นิพนธ์ต้นฉบับ
Original Article

ความไวของการตรวจด้วยวิธีตินเพร๊พโดยใช้ผ้าอนามัยแบบสอดเพื่อเก็บเซลล์จากช่องคลอดในสตรีที่มีผลแป๊ปสเมียร์ผิดปกติ

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บทคัดย่อ

การวิจัยนี้มีจุดประสงค์เพื่อศึกษาถึงความไวของการตรวจด้วยวิธีตินเพร๊พโดยใช้ผ้าอนามัยแบบสอดเพื่อเก็บเซลล์จากช่องคลอดในสตรีที่มีผลแป๊ปสเมียร์ผิดปกติ โดยเปรียบเทียบกับการตรวจทางพยาธิวิทยา และมีรูปแบบการศึกษาคือ แบบทดสอบวินิจฉัย ทำการศึกษาในสตรีจำนวน 81 รายที่มีผลการวินิจฉัยทางเซลล์วิทยาที่ได้จากการตรวจด้วยแป๊ปสเมียร์ผิดปกติภายใน 6 เดือน และมีแผนการที่จะวินิจฉัยทางพยาธิวิทยาที่คลินิคส่องกล้องบริเวณปากมดลูก โรงพยาบาลรามาธิบดี ช่วงเดือน กันยายน พ.ศ. 2552 ถึงพฤษภาคม พ.ศ. 2553 โดยผู้เข้าร่วมวิจัยสอดผ้าอนามัยแบบสอดด้วยตนเองก่อนที่จะรับการส่องกล้องบริเวณปากมดลูก ผู้วิจัยดึงผ้าอนามัยแบบสอดออกให้ นำไปแกว่งในสารละลายแล้วจึงส่งตรวจด้วยวิธีตินเพร๊พ ผลทางเซลล์วิทยาจากการตรวจด้วยวิธีตินเพร๊พจะนำไปเปรียบเทียบกับผลทางพยาธิวิทยาภายใน 3 เดือน

ผลการวิจัยพบว่า การตรวจด้วยวิธีตินเพร๊พโดยใช้ผ้าอนามัยแบบสอดเพื่อเก็บเซลล์จากช่องคลอดในสตรีที่มีผลแป๊ปสเมียร์ผิดปกติได้ผลดังนี้ sensitivity 35.1%, specificity 87.5%, PPV 86.9% , NPV 36.2% ความไวในการตรวจพบเฉพาะ CIN 3 ด้วยวิธีตินเพร๊พเท่ากับ 50% และความพอเพียงของสิ่งส่งตรวจเท่ากับ 67%

การตรวจด้วยวิธีตินเพร๊พโดยใช้ผ้าอนามัยแบบสอดเพื่อเก็บเซลล์จากช่องคลอดอาจเป็นอีกทางเลือกหนึ่งของการตรวจเซลล์ผิดปกติที่ปากมดลูกในสตรีที่มีผลแป๊ปสเมียร์ผิดปกติ การศึกษาเพิ่มเติมในอนาคตการนำวิธีนี้มาใช้ในการตรวจติดตามในสตรีที่มีพยาธิสภาพของปากมดลูกภายหลังการตรวจส่องกล้องคอลโปสโคปน่าจะเป็นที่น่าสนใจ

คำสำคัญ : มะเร็งปากมดลูก, การตรวจคัดกรองมะเร็งปากมดูกโดยใช้ pap smear, เซลล์วิทยา, ผ้าอนามัยแบบสอด, ตินเพร๊พ

Sensitivity of ThinPrep Test by Self-collected Vaginal Tampon in Women with Abnormal Pap Smear

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Abstract

The purpose of this study was to compare the sensitivity of the ThinPrep test by self-collected vaginal tampon for cervical cytology in women with abnormal Pap smears and their pathological diagnosis. The study design was a diagnostic test. Eighty-one women with abnormal results of Pap smear within the previous 6 months were recruited from the colposcopy clinic of Department of Obstetrics and Gynaecology, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand from September 2009 to May 2010.

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Participants inserted a vaginal tampon on the morning and removed it before a colposcopic examination on the afternoon. Vaginal tampons were then immersed into a vial of ThinPrep Presrv-Cyt solution and sent to a cytopathologist for analysis. Results were compared to the final pathological diagnosis. Outcomes of the ThinPrep test by self-collected vaginal tampon detecting any abnormalities (ASC-US, ASC-H, LSIL, HSIL, SCC, AGC, AGC-FN, AIS, Adenocarcinoma) compared to final pathological diagnosis.

The ThinPrep test with self-collected vaginal tampon detected abnormalities with the sensitivity of 35.1%, specificity of 87.5%, PPV of 86.9% and NPV of 36.2%. The sensitivity of our ThinPrep test to specifically diagnose CIN 3 was 50% when compared to the final pathological diagnosis. The adequacy of specimens for diagnosis with our ThinPrep test was 67%.

The ThinPrep test obtained by self-collected vaginal tampon was an alternative method for detection of abnormal cytology in women with abnormal Pap smear. Further studying of this technique as a follow-up method for women with abnormal cervical pathology after colposcopy evaluation would be interesting.

Keywords : Cervical cancer, conventional Pap smear, cytology, self- collected vaginal tampon, ThinPrep

Introduction

Cervical cancer is the second most common malignancy among Thai women and all over the world. It causes the death of 270,000 women per year[1]. Eighty percent of cervical cancer patients were found in developing countries. The number and incidence of death from cervical cancer was 2,195 women and 6.6 per 100,000 women, respectively, in Thailand during the year 2015[2]. Therefore, the estimated seven women die from cervical cancer each day in Thailand[1]. Cervical cancer was also the second most common cancer in the women approximately 16.7% in Ramathibodi Hospital in 2008[3]. Cervical cancer is preventable by early detection of a pre-cancerous lesion using Pap smear screening. A household survey conducted in Band PA-IN, Ayutthaya Province of Thailand in 1990-1991 (unpublished data) showed only 31.5% of women had ever had a conventional Pap smear. The factors for lack of performing Pap smear included poverty, lack of availability of health service, fear, embarrassment, and inconvenience to do the test.

A self-collected cytologic evaluation would be the alternative procedure to increase the number of cervical cancer screening. The advantages of self-collected samples are not only convenient for patients but it also reduces the needs for speculum examination. Self-collected vaginal tampons are reported that they are beneficial to the diagnosis of sexually transmitted infections such as gonorrhea, human papillomavirus, chlamydia and trichomonas[4-6].

The ThinPrep test decreases the presence of obscuring material including blood and mucus by dispersing cervical cytology specimens in a liquid suspension and subsequently centrifuge then pass through a filter[7]. The ThinPrep test tends to be more sensitive and specific than conventional Pap smear for detecting cervical dysplasia[8].

Although the self-administered tampon ThinPrep method would not be as good as Pap smear for detecting cervical abnormalities, it is a highly acceptable method for women[9]. The objective of this study was to assess the sensitivity of ThinPrep test obtained by self-collected vaginal tampon specimen for cervical cytology in women with abnormal Pap smear compared to the pathological diagnosis aiming to develop it as an alternative method for detecting cervical cytological abnormalities.

Material and Method

This study was approved by the Ethical Clearance Committee of the Faculty of Medicine, Ramathibodi Hospital, Mahidol University. Written informed consent was obtained from each participant. The cross-sectional study was performed at the colposcopic clinic of the Department of Obstetrics and Gynaecology, Faculty of Medicine, Ramathibodi Hospital, Mahidol University between September 2009 and May 2010.

Sample size was calculated, using alpha = 0.05, beta = 0.80 and the expected sensitivity of 0.8. The at least number of 77 cases was required. Eighty-one women with abnormal results of conventional Pap smear within the previous 6 months were recruited from the colposcopy clinic. Participants inserted a regular Jonson & Jonson tampon (O.B. Procomfort®, Austria) into their vagina on the morning and the tampon was then removed when performing colposcopic examination on the afternoon of the same day. The tampon was immersed it into a vial of ThinPrep Preserv-Cyt solution (Cytyc Corporation®, USA) and sent for analysis by a cyto-pathologist. The acceptability of self-collected vaginal tampon and the conventional Pap smear were evaluated before performing the colposcopy.

Women with abnormal results of conventional Pap smear were referred for colposcopic examination and pathological diagnosis including cervical biopsy, cervical conization e.g. large loop excision of transformation zone (LLETZ) or cold knife conization (CKC) if necessary by oncologic staff. Outcomes of ThinPrep test by self-collected vaginal tampon were compared to final pathological diagnosis.

Statistical analysis

All analysis was conducted using the Stata V11.0 (License number 40110514869). The data was presented as sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV). Performance for each variable was calculated as the following: performance = sensitivity + specificity -100. Pearson Chi-Square test was used for statistical analysis. $P < 0.05$ and 95% confidence intervals (CI), were the value regarded as statistically significant.

Results

The characteristics for the 81 women were summarized in Table 1. The median age was 43 years (ranged from 18 to 75 years) and BMI was 22.8 kg/m^2 (ranged from 15.7 to 33.6 kg/m^2). The median age at first sexual intercourse was 21 years old (ranged from 15 to 31 years). 74% had received the education above high school. In addition, 70% of the participants had multiparity, 34.5% and 6.2% revealed having multi-sexual partners and ever used a vaginal tampon, respectively.

Table 1 Participant Characteristics

Characteristics	Results (N=81)
Age (years), median (range)	43 (18-75)
BMI (kg/m2), median (range)	22.8 (15.7-33.6)
Age at first intercourse (years), median (range)	21 (15-31)
Education, n (%)	
None	4 (4.9)
Primary school	17 (21.0)
High school	26 (32.1)
Bachelor's degree	28 (34.6)
Postgraduate	6 (7.4)
Parity, n (%)	
0	24 (29.6)
1	19 (23.5)
2	29 (53.8)
≥ 3	9 (11.1)
Lifetime number of sexual partners, n (%)	
1	53 (65.5)
2	19 (23.5)
3	7 (8.6)
≥ 4	2 (2.4)
History of vaginal tampon used	5 (6.2)
Detail of abnormal conventional Pap smear	
ASC-US	51 (63.0)
ASC-H	5 (6.2)
AGC	3 (3.7)
LSIL	10 (12.3)
HSIL	12 (14.8)

BMI = body mass index, ASC-US=atypical squamous cells of undetermined significance, ASC-H=atypical squamous cells, cannot exclude HSIL, AGC=atypical glandular cells, LSIL=low-grade squamous intraepithelial lesion, HSIL= high-grade squamous intraepithelial lesion

The comparison of results of the ThinPrep test obtained by self-collected vaginal tampon and pathological diagnosis was shown in Table 2. Twenty-eight percents (23 to 81) had an abnormality on the ThinPrep test obtained by self-collected vaginal tampon (1 for ASC-US, 1 for ASC-H, 1 for AGC, 6 for LSIL and 14 for HSIL). Seventy percent (57 to 81) had final abnormal pathology (29 for CIN 1, 12 for CIN 2, 14 for CIN 3 and 2 for invasive cervical cancer).

Table 2 Results of ThinPrep test by self-collected vaginal tampon

Results of ThinPrep test by self-collected vaginal tampon	Final pathological diagnosis (n, % of total)					
	Negative (24)	CIN 1 (29)	CIN 2 (12)	CIN 3 (14)	Invasive cancer (2)	Total (n=81)
Negative	21 (12.3%)	26 (32%)	5 (6.1%)	4 (4.9%)	2 (2.4%)	58 (71.7%)
ASC-US	0	0	1 (1.2%)	0	0	1 (1.2%)
ASC-H	0	0	0	1 (1.2%)	0	1 (1.2%)
AGC	1 (1.2%)	0	0	0	0	1 (1.2%)
LSIL	2 (2.5%)	2 (2.5%)	1 (1.2%)	1 (1.2%)	0	6 (7.4%)
HSIL	0	1 (1.2%)	5 (6.2%)	8 (9.9%)	0	14 (17.3%)

CIN=cervical intraepithelial neoplasia, ASC-US=atypical squamous cells of undetermined significance, ASC-H=atypical squamous cells, cannot exclude HSIL, AGC=atypical glandular cells, LSIL=low-grade squamous intraepithelial lesion, HSIL= high-grade squamous intraepithelial lesion

The ThinPrep test obtained by self-collected vaginal tampon could detect abnormal cytology agree with pathological diagnosis 35.1% which was greater than 12.5% in the abnormal cytology disagree with pathological diagnosis group (p=0.04). Nevertheless, the ThinPrep test obtained by self-collected vaginal tampon could not detect two cases of invasive cervical cancer.

The sensitivity, specificity, PPV and NPV for the ThinPrep test obtained by self-collected vaginal tampon for detection all abnormal pathology, both pre-invasive and invasive, were 35.1, 87.5, 86.9 and 36.2%, respectively. (Table 3) For the final pathological diagnosis of CIN 3 the sensitivity was 50% which was higher than other groups.

Table 3 Diagnostics characteristics of ThinPrep test by self-collected vaginal tampon compared to the pathological diagnosis

Outcomes	Sensitivity	Specificity	PPV	NPV	Performance*
ASC-US	NA	98.7	NA	100.0	NA
ASC-H	NA	98.7	NA	100.0	NA
AGC	NA	98.7	NA	100.0	NA
LSIL	6.9	92	33.3	64.0	-1.1
HSIL	50.0	98.1	92.8	80.5	48.1
Total	35.1	87.5	86.9	36.2	22.6
(95% CI)	(24.7-45.5)	(80.3-94.7)	(79.6-94.2)	(25.7-46.7)	

ASC-US=atypical squamous cells of undetermined significance, ASC-H=atypical squamous cells, cannot exclude HSIL, AGC=atypical glandular cells, LSIL=low-grade squamous intraepithelial lesion, HSIL= high-grade squamous intraepithelial lesion, 95%CI=95% confidence interval, PPV=positive predictive value, NPV=negative predictive value

*Performance = Sensitivity + specificity -100

Satisfactory cytologic evaluation defined as a positive endocervical cell of self-collected vaginal tampon samples was 67%. All of the results of the ThinPrep test obtained by the self-collected vaginal tampon in the unsatisfactory group (27 cases) was normal whereas the abnormal pathology in this group was found 52% (14 of 27 cases; 6 cases for CIN 1, 5 cases for CIN 2 and 3 cases for CIN 3).

The median time of the vaginal tampon collection, duration from insertion of the tampon until removal, in the satisfactory and unsatisfactory specimen group revealed 5.52 and 5.89 hours which were not statistically significant different. (p=0.4)

Data from the questionnaire about acceptability for the self-collected vaginal tampon and the conventional Pap smear showed 38% of all women preferred the self-collected vaginal tampon, 18% of those decided to receive performing the conventional Pap smear and 44% of those refused evaluation by both tests. The advantages of the self-collected vaginal tampon were feeling of more comfortable, easier to perform, and less painful than performing pelvic examination for Pap smear. However, the participants concerned the effectiveness of the method because they were not sure whether they performed the self-collected vaginal tampon correctly. Women who preferred the conventional Pap smear provided the reason that it was the most reliable test. Moreover, they felt more confident when getting pelvic examination by a health provider thoroughly.

Discussion

Cervical cancer is preventable by early detection and treatment of the precancerous lesion. Previous data revealed that Pap smear screening test can prevent up to 90% of cervical squamous cell carcinoma cases[8]. However, conventional Pap smear screening tests could not reach the target of preventing cervical cancer in Thai women population, although almost all of them have adequate knowledge regarding cervical cancer.

The adequacy of specimens in the conventional Pap smear was 89% and the ThinPrep method was 96.7%[10]. Reowchotsakul et al. studied cytologic evaluation of smears obtained by the self-collected vaginal tampon. The quantity of cells for adequacy evaluation was 96%. They suggested that self-collected vaginal tampon might detect cytological abnormalities[11]. Nevertheless, the satisfactory cytologic evaluation in this study was only 67%, and the false negative from the self-collected vaginal tampon showed 45.4%. The high false negative rate would be from the absorption of some epithelial cells to tampon when it immersed into a vial ThinPrep Preserv-Cyt solution. An inherent problem with a self-collected vaginal tampon was an improper place of a tampon in the vagina causing an insufficient amount of cells shed from a cervix. For the duration of the tampon collection after vaginal insertion in the present study was less than the one in the other study but it was not significantly different between the satisfactory and unsatisfactory specimen groups. Therefore, the adequacy of specimens seems not correlate with duration of the vaginal tampon collection.

There were still some debates whether the presence of HSIL and/or the absence of endocervical cells contributes to the inadequacy of the sample. Selvaggi et al. showed in their retrospective study that there was no statistically significant difference in the detection of the HSIL in the ThinPrep samples comparing between the ones with and without the endocervical component[12].

This is the first study in Thailand which compares the efficacy of the ThinPrep test obtained by self-collected vaginal tampon to the pathological diagnosis. The sensitivity of ThinPrep test after previously abnormal Pap smears varied in many studies[13,14]. In our study the sensitivity for detection all abnormal pathology was 35.1% which was lower than the other studies. It may be explained by the error during collection of vaginal epithelial cells.

The results from the present study showed that the sensitivity of ThinPrep test obtained by self-collected vaginal tampon for ASC-US, ASC-H and AGC cannot be evaluated. The reason would be due to the small sample size in this group. The sensitivity and performance for HSIL was 50% and 48.1 which was found higher than the other groups. This method seems to be a good detector for high-grade abnormalities.

Importantly, the ThinPrep test obtained by self-collected vaginal tampon could not detect two cases of invasive cervical cancer while the result of conventional Pap smear from 2 cases demonstrated HSIL. However several recent meta-analyses have reported moderate to low Pap smear sensitivity in the range of 50%, or even as low as 20%[15]. The conventional Pap smear had a sensitivity of 44% and specificity of 91% for detecting HSIL[16]. Therefore, the conventional Pap smear had a high rate of false negative and reflecting that women must be screened frequently the same as the self-collected vaginal tampon. It was not the best cervical cancer screening method, a limitation of this method. Moreover, the cervical mucosa can be evaluated simultaneously while performing Pap smear by physicians.

Bugde et al. showed that the self-collected tampon test is more acceptable than the traditional doctor pelvic examination-approach Pap smear for women. Studying about the concern of women's attitudes to conventional Pap smear demonstrated 64% of women found it to be an unacceptable method for screening. It was uncomfortable, embarrassing or an invasion of their privacy[9]. Regarding acceptability for the self-collected vaginal tampon, the women in the present study preferred the ThinPrep test obtained by self-collected vaginal tampon to the conventional Pap smear only 38%. The acceptability for the self-collected vaginal tampon was lower than the one from Budge et al. The women provided the information that because it was a new method and lack of the accuracy of the data.

The present study evaluated the efficacy of ThinPrep test obtained by the self-collected vaginal tampon in women with abnormal Pap smear. From our result, the method would be a useful alternative for detection of abnormal cytology in women with the abnormal Pap smear. The limitation of the self-collected tampon for the ThinPrep test in our study would be 1) an obstacle to using it as a screening test 2) the cost of the whole procedure would be more expensive than conventional Pap smear. However, it would be a benefit for follow up in case patients had inadequate negative free margin from colposcopy. More research should be conducted with a large sample size for using the self-collected vaginal tampon as a follow-up tool and with other materials for the self-collected vaginal epithelial cell.

However, the self-collected vaginal tampon may be an alternative method for women who do not accept for the conventional doctor-administered Pap smear and in rural setting where lack of cervical cancer screening teams.

Conclusion

The results showed that the ThinPrep test obtained by self-collected vaginal tampon was an alternative method for detection of abnormal cytology in women with the abnormal Pap smear. Further study focusing on the role of the self-collected vaginal tampon with the ThinPrep as a follow-up method should be performed.

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Declaration of interest statement

The authors declare that there is no conflict of interest in this research.

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