

Original Research Article

Efficacy and safety of combination of nifuratel tablets with Baofukang suppository on treatment and recurrence of vaginitis in pregnancy

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Abstract

Purpose: To investigate the effect and safety of a combination of Nifuratel tablets and Baofukang suppository in the treatment and recurrence of vaginitis in pregnant patients.

Methods: A retrospective analysis was carried out on 100 in-patients admitted between February 2019 and April 2020. They were randomly assigned to control and study groups, with 50 in each group. The control group received Baofukang suppository treatment, whilst the study group was treated with Nifuratel tablets in addition to Baofukang suppository. The two groups were compared with regard to treatment effectiveness, incidence of adverse reactions, recurrence at 1, 2 and 3 months post-treatment; time taken for disappearance of clinical symptoms, and levels of inflammatory factors 1 week after treatment. Moreover, Mental Status Scale in Non-Psychiatric Settings (MSSNS) score, and Quality of Life Index (QLI) score were compared between the groups.

Results: The study group out-performed the control group with respect to treatment effectiveness and QLI score ($p < 0.05$). Patients in the study group had significantly lower incidence of adverse reactions, degree of recurrence at 1, 2 and 3 months post-treatment, time taken for disappearance of clinical symptoms, expression levels of inflammatory factors, and MSSNS score, when compared to those in control group ($p < 0.05$).

Conclusion: Combined use of Nifuratel tablets and Baofukang suppository in the treatment of pregnant patients with vaginitis leads to significant treatment efficacy and safety, and reduced recurrence and expression levels of inflammatory factors in patients.

Keywords: Nifuratel, Baofukang suppository, Vaginitis, Pregnancy, Therapeutic effect, Recurrence, Safety

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INTRODUCTION

Vaginitis is a common complaint among pregnant women. The main clinical manifestations are vaginal pain and itching, and abnormal secretion

of body fluids. Vaginitis, which may be due to fungal and bacterial infections, is classified into bacterial vaginitis, mycotic vaginitis and trichomoniasis vaginitis [1-3]. It probably occurs in pregnant women due to changes in hormonal

secretions during pregnancy. There is need for caution in drug intake during pregnancy, so as to avoid fetal malformation and other congenital diseases. Therefore, the health of pregnant women and their fetuses should be considered comprehensively in the treatment of vaginitis [4-6]. In addition, some pregnant women may ignore the importance of timely treatment of vaginitis. This may affect the delivery and health of the fetus. Generally, Nifuratel is a drug widely used for treating bacterial vaginosis, trichomoniasis vaginitis and other vaginal diseases due to its desirable effect [7,8]. *Baofukang* suppository is also used for treating diseases such as pruritus and vaginitis. This study was aimed at identifying a treatment method for pregnant patients with vaginitis. Pregnant women with vaginitis were retrospectively divided into study group and conventional-treatment control group. The two groups were compared with respect to percentage treatment effectiveness, incidence of adverse reactions, recurrence at 1 month, 2 months and 3 months post-treatment; time taken for disappearance of clinical symptoms, levels of inflammatory factors 1 week after treatment, MSSNS score and QLI score.

METHODS

General patient profile

A retrospective analysis was conducted among 100 pregnant patients with vaginitis admitted to our hospital from February 2019 to April 2020. They were randomly assigned to control group and study group, with 50 patients in each group. The patients in study group were aged 21 to 33 years, while those in the control group were aged 20 – 33 years. The protocol was approved by the ethics Committee of Shandong First Medical University, with the approved no. of 2018-CL-243 and the international guidelines for human studies that you followed [9]. There were no significant differences in age, gestational age

and other general data between the two groups ($p > 0.05$; Table 1).

Inclusion/exclusion criteria

Inclusion criteria

Patients aged 18 years and above, with clinical manifestations of vaginitis during pregnancy, and patients without other organic diseases or history of drug allergy, drug abuse or bad habits, were included in the study.

Exclusion criteria

Pregnant women at advanced gestational age, patients with other types of gynecological diseases, and those with gestational diabetes mellitus were excluded.

The study was approved by the ethics committee of our hospital. All patients voluntarily participated in the study and submitted signed informed consent forms.

Treatments

The control group patients were treated with *Baofukang* suppository (Hainan Bikai Pharmaceutical Co. Ltd.; SFDA approval No.: Z46020058; specification: 1.74 g). Before administering the drug, the patients were asked to wash their vulva with warm water, and slowly insert a suppository completely into their vaginas. The dose was 1 suppository per day, continuously for 7 days.

The study group received Nifuratel tablets (Yantai Luyin Pharmaceutical Co. Ltd.; SFDA approval no.: H20065237; specification: 0.2 g), in addition to *Baofukang* suppository at the same dose used in the control group. Nifuratel tablet was given orally at a dose of 1 tablet 3 times per day, 30 min after a meal. The drug was administered continuously for 7 days.

Table 1: General information on patients

Variable	Study group	Control group	t/ χ^2	P-value
Age (years)	26.28±3.00	26.51±3.17	0.37	0.71
Height (cm)	159.86±4.77	160.22±4.96	0.37	0.71
Weight (kg)	60.27±6.39	60.43±6.82	0.12	0.90
Duration (Months)	1.33±0.25	1.35±0.24	0.41	0.68
Gestational age (Weeks)	20.64±2.55	20.29±2.38	0.71	0.48
Hypertension (n)	5	8	0.80	0.37
Hyperlipemia (n)	6	5	0.10	0.75
BV(n)	19	21	0.17	0.68
Types				
Mycotic vaginitis(n)	20	16	0.69	0.41
Trichomonas vaginitis (n)	11	13	0.22	0.64

Indices evaluated

The study compared the two groups in terms of % treatment effectiveness, incidence of adverse reactions, recurrence at 1 month, 2 months and 3 months post-treatment; time taken for disappearance of clinical symptoms, expression levels of inflammatory factors 1 week after treatment, MSSNS score and QLI score. Treatment safety was judged by the incidence of adverse reactions viz: treatment was deemed *effective* when no adverse reactions appeared after treatment, and clinical manifestations basically disappeared; or *partially effective* if no adverse reactions appeared after treatment, with some reductions in clinical manifestations, or *ineffective* if the patient had serious adverse reactions, with clinical manifestations still present or even worse.

Expression levels of interleukin-2 (IL-2), tumor necrosis factor- α (TNF- α), and high-sensitivity C-reactive protein (hs-CRP) were used as indices inflammatory factors.

For MSSNS, a score below 60 indicated *normal mental state*, and a score within the range of 60 - 70 indicated *mild abnormal mental state*, while scores over 70 indicated *abnormal mental state* [10-12].

The QLI is usually based on factors such as activities of daily living, work, and interpersonal relationship, with a maximum score of 10 points. The higher the score, the better the quality of life of the patient.

Statistical analysis

Measurement data are presented as mean \pm SD and were analyzed using *t*-test. Enumeration data are expressed numbers and percentages [n

(%)], and were analyzed with χ^2 test. All statistical analyses were done with SPSS 20.0 software, while graphics were drawn with GraphPad Prism 7 (GraphPad Software, San Diego, USA). Statistical significance of difference was assumed at $p < 0.05$.

RESULTS

Treatment effectiveness

In study group, 28 cases were significantly effective, 19 cases were partially effective, and 3 cases were ineffective, with the overall effectiveness of 94 %. In control group, 17 cases were significantly effective, 18 cases partially effective, while 15 cases were ineffective, with an overall effectiveness of 70 %. Results showed that treatment effectiveness was significantly higher in the study group than in the control group ($\chi^2=9.76$, $P=0.002$), as shown in Table 2.

Incidence of adverse reactions

In the study group, there was 1 case of pruritus and 1 case of leucorrhea, with total incidence of 4 %. In the control group, there was 3 cases of pruritus, 5 cases of leucorrhea and 3 cases of nausea, with overall incidence of 22 %. Results showed significantly less adverse reactions in the study group than in the control group ($\chi^2 = 7.16$, $p = 0.007$), as shown in Table 3.

Recurrence rate at 1-, 2- and 3-month post-treatment

As shown in Table 4, values for percentage recurrence at 1, 2 and 3 months after treatment were significantly lower in the study group than in control group ($p < 0.05$).

Table 2: Comparison of treatment effectiveness between the two groups {n, (%)}

Variable	Markedly effective	Effective	Ineffective	Overall effectiveness
Study group (n=50)	28 (56)	19 (38)	3 (6)	47 (94)
Control group (n=50)	17 (34)	18 (36)	15 (30)	35
χ^2				9.76
<i>P</i> -value				0.002

Table 3: Comparison of incidence of adverse reactions between the two groups (n, %)

Group	Adverse reactions			Overall adverse reaction rates
	Pruritus	Leucorrhea	Nausea	
Study (n=50)	1 (2)	1 (2)	0	2 (4)
Control (n=50)	3 (6)	5 (10)	3 (6)	11 (22)
χ^2				7.16
<i>P</i> -value				0.007

Table 4: Comparison of recurrence rate at 1, 2 and 3 months post-treatment (n, %)

Group	1-month post-treatment	2-months post-treatment	3-months post-treatment
Study (n=50)	2 (4)	4 (8)	4(8)
Control (n=50)	16 (32)	20 (40)	26 (52)
χ^2	5.98	6.06	9.49
P-value	0.01	0.01	0.002

Time taken for disappearance of clinical manifestations

The clinical manifestations in patients disappeared 3.26 ± 0.64 d after treatment in the study group and 4.48 ± 1.29 d after treatment in the control group, much later than the control group ($t = 5.991$, $p < 0.001$).

Expression levels of inflammatory factors 1 week after treatment

The expression levels of IL-2, TNF- α and hs-CRP in the control group were 8.81 ± 2.30 pg/mL, 47.62 ± 7.59 pg/L, and 15.54 ± 3.51 mg/L, respectively; and those of the study group were 5.99 ± 1.42 pg/mL, 25.08 ± 5.73 pg/L, and 10.00 ± 3.03 mg/L, respectively. There were significantly lower expression levels of IL-2, TNF- α and hs-CRP in the study group than in control group ($p < 0.05$). These results are shown in Figure 1.

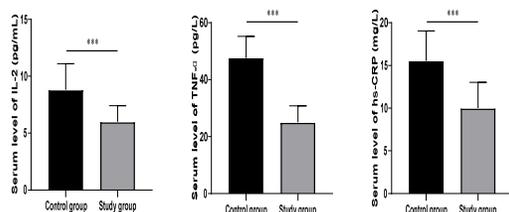


Figure 1: Comparison of expression levels of inflammatory factors 1 week after treatment. The left bar chart presents the expression levels of IL-2; the middle bar chart shows the expression levels of TNF- α ; while the right chart shows the expression levels of hs-CRP. *** $P < 0.001$

MSSNS and QLI scores 1 week after treatment

The MSSNS scores and QLI scores in the control group were 45.33 ± 5.20 and 63.19 ± 7.06 ; and those of the study group were 45.33 ± 5.20 and 72.25 ± 9.11 .

The study group had significantly lower MSSNS score and higher QLI score than the control group ($p < 0.05$). These results are shown in Figure 2.

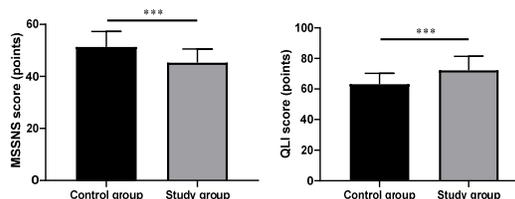


Figure 2: Comparison of MSSNS scores and QLI scores after treatment. The left figure presented the MSSNS scores, the right figure presented the QLI scores. *** $P < 0.001$

DISCUSSION

Vaginitis, a common gynecological disease during pregnancy, is caused by changes in hormonal secretion levels. Compared with non-pregnant women, pregnant women are more likely to be infected with bacteria and fungi which lead to vaginitis. Undoubtedly, vaginitis not only affects the physical health of pregnant women, it also has a certain influence on the outcome of delivery, delivery mode, and the health of the fetus [13,14]. In order to protect pregnant women and their fetuses, patients with vaginitis need timely treatment after diagnosis. Drugs used for treatment of vaginitis should be selected very carefully and used appropriately [15]. Nifuratel tablets and *Baofukang* suppository can be used in the treatment of vaginitis during pregnancy. Indeed, Nifuratel is widely used in treating various types of infectious vaginitis with acceptable curative effect, while *Baofukang* suppository is used for treating vaginitis and hydropyretic leucorrhoea [16,17].

This study determined the efficacy and safety of combination of the two drugs in the treatment of vaginitis in pregnant women. The results showed that the effectiveness and QLI score of study group treated with combination of *Baofukang* and Nifuratel tablets were significantly higher than those of the control group. The criteria for defining treatment effectiveness comprised disappearance of clinical manifestations and absence of adverse reactions. It was found that combination of *Baofukang* suppository and Nifuratel tablet significantly enhanced therapeutic effect and improved the quality of life of patients.

Pregnant women should maintain good living habits and mental state in pregnancy to ensure healthy development of the fetus [18]. The study investigated the quality of life of the patients so as to timely guide them. Furthermore, the study group had lower incidence of adverse reactions, lower percentage recurrence values at 1, 2 and 3 months after treatment; reduced expression levels of inflammatory factors 1 week after treatment, lower MSSNS scores, as well as quicker disappearance of clinical manifestations, when compared with the control group.

After treatment, vaginitis relapses easily, especially in pregnant women. Once the relapse appears, the patient may develop drug resistance which negatively affects treatment efficacy. In this study, the levels of inflammatory factors in patients with vaginitis were increased significantly, but they were decreased after medication. Therefore, the expression levels of inflammatory factors in patients could be used to assess therapeutic effect to a certain extent, thereby guiding further treatment [19]. The treatment of vaginitis in pregnant women is associated with certain risks such as adverse reactions caused by drugs and other physical issues.

This study used the incidence of adverse reactions as an index of the safety of vaginitis treatment. The results indicated that combination of Nifuratel tablet and *Baofukang* suppository enhanced the disappearance of clinical manifestations, reduced recurrence and the expression levels of inflammatory factors, and significantly improved the safety of treatment. In a previous study [20], it was demonstrated a group of vaginitis patients given combined treatment with Nifuratel tablets and *Baofukang* suppository significantly performed better than those on monotherapy, with respect to treatment effectiveness, time taken for disappearance of clinical manifestations, and recurrence after treatment. In addition, there was no significant difference between the two monotherapy groups in overall treatment effectiveness, time taken for disappearance of clinical manifestations, and recurrence, indicating that combination of Nifuratel tablets with *Baofukang* suppository produced a desirable effect and high safety in the treatment of pregnant women with vaginitis. This is in agreement with results of this study.

CONCLUSION

The combination of Nifuratel tablets and *Baofukang* suppository significantly improves the efficacy and safety of treatment in pregnant women with vaginitis, reduces recurrence, and

decreases the expression levels of inflammatory factors. Thus, this combination therapy may be useful for the management of vaginitis in pregnancy.

DECLARATIONS

Conflict of interest

No conflict of interest is associated with this work.

Contribution of authors

We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors.

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REFERENCES

1. Durić K, Kovčić Hadžiabdić S, Durić M, Nikšić H, Uzunović A, Džudžević Čančar H. Efficacy and safety of three plant extracts-based formulations of vaginories in the treatment of vaginitis: a randomized controlled trial. *Med Glas (Zenica)* 2021; 18: 47-54.
2. Plisko O, Zodzika J, Jermakova I, Pcolkina K, Prusakevica A, Liepniece-Karele I, Donders GGG, Rezeberga D. Aerobic Vaginitis-Underestimated Risk Factor for Cervical Intraepithelial Neoplasia. *Diagnostics (Basel)* 2021; 11: 97.
3. Zhang HT, Wang H, Wu HS, Zeng J, Yang Y. Comparison of viromes in vaginal secretion from pregnant women with and without vaginitis. *Viol J* 2021; 18: 11.
4. Wójkowska-Mach J, Pomorska-Wesołowska M, Romanik M, Romaniszyn D. Prevalence and Antimicrobial Susceptibility Profiles of Microorganisms Associated with Lower Reproductive Tract Infections in Women from Southern Poland-Retrospective Laboratory-Based Study. *Int J Environ Res Public Health* 2021; 18: 335.
5. Danby CS, Althouse AD, Hillier SL, Wiesenfeld HC. Nucleic Acid Amplification Testing Compared with Cultures, Gram Stain, and Microscopy in the Diagnosis of Vaginitis. *J Low Genit Tract Dis* 2021; 25: 76-80.

6. Mension E, Alonso I, Castelo-Branco C. Genitourinary Syndrome of Menopause: Current Treatment Options in Breast Cancer Survivors - Systematic Review. *Maturitas* 2021; 143: 47-58.
7. Poordast T, Ghaedian L, Ghaedian L, Najib FS, Alipour S, Hosseinzadeh M, Vardanjani HM, Salehi A, Hosseimehr SJ. Aloe Vera; A new treatment for atrophic vaginitis, A randomized double-blinded controlled trial. *J Ethnopharmacol* 2021; 270: 113760.
8. Juliana NCA, Suiters MJM, Al-Nasiry S, Morr  SA, Peters RPH, Ambrosino E. The Association Between Vaginal Microbiota Dysbiosis, Bacterial Vaginosis, and Aerobic Vaginitis, and Adverse Pregnancy Outcomes of Women Living in Sub-Saharan Africa: A Systematic Review. *Front Public Health* 2020; 8: 567885.
9. Department of Health, Education, and Welfare; National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The Belmont Report. Ethical principles and guidelines for the protection of human subjects of research. *J Am Coll Dent* 2014; 81: 4-13.
10. Critchley HOD, Babayev E, Bulun SE, Clark S, Garcia-Grau I, Gregersen PK, Kilcoyne A, Kim JJ, Lavender M, Marsh EE, et al. Menstruation: science and society. *Am J Obstet Gynecol* 2020; 223: 624-664.
11. Fidel PL Jr. The Neutral Vaginal pH in Mice That Is Typical of Most Mammalian Species Should Not Deter Research Using Experimental Murine Models of *Candida* Vaginitis. *Infect Immun* 2021; 89: e00624-20.
12. Okiki PA, Eromosele ES, Ade-Ojo P, Sobajo OA, Idris OO, Agbana RD. Occurrence of *mecA* and *blaZ* genes in methicillin-resistant *Staphylococcus aureus* associated with vaginitis among pregnant women in Ado-Ekiti, Nigeria. *New Microbes New Infect* 2020; 38: 100772.
13. Oerlemans EFM, Wuyts S, Bellen G, Wittouck S, De Boeck I, Ruban K, Allonsius CN, van den Broek MFL, Donders GGG, Lebeer S. The Dwindling Microbiota of Aerobic Vaginitis, an Inflammatory State Enriched in Pathobionts with Limited TLR Stimulation. *Diagnostics (Basel)* 2020; 10: 879.
14. Li Y, Xu Z, Qi H, Zhu Z, Chen S, Zhang G. Observation and Nursing of the Curative Effect of Ag/TiO₂ Nanomaterials on Bacterial Vaginosis and Trichomonal Vaginitis. *J Nanosci Nanotechnol* 2020; 20: 7419-7424.
15. Aduloju OP, Akintayo AA, Aduloju T. Prevalence of bacterial vaginosis in pregnancy in a tertiary health institution, south western Nigeria. *Pan Afr Med J* 2019; 33: 9.
16. Abu-Azzam O, Nasr M. In vitro anti-inflammatory potential of phloretin microemulsion as a new formulation for prospective treatment of vaginitis. *Pharm Dev Technol* 2020; 25: 930-935.
17. Fish ML, Grover R, Schwarz GS. Quality-of-Life Outcomes in Surgical vs Nonsurgical Treatment of Breast Cancer-Related Lymphedema: A Systematic Review. *JAMA Surg* 2020; 155: 513-519.
18. Sonthalia S, Aggarwal P, Das S, Sharma P, Sharma R, Singh S. Aerobic vaginitis - An underdiagnosed cause of vaginal discharge - Narrative review. *Int J STD AIDS* 2020; 31: 1018-1027.
19. Rigo GV, Tasca T. Vaginitis: Review on Drug Resistance. *Curr Drug Targets* 2020; 21: 1672-1686.
20. Ikegami K, Watanabe G, Kumagai J, Fujii Y, Watanabe H, Oite T. The apparition macrophage and D derlein bacillus is negatively correlated in class I Papanicolaou smear: A morphological examination. *Diagn Cytopathol* 2020; 48: 1205-1210.