ Accordingly, around 98% of gynaecologists in the current analysis considered efficacy of topical preparations which can work at acidic pH (vaginal pH) as an important parameter while treating patients with VVI.

Although topical azoles are preferred for management of VVI, but they may require a longer course of therapy.¹⁸ Nevertheless, there is a need for topical preparation which shows its effect within a shorter period of time.

A topical combination preparation of nadifloxacin (antibacterial), terbinafine (antifungal, antibacterial) and mometasone furoate (steroid) is available in the market and is used in the management of VVI by gynaecologists in India. Nadifloxacin, a topical fluoroquinolone antibiotic has anti-bacterial and anti-inflammatory properties. It acts by down-modulating the cutaneous immunity and interferes with the antigen-presenting ability of the epidermal cells.¹⁹ Nadifloxacin inhibits IL-12 and IFN- γ production to activate T cells and keratinocytes which results in reduction of bacterial infections.²⁰ Nadifloxacin is able to reduce a significant number of micro flora and is effective and safe in the management of bacterial skin infections.^{21,22} Our survey also indicated that overall 98% of gynaecologists opined that broad spectrum antibacterial activity of nadifloxacin is a very important or an important feature while using it in the treatment of suspected bacterial VVI.

Topical mometasone furoate, is a unique steroid and has demonstrated a higher degree of efficacy as well as local and systemic safety.^{23,24} A study reported that topical mometasone furoate has higher safety and efficacy for management of vulvar lichen sclerosus as compared to clobetasol propionate.²⁵ We observed that for application

on delicate areas like genital area, a lower potency steroid (mometasone) was a preferred choice by 82% of gynaecologists than a higher potency steroid (clobetasol). Higher potency steroids are sensitive and cause burning sensation on thin areas of skin.

Our survey also indicated that gynaecologists prefer terbinafine being an allylamine antifungal agent for management of VVI. Antifungal agents exert their effect by changing the permeability of fungal cell membrane;²⁶ Terbinafine, an allylamine antifungal agent, inhibits the ergosterol synthesis in fungi and thus destroy the integrity of fungal cell membrane and this depends on the concentration.²⁷ Further, terbinafine has the ability to manage VVI within two weeks and is considered superior than other azoles such as itraconazole, clotrimazole and fluconazole.^{28,29} But terbinafine fungicidal activity is active against few *Candida* like parapsiosis and static against *C. albicans* and others and few other *Candida* species. A previously published study suggest that fungicidal activity of terbinafine is rapid when compared to itraconazole and the minimal fungicidal concentration(MFC) to minimal inhibitory concentration(MIC) ratio for terbinafine is lower than itraconazole; fungicidal activity of terbinafine was excellent and initiated rapidly (by 7 hours) as compared to itraconazole.³⁰

Mild vaginal infections usually respond to a single dose or short duration of treatment, i.e, 1–3 days, whereas more severe signs and symptoms need topical therapy for 5–7 days.³¹ In the present survey, around half of the gynaecologists were found recommending triple drug topical preparations for a period of two weeks while 22% recommending it for a week in the management of VVI.

Triple drug topical therapy like combination of nadifloxacin, terbinafine and mometasone, is found to be well-supported by the gynaecologists in our survey probably because of its broad spectrum effect in management and control of symptoms in VVI patients. A combination of antibacterial, antifungal and steroid components of triple drug topical preparation can provide early onset of relief from VVI. Hence, a triple drug topical preparation offers a potential for therapeutic benefit in the form of short duration of application required due to early resolution of symptoms and control over microbial infection while going for empirical treatment in VVI.

Our survey highlights about gynaecologists' perspective on management of VVI and the use of combination topical preparation in it. However it had some limitations including the cross-sectional design which makes us unable to analyse behaviour over a period of time and does not help to determine the cause and effect relationship.

5. Conclusion

This survey indicated that triple drug topical combination of nadifloxacin, terbinafine and mometasone is commonly used by gynaecologists in the management of VVI with

satisfactory results.

Limitation of the study- Due to cross-sectional design of this study we failed to analyse the behaviour over a period of time. You can add any related limitation of the study example like we have not assessed severity of VVI as it is overall opinion of gynaecologists and as per severity, duration of treatment can change.

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7. Source of Funding

None.

8. Conflict of Interest

None.

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