



The role of an over-the-counter vaginal pH self-test device package insert: Can subjects learn what the device is for and how to use it?

S. Roy, MSPH, MD,^{a,*} J. C. Caillouette, MD,^a J. S. Faden, PhD,^b T. Roy, MSPH^c

Obstetrics and Gynecology, Keck School of Medicine of the University of Southern California, Women's and Children's Hospital,^a Los Angeles, CA, US Food and Drug Administration, Washington, DC^b and Regulatory Consultant, Statistical Consultant, Bethel, CT^c

KEY WORDS

Vaginal pH self-test device
Vaginitis
Over-the-counter
Antifungal

Objective: This study was undertaken to determine whether subjects could read and understand the package insert of a vaginal pH self-test device to improve self-diagnostic accuracy.

Study design: This study was performed at 8 clinic locations with 206 women of varying ages, ethnicity, and education. A package insert explaining the indications and clinical facts associated with the use of a vaginal pH self-test device was used. A 16-item questionnaire was administered to assess comprehension.

Results: The cumulative probability of having 12 or more correct answers of 16 was $P = .038$, significantly different than by chance alone, representing 200 (97.1%) of subjects in this trial.

Conclusion: The package insert for the vaginal pH self-test device was read and understood by subjects. Indeed, they correctly understood the role of vaginal pH as an aid in the diagnosis of vaginal symptoms while improving decisions to use an over-the-counter antifungal medication or to see a health care provider.

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Ferris et al¹ recently examined whether consumers who read current over-the-counter (OTC) package inserts for vaginal antifungals make better decisions regarding when to begin therapy compared with those

who did not. They did not find any improvement because of a lack of concordance with a prior history of candidal vulvovaginitis and the current diagnosis. They specifically stated that OTC package inserts “did not prescreen or provide an educational intervention to maximize self-diagnostic accuracy.”² To address this limitation, we wondered if subjects could be educated by having them read an informative and educational package insert for a vaginal pH self-test device. This tool is intended to help them decide which choice to make. Our assumption was that with this information, subjects could make better decisions either to institute therapy with an antifungal medication or to see a health care provider. This report summarizes our findings.

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* Reprint requests: Subir Roy, MD, Department of Obstetrics and Gynecology, Keck School of Medicine of the University of Southern California, Women's and Children's Hospital, 1240 N. Mission Rd, Room L1022, Los Angeles, CA 90033.

E-mail: subirro@usc.edu

Table I Distribution of subjects by investigational site

Investigational site	N of subjects
1	15
2	26
3	20
4	30
5	28
6	40
7	35
8	12
Total	206

Material and methods

This study was conducted under the oversight of the IRB Company, Camino de los Mares, Calif. The questionnaire associated with this study is presented in the Results section of this article and the package insert is provided in [Appendix 1](#).

A questionnaire was developed specific to the package insert. This study was open to all women who attended the 8 clinics. Women were asked to participate as they presented. Each subject was required to read and sign the informed consent before participating in this evaluation. They were asked to read the package insert and complete the questionnaire. All subjects were able to read and understand English. A sample size of approximately 200 was selected to account for the various ethnic, educational, age, and clinic locations from which subjects were selected to be certain that a success rate of 80% for 16 questions was not by chance alone.

The questionnaire results were analyzed with the use of standard statistical methods such as the generation of exact 95% CI around a proportion to determine whether a proportion was different from 0.5 (50%), the likelihood of a correct answer by chance alone, the cumulative probability of correct answers, Fisher exact test (FET), including stepwise logistic regression according to clinic site, age, ethnicity, and educational group with the use of SAS version 8.01 (SAS Institute, Inc, Cary, NC) and Proc-StatXact 4 for SAS (Cytel Software Corp, Cambridge, Mass).

Results

A total of 206 women were enrolled in this study. The distribution of subjects by investigational site is provided in [Table I](#). The demographics of the enrolled subjects are provided in the [Table II](#). The women ranged in age from 17 to 61 years old (average 33.0 years). The study included women with a diversity of ethnic backgrounds. The educational backgrounds of the women were also diverse, ranging from 7 years of formal education to graduate school.

Table II Demographic characteristics of subjects

Demographic characteristic	Value/number of subjects	Percent of subjects
Age (y)*		
Average (n = 205)	33.0	—
Minimum	17	—
Maximum	61	—
No answer given	1	—
Ethnicity		
1. White	31	15%
2. Hispanic	102	50%
3. Black	40	19%
4. Asian American	28	14%
5. Other	5	2%
Years of education (y)†		
7-12 (actual range)	85	41%
12-16	103	50%
> 16 (graduate)	15	7%
No response given	3	1%

* Age: 1 = 15-19; 2 = 20-24; 3 = 25-29; 4 = 30-34; 5 = 35-39; 6 = 40-44; 7 = 45-49; 8 = 50+.

† Education: 1 = 7-11 years; 2 = 12; 3 = 13-15; 4 = 16; 5 = 17+.

The questionnaire included 16 questions about all aspects of the material contained in the package insert. The questions are provided verbatim in [Table III](#), along with the percentage of correct answers given by the women. The correct answers in brackets are provided for clarity. The percentages of correct answers are considered a worse-case value because when no response was given by the subject, it was considered an incorrect answer in the calculation. The number of questions for which a subject gave no answer was small and ranged from 1 to 3, depending on the question, except for 1 subject who did not answer any of the questions.

Except for question 14, at least 87.6% of the responses for any individual question were correct. Question 14 had 64% correct answers (exact 95% CI: 57.1-70.6, which is significantly greater than 50%, $P < .0001$, the expected percent of correct answers by chance alone). The distribution of correct answers and probabilities are shown in [Table IV](#). The cumulative probability of having 12 or more correct answers of 16 was $P = .038$, significantly different from having 8 or 9 correct answers of 16 questions, the number expected by chance alone, representing 200 (97.1%) of subjects in this trial, with 162 (78.7%) of them having either none or only 1 incorrect answer. Only 6 (2.9%) had 5 or more incorrect answers. Three subjects had 5, 1 subject had 6, and 1 subject had 10 incorrect answers. One subject did not attempt to answer any questions and was, by default, considered to have answered all questions incorrectly.

The stepwise logistic regression analysis indicated that the following variables were of greatest importance and should be further tested by pairwise comparisons. Using pairwise comparisons, we observed the following

Table III Questions asked of subjects after reading package insert and percent (%) of subjects providing correct answers*

Questions asked of subject	Percent of correct answers
1 pHEM-ALERT is a device used to test vaginal pH. [correct answer is yes]	99
2 pHEM-ALERT requires insertion of the device into the vagina to moisten the pH paper. [correct answer is yes]	98
3 Normal vaginal pH is 4.5. [correct answer is yes]	99
4 Vaginal pH with a yeast infection alone is usually 4.5. [correct answer is yes]	86
5 Vaginal pH with a bacterial infection is greater than 4.5. [correct answer is yes]	91
6 A health care provider should be consulted if the vaginal pH is 5.0-7.5. [correct answer is yes]	97
7 pHEM-ALERT is intended for women with symptoms of vaginal itching, burning, unpleasant odor, or unusual discharge. [correct answer is yes]	98
8 This test is only for women with normal periodic menstrual bleeding. [correct answer is yes]	88
9 Is pHEM-ALERT a test for HIV, chlamydia, herpes, gonorrhea, syphilis or group B streptococcus? [correct answer is no]	96
10 Should you wait 72 hours after the use of vaginal contraceptive cream or antifungal agents before using the test? [correct answer is yes]	97
11 Should you wait 48 hours after sexual intercourse or douching before using the test? [correct answer is yes]	98
12 Should you wait 5 days after your period is completed before using the test? [correct answer is yes]	99
13 Should you compare the color of the pH paper with the color chart either under a light bulb or in daylight? [correct answer is yes]	99
14 Is more than 30% of vaginal itching due to bacterial infection? [correct answer is yes]	64
15 If vaginal pH is 4.5 with vaginal itching and discharge, is it okay to try anti-yeast medication? [correct answer is yes]	91
16 Should you use the vaginal pH test during your period or if you have medication in your vagina? [correct answer is no]	97

* Correct answers, provided in brackets, were not in the original questionnaire, but are provided here for clarity.

significant findings ($P \leq .05$, by FET permutation adjusted for multiplicity): For question 14, subjects from sites 5 and 7 answered correctly significantly better than those subjects from all other sites. Subjects aged 15 to 19 years were more likely to answer questions 4 and 14 improperly compared with the other ages. Ethnic group 3 gave more incorrect responses compared with group 4 for questions 4 and 14 and compared with group 2 for question 14. Education group 2 gave more incorrect answers compared with education groups 1 and 3 for question 14, whereas education group 3 gave more incorrect answers compared with education group 4 for question 14.

Comment

This study has shown that it is possible to develop an informative and educational package insert for a vaginal

pH self-test device that subjects can read and understand. For example, the common yet mistaken belief is that almost all symptomatic vaginal infections are caused by yeast.³ However, after reading the package insert, the majority of subjects (64%) correctly acknowledged that more than 30% of vaginal itching is due to bacterial infections, significantly greater than 50%, the expected percent of correct answers by chance alone. Although there were statistically significant differences in correct responses on the basis of site, age, ethnicity, and education for questions 4 and 14, overall, these did not result in clinical significance because the correct responses for all groups was significantly greater than 50%. Except for the single question above, subjects were able to assimilate and respond correctly to the majority of questions (ie, with >87.6% correct answers) and nearly all the subjects gave correct answers. Indeed, 200 subjects (97.1%) gave correct answers to at least three

Table IV Distribution and binomial probabilities of questions answered correctly

Obs	P^*	N^\dagger	x^\ddagger	$Pdfb^\S$	$Cdfb^\parallel$	N^\natural	$Pct^\#$
1	.5	16	16	0.000015	0.000015	97	47.1
2	.5	16	15	0.000244	0.000259	65	31.6
3	.5	16	14	0.001831	0.002090	19	9.2
4	.5	16	13	0.008545	0.010635	15	7.3
5	.5	16	12	0.027771	0.038406	4	1.9
6	.5	16	11	0.066650	0.105057	3	1.5
7	.5	16	10	0.122192	0.227249	1	0.5
8	.5	16	9	0.174561	0.401810	0	0.0
9	.5	16	8	0.196381	0.598190	0	0.0
10	.5	16	7	0.174561	0.772751	0	0.0
11	.5	16	6	0.122192	0.894943	1	0.5
12	.5	16	5	0.066650	0.961594	0	0.0
13	.5	16	4	0.027771	0.989365	0	0.0
14	.5	16	3	0.008545	0.997910	0	0.0
15	.5	16	2	0.001831	0.999741	0	0.0
16	.5	16	1	0.000244	0.999985	0	0.0
17	.5	16	0	0.000015	1.000000	1	0.5

* Probability of success by chance alone.

† Number of questions.

‡ Number of correct answers.

§ Probability distribution function for binomial, $Pdfb$, is the probability of x successes in n questions

($Pdfb = [n!/(x!(n-x)!)](p^x)[(1-p)^{(n-x)}]$).

|| Cumulative distribution function for binomial, $Cdfb$, is the cumulative binomial probability with probability of success per questions of p .

¶ The number of subjects with x (correct answers) corresponding to the pct of subjects.

Percentage of subjects (pct).

quarters of the questions, mostly with none or a single incorrect answer, significantly better than the number expected by chance alone. This demonstrates a remarkable degree of educational success. In a companion study,⁴ subjects complaining of symptoms of vaginal infections demonstrated that they could read the package insert, use this device, and obtain the same pH readings as health care providers. Furthermore, if the vaginal pH was less than 4.5, they could reduce inappropriate use of OTC antifungal preparations by greater than 50%. Last, if the vaginal pH was greater than 4.5, they would see a health care provider for proper evaluation and therapy. On the basis of these 2 studies, clinicians should educate patients in the use of this tool to improve decisions regarding their vaginal health.

(The US Food and Drug Administration [FDA] cleared use of the OTC vaginal pH self-test device and the package insert in October 2001 because of the following factors: First, a clinical study demonstrated the validity of the vaginal pH self-test device.⁴ Second, the questions that the FDA raised for an OTC device were answered. Third, the use of the vaginal pH self-test device is substantially equivalent to the professional version already approved for use. The OTC vaginal pH self-test device is currently marketed as pHEM-ALERT, distributed by GYNEX, 2719 152nd Ave NE, Redmond, Wash. It is comprised of a plastic probe with pH paper on one end, a color chart, and a package insert. The pH paper calibration used indicates ≤ 4.5 in vivid

yellow with a clear shift from light, medium, and dark olive to light and dark blue to indigo as the pH increases in increments of 0.5 from <4.5 -7.5.)

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Editor's note: This manuscript was revised after these discussions were presented.

Discussion

DR DURLIN HICKOK, Seattle, Wash. Vaginitis is one of the most common problems in clinical medicine and the reason cited most often for visits to obstetricians and gynecologists. Aside from discomfort associated with the symptoms and potential of infection of a sexual partner, the organisms associated with vaginitis are associated with a number of other risks. In nonpregnant women, vaginitis is linked with posthysterectomy vaginal cuff cellulitis, plasma cell endometritis, and postabortion pelvic inflammatory disease. Pregnancy-associated complications from bacterial vaginal infections may include premature rupture of membranes, preterm delivery, and postpartum endometritis.

Traditional evaluation for differentiating the common causes of vaginal infection includes both visual examination and laboratory procedures. These include determination of vaginal pH, detection of a fishy odor on adding 10% potassium hydroxide, and microscopic examination of vaginal fluid. This approach has several potential shortcomings. First, many time-pressed physicians attempt to make a diagnosis on the basis of symptoms alone or solely from a wet mount. Second, many elements of the process are quite subjective, especially the assessment of vaginal amines.

The FDA has cleared several diagnostic devices as an aid to, or in some cases, an alternative to traditional methods for evaluation vaginal symptoms. Some of these are designed for professional use in the office, and other are sold OTC. Most test kits are based on a visual colorimetric reaction reflecting the pH of vaginal secretions. Ordinarily, vaginal secretions have a pH of less than 4.5, but this value may be elevated in the presence of abnormal conditions. Some test kits available on the market also incorporate detection of trimethylamines or proline iminopeptidase activity that may be present with bacterial vaginosis. A vaginal pH of greater than 4.5, especially when combined with evidence of vaginal amines, is highly predictive of bacterial vaginosis. In contrast, vaginal infections caused by *Candida* species are likely to be associated with a pH of less than 4.5.

Dr Roy and his coauthors performed this study in response to information suggesting that consumers who read standard OTC package inserts for antifungal medications do not make better decisions regarding when to begin therapy compared with those who did not. The purpose of their investigation was to determine whether consumers could be educated by reading an informative package insert for a vaginal pH self-test device. The implication is that women should be able to use this information to make better decisions whether to

institute therapy on their own or to seek testing and advice from a health care provider.

The pHEM-ALERT pH self-test device used in this study has a package insert explaining the indications and use of the vaginal self-test device. In addition, the OTC insert for this product has a Questions and Answers section for consumers to further explain this content. The authors designed a study questionnaire to address a subject's knowledge of information contained in the package insert. The questionnaire was composed of 16 yes or no responses. This tool was administered to 206 women of varying age, ethnicity, and educational attainment from 8 study sites. The proportion of correct answers to specific questions ranged from 64% to 99%, and 78.7% of study participants either answered all questions correctly or had only 1 error. Thus, the authors concluded that the subject of this study correctly understood the role of vaginal pH as an aid in the diagnosis of vaginal symptoms.

I would like to commend the authors for their investigation into an aspect of patient education that is often overlooked or not given the attention that it deserves. As health care providers we assume that our advice, as well as that given by producers of medical devices and tests, is always understood by our patients—this is clearly not always so. This study demonstrates that the addition of educational information in a package insert for a vaginal pH self test device results in a high degree of knowledge regarding the use of the test.

I have the following questions for Dr Roy:

1. Are you aware of studies examining potential cost saving from an algorithm using self-testing as the first step in diagnosis and treatment of symptoms suggestive of vaginitis?
2. Are there advantages or disadvantages from the addition of a measure for the presence of amines?

DR EMMET LAMB, Palm Desert, Calif. Your statistical analysis is based on the premise that the controls are equivalent to a coin toss, a 50/50 chance of a “yes” or “no” answer. Have you any data on how patients who had not read the package insert answered the questions? Is the 50/50 estimate a good one or should you test against some other proportion?

DR PAUL KAPLAN, Eugene, Ore. Did you pay the women who completed the questionnaire or compensate them in some way? I ask this as I am wondering if you can definitely generalize your results to all women. I raise this question because I am notorious for purchasing something and trying to figure it out without reading the instructions.

DR HEDRIC HANSON, Anchorage, Alaska. Is this product approved for use in pregnancy? Regarding the design of the product, Dr Eric Saling, the Professor Emeritus from the Free University in Berlin, developed a product that had an insertion device for determining