Int J Gynecol Cancer 2005, **15,** 489–492

Can we substitute brush cytology for biopsy in the evaluation of cervical lesions under the guidance of colposcopy?

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Abstract. Eftekhar Z, Izadi-Mood N, Yarandi F, Khodamoradi M, Rahimi-Moghaddam P. Can we substitute brush cytology for biopsy in the evaluation of cervical lesions under the guidance of colposcopy? *Int J Gynecol Cancer* 2005;**15:**489–492.

In cervical cancer screening, colposcopically directed biopsy is the gold standard method for identifying intraepithelial and occult invasive lesions of the uterine cervix. As biopsy needs special expertise and the procedure is not convenient for the patients, we sought to evaluate colposcopically directed brush cytology as a substitute for biopsy of cervical lesions. We studied a series of 150 women who were referred for colposcopic evaluation. Colposcopically directed brush cytology and biopsy were performed for all patients with abnormal colposcopic findings. A total of 40 samples were excluded due to unsatisfactory report of brush cytology. Of the remaining 110 samples, 34 abnormal pathologies were reported in biopsy evaluations, while only 9 abnormal cytologies were reported in brush cytology specimens. Brush cytology sensitivity and specificity were 26% and 97%, respectively. We conclude that colposcopically directed brush cytology is not a safe substitute for biopsy in the evaluation of cervical lesions.

KEYWORDS: biopsy, brush cytology, cervical screening test, colposcopy.

Cervical cancer is the second most common neoplastic disease among women[1]. An effective and convenient cancer screening followed by early, appropriate treatment could reduce cancer-associated death in women. In colposcopically abnormal findings suspected to be dysplastic, biopsy is the only test to confirm or rule out premalignant or malignant lesions. Many patients are reluctant to undergo the test because of biopsy complications such as bleeding, abdominal pain, and vaginal infection. Also, the preparation of samples needs specific time, expertise, and facilities. Therefore, economically biopsy is a costly test for both patients and health systems. A study has shown that biopsy could be safely substituted by brush cytology in pregnant women[2]. A good number of endocervical cells could be obtained by endocervical brushing[3]. In this study, we evaluated the potential use of colposcopically directed brush cytology instead of biopsy for detection of dysplasia.

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Materials and methods

The study population consisted of 150 women referred to the colposcopy center at Mirza Koochak Khan Hospital from January 2000 to January 2001. The reasons for reference to the center were abnormal Pap smear test, abnormal appearance of cervix observed with the naked eye, postcoital bleeding, or follow-up for previously diagnosed dysplastic lesion. Ethically, informed consent, privacy, and confidentiality were observed based on the Ethical Committee in the Tehran University of Medical Sciences, Iran. Before the screening procedure, information about age, marriage status, pregnancies, labors, abortions, live children, history of smoking, vaginal discharge, and contraception method were obtained. All examinations and biopsies were done by one expert (Z.E.). For each sampling, the patient was placed in the lithotomy position and a speculum was inserted into the vagina. If the patient had not undergone Pap smear for the last 2 months, a Pap smear was obtained. Then, a 3–5% acetic acid solution was applied to the cervicovaginal surface to visualize any evidence of dysplasia with the naked eye[4,5]. After concise visualization of squamocolumnar junction (transitional zone), total area of transformation zone was carefully observed. In the case of observation of any abnormal vessel, leukoplakia, or acetowhite lesion, a brush cytology specimen was collected from that site, using a single Cytobrush (Medscand, Malmö, Sweden). To expose a larger surface of Cytobrush swab to the selected site, the Cytobrush was bent 45° (Fig. 1). Then, each specimen was obtained by scraping back and forth across the area several times. The sample was spread onto a glass slide, which then was placed in 95% ethanol fixative. Then, a cervical biopsy was performed at the same area of lesion. All brush cytology and biopsy samples were evaluated by one expert pathologist (N.I-M.) and reported according to the 2001 Bethesda System[6] and Modified Richart Classification[7], respectively.

Based on the pathologic findings, the results were divided into three subgroups: a) no change or some reactive changes, namely atypical squamous cells of undetermined significance; b) cervical intraepithelial neoplasia (CIN) grade I in biopsy samples or low-grade squamous intraepithelial lesion in brush samples; and c) CIN-II and CIN-III or high-grade squamous intraepithelial lesion.

Statistical evaluations included analyses of sensitivity and specificity (with 95% confidence interval [$CI_{95\%}$]) and the kappa statistic using SPSS Software, Version 9.0.

Results

Of the 150 women who were screened, 150 sample pairs of brush cytology and biopsy were prepared. Forty samples were excluded from the study because of inadequate sample size due to obscuring blood in brush cytology samples, leaving 110 samples pairs for analyses. Based on Bethesda System classification(6), 40 samples were unsatisfactory for evaluation because more than 75% of smear surface was covered by blood, and among observable cells, no abnormal cell was seen. The high number of unsatisfactory slides might be due to use of the conventional method for smear preparation, as in this method removal of blood was not possible.

Based on the demographic data, the patients were between 20 and 66 years of age (38.5 ± 9.4). Only 4.5% of patients had never been pregnant. Seventy-three patients (66.4%) did not mention any history of cervical dysplasia. Seventeen patients (15.5%) had unsatisfactory colposcopy.

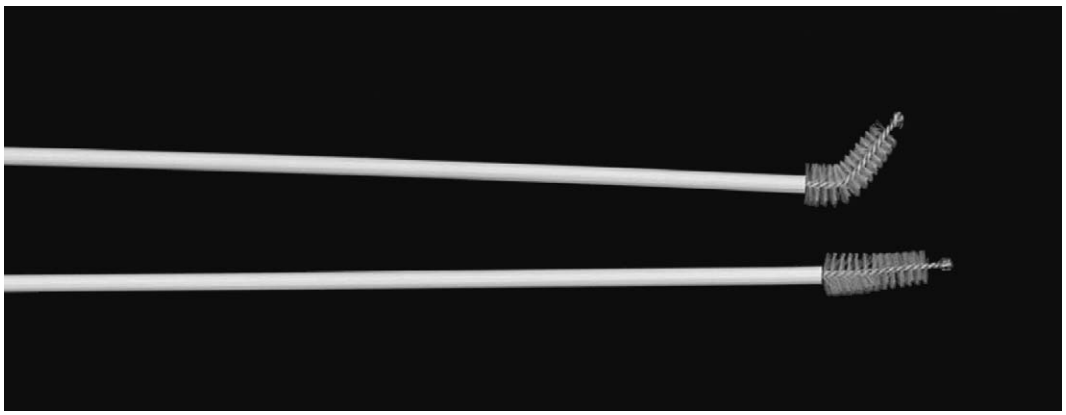

Figure 1. The straight cytobrush (the lower one) is bent about 45° (the upper one) to expose more brushing surface to the site of sampling.

Table 1 compares the test results obtained by brush and biopsy techniques. Among 110 biopsied samples, 32 showed low-grade CIN-I and 2 were identified as high-grade CIN-II and CIN-III based on the Modified Richart Classification[7]. The directed brush cytology demonstrated relatively poor agreement with the corresponding biopsy ($\kappa = 0.29$) as it detected both cases of high-grade squamous intraepithelial lesion (CIN-II and CIN-III), but only seven cases of low-grade squamous intraepithelial lesion (CIN-I). Overall brush cytology identified 9 of 34 biopsy-proved dysplasia, therefore, the sensitivity of directed brush cytology was 26% ($CI_{95\%} = 13.5–44.7$), while its specificity was 97.4% ($CI_{95\%} = 90–99.5$) with an accuracy rate of 75.5%.

Discussion

Cervical cancer screening in less-developed countries is based on annual Pap smears. When Pap smears show abnormal cervical cytology, the next step is biopsy, which is usually a costly procedure that causes discomfort for patients. In one study, Lieberman *et al.* showed that in pregnant women brush cytology could be used as a substitute for biopsy[2]. The brush cytology technique is much easier to perform than biopsy. Also, there are fewer complications such as bleeding and abdominal cramps.

In obtaining samples for cervical smears, brushing is an efficient cell-collecting device[8–10]. Also, endocervical cytobrush sampling was proved to be a suitable procedure in the detection of intraepithelial neoplastic lesions[11]. Also, it has been demonstrated that brush cytology shows a safe adjunct to the colposcopic evaluation when endocervical curettage is not possible[3,12]. Brush cytology has been used in the screening procedures of some other neoplastic lesions such as nasopharyngeal carcinoma, gastric malignancy, pancreas cancer, and lung tumors[13–16].

Based on the apparent usefulness of brush cytology in the early diagnosis of CIN, we compared the test results of colposcopically directed brush cytology to that of biopsy as the gold standard test. The brush cytology confirmed 9 of 34 specimens with dysplasia proved in biopsy (26% sensitivity). Brush cytology confirmed both high-grade preneoplastic lesions, similar to that observed by Lieberman *et al.* in their studies[2]. This may be due to the presence of more exfoliated abnormal cells in the area of sampling as dysplastic cells tend to detach from each other.

Overall, our results show that cytobrush is not a safe substitute for biopsy. The sensitivity of brush cytology (26%) is much lower than that (86%) of the study by Lieberman *et al.*[2]. This might be due to the fact that they did their study on pregnant women, while none of our patients were pregnant. In pregnancy, the cervical cellularity increases. This may lead to better and easier sampling by brushing. Further studies on larger patient populations may show usefulness of brush cytology in evaluation of cervical dysplasia. As we did not have the sample size in mind when we planned the study, this study can be considered a pilot study. Some confounding factors might be ignored in the present work such as limitation of the study to one specific group. Also, use of thin-PREP instead of conventional smears may improve the accuracy of our test result as several studies in recent years declare a significant improvement in sensitivity of disease detection using thin-layer preparations as compared to the conventional Pap smears[17–20].

Table 1. Comparison of biopsy and brush diagnosis

	Biopsy diagnosis in 110 samples[a]		
Brush diagnosis in 110 samples[a]	Normal-ASCUS	CIN-I (LSIL)	CIN-II and III-II (HSIL)
Normal-ASCUS	76	25	0
LSIL (CIN-I)	0	7	0
HSIL (CIN-II and CIN-III)	0	0	2

ASCUS, atypical squamous cells of undetermined significance; CIN, cervical intraepithelial neoplasia; LSIL, low-grade squamous intraepithelial lesion; HSIL, high-grade squamous intraepithelial lesion.

[a]Of the 150 specimens, 40 samples were excluded because of unsatisfactory smear for evaluation (see Results for more details).

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Accepted for publication April 27, 2004