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Assessment of a Dazel-Kit (Fluconazole 150 mg, Azithromycin 1 gm, Secnidazole 1 g Two Tablets) for Syndromic Management of Abnormal Vaginal Discharge in Women of Kazakhstan

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Authors' contributions

This work was carried out in collaboration between all authors. All authors read and approved the final manuscript.

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Short Research Article

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ABSTRACT

Objective: Present study aimed to assess the effectiveness and safety of Dazel kit (fluconazole 150 mg, azithromycin 1 gm, secnidazole 1 g two tablets) among patients with vaginal infections.
Materials and Methods: In this observational study, 705 clinically diagnosed patients with abnormal vaginal discharge were enrolled in four different cities of Kazakhstan. Clinical features, treatment given, improvement in symptoms and adverse events were noted. Improvement in clinical features with Dazel kit was rated on a 4-point scale; 1=no effect; 2=somewhat effective; 3=effective; 4= highly effective.
Results: Abnormal vaginal discharge was the most common symptom (91.5%), followed by itching

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(88.2%) and lower abdominal pain (59.6%). For all patients, Dazel kit was recommended, whereas in 617 patients (87.5%), it was recommended for their partner(s) too. In 90 patients (12.8%) only Dazel kit was recommended alone whereas, in 615 patients (87.23%), vaginal treatment was recommended in addition to Dazel kit. In 99.2% patients with abnormal vaginal discharge and vaginal itching, treatment was effective or highly effective. For the control of dyspareunia, lower abdominal pain and burning sensation with urination, treatment was found to be effective or highly effective in 64.3%, 98.7% and 95.4% patients, respectively. No significant difference was observed in the "highly effective" and "effective" response for any of the symptoms between treatment only to the female patient and treatment to patient and her partner(s) [abnormal vaginal discharge (*p*= 0.755), vaginal itching (*p*= *0.512*), dyspareunia (p= 0.791), lower abdominal pain (*p*= 0.964) or burning sensation (*Pp*= 0.804)].

Conclusion: Dazel kit was found to be effective in the treatment of vaginal symptoms in majority of the patients without significant adverse events.

Keywords: Azithromycin; fluconazole; secnidazole; vaginal discharge; Dazel-Kit.

1. INTRODUCTION

Vaginitis is an important public health concern [1] and a common problem encountered in clinical practice. In about 20-25% women attending gynaecology outpatient clinic have the problem of vaginitis, and among them, more than 60% have it because of an infection [2].

The common causes of vaginal issue include bacterial vaginosis, trichomoniasis and vulvovaginal candidiasis [3,4]. These three infections account for about 90% of all vaginal infections [5]. In a study from India among patients (n=319) with vaginal discharge, bacterial vaginosis and candidiasis were seen in 26% and 25.4% of patients, respectively. Chlamydia trachomatis and trichomoniasis were present in 12.2% and 10% of patients, respectively whereas diagnosis was not possible in 40.1% [6].

Most of the untreated vaginitis can result in pelvic inflammatory disease [7] which is one of the most common and debilitating diseases in women [8]. The symptoms of pelvic inflammatory disease include general symptoms such as pain in the lower part of the abdomen, back pain, fever, vomiting, dyspareunia and vaginal symptoms including discharge or bleeding, itching and odour [9]. In addition to the listed bothersome symptoms, pelvic inflammatory disease may be associated with more serious complications such as infertility or ectopic pregnancy [9-11]. Early diagnosis and treatment of pelvic inflammatory disease are important to avoid these complications.

Due to polymicrobial origin, patients with pelvic inflammatory diseases are often treated with broad spectrum antimicrobial agents [12,13]. According to the WHO guidelines [14] on management of sexually transmitted infection, all women presenting with abnormal vaginal discharge should be treated for trichomoniasis and bacterial vaginosis. Laboratory tests are recommended only if resources are available.

Vaginal infections are often managed with empirical treatment because it is often cost-effective option. Abnormal vaginal discharge is also often polymicrobial; hence it needs to be treated as a syndrome rather than a single cause [15]. Combination of antibiotic covering aerobic and anaerobic pathogens and antifungal is often useful.

Nitroimidazoles can be used for the treatment of trichomoniasis and bacterial vaginosis. Metronidazole, a commonly used nitroimidazole is associated with rising rates of resistance. Secnidazole, an agent with longer half-life is an alternative option with better compliance because of single dose (2 gm) [2]. Vulvovaginal candidiasis needs treatment with the antifungal agent [3]. Topical treatment is not preferred because of inconvenience and social issues. Oral fluconazole 150 mg given as a single dose is an effective option for the treatment of vulvovaginal candidiasis [16]. It also reduces the risk of recurrence because of the elimination of rectal fungal pathogens [2]. A randomised trial showed 97% efficacy of 1 gm oral single dose of azithromycin for urogenital *Chlamydia trachomatis* infection [17]. Thus, azithromycin [18], fluconazole [19] and secnidazole [20] all three are useful antimicrobial agents for the treatment of genital infections [18-20]. Dazel-Kit is a single day treatment thereby; all pills need to be consumed in a single day. Dazel kit contains one tablet of fluconazole 150 mg, one tablet of

azithromycin 1 gm, two tablets of secnidazole 1 gm. It is marketed for the treatment of vaginal discharge. Although there is a wide clinical experience of using this combination in patients with vaginal infection, the published evidence is limited all across the globe. The study was conducted to assess the effectiveness and safety of Dazel kit among patients with vaginal discharge.

2. MATERIALS AND METHODS

This observational data on Dazet kit experience were collected from 21 doctors from four cities in Kazakhstan i.e. Shymkent, Taraz, Almaty and Pavlodar. Data of 705 patients with different symptoms of vaginal infection were collected. Diagnosis of vaginal infection was done clinically. Clinical features of the patients, type of treatment recommended by the clinician, recommendation of Dazel kit to the patient, recommendation of treatment to the partner(s), and improvement in symptoms post-treatment were collected through feedback of doctor's form prepared by the team of Ajanta Pharmaceutical Medical & Clinical Service Department. After the treatment, observation was done on Day 14. Improvement in clinical features was rated on a 4-point scale; 1=no effect; 2=somewhat effective; 3=effective; 4= highly effective. The incidence of adverse event was recorded to evaluate safety of the given treatment.

2.1 Statistical Analysis

Data were presented as numbers and percentages for clinical features, treatment recommendation, effectiveness of the medicine and adverse events. Chi-square test was performed to examine the difference in effectiveness when Dazel kit was given for treatment only to the female partner(s) versus when given to patient and her partner(s). p value less than 0.05 was considered statistically significant.

3. RESULTS

The most common symptom among patients was abnormal vaginal discharge [645 (91.5%)]. The other symptoms included itching [622 (88.2%)], lower abdominal pain [420 (59.6%)], foul discharge [388 (55.0%)], burning sensation during urination [359 (50.9%)] and dyspareunia [87 (12.3%)] (Fig. 1).

For all patients, Dazel kit was recommended whereas in 617 patients (87.5%), Dazel kit was also recommended for their partner(s) (Table 1).

In 90 patients (12.8%), only Dazel kit was recommended whereas in 615 patients (87.23%), vaginal treatment with antifungal was recommended in addition to Dazel kit orally (Table 2).

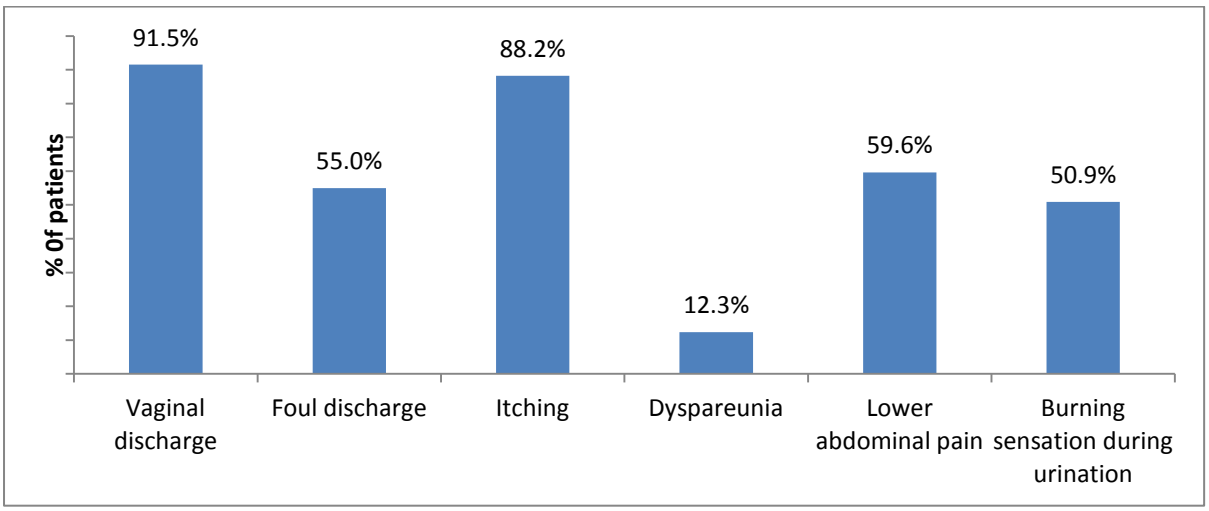

Fig. 1. Clinical features of patients

Table 1. Treatment recommendations

Dazel kit recommendation to patient	Dazel kit recommendation to patient and her partner(s)
705 (100%)	617 (87.5%)

Table 2. Distribution of patients with only Dazel kit recommendation and Dazel kit plus vaginal treatment recommendation

Dazel kit alone	Dazel kit along with vaginal treatment
90 (12.8%)	615 (87.23%)

Antibiotic was prescribed in 173 patients (24.5%), whereas antifungal, antispasmodic and anti-inflammatory agents were prescribed in 109 (15.5%), 73 (10.4%) and 127 (18.0%) patients respectively (Fig. 2).

In 99.2% patients with abnormal vaginal discharge and vaginal itching, treatment was effective or highly effective. For the control of dyspareunia, lower abdominal pain and burning sensation while urination, treatment was found to be effective or highly effective in 64.3%, 98.7% and 95.4% patients respectively (Fig. 3). Fig. 4 shows the percentages of patients with effectiveness when treatment was given to the patient and her partner(s).

There was no significant difference in the "highly effective" and "effective" response for any of the symptoms between two groups i.e. treatment only to the female patient and treatment to patients and her partner(s) [abnormal vaginal discharge (*p= 0.755*), vaginal itching (*Pp= 0.512*), dyspareunia (*p= 0.791*), lower abdominal pain (*p= 0.964*) or burning sensation (*p= 0.804*)].

3.1 Safety

Adverse events were reported by 54 patients (7.7%). Common adverse events observed were diarrhoea [20 (2.8%)], nausea [15 (2.1%)] and epigastric pain [10 (1.4%)]. Other adverse events are shown in Table 3.

4. DISCUSSION

Vaginitis is an important public health concern in women of all ages. Nature of vaginitis could be infectious or inflammatory [1]. Infectious vaginitis accounts for the majority of vaginal infections in women in the reproductive age group [21].

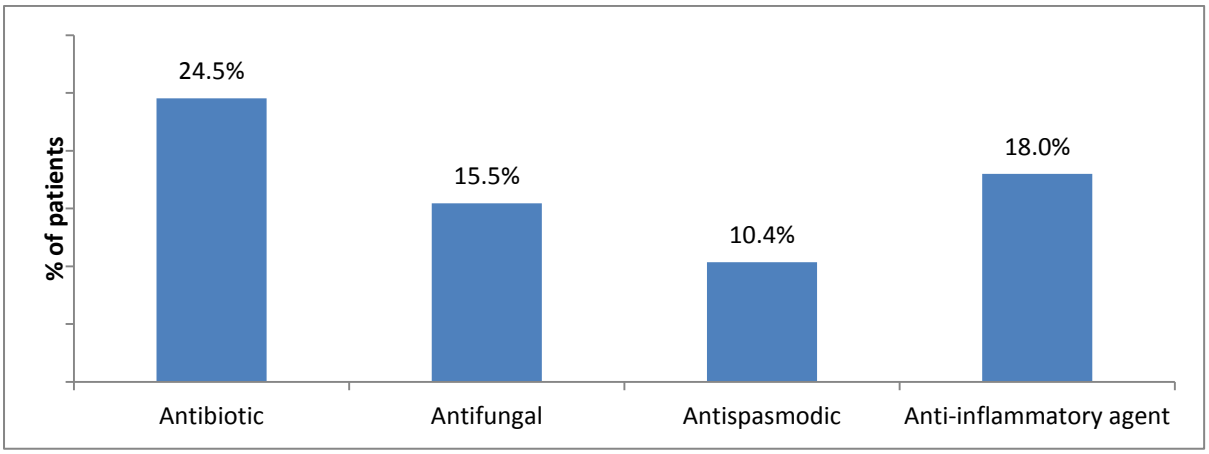

Fig. 2. Other medications prescribed along with Dazel kit

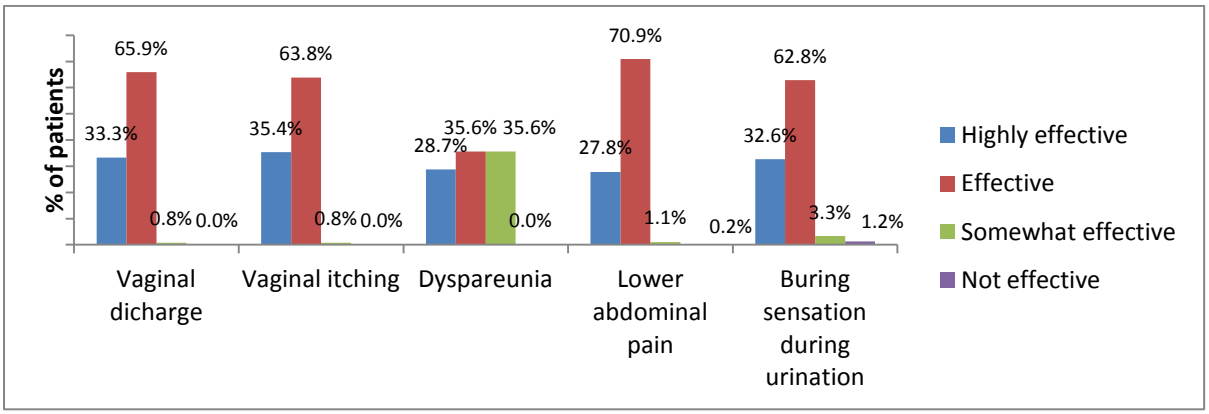

Fig. 3. Effectiveness of Dazel kit when treatment given only to female patient

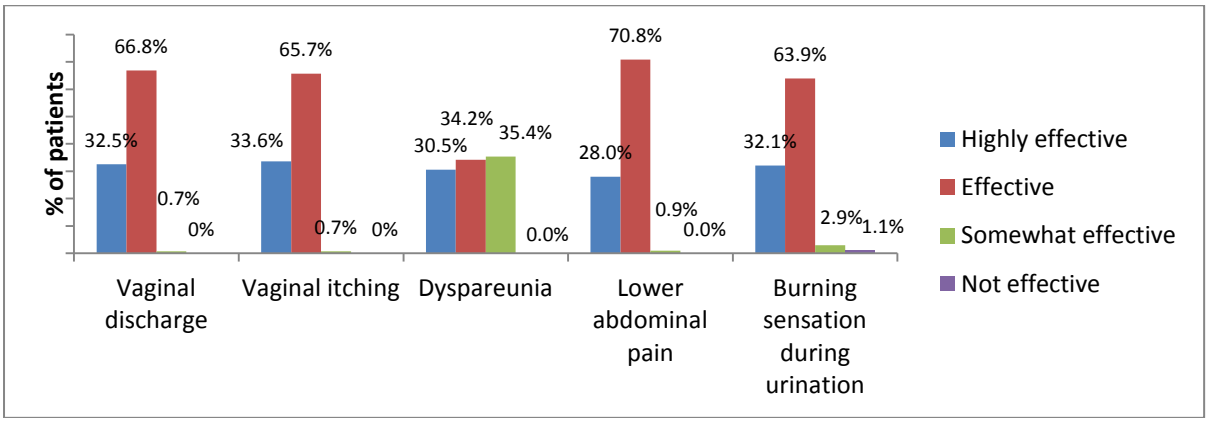

Fig. 4. Effectiveness of Dazel kit when treatment given to patients and her partner(s)

Table 3. Incidence of adverse event

Adverse event	N (%)
Nausea	15 (2.13%)
Dizziness	4 (0.57%)
Epigastric pain	10 (1.42%)
Vomiting	3 (0.43%)
Diarrhoea	20 (2.84%)
Weakness	4 (0.57%)
Headache	4 (0.57%)
Lowe abdominal pain	1 (0.14%)
Pain	5 (0.71%)
Metallic taste in mouth	4 (0.71%)
Skin rash/hive	2 (0.28%)
Nocturnal urges	1 (0.14%)
Potency disorder	1 (0.14%)
Pruritus	1 (0.14%)
Signs of infertility	1 (0.14%)
Heaviness in the stomach	1 (0.14%)

The common symptoms of vaginitis include abnormal vaginal discharge, itching, burning and discomfort [1]. In our study group, the most common symptom was abnormal vaginal discharge followed by itching and lower abdominal pain. Dyspareunia i.e. pain with sexual activity [22] was presented in 12.3% patients in this study. Dyspareunia can cause significant problems in women including mental stress and conflict in a relationship with partner(s) [22].

The risk factors for infections include low socio-economic status, lack of awareness, use of intra-uterine device, sex with multiple partner(s) and early marriage [7]. Poor hygiene, multiple sexual partner(s) and intra-uterine device can also cause recurrent vaginal infections [23]. Abnormal vaginal discharge can be a symptom of pelvic inflammatory disease [24].

It is important for the healthcare providers to educate patients about the aspects which help to prevent the occurrence of such infections [21].

The episodes of vaginal infections need effective treatment. Oral as well topic antimicrobials are used in the treatment of bacterial vaginosis for the eradication of pathogens. Secnidazole is effective for the treatment of trichomoniasis and bacterial vaginosis with cure rates ranging between 90-97% and 85-95% respectively [25]. Single dose azithromycin is an effective treatment of urogenital C. trachomatis infection [17]. The advantages of azithromycin include high tissue bioavailability and longer tissue half-life resulting in high antimicrobial activity at the site of infection [18]. Single dose 150 mg fluconazole has also been shown to be an effective and well-tolerated treatment for vaginal candidiasis [19]. In a recent study, secnidazole 2 g single dose was found to be effective and well tolerated for the treatment of bacterial vaginosis [20]. Because of the polymicrobial nature of vaginitis [15], it needs treatment with broad spectrum antimicrobial agents. Combination kit therapy containing fluconazole, azithromycin and secnidazole is a simple approach for a high cure rate in patients with abnormal vaginal discharge complaints [2]. In this study, we evaluated the effectiveness and safety of triple drug combination of azithromycin, secnidazole and fluconazole. A study from India has shown an excellent efficacy in majority of patients with abnormal vaginal discharge [2].

Present study recorded the effectiveness of triple drug combination in improvement of majority of patients. Similar observations have been reported in another study conducted by Malhotra and colleagues [26]. In a randomised study from India involving 165 women with pelvic

inflammatory disease in compared to the treatment with three regimens; ciprofloxacin (500 mg) and tinidazole (600 mg) twice daily, fluconazole (150 mg), azithromycin (1 gm) and secnidazole (2 mg) and Doxycycline 100mg twice daily and metronidazole 200 mg thrice daily. The kit containing fluconazole, azithromycin and secnidazole resulted in a cure rate of 93.5% [26]. In sexually transmitted disease, treatment of partner(s) is also important [5]. In a study from India, combination therapy in the form of a kit was recommended to patients and her partner(s) husband and wife [2]. In our study, treatment was recommended for 87.5% patient partner(s).

Treatment was well tolerated by majority of the patients with no major adverse events. The incidence of adverse events was 7.7% with gastrointestinal disturbance as a common adverse event. There was no serious adverse event reported in the study.

Single centre, single arm, observational study design, clinical diagnosis, empirical treatment and limited period of follow up are the limitations of our study. Further studies with long-term follow up are required to find out the recurrence of infections after initial treatment.

5. CONCLUSION

Single dose combination of azithromycin, fluconazole and secnidazole in the form of a kit (Dazel kit) is effective in improvement of vaginal symptoms in majority of the patients. There was no difference in the effectiveness when treatment was given only to the female patient versus treatment for patients and her partner(s). Treatment is well tolerated by the patients without clinically significant adverse event.

CONSENT

Patients were treated by physician in their routine practice. Patient confidentiality was not revealed by physician when data provided to authors. All disease and treatment related things explained to patient during patient physician interactions.

ETHICAL APPROVAL

This data was obtained from physicians in their routine Practice. Patient confidentiality had not revealed by physicians when data was provided to authors. This study did not have any fix clinical protocol as mentioned, so that we could harmonise the treatment of each physician. It was their individual judgement. It is analysis of the feedback of treating physicians from their routine clinical practice. In Clinical practice physicians used both topical and systemic antibiotic / antifungal agent depending on their acumen and clinical experience. They may have added additional antibiotic and antifungal agent in suppository form (topical), details of which were not captured. Dazel kit is an oral one-day treatment. Application of topical (suppository) antibiotic/antifungal agent along with oral agent was used.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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