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Performance of a rapid yeast test in detecting *Candida* spp. in the vagina☆

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Abstract

We compared the performance of a rapid vaginal yeast assay (*Savvycheck*) with that of microscopic examination of a Gram-stained smear and culture of vaginal discharge in detecting *Candida* spp. Two hundred thirty-one women with vaginal symptoms were studied prospectively. Vaginal specimens obtained from all participants were studied by the *Savvycheck* rapid yeast test, microscopic evaluation of Gram-stained vaginal smears, and yeast culture. *Savvycheck* rapid yeast test was positive in 79% of women with positive cultures and in 3.6% of women with negative cultures. The *Savvycheck* test detected yeasts in 93% of subjects with positive Gram stain and in 5.5% of subjects with negative Gram stain. The *Savvycheck* rapid yeast test showed 93% sensitivity, 95% specificity, and a 97% negative predictive value compared with the Gram stain. It revealed 79% sensitivity, 96% specificity, and an 87% negative predictive value compared with culture. The *Savvycheck* rapid yeast test can be used in the busy office instead of microscopy as a point-of-care tool for diagnosing vulvovaginal candidiasis. It can also reduce the need for yeast cultures in patients with vaginitis.

Keywords: *Candida* spp.; Rapid yeast test; Vulvovaginal candidiasis; Sensitivity and specificity

1. Introduction

The main challenge for the clinician seeing women with vulvovaginal complaints is in determining the cause of the condition because a variety of infectious and noninfectious factors may cause identical signs and symptoms. Vulvovaginal candidiasis results from the overgrowth of the various *Candida* spp. that may already be present in the vagina as a commensal, and symptomatic infection correlates with a high vaginal fungal burden (Sobel et al., 1998). Unfortunately, none of the clinical signs and symptoms of vulvovaginal candidiasis, which include vulvovaginal pruritus, irritation, soreness, dyspareunia, burning on micturition, and whitish, cheesy discharge, are pathognomonic either individually or collectively (Sobel et al., 1998). It has been repeatedly demonstrated that symptoms such as pruritus and the characteristics of the discharge do not reliably predict the cause of acute vaginitis; the amount and color of vaginal discharge are among the least reliable features for predicting the cause of vaginitis (Anderson et al., 2004). Hence, a reliable diagnosis cannot be made on the basis of the history and physical examination without the confirming evidence of laboratory tests.

Microscopic evaluation of vaginal fluid is the mainstay of diagnosis of acute vaginitis. According to the current guidelines by the Centers for Disease Control and Prevention (CDC), the diagnosis of vulvovaginal candidiasis is made in a woman who has signs and symptoms of vaginitis when a wet preparation (saline, 10% KOH) or Gram stain of vaginal discharge demonstrates yeasts or pseudohyphae (CDC, 2006). Accordingly, in a patient with a compatible clinical syndrome, who has a normal vaginal pH and in whom yeast

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is identified microscopically, a culture is not required (Anderson et al., 2004). Vaginal cultures for *Candida* should be considered for the symptomatic woman with negative microscopy (CDC, 2006). Because up to 80% of patients with symptomatic vulvovaginal candidiasis have positive microscopic findings (Sobel et al., 1998), most cases can be diagnosed correctly by microscopic evaluation at the office visit, the diagnosis being established immediately while saving the costs of yeast cultures. Omitting the microscopic evaluation will delay the correct diagnosis, reduce its specificity, and increase its costs.

Unfortunately, many physicians assessing women with vulvovaginal symptoms in the United States (and probably elsewhere) do not perform a microscopic examination. A major reason for the abandonment of office microscopic examination by US physicians has been the imposition of certification by the Clinical Laboratory Improvement Amendment. The added paperwork and liability associated with performance of wet saline mount and potassium hydroxide testing have forced some physicians who did microscopic examination to abandon its use within a doctor's office laboratory. Other reasons for not using office microscopy (or using it incorrectly) would be high patient load and lack of microscopic skills (Ledger and Monif, 2004; Sobel et al., 1998). Moreover, vaginal cultures for yeast are an underused diagnostic test, and despite their undisputable value, they are not routinely required in the diagnosis of vulvovaginal candidiasis (Sobel et al., 1998). Consequently, vulvovaginal candidiasis is routinely diagnosed without benefit of microscopy or culture, and in as many as half of the cases so diagnosed, the women may be uninfected or have other conditions (Sobel et al., 1998).

The general inability to diagnose correctly the condition and the assumption by many that vaginitis is never life threatening and that empirical therapy is always harmless has opened the doors to over-the-counter treatments for vulvovaginal candidiasis. Increasing numbers of women are self-diagnosing vulvovaginal candidiasis and purchasing antifungal preparations over the counter. However, misdiagnosis is common, and studies have shown that as many as two-thirds of all over-the-counter drugs for vulvovaginal candidiasis were used by women without the disease. Overuse of these medications can increase the risk of the development of resistance to antifungals. The only way to restrain the abuse of over-the-counter antifungals and to reduce the risk of resistance is by improving the ability of women to self-diagnose *Candida* vaginitis. This can be achieved by making available a rapid diagnostic tool that can be used by the patient with self-collected vaginal swabs.

A point-of-care test able to detect yeasts in vaginal discharge with sensitivity and specificity comparable to that of microscopy, which is easy to perform and is not time consuming, is highly needed. In the present report, we present the results of a prospective evaluation of a new rapid vaginal yeast detection assay in comparison with microscopic examination of Gram-stained vaginal smears.

2. Materials and methods

Patients with symptoms suggestive for vulvovaginal infection were recruited prospectively and consecutively at a general gynecology practice. Symptoms included at least one of the following: vaginal discharge, itching, burning, and dyspareunia. Women below 18 years of age were excluded. Vaginal samples were taken for Gram stain, yeast culture, and the rapid *Candida* test (*Savvycheck*; Savyon Diagnostics, Ashdod, Israel). All Gram-stained smears were examined by the same physician (M. Dan) within 2 weeks from recruitment. We elected to use the Gram stain technique for immediate identification of yeast because of technical considerations and the ability to store the slides if the need of ulterior reevaluation arose. The vaginal fluid specimens that were obtained for culture were processed and analyzed at a single laboratory. The specimens were inoculated on Sabouraud agar with chloramphenicol and incubated at 37 °C; the plates were examined each day for 7 days. A yeast culture was reported as positive, even if it grew only 1 colony. The rapid *Candida* detection test was based on the concept of lateral flow immunoassay systems. Briefly, a vaginal fluid sample is obtained by a Copan Sterile Dacron swab (Copan Italia, Brescia, Italy), which is then mixed with an extraction buffer liquid placed in a cap situated at the proximal end of the device. Turning the cap will convey the liquid into the test strip, which is housed in the device. The sample then flows by capillary force along the different strip components. The first immunologic interaction occurs between the extracted yeast antigen and the anti-*Candida* polyclonal antibody conjugated to a colored bead, forming a colored antibody–antigen complex. The newly formed complex further migrates toward a second anti-*Candida* polyclonal antibody, which is immobilized to the membrane at the test line. This second immunologic interaction will produce a visual signal across the strip because of formation of concentrated colored tags at this position. The presence of this blue line in the test region indicates a positive result, whereas its absence indicates a negative result. To serve as a procedural control, a blue line appears in the control region, located downstream to the test region, indicating a proper function of the test. The excess of the fluid is absorbed by an absorbent pad, located at the distal end of the assay strip (Rapid Lateral Flow Test Strip, 2003). The *Savvycheck* rapid test results were read after 10 and 20 min concomitantly by 2 of the authors (A. Yeshaya and Y. Leshem). The readers of the rapid test were blind to the results of Gram stain and culture, and vice versa.

The study protocol was approved by the institutional review board of Maccabi Health Services, Tel Aviv, Israel (approval no. 2006019).

3. Results

A total of 231 symptomatic patients were included in the study, and the analysis of their results is presented here

Table 1
Results of *Savvycheck* rapid testing compared to culture findings

Savvycheck rapid yeast test	Culture		
	Positive	Negative	Total
Positive	75	5	80
Negative	20	131	151
Total	95	136	231

Sensitivity: 75/95 = 79%; specificity: 131/136 = 96%; accuracy: 206/231 = 89%.
Positive predictive value = 75/80 = 94%; negative predictive value = 131/151 = 87%.

(Tables 1 and 2). Yeast cultures were positive in 95 (41.1%) patients. Yeasts were seen in 75 (34.4%) of the 218 participants with available Gram-stained smears (results were not available for 13 patients). All positive smears were in patients with positive cultures, the positivity rate being 83%. The *Savvycheck* rapid yeast test showed positive results in 80 patients (34.6%). The test was positive in 75 (79%) of 95 patients with positive cultures and in 5 (3.6 %) of 136 patients with negative cultures. Compared to culture, the *Savvycheck* rapid yeast test sensitivity was 79%, specificity was 96%, and accuracy was 89% (Table 1). Of the 72 patients who had positive microscopy, the *Savvycheck* rapid yeast test was positive in 67 patients (93%); the test was positive in 8 (5.5%) of 145 patients with negative microscopy. Compared to microscopy, the *Savvycheck* rapid yeast test showed 93% sensitivity, 95% specificity, and 94% accuracy (Table 2).

4. Discussion

The *Savvycheck* rapid yeast test has demonstrated excellent sensitivity and specificity compared to the Gram stain technique (93% and 95%, respectively). The specificity of the test was also very high when compared to culture (96%), whereas the sensitivity was similar to that of other antigen detection techniques used for various pathogens (~80%) (Huppert et al., 2007; Saison et al., 2007). It should be recognized that the sensitivity of the test compared to culture might be underestimated. Unlike the case of other pathogens, such as *Trichomonas* and *Chlamydia*, for which any positive culture is clinically and therapeutically significant, a positive *Candida* culture is not necessarily clinically relevant because of the relatively high rate of positive cultures in asymptomatic cases for which treatment is not indicated (Sobel et al., 1998).

Table 2
Results of *Savvycheck* rapid testing compared to Gram stain findings

Savvycheck rapid yeast test	Microscope		
	Positive	Negative	Total
Positive	67	8	75
Negative	5	137	142
Total	72	145	217

Sensitivity: 67/72 = 93%; specificity: 137/145 = 95%; accuracy: 204/217 = 94%.
Positive predictive value = 67/75 = 89%; negative predictive value = 137/142 = 97%.

In a previously published study of the same rapid detection kit (Chatwani et al., 2007), the sensitivity of the *Savvycheck* rapid yeast test compared to culture (77.4%) was similar to that in the present evaluation (79%); the specificity, however, was much lower (76.9% versus 96%). The increased specificity observed in the present study is at least partly due to biologic and technical improvements introduced into the kit, such as changes in the conjugate production, and improved reading of the test line and internal control. It should also be noted that, in the other study, the sensitivity and specificity of the wet mount were quite low compared to the Gram stain findings in the present study results (51.6% versus 83% and 89.7% versus 100%, respectively) (Chatwani et al., 2007). It is unlikely that the differences in results were due to the difference in techniques used for direct detection of yeasts (based on unpublished personal experience).

The results of the present study have shown that the *Savvycheck* rapid yeast test performed as well as the microscopic examination of Gram-stained vaginal smear. Gram stain, together with the wet preparation, is considered as the gold standard for rapid diagnosis of vulvovaginal candidiasis (CDC, 2006). Hence, the *Savvycheck* rapid yeast test can serve as a valid substitute of the office microscope for the diagnosis of vulvovaginal candidiasis. The *Savvycheck* rapid yeast test can offer a valuable solution for clinics not using microscopic examination either because of microscope unavailability or lack of microscopic skills. The kit focuses, however, only on the diagnosis of *Candida* infections, leaving unanswered the issue of the 2 other common causes of vaginitis. The diagnostic relevance of bacterial vaginosis and trichomoniasis can be easily clarified using a couple of simple, rapid, and low-cost tests, namely, pH determination and the whiff test (Eckert, 2006). In a woman with vaginitis symptoms, a pH of ≤4.5 and a negative whiff test can rule out the diagnosis of bacterial vaginosis and trichomoniasis with very high probability. However, the *Savvycheck* rapid yeast test may be also used in cases with pH of >4.5, when the diagnosis of bacterial vaginosis and trichomoniasis should be considered, to test for a concomitant *Candida* infection. Several point-of-care tests are available for the diagnosis of bacterial vaginosis and trichomoniasis (QuickVue Advance and OSOM BV Blue for bacterial vaginosis, OSOM for trichomoniasis) (Eckert, 2006).

The *Savvycheck* rapid yeast test, which can be administered either by a health care professional or by the patient herself (Chatwani et al., 2007), does not require sophisticated equipment, is simple to use, and is easy to interpret. The test can be used to identify vaginal *Candida* infection in symptomatic patients during the office visit and thereby

leads to prompt and accurate therapy, saving time, improving compliance, and shortening suffering. The availability of the *Savvycheck* rapid yeast test as an over-the-counter product would allow women to self-diagnose accurately and self-treat correctly, saving many physician office visits and thereby reducing office overload. Hence, the *Savvycheck* rapid yeast test can contribute to health care costs' savings by reducing office visits of women who elect to self-diagnose and self-treat, eliminating office revisits because of initial wrong empiric diagnosis, and avoiding unnecessary fungal cultures. Costs will also be saved by limiting the use of unnecessary or unsuitable drugs by physicians and by self-medicating patients.

The *Savvycheck* rapid yeast test is a promising easy-to-operate tool that can be used by both physicians and patients to correctly diagnose and treat vulvovaginal candidiasis. The test is very useful when no other diagnostic tests is employed, is more accurate than just pH measurement, and could easily be used by every practitioner who knows its limitations (which are similar to those of the microscopic diagnosis). It can decrease unnecessary office visits, cultures, and medication use and, thereby, reduce health care costs.

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