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Original Research Article

Oral itraconazole combined with local isoconazole in the treatment chronic candida vulvovaginitis

Mostafa Adulla Elsayed*

Department of Obstetrics and Gynecology, Benha University, Egypt

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***Correspondence:**
Dr. Mostafa Adulla Elsayed,
E-mail: Mostafaabdulla7@gmail.com

ABSTRACT

Background: Chronic vulvovaginal candidiasis is a major problem and common with poor quality of life from itching and discharge and it is difficult to treat because fungi are slow growers.
Methods: Two hundred cases recruited from JAM clinic in Benha city, Egypt divided into two groups to study combination of oral itraconazole and local isoconazole in comparison with the use of local isoconazole only in chronic monilial vulvovaginitis and main outcome was relief of symptoms and signs with absent laboratory evidence of monilial infection by culture. Group one included 100 cases treated with combined oral itraconazole with three alternate days dose of local isoconazole (gynotrazonagen) and group two (local isoconazole only) included 100 cases treated with local isoconazole ovules on alternate days for 3 doses and week period.
Results: Regarding the cure rate there were 90 clinically cured rate in the combined group compared to 70 in the local treatment group with p value of 0.0004 which was a very high statistically significant difference. Clinical cure included alleviation of the symptoms of discharge dysuria dyspareunia burning itching with also by clinical examination cure and disappearance of redness erythema edema fissures with absent pseudomycelia by microscopic examination. Usually, a symptom score of less than 2 is a positive one. Regarding the laboratory cure which means absent or negative candida culture on Sabaraud agar medium there were a laboratory cure rate of 84 out of 100 in the combined treatment group compared to 65 out of 100 in the local treatment group with p value of 0.002 and a high statistically significant difference.
Conclusions: Oral itraconazole combined with local isoconazole is highly effective in treating chronic monilial vulvovaginitis.

Keywords: Candida vulvovaginitis, Isoconazole, Itraconazole

INTRODUCTION

Fungal infections are common in females, especially monilial vaginitis.[1,2]

The problem with fungal infections is the chronic course and the slow healing process because fungi are slow growers with little need for nutritional support.

Many conditions contribute to the causes of fungal infections like maternal immunosuppressive states, autoimmune disorders, endocrinopathies like diabetes and prolonged corticosteroid use.

Local irritation with candida vaginitis can lead to erythema edema and ulcerations and fissuring with itching burning sensations dyspareunia and dysuria.[3,4]

Female hygiene is important in preventing fungal infection and also the healthy nutrition especially with food containing flavonoids like fruits that explicit antifungal activity.

Several drugs are invented for treatment of monilial vaginitis like ketoconazole, fluconazole, and the recent drug itraconazole with broad spectrum antifungal activity.

Local azole groups like clotrimazole, isoconazole also effective alone or in combination in treating monilial vulvovaginitis.[5]

The most common species causing fungal vaginitis is candida albicans, but there are many other fungi like *Candida (C.) tropicalis*, *C. pesudotropicalis* and *P. creusii* that contribute also to vaginal infection.

The most important step in treating chronic fungal infections us to raise the immunity state of patients plus good hygiene.[6]

The main symptom of monilial vaginitis is the white curdy vaginal discharge and the associated itching sensation together with redness and swelling.

The drawback of monilial vaginitis is that it can highly reduce the quality of life in infected patients so treatment is important.[7]

Efforts made throughout centuries to cure this condition but radical cure is very difficult.

For chronic infection oral fluconazole is a good option and also different forms of oral treatment like ketoconazole had a good result.[8]

The main objective of the study was to determine the efficacy of combined oral broad-spectrum antifungal treatment itraconazole with local isoconazole in chronic vulvovaginal candidiasis.

METHODS

The study was a controlled trial comparing two regimens in treatment of monilial vulvovaginitis. The study was conducted at JAM clinic private clinic in Benha city. The study was conducted from January 2012 to January 2022.

Sample size

The sample size consisted of 200 hundred cases divided into two groups each group is 100 hundred.

Ethical consideration

Written consent was taken from the institutional ethics committee.

Inclusion criteria

Cases with clinical symptoms of monilial vaginitis like white curdy discharge dysuria dyspareunia were included in the study. First, there were clinical features of fungal infection (discharge, pruritus, dysuria/dyspareunia, redness, fissuring, and edema); the patient was between 16 and 60 years of age, there was laboratory confirmation of infection. Symptoms are recurring in the last three month or continuous.

Exclusion criteria

Patients with concomitant infection with chlamydia, bacterial vaginosis, comorbid immune-suppressive disease like diabetes, chronic renal insufficiency and chronic hepatic insufficiency, immunosuppressive drugs like prolonged antibiotic therapy or corticosteroid dependency and pregnancy were excluded.

Participant evaluation

History taking special the current symptoms and each symptom scored by one 1 figure.

There were 5 main symptoms: white curdy discharge, dysuria, dyspareunia, burning, and itching or pruritus.

Clinical examination

Clinical examination for cases done with generally vital signs and chest and heart examination to exclude chronic chest disease that warranted corticosteroid use.

Local examination

Visualization of the introitus, vagina and cervix for evidence of redness, swelling, fissuring and discharge. And presence of psudomycelia seen by wet drop preparation under light microscopy.

Inspection for erythema and edema discharge

Speculum examination done for local inspection and then a cotton tipped applicator introduced to take a discharge sample for two reasons examination with microscopy for the presence of pseudo mycelia.

Exclusion of clue cells cases was done to avoid treatment overlap.

Then the other purpose was to send sample for culture to confirm manilial vaginitis.

Then endo-cervical samples taken for microscopic and laboratory examination for concomitant cervical infections with chlamydia or gonorrhea.

Wet drop preparation with a drop of discharge taken to be examined under light microscopy.

Laboratory evaluation for cases

They include: complete blood count, fasting blood sugar, glycated hemoglobin (HbA1C), thyroid stimulating hormone (TSH), triiodothyronine (T3), thyroxine (T4), vitamin D3 level, serum (S.) calcium, S. glutamic-oxalacetic transaminase (SGOT), S. glutamic-pyruvic transaminase (SGPT), bilirubin, urea and creatinine and quantitative human chorionic gonadotropin (hCG).

The patients were divided into two groups according to the intervention.

Group one

Combined treatment group implied the administration of oral itraconazole (itranox) 100 mg capsule twice daily for two days combined with local isoconazole (gynotrazonagen) 600 every other day for 3 doses and week duration.

Group two

Given local isoconazole nitrate 600 locally ovules every other day for 3 doses.

Monitoring

Patients kept a symptom diary which was reviewed in a three-day post-treatment telephone call and at subsequent follow-up visits.

Patients were instructed to have a diary fir daily evaluation and each item of the symptom is written like: discharge, dyspareunia, dysuria, itching, and burning. Clinical cure was defined as absent symptoms and of signs of infection on perineal and speculum examination.

A laboratory monilial cure was considered to have occurred when microscopy (wet mount/gram stain) and culture were negative.

RESULTS

The two groups did not differ in age, weight, duration of current vulvovaginitis attack.

Regarding the cure rate there were 90 clinically cured rate in the combined group compared to 70 in the local treatment group with p value of 0.0004 which was a very high statistically significant difference.

Clinical cure included alleviation of the symptoms of discharge dysuria dyspareunia burning itching with also by clinical examination cure and disappearance of redness erythema edema fissures with absent psudomycelia by microscopic examination.

Usually, a symptom score of less than 2 is a positive one. Regarding the laboratory cure which means absent or negative candida culture on Sabaraud agar medium there were a laboratory cure rate of 84 out of 100 in the combined treatment group compared to 65 out of 100 in the local treatment group with p value of 0.002 and a high statistically significant difference.

Table 1: Demographic data.

Demographics	Group one combined	Group two single local	P value
Age	30.2	30.1	0.9
Body mass index	27.3	27.2	0.9
Ethnicity	Caucasian	Caucasian	

Table 2: Cure rates.

Parameters	Group one combined 100	Group two local only 100	P value
Clinical	90	70	0.0004
Laboratory	84	65	0.002

No significant difference was seen regarding demographic data (Table 1).

DISCUSSION

Genital infections in females are common complaints especially vaginal infections and one of the commonest pathogens is monilial infection which is a fungal infection caused by *Candida albicans*.[9]

The problem with fungal infection is that it takes a very long time to heal because fungi are slow growers and need minimal blood supply to grow also, they are strongly attached to the cells.

Patients with moilial vaginitis may complain about white curdy discharge dysuria dyspareunia, itching and burning vaginal sensations and rapidly deteriorate the quality of life and resting comfort.

Certain morbidities are associated with high rates of *Candida* vulvovaginintis like hypothyroidism, diabetes, autoimmune disorders like system lupus and other autoimmune conditions.[10,11]

Chronic mental stress or emotional stress also may alter immunity in the form of reduction of the total count and functions of natural killer cells that is a major immune cell that scan and kill fungal infections.[12]

Local treatment may be irritant to many patients and those types of cases requested the oral treatment also oral treatment is a good choice for virgins, the discovery of azole groups solved many of these problems like ketoconazole but it is limited by its hepatotoxicity.[13,15]

Woolley in studied three drugs in treatment of acute candida vulvovaginitis and found high cure rates with local clotrimazole and oral itraconazole.[14]

The presented work studied the efficacy and cure rates of using oral treatment itraconazole together with local vaginal isoconazole 600 and compared to local isoconazole only and study included two hundred women recruited from jam clinic in Benha city, Egypt.

The main symptom score categorizes patients as mild moderate severe according to main 5 symptoms like white curdy discharge, dysuria, dyspareunia, itching and burning. All groups' participants followed clinically through resolution of symptoms and also laboratory by absence of fungal colonization with cultures.

Regarding the cure rate, there were 90 clinically cured rate in the case combined group compared to 70 in the local treatment group with p value of 0.0004 which was a very high statistically significant difference.

Clinical cure included alleviation of the symptoms of discharge dysuria dyspareunia burning itching with also by clinical examination cure and disappearance of redness erythema edema fissures with absent psudomycelia by microscopic examination usually a symptom score of less than 2 is a positive one.

Regarding the laboratory cure which means absent or negative candida culture on Sabaraud agar medium there were a laboratory cure rate of 84 out of 100 in the combined treatment group compared to 65 out of 100 in the local treatment group with p value of 0.002 and a high statistically significant difference. So, oral itraconazole was highly effective in treating chronic *Candida* vulvo-vaginitis.

Limitations

Limitation of the study was the limited number of patients so in the future further studies may be done on a large scale of cases.

CONCLUSION

Oral itraconazole is a significant treatment option for patients with chronic *Candida* vulvovaginitis.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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