

Comparison of Specimen Adequacy and Smear Quality in Conventional and Liquid-Based Pap Tests

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Abstract

Background: Since the best method of cervical smear is a controversial subject, this study was designed to compare two methods of cervical sampling, consisting of conventional versus liquid base.

Objectives: Pap smear is a screening test used to detect pre malignant and malignant processes in the endocervical canal of the female reproductive system. There are two methods, consisting of conventional Pap, in which samples are smeared directly on a microscope slide after collection, and liquid based cytology, in which the smear sample is placed in a bottle of preservative for transport to the laboratory, where it is then smeared on the slide. In this study it was decided to compare these two methods of sampling.

Methods: This randomized trial was carried out at the Amir Hospital of Semnan, Iran on 240 females undergoing Pap smear screening from April to September 2012. Patients were divided to two groups including conventional (n = 120) and liquid base cytology smear (n = 120). The results of cytological reports of both groups were compared in regards to sufficiency of sample, presence of blood in the sample, presence of infection and premalignant or malignant condition.

Results: Specimen adequacy and smear quality were significantly better in liquid base sampling (P = 0.03); presence of benign cellular changes was not different between the two groups (P = 0.389). Diagnosis of bacterial vaginosis was significantly better with the conventional method (P = 0.007). Also, severe inflammation was more commonly reported in the conventional method than liquid base sampling test (P = 0.029).

Conclusions: Specimen adequacy and diagnosis of inflammatory reaction were better in liquid base smear and convention smear, respectively.

Keywords: Pap Smear, Liquid Base, Conventional

1. Background

Early detection of cervical cancer could be performed by the Pap smear, colposcopy and Human Papilloma Virus (HPV) testing (1). Incidence and mortality of cervical cancer have declined with organized cytology-based screening programs (2). Cervical Intra-epithelial Neoplasia (CIN) and cervical cancer are the most important health problems in females in the entire world (3). Cervical cytology is the gold standard for cervical cancer screening and the Pap smear is broadly done as the method of screening (4).

There is a lot of evidence that cervical cancer screening with conventional cytology (CC) has led to a decrease in mortality. There are two new modalities for cervical cancer screening. One is liquid-based cytology (LBC) and the other is HPV test. The LBC and CC have the same outcome in terms of sensitivity and specificity for detection of CIN2 or CIN3. Human papilloma virus tests are better than CC in sensitiv-

ity but have a lower specificity for diagnosis of CIN2 or CIN3 (5). Liquid-Based Cytology has become a common screening test for cervical cancer in the unitedstates and also, this method was used in nearly 75% of Pap tests in 2006 and 2007 (6). Sensitivity in diagnosis and the ability to perform molecular assays with the LBC method are its advantages over CC, while it is also superior to CC for detection of lesion in high-risk patients (7). Also, LBC shows a complete elimination of most causes of unsatisfactory samples (8).

In a case-control study by Paulin et al. using an optimal collection technique, especially in older age groups for prevention of unsuit factory pap sample is recommended (9). In another study, the quality of smear was an important factor in screening of cervical cancer (10). Also, in the study of Confortini et al., cytologic reports of two methods of sampling, consisting of conventional versus liquid base, was the same and the sensitivity of liquid base in detecting

CIN2 of cervix was comparable with the conventional sample (11).

2. Objectives

Regarding the controversy about the best method of sampling and because the sampling method of choice at our center was CC, it was decided to compare two methods of cervical pap test, CC versus LBC.

3. Methods

In this prospective randomized trial, 240 females, aged between 20 and 56 years old that had undergone Pap smear screening, were recruited. Patients were allocated to two groups including conventional (n = 120) and liquid base cytology smear (n = 120) from April to September 2012 at the Amir Hospital of Semnan, Iran. The study was approved by the ethical committee of Semnan University of Sciences and written informed consent was obtained from all cases. Main outcome measures were defined as adequacy of specimen, bloody specimen, presence of infection, presence of benign cellular change and premalignant and malignant conditions. Pap smear was obtained in mid cycle (12 to 16 days of cycles) in both groups. Patients, who had any vaginal apparent cervicitis or vaginitis, were excluded from the study. Cytobrush was used for taking the samples in both groups and the samples were sent to the same laboratory for cytologic evaluation.

The results of cytological reports of both groups, which were based on Bethesda system were compared in regards to sufficiency of sample, presence of blood in the sample, presence of infection such as bacterial vaginosis, presence of benign cellular change and premalignant or malignant condition.

Statistical analyses were performed using Mann-Whitney, Pearson chi square and Fisher's exact tests with the excel computer software. P-values of less than 0.05 were considered statistically significant.

4. Results

The mean \pm Standard Deviation (SD) of age of patients in the liquid-based group was 32.52 ± 10.45 and conventional group was 34.08 ± 10.06 ($P = 0.217$). The mean parity of liquid base group was 1.53 ± 1.87 and in conventional group was 1.59 ± 1.44 ($P = 0.218$). There was no significant difference in term of age and parity between the two groups.

Inadequate sample was observed among five cases (4.2%) of conventional and none of the cases of the liquid

base group. Data analysis by Fisher's exact test revealed that the liquid base method is significantly better for gathering adequate samples than the conventional method ($P = 0.03$). A bloody sample was reported among eight cases of the conventional group and none of the cases of the liquid base group. Fisher's exact test showed that the liquid base method is significantly better for gathering non-bloody samples than the conventional method ($P = 0.03$).

Benign cellular changes were reported in ten cases of conventional versus fourteen cases of the liquid base group; analysis by Pearson chi-square and Fisher's exact test revealed that there was no significant difference between the two groups in regards to presence of benign cellular changes ($P = 0.389$).

Bacterial vaginosis was present in eight cases of conventional versus no case of the liquid base group and statistical analysis by Fisher's exact test showed that the conventional method was significantly better for diagnosis of bacterial vaginosis than the liquid base method ($P = 0.007$).

Severe inflammation was reported in six cases of the conventional group versus no case of the liquid base group, and statistical analysis by Fisher's exact test revealed that report of severe inflammation with the conventional method was significantly more common than the liquid base method ($P = 0.029$), (Table 1).

5. Discussion

Cervical cytology smears have been reported as unsatisfactory methods and also, represent an unsuccessful form of screening and might have high laboratory and patient costs. Generally, 1.1% of all Pap smears have been reported as unsatisfactory, therefore, identifying the causes of unsatisfactory smear is very important (9). This study showed that the adequacy of specimen is significantly more in liquid base cytology test than conventional test and it prevents the need for obtaining further specimens and consequently will reduce the costs.

Smear quality is an important factor involved in the success of cytology in screening programs for cervical cancer (10). Our study showed that gathering non-bloody specimens in the liquid base method was significantly more than the conventional method.

The study of Confortini et al. compared the LBC results of 99 patients with their previous screening using the CC method. This study showed that the CC and LBC provide comparable cytological reports and that the LBC is not less sensitive than the CC in detecting of CIN2 + lesions of the cervix (11). Similarly, in the present study, the two methods of sampling (CC versus LBL) had similar cytological reports.

Table 1. Distribution of the Characteristics of the Study Groups

Characteristics	Count (%) by Method		Total Count (%) (n = 240)	P
	Conventional (n = 120)	Liquid Base (n = 120)		
Age group, y				0.1
≤ 20	4 (3.3)	12 (10.0)	16 (6.7)	
> 20 & ≤ 30	54 (45.0)	57 (47.5)	111 (46.2)	
> 30 & ≤ 40	27 (22.5)	19 (15.8)	46 (19.2)	
> 40	35 (29.2)	32 (26.7)	67 (27.9)	
Parity				0.1
0	33 (27.5)	47 (39.2)	80 (33.3)	
1	33 (27.5)	24 (20.0)	57 (23.8)	
≥ 2	54 (45.0)	49 (40.8)	103 (42.9)	
Sufficiency of samples				0.03 ^a
Sufficient	115 (95.8)	120 (100.0)	235 (97.9)	
Insufficient	5 (4.2)	0 (0.0)	5 (2.1)	
Presence of bloody specimen				0.003 ^a
Not-Bloody	112 (93.3)	120 (100.0)	232 (96.7)	
Bloody	8 (6.7)	0 (0.0)	8 (3.3)	
Presence of BCC				0.4
No	110 (91.7)	106 (88.3)	216 (90.0)	
Yes	10 (8.3)	14 (11.7)	24 (10.0)	
Presence of BV				0.003 ^a
No	112 (93.3)	120 (100.0)	232 (96.7)	
Yes	8 (6.7)	0 (0.0)	8 (3.3)	
Presence of inflammation				0.01 ^a
Not-severe ^b	114 (95.0)	119 (100.0)	234 (97.5)	
Severe	6 (5.0)	0 (0.0)	6 (2.5)	

Abbreviations: BCC, benign cellular change; BV, bacterial vaginosis.

^aOne-sided Fisher's exact test.

^bNo/Mild/Moderate.

In one study, 6332 females were screened for cervical cancer in a one-year period and 169 abnormal Pap smears were found. In this study, 497 cases by LBC and 5835 cases by CC were screened, respectively. The prevalence of abnormal Pap smear was 4.0% and 2.6 % in LBC and CC groups, respectively. The incidence of atypical smear and false positive results between LBC and CC were not different (12). In our study, no cases of abnormal Pap smear was observed amongst the two groups and all 240 cases had normal findings in the cytological survey. The difference between the study of Suwannarurk et al. (12) and our study was related to the number of cases involved in the research.

Sams et al. showed that the sensitivity detection of endometrial carcinoma by LBC (88%) is considerably higher

than that reported for CC (20%-30%) (13). In the present study, we had no cases of endometrial cancer.

New technologies for cervical cancer screening try to provide an accurate and cost-effective way for detection of females at risk for cervical cancer. Human papilloma virus DNA testing combined with cytology was used recently but it needs multiple visits and is very costly for the patient and the society (14). The incidence and mortality of squamous cervical carcinoma of cervix has been reduced noticeably as a result of successful screening in many countries but the incidence of cervical adenocarcinoma continues to increase. Early detection and screening by using molecular biomarker assays should be considered (15). The American college of obstetricians and gynecologists recommen-

datations in 2009 for cervical cancer screening calls for less frequent but smarter screening that integrates human papillomavirus infection testing with the Pap smear test (16). In our study, due to great cost of HPV testing, we did not use the above new technologies and only a comparison was done between conventional and liquid base cytology.

In the study of Atilgan et al., among 32026 conventional cytology tests that were collected from three hospitals, 900 (2.8%) cases had epithelial abnormalities. The epithelial abnormalities were as follows: atypical squamous cell of undetermined significance (ASCUS, n = 615, 1.9%), atypical squamous cell suspicious for high-grade squamous intraepithelial lesion (ASC-H; n = 27, 0.1%), atypical glandular cell of undetermined significance (AGUS, n = 73, 0.2%), low grade squamous intraepithelial lesion (LSIL, n=147, 0.5%), high-grade squamous intraepithelial lesion (HSIL, n = 35, 0.1%), and squamous cell carcinoma (SCC, n = 3, 0.0%). The prevalence of cervical cytological abnormality in this study was 2.8% (17). The low sample size of the present study was the cause of absence of epithelial abnormality because the aim of the present study was to compare the adequate rate and quality of sampling of two methods. There were no cases with epithelial abnormality among our cases yet with regards to the presence of benign epithelial change, both methods had comparable cytological reports.

This study revealed that the conventional method could detect more bacterial vaginosis and severe inflammation than liquid base type and there is no scientific evidence for these results, therefore it is necessary to have more research about these findings.

One of the most important limitations of this study was related to the methodology, as we compared the findings of two different tests on two different populations. This may cause error and reporting of false results. Also, the other limitation of the study was related to patients who were not referred for doing a second test and it forced us to continue until access the sample size which this result in missing data.

In conclusion, liquid base smear provides more adequate, non-bloody and better sample for cytologic evaluation but the conventional smear is better for diagnosis of inflammatory reaction. We recommend doing LBC smear for better-qualified samples. However, it is recommended to perform further studies in regards to inflammatory reactions in smear.

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