Treatment and prevention of trichomoniasis, bacterial vaginosis and candidiasis with a new 7-day regime containing metronidazole and miconazole in a single vaginal pessary

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ABSTRACT — OBJECTIVE: *To evaluate the efficacy of a new pessary combination of metronidazole 750 mg + miconazole nitrate 200 mg in candidal, bacterial and trichomonal vaginitis and in mixed vaginal infections.*

PATIENTS AND METHODS: *104 patients with clinical diagnosis of vaginitis entered this open, non-comparative study. Each patient inserted one pessary once daily for seven days. Gynecological and microbiological assessments were carried out before and 8-10 and 21-23 days after the start of treatment.*

RESULTS: *Vaginitis symptoms were resolved in 97% of the 99 patients evaluated, and improved in the remaining 3%. Microbiological cure rates were 100% for trichomoniasis, 96.2% for bacterial vaginosis and 90% for candidiasis. Recurrence rates were 2.7%, 5.7% and 15.3%, respectively. The overall microbiological cure rate for mixed infections was 92%, with 97% for trichomonal + bacterial and 80% for bacterial + candidal vaginitis. In 2 out of 2 cases each with trichomonal + candidal and trichomonas l + bacterial + candidal infection, the microorganisms were eradicated completely.*

CONCLUSIONS: *Metronidazole and miconazole in a dosage of 750 mg + 200 mg respectively as a single pessary provide immediate and effective treatment for vaginitis, irrespective of single or multiple infection, even when the diagnosis may be uncertain. This medical approached represents an improvement in the management of these diseases as effective and improved compliance rates are achieved with this new dosage regime.*

KEYWORDS
Trichomoniasis, Candidiasis bacterial vaginosis, Mixed vaginal infections, Metronidazole, Miconazole.

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INTRODUCTION

Infection of the vulva and vagina are among the most common medical problems seen in general practice. There are three common types of vaginitis: vulvovaginal candidiasis, bacterial vaginosis and trichomonal vaginitis[1,2]. Vaginitis due to simultaneous infection with at least two pathogens (mixed infection, e.g. bacterial vaginosis in a patient with vulvovaginal candidiasis) is also highly prevalent and make up approximately 30% of all cases[3-6].

Effective management of vaginitis depends on accurate diagnosis, selection and administration of effective specific therapy and good compliance of the patient.

Since classic signs and symptoms of common types of vaginitis are often equivocal, the diagnosis cannot always be established on the basis of clinical manifestations alone[2,6]. Laboratory support is necessary for a differential diagnosis or to confirm the clinical diagnosis. However, accurate identification of the causative microorganism is technically difficult, often affected by a wide variety of factors and therefore, clinical diagnosis of the cause of vaginitis is often incorrect[7].

Metronidazole 500 mg and miconazole nitrate 100 mg (Neo-Penotran®, Exeltis, Istanbul, Turkey), were indicated for the treatment of vulvovaginal candidiasis, bacterial vaginosis and trichomonal vaginitis[8]. The recommended dosage schedule was one pessary at night and one pessary in the morning for seven days or one pessary at night for 14 days. Clinical studies[8-12] have shown that with both dosage regimens, once daily for 14 days or twice daily for seven days, high clinical and microbiological cure rates were achieved with an excellent safety profile[8-11]. One other study[12] also showed a high efficacy for the immediate treatment of single and/or mixed vaginal infection. In addition, there appeared to be no significant difference regarding efficacy and safety between the 7-day and 14-day dosage regimens[12].

Appropriate therapy is fundamental for a successful treatment of vaginitis. However, successful treatment can be contingent upon completion of the full course of therapy. With this in mind, a new combination of metronidazole (750 mg) and miconazole nitrate (200 mg) (Exeltis, Istanbul, Turkey) was developed for once daily administration in the therapy of vaginitis. A tolerance, acceptability, and absorption study[13] of this combination with and without lidocaine in healthy volunteers has shown that the pessaries are well tolerated. Ten subjects received metronidazole 750 mg + miconazole nitrate 200 mg + lidocaine 100 mg for the first three days, and the same combination without lidocaine for the subsequent 4 days of pessary administrations. Systemic absorption of metronidazole revealed steady state plasma levels in a range approximately comparable with the standard 200 mg oral dose. Lidocaine was minimally absorbed and miconazole was not absorbed vaginally.

Therefore, the objective of this study was to evaluate the efficacy and tolerability of a new formulation with metronidazole + miconatol pessaries, administered once daily for seven days for the treatment of bacterial, trichomonal or candidal vaginitis and in mixed vaginal infections having in mind an improvement in patient compliance with a low side effect profile of the new drug formulation.

PATIENTS AND METHODS

Patients

One hundred and four gynecological outpatients attending the Central Clinical Research Hospital, Ashgabad, Turkmenistan, were recruited. The study protocol was approved by the Local Ethics Committee and patients were enrolled into the study after their informed written consents had been obtained. Women in reproductive period (age between 18 and 50 years) and with a clinical diagnosis of trichomonal, bacterial and/or candidal vaginitis, were included.

Patients were excluded from the trial if they had known sensitivity to metronidazole or miconazole, were pregnant or lactating or had any gynecological condition that contraindicated the use of pessaries. Those who had treatment with any systemic/local antibacterial, antiprotozoal or antifungal agent in the two weeks preceding the study or during the study period, as well as patients with any sexually transmitted disease except vaginitis and women using oral contraceptives, were also excluded.

Patients were treated once daily (each evening) for 7 days and assessed clinically and microbiologically at the beginning of the study and 8-10 days and 21-23 days after the start of the study.

Procedures/Assessments

At visit 1 (entry, day 1), a detailed medical and gynecological history was evaluated and a physical examination was performed. A gynecological examination was carried out and the apparent condition of the external genitalia and of the vagina and cervix was recorded. Duration of vaginitis and details of key symptoms (i.e. discharge, irritation, itching, odor, coital pain) as well as signs (i.e. inflammation, discharge or non-menstrual bleeding) of vaginitis were recorded. Treatment was started before microbiological confirmation.

Microbiological sampling was performed by taking vaginal swabs from the posterior fornix at

the time of the gynecological examination. Since transport time to the laboratory did not exceed two hours, the swabs were placed in tubes containing 0.3 ml of normal saline to maintain viability of the microorganisms.

Patients with clinical diagnosis of vaginitis were given a package of 7 pessaries, each containing 750 mg of metronidazole and 200 mg of miconazole nitrate and they were instructed to insert one pessary each night (at bedtime) for 7 days, using the finger stalls provided in the medication package.

The patients were advised to abstain from sexual intercourse and alcohol as well as to employ good hygiene conditions and not to use any agents, which could alter vaginal pH (e.g. vaginal douche) during the one week of treatment.

Concomitant medication (except any systemic/local antifungal/antibacterial/antiprotozoal medication) was allowed for the duration of the trial, if considered necessary for the patient's welfare.

Patients were given two record forms to be completed each day for 7 days. Patient compliance to the study medication (time of application) and usage of other drugs (concomitant medication) were recorded in the first record form. Occurrence of wetness, and any complaints of irritation (i.e. burning) were recorded in the second questionnaire using a graded scoring system (1= not different from normal; 2= mild, i.e. noticeable but not causing discomfort; 3=significant, i.e., causing discomfort).

At visit 2 (end of 7-days' treatment, Days 8-10), gynecological examination and recording of symptoms of vaginitis were performed as at visit 1. Microbiological samples were taken and any side effects or adverse events experienced were recorded by the physician by asking the patient: "Have you felt different in any way since your last visit?". The investigator evaluated and recorded the reported side effects or adverse events according to the following graded scoring system: 1=mild, i.e. noticeable but not causing discomfort 2=moderate, i.e. causing discomfort; 3= severe, i.e. discomfort sufficient to interfere with normal activities.

The patients were asked to return for a follow-up evaluation two weeks after the end of treatment. The record form for compliance, usage of other drugs (concomitant drugs) and the record form for subjective recordings of wetness and irritation were collected.

At visit 3 (follow-up, Days 21-23), gynecological examination and microbiological sampling were repeated as at previous visits. A reduction in total symptom score greater than 75% was regarded as "clinical cure", which was recorded at visit 2.

Patients with missing microbiological sampling at visit 1 and those with missing gynecological/microbiological post-treatment assessments were excluded from the efficacy evaluation. Patients with pathogens other than those responsible for candida, trichomonas or bacterial vaginitis (e.g., N. gonorrhea) in their vaginal swabs at visit 1 were also excluded from the efficacy evaluation.

Clinical Evaluation

Vaginitis and symptomatic improvement were assessed by recording detailed symptoms of vaginitis and by gynecological examination, especially the description of external genitalia and results of visualization of the vagina and cervix. Patients with two or more key symptoms (i.e. discharge, irritation, itching, odor, coital pain) and one or more signs of vaginitis (i.e. inflammation, discharge or non-menstrual bleeding) at visit 1 were clinically diagnosed as having vaginitis and received the medication package without waiting for the microbiological test results. The severity of symptoms of vaginitis was recorded using a graded scoring system (0=none/absent; 1=mild; i.e. noticeable but not causing discomfort; 2=moderate, i.e. causing discomfort; 3=severe, i.e. discomfort sufficient to interfere with normal activities). Therefore, patients' symptom scores were assessed between 0 and 15 points.

Patients with missing microbiological sampling at visit 1 and those with missing gynecological/microbiological post-treatment assessments were excluded from the clinical evaluation.

Microbiological Evaluation

The laboratory diagnosis of vaginitis was based on the following tests carried out on vaginal swab samples. Bacterial vaginosis: release of fishy amine odor from the vaginal fluid when mixed with 10% KOH solution (positive odor test) and presence of "clue cells" on wet mount or Gram stain vaginal specimens.

Vulvovaginal candidiasis: identification of the pseudo hyphae on potassium wet mount (10% potassium hydroxide solution).

Trichomonas vaginitis: detection of the typical motile protozoa in a wet mount preparation using physiologic saline. *T. vaginalis* culture was performed, unless the motility of *T. vaginalis* was observed (Trichomonas specific culture, GBL - 0725, Istanbul, Turkey).

RESULTS

Of the 104 patients initially recruited, a total of 99 patients (95%) fulfilled the criteria for efficacy evaluation. At visit 1, reasons for exclusion from the study were allergic reaction against metronidazole

in the medical history (1 patient) and menopause (1 patient). Three patients were excluded from the efficacy evaluation: missed microbiological testing (1 patient) and presence of N. gonorrhea at microbiological examination (2 patients).

The mean age of the study population was 33 years (range 18-50 years). All patients complied with the dosing regimen and instructions, inserting one study pessary at night (at bedtime) for seven days. Only one patient used concomitant medication during the therapy period with the study medication (reserpine 200 mcg/day and nifedipine 30 mg/day).

Microbiological Diagnosis

Microbiological diagnosis revealed that 37.4% of the 99 patients had *Trichomonas vaginalis,* 59.6% had *Candida ssp.* and 53.5% had anaerobic bacteria in their vaginal swabs. Single infections were detected in 4.0% (*Trichomonas vaginalis*), 40.4% (*Candida ssp.*) and 7.1% (anaerobic bacteria) of the patients. In 48 (48.5%) of the 99 patients, at least two pathogens responsible for the most common types of vaginitis (i.e. *Candida* species, *Trichomonas vaginalis* and anaerobic bacteria, including *Gardnerella vaginalis*) were simultaneously present in the vaginal specimens (Table 1).

Treatment Results

Microbiological

The microbiological cure rates (return of vaginal flora to normal at visit 2) for all patients were 100% (37 out of 37 cases) for the treatment of trichomonial vaginitis, 96.2% (51 out of 53 cases) for bacterial vaginosis and 89.8% (53 out of 59 cases) for vulvovaginal candidiasis (mixed infections included). Microbiological recurrence rates were 2.7% for trichomonial vaginitis (1 out of 37), 5.7% (3 out of 53 cases) for bacterial vaginosis and 15.3% (9 out of 59 cases) for vulvovaginal candidiasis (Table 2).

The cure rates for patients with single infections were 100% (4 out of 4 cases) for the treatment of trichomonas vaginitis, 85.7% (6 out of 7 cases) for bacterial vaginosis and 92.5% (37 out of 40 cases) for vulvovaginal candidiasis (mixed infections excluded). Microbiological recurrence rates were 0% for trichomonas vaginitis (0 out of 4), 0% (0 out of 7 cases) for bacterial vaginosis and 12.5% (5 out of 40 cases) for vulvovaginal candidiasis (Table 2).

Overall microbiological cure rate in patients with mixed infections was 91.7% (44 out of 48 cases). Microbiological eradication was achieved in 96.6% (28 out of 29 cases) of patients with trichomonal + bacterial infection, in 80% (12 out of 15 cases) with bacterial + candidal infection. In the two patients with trichomonas l + candidal infection, both pathogens, and in the two patients with bacterial + candida + trichomonal infection, all three microorganisms were eradicated completely. Microbiological recurrence rates were 6.9% for trichomonal + bacterial vaginitis (2 out of 29), 40.0% (6 out of 15 cases) for bacterial + candidal vaginitis, 0% (0 out of 2 cases) for trichomonal + candidal infection and 0% (0 out of 2) for bacterial + candida + trichomonal infection. Overall, the recurrence rate at visit 3 was 16.7% (8 out of 48 cases) (Table 2 and Figure 1).

Table I. Microbiological test results.

All patients (N =99)		
Trichomoniasis	37	37
Candidiasis	59	59
Bacterial Vaginosis	53	54
Single infections (N = 51)		
– Trichomoniasis	4	4
– Candidiasis	40	40
– Bacterial Vaginosis	7	7
Mixed Infections (N = 48)		
– Bacterial Vaginosis and Trichomoniasis	29	29
– Bacterial Vaginosis and Candidiasis	15	15
– Bacterial Vaginosis, Trichomoniasis, and Candidiasis	2	2

Table II. Microbiological cure rates and recurrence rates (%).

Diagnosis	Cure Rates %	Recurrence Rate %
All patients (N = 99)		
– Trichomoniasis	100	2.7
– Bacterial Vaginosis	96.2	5.7
– Candidiasis	89.8	15.3
Single infections (N = 51)		
– Trichomoniasis	100	0
– Bacterial Vaginosis	85.7	0
– Candidiasis	92.5	12.5
Mixed infections (N = 48)		
– Trichomoniasis and Candidiasis	100 (2/2)	0
– Trichomoniasis, – Candidiasis, and Bacterial Vaginosis	100 (2/2)	0
– Trichomoniasis and – Bacterial Vaginosis	96.6	6.9
– Candidiasis and Bacterial Vaginosis	80	40
– Overall Cure Mixed infections	91.7	16.7

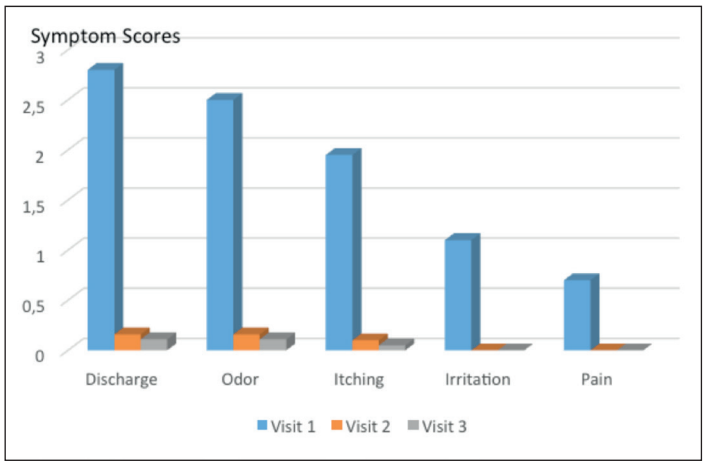

Figure 1. Single symptom scores at visits 1, 2 and 3 (mixed infections included).

Clinical

The clinical cure rates were 97.3% (36 out of 37 cases) for the treatment of trichomonal vaginitis, 98.1% (52 out of 53 cases) for bacterial vaginosis and 96.6% (57 out of 59 cases) for vulvovaginal candidiasis (mixed infections included). Clinical recurrence rates were 2.7% for trichomonal vaginitis (1 out of 37), 3.8% (2 out of 53 cases) for bacterial vaginosis and 3.4% (2 out of 59 cases) for vulvovaginal candidiasis (Table 3).

The clinical cure rates for patients with single infections were 100% (4 out of 4 cases) for the treatment of trichomonal vaginitis, 100% (7 out of 7 cases) for bacterial vaginosis and 95% (38 out of 40 cases) for vulvovaginal candidiasis (mixed infections excluded). Clinical recurrence rates were 0% for trichomonal vaginitis (0 out of 4), 0% (0 out of 7 cases) for bacterial vaginosis and 5% (2 out of 40 cases) for vulvovaginal candidiasis (Table 3).

Overall clinical cure rate for patients with mixed infections was 98% (47 out of 48 cases). Clinical cure was achieved in 96.6% (28 out of 29 cases) of patients with trichomonal + bacterial infection, in 100% (15 out of 15 cases) with bacterial + candidal infection. In the two patients with trichomonal + candidal infection and in the two patients with bacterial + candida + trichomonal infection, complete clinical cure was achieved. Clinical recurrence rates were 6.9% for trichomonal + bacterial vaginitis (2 out of 29), 6.7% (1 out of 15 cases) for bacterial+ candidal vaginitis and 0% (0 out of 2 cases) for trichomonal + candidal infection and 0% (0 out of 2) for bacterial + candida + trichomonal infection. Overall clinical recurrence rate was 6.3% (3 out of 48 cases) (Table 3).

Table III. Clinical cure rates and recurrence rates (%).

Diagnosis	Cure Rates	Improvement	Ineffective	Recurrence Rates
All patients (N = 99)				
– Bacterial Vaginosis	98.1	1.9	0	3.8
– Trichomoniasis	97.3	2.7	0	2.7
– Candidiasis	96.6	3.4	0	3.4
– Overall Cure	97	3	0	5.1
Single Infections (N = 51)				
– Trichomoniasis	100	0	0	0
– Bacterial Vaginosis	100	0	0	0
– Candidiasis	95	5	0	0
Mixed Infections (N = 48)				
– Trichomoniasis and Bacterial Vaginosis and Candidiasis	100	0	0	0
– Trichomoniasis and Candidiasis	100	0	0	0
– Bacterial Vaginosis and Candidiasis	100	0	0	6.7
– Bacterial Vaginosis and Trichomoniasis	96.6	3.4	0	6.9
– Overall Cure	97.9	2.1	0	6.3

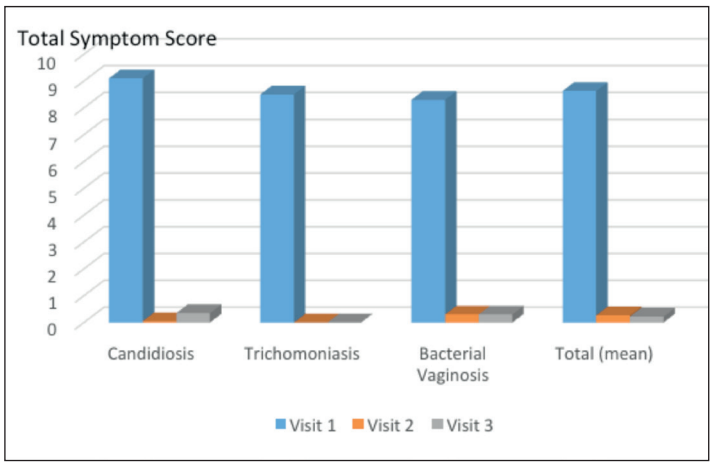

Figure 2. Total symptom scores at visits 1, 2 and 3 (mixed infections included).

According to the subjective and objective clinical evaluation criteria mentioned in the "Patients and Methods" section, clinical symptoms vaginitis were resolved in 97.0% of the patients, and improved in a further 3.03%, regardless of the pathogen(s) responsible for the vaginitis. Total symptom score for vaginitis declined from 8.63 (visit 1) to 0.27 (visit 2) and to 0.22 (visit 3) (mixed infections included) (Figure 2). The overall clinical recurrence rate was 5.05% (at visit 3) (Table 3).

For the clinical and microbiological evaluation, the responses were statistically significant both at the end of treatment and at follow-up: a reduction of anaerobes, *Trichomonas* and *Candida* in vaginal swabs between visit 1 and visits 2 and 3 (p <0. 05, Friedman's x^2-test), and a reduction in the symptoms of vaginitis (discharge, irritation, itching, odor and pain) between visit 1 and visits 2 and 3 (p = 0. 000). There were significant improvements in vaginal inflammation and vaginal discharge after treatment, as assessed by gynecological examination (Cochran's Q =12,28; p < 0. 05).

Side effects/Adverse events

The used pessaries were subjectively well tolerated by the patients and only mild and transient local or non-local side effects/adverse events were recorded.

Scores for patient's questionnaire for occurrence of local side effects such as wetness and irritation (i.e. burning) were: 1= not different from normal; 2= mild, i.e. noticeable but not causing discomfort; 3= significant, i.e., causing discomfort.

Non-local adverse events reported by the patients and recorded by the investigator in the side effects/adverse events form were scored as follows: 1=mild, i.e. noticeable but not causing discomfort; 2=moderate, i.e. causing discomfort; 3= severe, i.e. discomfort sufficient to interfere with normal activities.

16 patients reported mild and transient burning sensation (severity score: 2=mild, i.e. noticeable but not causing discomfort) in the first few days of the treatment, which lasted mostly 30 minutes-2 hours (Table 4). None of the subjects reported significant vaginal burning and/or increase in vaginal wetness (due to leakage of the pessary), which would cause discomfort sufficient to interfere with normal activities. None of the patients discontinued the treatment due to local side effects/adverse events or needed medical/nonmedical treatment for the relief of the symptoms experienced.

A total number of 10 patients reported untoward clinical events at visit 2 (end of the 7 day's treatment period). These were mild to moderate metallic taste (six patients), dizziness (two patients), diarrhea (one patient) and abdominal pain (one patient) (Table 4).

The metallic taste experienced by the six patients was regarded as being related to the systemic absorption of metronidazole from the study medication. Other side effects/adverse events given in Table 4 were regarded as possibly related to the study medication. None of these non-local side effects/adverse events necessitated medical/nonmedical treatment and/or discontinuation of the study medication.

DISCUSSION

Vulvovaginal candidiasis, trichomonal vaginitis and bacterial vaginosis are the most prevalent forms of vaginitis. Infection of the vagina with multiple pathogens is also very common; mixed forms of vaginitis, which

Table IV. Microbiological test results.

Side effects	Severity
Local (N = 16)	
Vaginal burning (N = 16)	Mild (16)
Non Local (N = 10)	
Metallic Taste (N = 6)	Mild (3) Moderate (3)
Dizziness (2)	Mild (1) Moderate (1)
Diarrhoea (1)	Mild (1)
Abdominal Pain (1)	Moderate (1)

complicate the diagnosis and treatment of vaginitis, may be observed at a rate between 10 to 30%[3-6].

Since effective management of vaginitis depends on accurate diagnosis, selection and administration of effective specific therapy and good compliance of the patient, a single form of medication capable of treating candidal, bacterial and trichomonal vaginitis should provide a valuable form of therapy, especially in cases where the cause of vaginitis is unconfirmed and may be of mixed origin.

It is known that 200 mg miconazole vaginally and 750 mg metronidazole oral per day for a period of 7 days, are the standard medication in the management of candidiasis and trichomoniasis and bacterial vaginosis[14].

The logical combination of metronidazole (500 mg) and miconazole nitrate (100 mg), both standard medications at these doses, have been evaluated in previous clinical studies[8-12]. It was shown that with this combination, very high clinical and microbiological cure rates are achieved in patients with candidal, bacterial and trichomonal vaginitis and in mixed vaginal infections.

As patient compliance is a major problem, and dosages similar to the oral established dosages should be used a combination of metronidazole (750 mg) and miconazole nitrate (200 mg), it was developed for once daily administration in the therapy of vaginitis.

This study, for the first time, could demonstrate that the new posology with the metronidazole and miconazole pessaries, administered once daily for seven days, provided effective and safe treatment in common types of vaginitis, as well as in mixed vaginal infections.

The pessary was well tolerated and there was a drastic reduction in signs and symptoms of vaginitis at the end of seven days' treatment (visit 2) and follow-up examination carried out two weeks later (visit 3). Overall clinical cure rate was 97% with a further improvement in 3% of the patients. Microbiological cure rates were 81, 87 and 97% for candidal, bacterial and trichomonal vaginitis, respectively, and 92% for mixed vaginal infections.

The results for the microbiological evaluation are compared below with those from other trials carried out with Neo-Penotran®, as well as other published studies with metronidazole or miconazole. Lugo-Miro et al[15] published a meta-analysis of results of the treatment of bacterial vaginosis with metronidazole. Altogether, 10 papers and 23 treatment regimens were analyzed. The combined cure rates, corresponding to the results at the end of treatment with the old metronidazole + miconazole regime, ranged according to treatment regimen from 85 to 87%.

In previous clinical studies with metronidazole + miconazole in the dosage of 500 mg and 100 mg respectively, the microbiological cure rates were 95.2[8], 93.3[9], 89.5[10] and 87%[12] for bacterial vaginosis. In the present study, the microbiological cure rate (eradication of all microbes) was 96% at the end of once daily, 7-days' treatment (mixed infections included). This was highly comparable to the results of the meta-analysis of Lugo et al[15], as well as the cure rates obtained in previous studies carried out with two different dosage regimens of metronidazole and miconazole (i.e. twice daily for 14 days or twice daily for 7 days). Microbiological recurrence rate in bacterial vaginosis was 5.7% in the present study (mixed infections included), which is very similar to the results with previous studies and to other published studies with metronidazole.

In eight published trials[16-23] with miconazole in the treatment of candidal vaginitis, the mycological cure rate at the end of treatment ranged from 62.5 to 91%. Corresponding mycological cure rates obtained in earlier studies with miconazole 100 mg twice per day were 97.6[8], 93.3[9], 86.4[10] and 81%[12]. The equivalent cure rate in the present trial was 90% (mixed infections included). Re-appearance of vulvovaginal candidal growth was found to be 15.3%, which is within the range of results previously published in the literature.

Published success rates for metronidazole in the treatment of trichomonal vaginitis vary between 50-97%, depending on the dosage regimen and the route of administration employed[2]. Microbiological cure rates for trichomonal vaginitis obtained in previous trials with the 7-day regimen were 80[9], 82[10] and 97%[12] respectively. The microbiological cure rate obtained with once daily 7-days' treatment in the present study was 100% (mixed infections included). Microbiological recurrence rate was 2.7% in this study, highly comparable to previous trials and to those found in the literature.

48 out of 99 women (48.5%) presented multiple causative pathogens for vaginitis in their vaginal swabs. After once daily, seven days' treatment with the study medication, microbiological eradication was achieved in 97% of patients with trichomonal + bacterial and in 80% with bacterial and candidiasis infection with recurrence rates of 7 and 40%, respectively. In the two cases with candida + trichomonal and in the two patients with bacterial + candida + trichomonal infection, the microorganisms were eradicated completely without any recurrence at visit 3. The overall microbiological cure rate for mixed infections was 92%.

CONCLUSIONS

This new pessary containing 750 mg metronidazole + 200 mg miconazole provides an effective treatment for candidal, bacterial and trichomonal vaginitis and in vaginitis due to mixed infections with clinical cure rates of up to 97.9% and recurrence rates of only 6.3%.

There appears to be no significant difference regarding efficacy and safety between the once daily 7-day dosage and twice daily 7- or 14-day dosage regimens recommended before.

The easy and patient friendly mode of application by the only vaginal use of 7 pessaries once per day over 7 days represents an improvement in the compliance and management of vaginal infections of women during their reproductive live.

Conflicts of interest:
The Authors declare that they have no conflict of interests.

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