Research Article

Efficacy of Amla (*Emblica officinanis*) and Shibe yamani (*potash alum*) in the management of Candida vaginitis: a randomized standard controlled trial

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ABSTRACT

Background: It has been estimated that 75% of all females experience at least one episode of Candida vaginitis with approximately 40-50% reporting a recurrence during their lifetime. The symptoms of vulvovaginal candidiasis are often painful and uncomfortable to the patient. The objective of this study was to assess the efficacy of Amla and Shibe yamani in the management of Candida vaginitis.

Methods: This randomized, single blind, standard controlled study was done to compare the efficacy of Amla and *Shibe yamani* against fluconazole and 2% miconazole on diagnosed subjects of Candida vaginitis. Test group (n=30) received *Amla* with honey orally and *Shibe yamani* intra-vaginally at bed time for 3 wks. Whereas control group received standard regime of single dose fluconazole 150 mg orally and 5g of miconazole 2% cream intravaginally for 7 days. The primary outcome measure was relief in the vulvovaginal pruritus (reduction in 5D itch score). Secondary outcome measures included change in wet mount and improvement in vaginal discharge.

Results: Vulvovaginal pruritus significantly decreased (P<0.001) after intervention in the two groups. Marked improvement was observed in vaginal discharge (P<0.001) in both the groups. 70% of patients in test group and 80% in control group showed change in wet mount.

Conclusions: Test drugs provide statistically significant improvement in vulvovaginal pruritus, vaginal discharge and in wet mount test without any apparent side effects. It can serve as an alternative treatment for Candida vaginitis.

Keywords: Candida vaginitis, Amla; Shibe yamani, Fluconazole, Vulvovaginal pruritus

INTRODUCTION

Candida vaginitis is a common cause of infective vaginal discharge experienced by women.[1] Each year an estimated 10 million health care office visits to gynaecologists are due to vulvovaginitis.[2] Among the many causes of vaginitis, Candida vaginitis is the second most common cause after bacterial vaginosis and is diagnosed in up to 40% of women with vaginal complaints.[3] It is a disease caused by abnormal growth of yeast-like fungi in the mucosa of female genital tract, classified by WHO as a sexually transmitted disease of frequent sexual transmission.[4] Several behavioural factors such as frequent sexual intercourse, oral sex, use of high oestrogen oral contraceptives, condoms,

spermicides etc. and host-related risk factors such as antibiotics use, uncontrolled diabetes, conditions with high reproductive hormone levels, genetic predisposition etc. have been associated with VVC and recurrent episodes.[3] Although vaginal candidiasis is treatable, when left untreated is a possible risk for acquisition of HIV/AIDS as well as other complications such as PID, infertility, ectopic pregnancy, pelvic abscess, menstrual disorders, spontaneous abortion and premature delivery.[5] Studies have found that women with recurrent vaginal yeast infections are more likely to experiment with alternative therapies due to relatively lower cost. An estimated 42% of patients with RVVC have resorted to alternative therapies.[2] Candida infections are usually treated with an array of antimycotic agents such as

azoles, polyenes, echinocandins, allylamines and other derivatives but the emergence of antimycotic resistant candidal pathogens, especially the potential widespread dissemination of resistance has become a major public health concern. The prevalence of VVC is therefore expected to increase. Antifungal resistance has been reported in most Candida species, which are the aetiological agents of VVC in addition to other adverse effects of the drugs. Thus there is a need for alternative or adjunct bio-antimycotic means of controlling pathogenic Candida species that infect humans. Studies are also being conducted on the prospects for development of vaccine to prevent and control vaginal candidiasis, which would benefit a large number of women who suffer from this debilitating syndrome.[6] Amla has got habis, qabiz, mubarrid, mussaffie khoon properties and Shibe yamani is having qabiz, habis, mujaffif, musakkin and mane' sailan effect.[7-13] Pharmacological studies has also confirmed that Amla contains antifungal, antibacterial, antiviral, anti-inflammatory, analgesic, cooling, antidiabetic, antioxidant, immunomodulator, astringent and resistance building properties.[14-16] Whereas Shibe yamani is having antifungal, antibacterial, anti-inflammatory and astringent properties.[17-20] Keeping in view the properties of Amla and Shibe yamani this study was carried out to scientifically evaluate their efficacy in the management of Candida vaginitis.

METHODS

This randomized single blind standard controlled study was conducted in the Dept. of Ilmul Qabalat Wa Amraze Niswan, National Institute of Unani Medicine Hospital, Bangalore, from Feb 2013 to Feb 2014. Keeping in consideration the availability of patients and limited resources 45 patients were recruited for the present study. Patients were allocated randomly to either of the test (n=30) or control group (n=15). Randomisation was done by lottery method/random number table. Prior to initiation of the study, the protocol and informed consent were reviewed and approved by institutional ethical committee, NIUM, Bangalore, with IEC No: NIUM/IEC/2011-12/12/ANQ/04. Data were collected by history, clinical examination and Laboratory investigations.

Inclusion criteria

Married patients in the age group of 18- 45 years complaining of vulvovaginal pruritus, vaginal discharge, dysuria and dyspareunia.

Exclusion criteria

Systemic illness, blood stained discharge, sexually transmitted infections, malignancy, pregnant and lactating women and the patients who had received antifungals or antibiotics within previous two weeks.

Patients fulfilling inclusion criteria were enrolled in the study after obtaining informed consent. In each patient a detailed history was evaluated with basic information. Duration of presence of presenting complaint and associated symptoms were enquired. Participants underwent a complete general physical examination including height, weight, BMI and measurements of vitals. Systemic examination of CNS, CVS, RS, abdominal examination and gynaecological examination (P/S, P/V and breast examination) was done in each patient. Per speculum and per vaginal examinations were done by placing the patient in lithotomy position after emptying the bladder. Under a good source of light local examination of external genitalia to look for signs of erythema, oedema and excoriation was made. A sterile speculum without lubricant was placed; vagina and cervix were examined for abnormal inflammation and secretions in terms of colour, consistency and odour. Cases revealing cheesy or white, thick and curdy discharge adherent to vaginal wall were suggestive of Candida vaginitis. Sample of vaginal discharge was taken from the upper wall of the vagina and placed on clean dry slide. A drop of 10% KOH solution was added and covered with a clean cover slip. Then the slide was examined microscopically to notice the presence of budding yeast or pseudohyphae. After speculum examination bimanual vaginal examination was done for assessment of uterine size, position, mobility and condition of adnexa. Any mass, tenderness in the fornices and pouch of Douglas was noted. Following thorough evaluation of history and clinical examination, patients were subjected to baseline investigations CBP, ESR, CUE, HIV, VDRL, LFT, RFT, thyroid profile, RBS, Pap smear, USG pelvis.

Test group (n=30) received Amla (*Emblica officinalis*) with honey orally and *Shibe yamani* (potash alum) intra-vaginally at bed time for 3 wks. Dried fruit of Amla was grinded to make fine powder (sufoof). In each 4gms of sufoof e Amla 7 ml of pure honey was mixed for one dose. Accordingly in 28gms of sufoof e Amla, 50 ml of honey was mixed for one week dose and was dispensed in air tight pet jar weekly. Honey was used as corrective (musleh) of Amla. Shibe yamani biryan 4gms had to be mixed with 30ml of distilled water for one dose. Shibe yamani biryan was dispensed in lock bag and distilled water in 250ml bottle for one week dose. Patients were advised to take preparation in a dosage of 4gms orally twice a day. Tampons dipped in lotion of Shibe yamani biryan (4gms/30ml) had to be used intra-vaginally at bed time daily. In control group one tablet of fluconazole 150mg was given in a lock bag and miconazole 2% cream was given in 50gm pet jar. Fluconazole 150mg tablet had to be taken orally whereas 5gms of miconazole 2% cream had to be applied intra-vaginally daily at bed time for 7 consecutive days. Treatment was subsequently started in patients fulfilling the inclusion criteria. The test drug was given for 3 weeks and standard drug was given for 7 days. After which an assessment of white discharge and pruritus were made. Biochemical estimations were repeated after the completion of trial.

Effectiveness of trial drugs were assessed by subjective and objective parameters. Subjective parameters included

the severity of pruritus vulva assessed at baseline, for three consecutive weeks during treatment and fortnightly for two visits after treatment. For assessment of pruritus vulva 5-D itch scale was used. It is a brief, single page questionnaire for the multidimensional quantification of pruritus that is sensitive to change over time. 5-D scores can potentially range between 5 (no pruritus) and 25 (most severe pruritus). Objective parameters included quantity and character of white discharge assessed by per speculum examination and presence or absence of fungal spores and hyphae assessed by KOH wet mount. Objective parameters were assessed before and after treatment.

Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (inter group analysis) and paired proportion test has been used for within groups (intra group) analysis on metric parameters. Student t test (two tailed, dependent) has been used to find the significance of study parameters on continuous scale within each group. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups.

RESULTS

Table 1: Baseline demography of the patients with Candida vaginitis in test and control group.

Characteristics	Test group(n=30)	Control group (n=15)	Total (n=45)	P value
Age (years)				
21-25	8(26.7%)	1(6.7%)	9(20%)	
26-30	10(33.3%)	6(40%)	16(35.6%)	
31-35	5(16.7%)	5(33.3%)	10(22.2%)	P=0.500
36-40	6(20%)	3(20%)	9(20%)	
>40	1(3.3%)	0(0%)	1(2.2%)	
Mean ± SD	30.13±6.22	31.40±5.15	30.56±5.86	
Occupation				
House wife	23(76.7%)	14(93.3%)	37(82.2%)	
House maid	1(3.3%)	0(0%)	11(2.2%)	
Factory worker	1(3.3%)	0(0%)	1(2.2%)	P=0.897
Tailor	4(13.3%)	1(6.7%)	5(11.1%)	
Teacher	1(3.3%)	0(0%)	1(2.2%)	
Education				
Illiterate	2(6.7%)	2(13.3%)	4(8.9%)	
Primary	14(46.7%)	7(46.7%)	21(46.7%)	
Secondary	10(33.3%)	4(26.7%)	14(31.1%)	P=0.941
Higher secondary	3(10%)	1(6.7%)	4(8.9%)	
Graduate	1(3.3%)	1(6.7%)	2(4.4%)	
Diet				
Mixed/non-veg	28(93.3%)	14(93.3%)	42(93.3%)	P=1.000
Veg	2(6.7%)	1(6.7%)	3(6.7%)	
Nutritional status				
Poor	4(13.3%)	2(13.3%)	6(13.3%)	
Average	18(60%)	8(53.3%)	26(57.8%)	P=0.903
Good	8(26.7%)	5(33.3%)	13(28.9%)	
BMI (kg/m^2)				
<25	17(56.7%)	9(60%)	26(57.8%)	
25-30	12(40%)	4(26.7%)	16(35.6%)	P=0.681
>30	1(3.3%)	2(13.3%)	3(6.7%)	
Total Mean ± SD	24.55±3.44	24.05±4.49	24.39±3.78	
SES				
Lower	1(3.3%)	1(6.7%)	2(4.4%)	
Upper lower	13(43.3%)	8(53.3%)	21(46.7%)	P=0.849
Lower middle	11(36.7%)	4(26.7%)	15(33.3%)	
Upper middle	5(16.7%)	2(13.3%)	7(15.6%)	

Table 2: Comparative evaluation of vulvovaginal pruritus (5D itch score).

VVP	Test group	Control group	P value
Before treatment	19.10±3.21	18.40±2.79	0.476
After treatment	6.67±3.57	5.93±1.67	0.455
Difference	12.43	12.47	-
P value	<0.001**	<0.001**	-

Table 3: Comparative evaluations of KOH wet mount.

KOH wet mount	BT	AT	% change	P value
Test group				
Positive	30(100%)	9(30%)	-70.0	<0.001**
Negative	0(0%)	21(70%)	+70.0	
Control group				
Positive	15(100%)	3(20%)	-80.0	
Negative	0(0%)	12(80%)	+80.0	<0.001**
P value	1.000	0.475	-	

Table 4: Comparative evaluation of white discharge per speculum.

WDPV	BT	AT	% change	P value
Test group				
Nil	0(0%)	21(70%)	+70.0	
Mild	7(23.3%)	9(30%)	+6.7	
Moderate	23(76.7%)	0(0%)	-76.7	<0.001**
Profuse	0(0%)	0(0%)	0.0	
Control				
Nil	0(0%)	8(53.3%)	+53.3	
Mild	6(40%)	7(46.7%)	+6.7	
Moderate	9(60%)	0(0%)	-60.0	
Profuse	0(0%)	0(0%)	0.0	<0.003**
P value	0.245	0.271	-	

There were no significant difference between the groups concerning baseline characteristics with P>0.05 (Table 1). The mean range of VVP (5D itch score) in test group before treatment was 19.10±3.21 and it reduced to 6.67±3.57 after treatment with a difference of 12.43. In control group it was 18.40±2.79 before treatment and reduced to 5.93±1.67 after treatment with a difference of 12.47. The intra group difference of 5D itch score is highly significant in both the study groups with P<0.001 (Table 2). As shown in table.3 before intervention all the study subjects (100%) in both the groups presented with fungal buds or hyphae on KOH wet mount test. After completion of treatment no fungal buds or hyphae were detected in 70% of test group and 80% of control group participants. Here intra group analysis gives a highly significant (P<0.001) value whereas no significant difference was observed in inter group analysis. It is approximately similar in both the groups showing

equivalent efficacy of test drug to control drug. On speculum examination all participants presented with white discharge which was significantly improved after treatment (Table 4). In test group improvement was 70% and control group exhibited 53.3% improvement in WDPV. Intra group analysis before and after treatment was highly significant (P<0.001) in both the groups and inter group analysis exhibited no significant difference (P>0.05) after treatment i.e. effect of both the intervention were comparable.
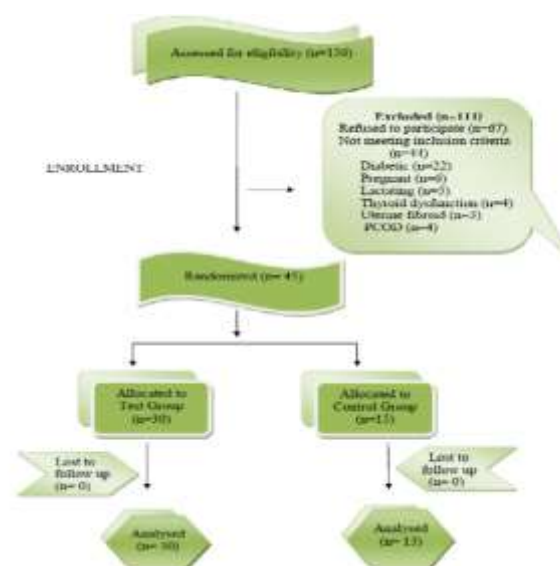
Figure 1: Flow diagram of participants.

DISCUSSION

Candida vaginitis presents with common symptoms like itching, vaginal discharge and burning sensation that affects the quality of life of many women. Generally the affected women will turn to self-medication with over the counter antifungal drugs. It is prudent that the side effects of oral antifungals have to be born in mind in treating a relatively harmless non-life threatening condition. Patients who opt for oral antifungal agents for personal preference should be adequately informed of its potential side effects, if long term usage is required. On the other hand Unani system of medicine is bestowed with a cache of herbal and mineral origin medicinal wealth. A number of drugs have been mentioned in Unani authentic literature to treat vaginal discharge and vulvovaginal pruritus which are the salient features of Candida vaginitis.

There was no significant difference between the groups concerning baseline characteristics with P>0.05 (Table 1). Mean age of the patients included in study was 30.13±6.22 in test group and 31.40±5.15 in control group ranging from 21-45 years. Maximum number of participants (55%) belongs to age group of 21-30 years. Aring et al also reported highest incidence of VVC in age group 21-30 years (64.9%) followed by 31-40 years (17.45%) and lower incidence in age above 40yrs (7%).

82% of patients included in this study were housewives. Similar findings were observed by Reza et al. in which 81% of women were housewives and rest were working women.[21] In present study majority of participants (84%) belong to low socioeconomic class (upper lower, lower middle, lower). This is in accordance to the Unani concept. Eminent Unani physicians has highlighted the association of low socioeconomic status with occurrence of sailanur rehm.[22] Sarain et al. also found an association of low socioeconomic status with prevalence of Candida species in 87% of participants of their study.[23]

Unani physicians described the cause of disease as zofe in quwae rehm and accumulation of rutoobat.[13] The excellent response of test drugs was due to the qabiz[7-9,12] effect of Amla which helped in absorption of excessive rutoobat. It strengthens the quwae rehm also by its muqawwi action.[9,12] Along with the local effect produced by Shibe yamani which absorbs excessive discharge due to its mujaffif and qabiz action.[10,11,13] Thus there was no culture media for yeast to grow and proliferate. In the absence of discharge (irritant) and active organism, as well as due to the musakkin (soothing) effect of alum there was a relief in vulvovaginal pruritus.[12] This improvement in the vaginal discharge may be attributed to the higher content of tannins, flavonoids, alkaloids, phenolic compounds, antioxidants and considerable amount of micronutrients such as chromium, zinc and copper present in the Emblica officinalis.[15]

Improvement in the KOH wet mount may be due to antifungal properties of Amla and Shibe yamani proved by earlier research.[17,23] Regarding the nature and quantity of discharge in all the study participants the colour of discharge was white. 64.4% of patients had moderate discharge, 28.9% had scanty discharge and only 6.7% had profuse discharge. Curdy discharge was present in 88.9% of patients and rest had (11.1%) mucoid discharge. In 97.8% of patients, discharge was non-offensive whereas in 2.2% malodorous discharge was present. This is in accordance with Unani concept that specifies odourless and colourless discharge as an indication of ghalbae balgham.[25] In present study majority of patients had balghami mizaj. Hence from this statement it can be inferred that Candia vaginitis is a type of sailanur rehm which occurs due to alteration in the quality and quantity of balgham. In other words Candida vaginitis is a disease condition described centuries back in classical Unani text as sailane balghami. Normalcy of abnormal balgham was restored by dafe balgham and musaffie akhlat property of Amla.[9]

It can be inferred from the above findings that Amla and Shibe yamani was found as an effective alternative treatment in the treatment of Candida vaginitis with no obvious adverse effects rather it is equivalent in efficacy to standard drugs i.e. fluconazole and miconazole. Being natural agent and free of side effects, it can be considered superior to standard control. It can provide an alternative substitute for costly antifungal drugs, especially in the country like India where majority of population belong to lower socioeconomic group.

CONCLUSION

Amla and Shibe yamani are equivalent in efficacy to fluconazole and miconazole in the management of Candida vaginitis. A remarkable relief in vulvovaginal pruritus and white discharge was found after treatment. Relief in symptoms was due to the habis, qabiz, mujaffif, mane' sailan, musakkin, mubarrid, and musaffie khoon properties as well as effects of tannins, flavonoids and antioxidants present in test drugs. The promising results of the study have certain limitations due to a non elevated number of patients and a short follow-up period. There is need to perform similar study in large number and for a longer duration.

Candida vaginitis is prevalent in diabetics. Hence it is recommended to conduct clinical trial of Amla without honey (used as musleh of Amla) by using other muslehat for islah of Amla as mentioned in Unani literature. So that result can be generalised to all the patients of Candida vaginitis.

In conclusion, the results of this clinical study/trial indicate that Amla and Shibe yamani possess properties that warrant further clinical studies in a larger number of patients with vulvovaginal yeast infection to confirm its efficacy and tolerability.

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