

## Assessment of a Dazel-Kit (fluconazole 150 mg, azithromycin 1 gm, secnidazole 1 g two tablets) for Syndromic Management of Vaginal Discharge in Women of Kazakhstan

### ABSTRACT:

**Objective:** To assess effectiveness and safety of Dazel kit (fluconazole 150 mg, azithromycin 1 gm, secnidazole 1 g two tablets) among patients with vaginal infections.

**Material and methods:** In this observational study, 705 clinically diagnosed patients with 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 4-point scale; 1=no effect; 2=somewhat effective; 3=effective; 4= highly effective.

**Results:** Vaginal discharge was the most common symptom (91.5%), followed by itching (88.2%) and lower abdominal pain (59.6%). For all patients Dazel kit was recommended whereas in 617 (87.5%) patients, it was recommended for their partners too. In 90 (12.8%) patients only Dazel kit was recommended alone whereas in 615 (87.23%) patients, vaginal treatment was recommended in addition to Dazel kit. In 99.2% patients with 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. 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 both partners [vaginal discharge ( $P=0.755$ ), vaginal itching ( $P=0.512$ ), dyspareunia ( $P=0.791$ ), lower abdominal pain ( $P=0.964$ ) or burning sensation ( $P=0.804$ )]

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

**Key words:** *Azithromycin, Fluconazole, Secnidazole, Vaginal discharge, Dazel-Kit*

### 1. INTRODUCTION

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

33 [2].

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

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

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

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

55 Nitroimidazoles can be used for the treatment of trichomoniasis and bacterial vaginosis.  
56 Metronidazole, a commonly used nitroimidazole is associated with rising rates of resistance.  
57 Secznidazole, an agent with longer half-life is an alternative option with better compliance because of  
58 single dose (2 gm) [2]. Vulvovaginal candidiasis needs treatment with antifungal agent [3]. Topical  
59 treatment is not preferred because of inconvenience and social issues. Oral fluconazole 150 mg given  
60 as a single dose is effective option for the treatment of vulvo-vaginal candidiasis [16]. It also reduces  
61 the risk of recurrence because of the elimination of rectal fungal pathogens [2]. A randomized trial  
62 showed 97% efficacy of 1 gm oral single dose azithromycin urogenital Chlamydia trachomatis  
63 infection [17]. Thus, azithromycin [18], fluconazole [19] and secnidazole [20] all three are useful  
64 antimicrobial agents for treatment of genital infections [18-20]. Dazel-Kit is a single day treatment. All  
65 pills in Dazel kit to be consumed in a single day. Dazel kit contains one tablet of fluconazole 150 mg,  
66 one tablet of azithromycin 1 gm, two tablet of secnidazole 1 gm). It is marketed for the treatment of  
67 vaginal discharge. Although there is wide clinical experience of using this combination in patients with  
68 vaginal infection, the published evidence is limited all across the globe is very limited. The study was  
69 conducted to assess effectiveness and safety of Dazel kit among patients with vaginal discharge.

## 70 2. MATERIAL AND METHODS

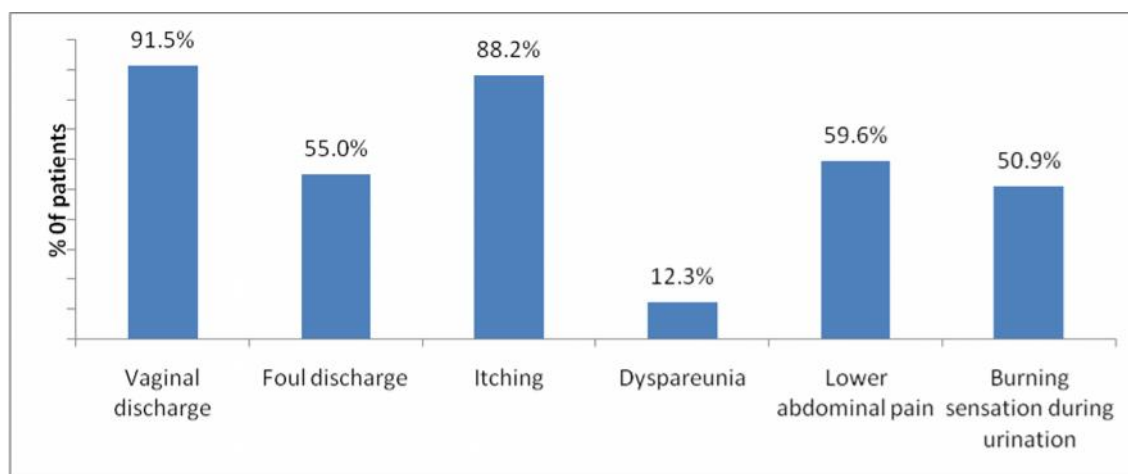
71 This observational study data on Dazel kit experience were collected from 21 doctors from four cities  
72 of Kazakhstan i.e. Shymkent, Tarar, Almaty and Pavlodar. Data of 705 patients with different  
73 symptoms of vaginal infection were collected. Diagnosis of vaginal infection was done clinically.  
74 Clinical features of the patients, type of treatment recommendation by the clinician, recommendation  
75 of Dazel kit to the patient, recommendation of treatment to the partner, and improvement in symptoms  
76 post treatment was collected through a feedback of doctors form prepared by the team of Ajanta  
77 Pharmaceutical Medical & clinical service department. After the treatment observation was done on  
78 Day 14. Improvement in clinical features was rated on 4-point scale; 1=no effect; 2=somewhat  
79 effective; 3=effective; 4= highly effective. Incidence of adverse event was noted to evaluate safety of  
80 the given treatment

### 81 2.1 Statistical Analysis:

82 Data are presented as numbers and percentages for clinical features, treatment recommendation,  
83 effectiveness of the medicine and adverse events. Chi square test was used to examine difference in  
84 effectiveness when Dazel kit was given for treatment only to the female partner versus when given to  
85 both partners. P value less than 0.05 was considered statistically significant.

## 86 3. RESULTS

87 The most common symptom among patients was vaginal discharge [645 (91.5%)]. The other  
88 symptoms included itching [622 (88.2%)], lower abdominal pain [420 (59.6%)], foul discharge [388  
89 (55.0%)], burning sensation during urination [359 (50.9%)] and dyspareunia [87 (12.3%); Fig. 1].



90

91 **Fig. 1. Clinical features of patients**

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94 **Table 1. Treatment recommendations**

Dazel kit recommendation to patient	Dazel kit recommendation to both partners
705 (100%)	617 (87.5%)

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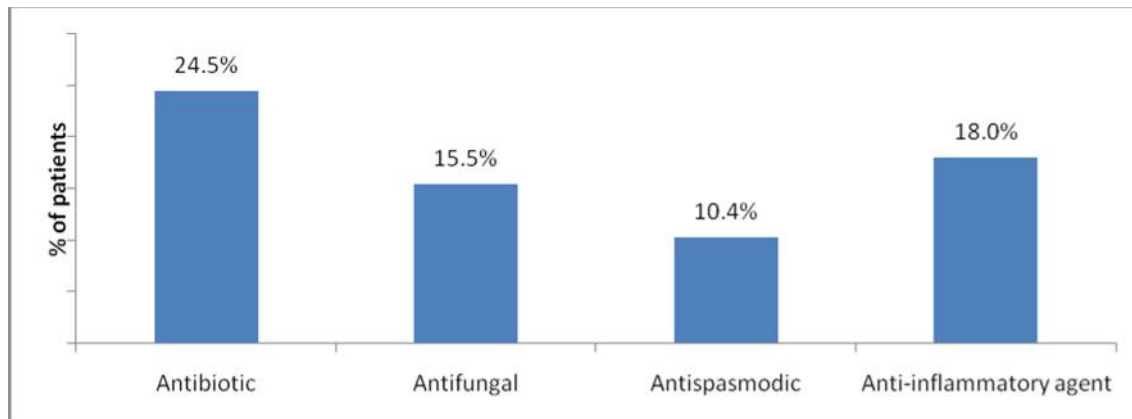
96 For all patients Dazel kit was recommended whereas in 617 (87.5%) patients, Dazel kit was also  
 97 recommended for their partners (Table 1).

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

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

100

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

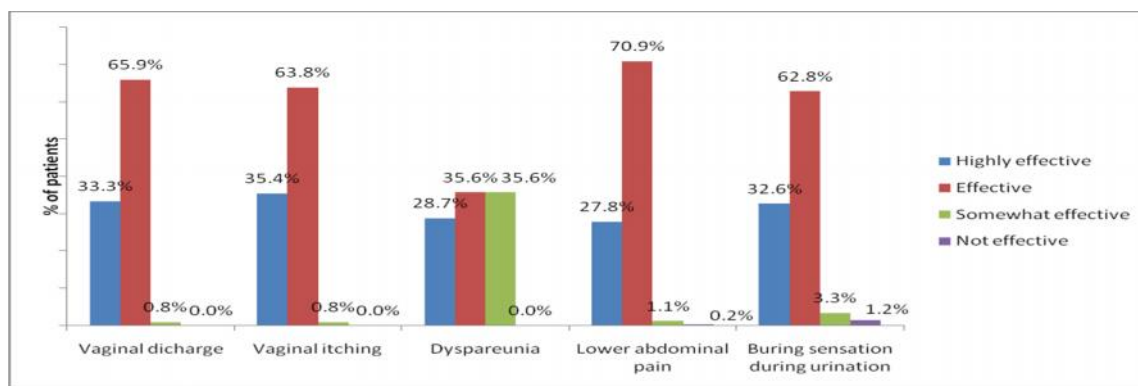


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104 **Fig. 2: Other medications prescribed along with Dazel kit**

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

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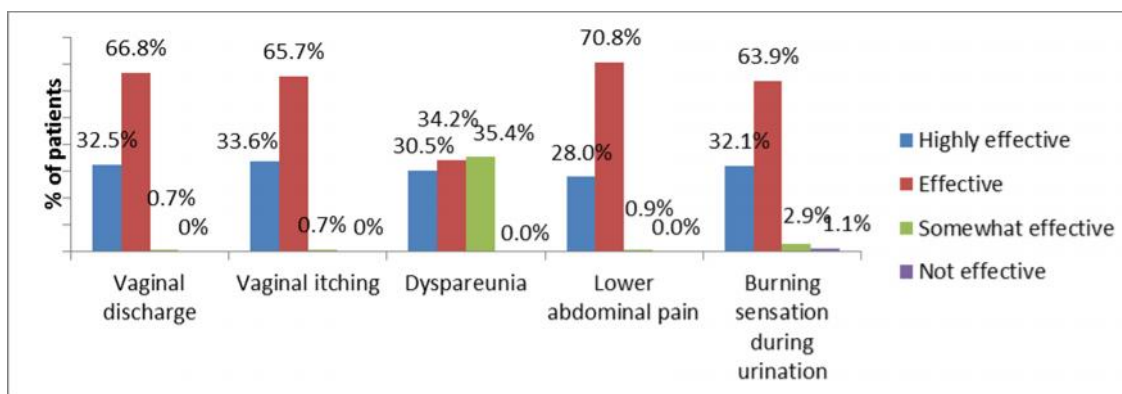


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110 **Fig. 3. Effectiveness of Dazel kit when treatment given only to female patient**

111 In 99.2% patients with vaginal discharge and vaginal itching treatment was effective or highly  
 112 effective. For the control of dyspareunia, lower abdominal pain and burning sensation while urination,  
 113 treatment was found to be effective or highly effective in 64.3%, 98.7% and 95.4% patients  
 114 respectively (Figure 3). Figure 4 shows percentages of patients with effectiveness when treatment  
 115 was given to both partners.

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117

118 **Fig. 4. Effectiveness of Dazel kit when treatment given to both partners**

119 There was no significant difference in the “highly effective” and “effective” response for any of the  
 120 symptoms between two groups i.e. treatment only to the female patient and treatment to both partners  
 121 [vaginal discharge ( $P=0.755$ ), vaginal itching ( $P=0.512$ ), dyspareunia ( $P=0.791$ ), lower abdominal pain  
 122 ( $P=0.964$ ) or burning sensation ( $P=0.804$ )]

123 **3.1 Safety:**

124 **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%)
Diarrhea	20 (2.84%)
Weakness	4 (0.57%)
Headache	4 (0.57%)
Low 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%)

125

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

#### 129 **4. DISCUSSION**

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

133 The common symptoms of vaginitis include abnormal vaginal discharge, itching, burning and  
 134 discomfort [1]. In our study group, the most common symptom was vaginal discharge followed by  
 135 itching and lower abdominal pain. Dyspareunia i.e. pain with sexual activity [22] was present in  
 136 12.3% patients in this study. Dyspareunia can cause significant problems in women including mental  
 137 stress and conflict in relationship with partners [22].

138 The risk factors for infections include low socio-economic status, lack of awareness, use of use of  
 139 intra-uterine device, sex with multiple partners and early marriage [6]. Poor hygiene, multiple sexual  
 140 partners and intra-uterine device can also cause recurrent vaginal infections [23]. Abnormal vaginal  
 141 discharge can be a symptom of pelvic inflammatory disease [24].

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

144

145 The episodes of vaginal infections need effective treatment. Oral as well topic antimicrobials are used  
 146 in the treatment of bacterial vaginosis for eradication of pathogens.<sup>3</sup>Secnidazole is effective for the  
 147 treatment of trichomoniasis and bacterial vaginosis with cure rates ranging between 90-97% and 85-  
 148 95% respectively [25]. Single dose azithromycin is effective treatment of urogenital *C. trachomatis*  
 149 infection [17]. The advantages of azithromycin include high tissue bioavailability and longer tissue  
 150 half-life resulting in high antimicrobial activity at the site of infection [18]. Single dose 150 mg  
 151 fluconazole has also been shown to be effective and well tolerated treatment for vaginal candidiasis  
 152 [19]. In a recent study secnidazole 2 g single dose was found to be effective and well tolerated in the  
 153 treatment of bacterial vaginosis [20]. Because of polymicrobial nature of vaginitis [15], it need

154 treatment with broad spectrum antimicrobial agents. Combination kit therapy containing fluconazole,  
155 azithromycin and secnidazole is a simple approach for high cure rate in patients with vaginal  
156 discharge [2]. In this study, we evaluated the effectiveness and safety of triple drug combination of  
157 azithromycin, secnidazole and fluconazole. A study from India shown has shown excellent efficacy in  
158 majority of patients with vaginal discharge [2].

159 We observed effectiveness of the triple drug combination in improvement of majority of patients.  
160 Similar observations have been reported in another study conducted by Malhotra and colleagues [26].  
161 In a randomized study from India involving 165 women with pelvic inflammatory disease compared  
162 treatment with three regimens; ciprofloxacin (500 mg) and tinidazole (600 mg) twice daily, fluconazole  
163 (150 mg), azithromycin (1 gm) and secnidazole (2 mg) and Doxycycline 100mg twice daily and  
164 metronidazole 200 mg thrice daily. The kit containing fluconazole, azithromycin and secnidazole  
165 resulted in cure rate of 93.5% [26]. In sexually transmitted disease, treatment of partners is also  
166 important [5]. In a study from India, combination therapy in the form of a kit was recommended to both  
167 husband and wife [2]. In our study, treatment was recommended for 87.5% patient partners.  
168 Treatment was well tolerated by majority of the patients with no major adverse events. Incidence of  
169 adverse events was 7.7% with gastrointestinal disturbance as a common adverse event. There was  
170 no serious adverse event reported in the study.

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

## 174 **5. CONCLUSION**

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

## 179 **CONSENT:**

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

## 183 **ETHICAL APPROVAL:**

184 This data was obtained from physicians in their routine Practice. Patient confidentiality is not revealed  
185 by physician when data was provided to authors.

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