

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

5
6 **ABSTRACT:**

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

9 **Material and methods:** In this observational study, 705 clinically diagnosed patients with
10 abnormal vaginal discharge were enrolled in four different cities of Kazakhstan. Clinical
11 features, treatment given, improvement in symptoms and adverse events were noted.
12 Improvement in clinical features with Dazel kit was rated on 4-point scale; 1=no effect;
13 2=somewhat effective; 3=effective; 4= highly effective.

14 **Results:** Abnormal vaginal discharge was the most common symptom (91.5%), followed by
15 itching (88.2%) and lower abdominal pain (59.6%). For all patients Dazel kit was
16 recommended whereas in 617 (87.5%) patients, it was recommended for their partner(s) too.
17 In 90 (12.8%) patients only Dazel kit was recommended alone whereas in 615 (87.23%)
18 patients, vaginal treatment was recommended in addition to Dazel kit. In 99.2% patients with
19 abnormal vaginal discharge and vaginal itching treatment was effective or highly effective.
20 For the control of dyspareunia, lower abdominal pain and burning sensation with urination,
21 treatment was found to be effective or highly effective in 64.3%, 98.7% and 95.4% patients
22 respectively. No significant difference was observed in the “highly effective” and “effective”
23 response for any of the symptoms between treatment only to the female patient and
24 treatment to patient and her partner(s) [abnormal vaginal discharge ($P=0.755$), vaginal
25 itching ($P=0.512$), dyspareunia ($P=0.791$), lower abdominal pain ($P=0.964$) or burning
26 sensation ($P=0.804$)]

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

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

30 **1. INTRODUCTION**

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

34 [2].

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

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

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

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

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

68 of vaginal discharge. Although there is wide clinical experience of using this combination in patients
69 with vaginal infection, the published evidence is limited all across the globe is very limited. The study
70 was conducted to assess effectiveness and safety of Dazel kit among patients with vaginal discharge.

71 2. MATERIAL AND METHODS

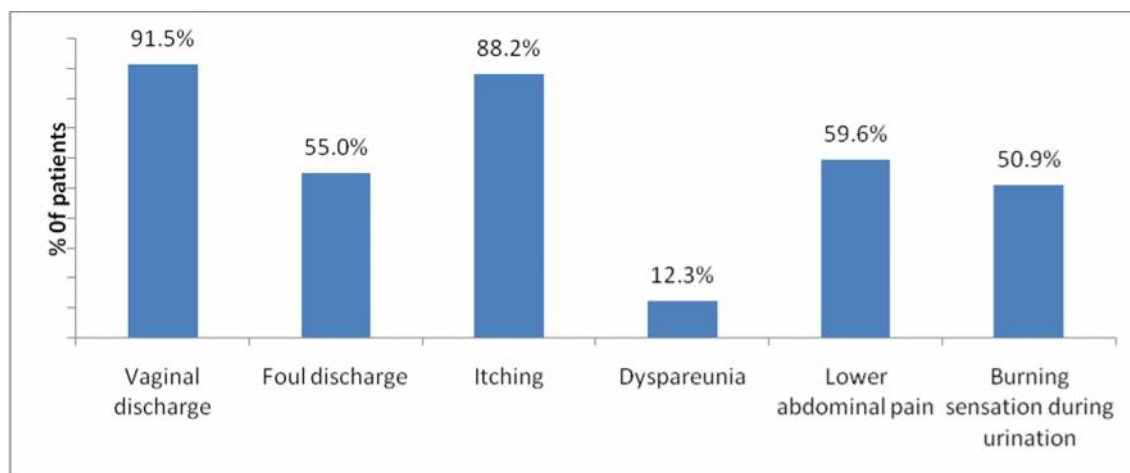
72 This observational study data on Dazel kit experience were collected from 21 doctors from four cities
73 of Kazakhstan i.e. Shymkent, Taraz, Almaty and Pavlodar. Data of 705 patients with different
74 symptoms of vaginal infection were collected. Diagnosis of vaginal infection was done clinically.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

82 2.1 Statistical Analysis:

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

87 3. RESULTS

88 The most common symptom among patients was abnormal vaginal discharge [645 (91.5%)]. The
89 other symptoms included itching [622 (88.2%)], lower abdominal pain [420 (59.6%)], foul discharge
90 [388 (55.0%)], burning sensation during urination [359 (50.9%)] and dyspareunia [87 (12.3%); Fig. 1].



91

92 Fig. 1. Clinical features of patients

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94

95 **Table 1. Treatment recommendations**

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

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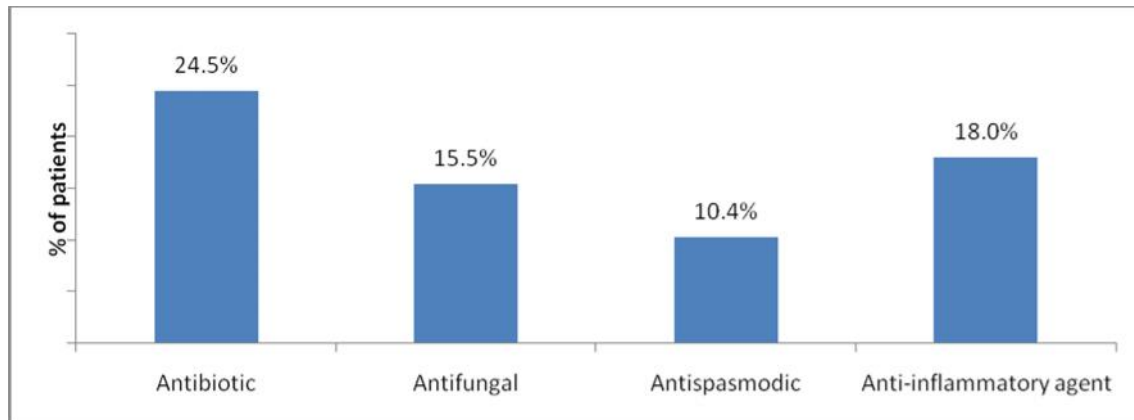
97 For all patients Dazel kit was recommended whereas in 617 (87.5%) patients, Dazel kit was also
98 recommended for their partner(s) (Table 1).

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

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

101

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

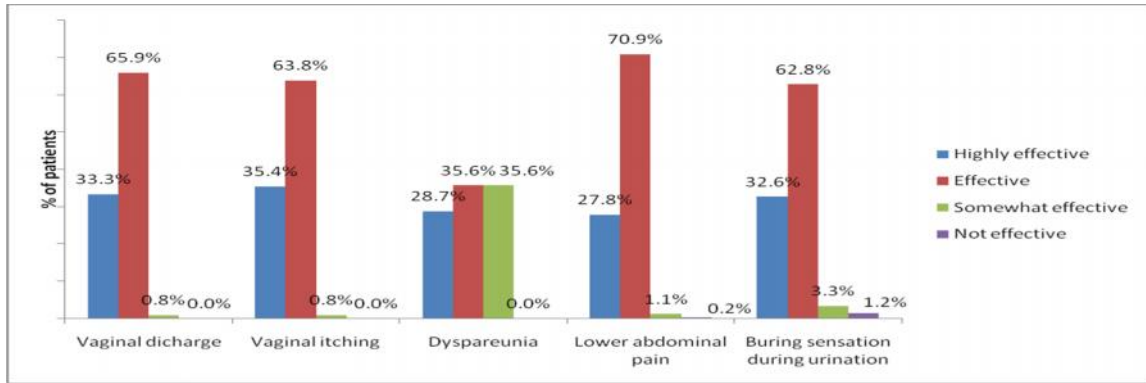


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105 **Fig. 2: Other medications prescribed along with Dazel kit**

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

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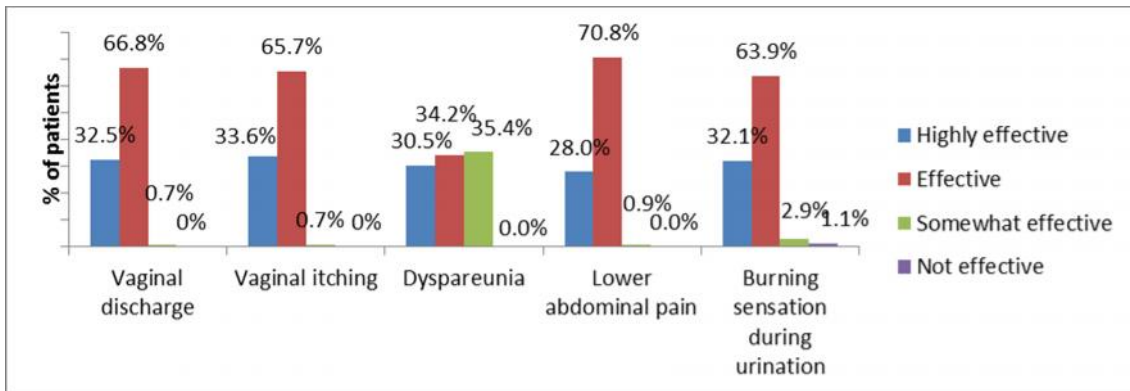


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111 **Fig. 3. Effectiveness of Dazel kit when treatment given only to female patient**

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

117



118

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

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

124 **3.1 Safety:**

125 **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%)

126

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

130 4. DISCUSSION

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

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

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

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

145

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

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

160 We observed effectiveness of the triple drug combination in improvement of majority of patients.
161 Similar observations have been reported in another study conducted by Malhotra and colleagues [26].
162 In a randomized study from India involving 165 women with pelvic inflammatory disease compared
163 treatment with three regimens; ciprofloxacin (500 mg) and tinidazole (600 mg) twice daily, fluconazole
164 (150 mg), azithromycin (1 gm) and secnidazole (2 mg) and Doxycycline 100mg twice daily and
165 metronidazole 200 mg thrice daily. The kit containing fluconazole, azithromycin and secnidazole
166 resulted in cure rate of 93.5% [26]. In sexually transmitted disease, treatment of partner(s) is also
167 important [5]. In a study from India, combination therapy in the form of a kit was recommended to
168 **patients and her partner(s)** husband and wife [2]. In our study, treatment was recommended for
169 87.5% patient partner(s).

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

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

176 **5. CONCLUSION**

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

182 **CONSENT:**

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

186 **ETHICAL APPROVAL:**

187 This data was obtained from physicians in their routine Practice. Patient confidentiality had not
188 revealed by physician when data was provided to authors.

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