Gynecologic Oncology Reports 24 (2018) 18–20

Contents lists available at ScienceDirect

Gynecologic Oncology Reports

journal homepage: www.elsevier.com/locate/gynor

Review article

The value of visual inspection with acetic acid and Pap smear in cervical cancer screening program in low resource settings – A population-based study

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ARTICLE INFO

Keywords:
VIA
Pap smear
Cervical cancer screening

ABSTRACT

This study aims to determine the diagnostic values of visual inspection with acetic acid (VIA) and Pap smear in a cervical cancer screening program at a community level in Vietnam. A cross-sectional analysis was obtained, including 1034 women of reproductive age from Thua Thien Hue Province, Vietnam from 09/2012 to 09/2013. Samples were taken from cervixes for Pap smear testing, followed by visual inspection with acetic acid. Subjects with abnormal VIA and/or positive cytology results were invited for colposcopy and biopsy. Histologic confirmed cervical intraepithelial neoplasia (CIN2+) served as gold standards for diagnostic values analysis. Abnormal VIA results were recorded in 87 cases (7.7%). The sensitivity, specificity, accuracy, positive predictive value (PPV) and negative predictive value (NPV) of VIA for CIN2+ were 88.8%, 43.8%, 63.4%, 51.2% and 83.3%, respectively. Diagnostic values of Pap smear were 58.0%, 85.2%, 69.9%, 83.3% and 61.3% for its sensitivity, specificity, accuracy, PPV and NPV, respectively. VIA yielded high sensitivity but its accuracy is still limited in pre-cancerous lesions during cervical cancer screening. The Pap smear has acceptable sensitivity and specificity, but its false-negative rate is still high. We recommend a combination of different tests to increase the efficiency of screening in our community.

1. Introduction

According to World Health Organization, about 520,000 new cases of cervical cancer were diagnosed annually worldwide, with over 85% from developing countries (World Health Organization, 2014). In Vietnam, the incidence of cervical cancer is 16 per 100,000 women/year; annually there are 6500 new cases and about 3000 women will die from cervical cancer. In contrast, cervical cancer incidence in developed countries is substantially lower due to the effective and efficient organized mass screening programs and appropriate interventions after detection of abnormal cases (Adam et al., 2000; de Sanjosé et al., 2007). Cervical cancer has a long natural history and progression interval. Early detection of precancerous lesions by conventional screening and diagnosis modalities such as cervical cytology, colposcopy, cervical biopsy, endocervical curettage allows for treatment of these precancerous lesions before progression to invasive cancers.

Pap smear screening has markedly reduced mortality from cervical cancer in developed countries. In Vietnam there has been many efforts for cervical cancer screening using routine Pap smears in major centers; however, the cytologic screening coverage is still very low outside of the urban regions. Moreover, VIA is considered as an attractive alternative to cytology-based screening in low-resource settings, it is a simple and cost-effective technique acceptable to women and providers. High-risk HPV DNA has been identified in 99.9% of invasive cervical cancers specimens (Franco et al., 2001). The sensitivity and specificity of VIA and HPV when used sequentially were 63.6 and 81.9%, respectively (Bornstein et al., 2012). This study aims to determine the diagnostic values of VIA and Pap smear in a cervical cancer screening program at a rural community in Thua Thien Hue Province, Vietnam.

2. Subjects and methods

This cross-sectional descriptive study on 1034 married or sexually active reproductive-age women (15–49 years) from Thua Thien Hue

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https://doi.org/10.1016/j.gore.2018.02.004
Received 21 September 2017; Received in revised form 27 January 2018; Accepted 13 February 2018
Available online 15 February 2018

Province was carried out from September 2012 to May 2013. Women who had a prior hysterectomy, who were menstruating, pregnant or in the post-partum period, used vaginal douching 24 h before examination, had existing precancerous-cancerous cervical lesions or a history of gynecologic malignancies, or had received pelvic radiation were excluded from the study.

Sample size was calculated for rate estimate investigation:

$$n = Z^2_{\alpha/2}\frac{p(1-p)}{\Delta^2}$$

with the prevalence p = 12%, Δ = 0,02, α = 0,05, $Z_{\alpha/2}$ = 1,96, minimum sample size is 1015 women. In total, 1100 women were invited for gynecologic examination.

The study was carried-out in 3 districts that were representative of geographic and socio-economic characteristics for Thua Thien Hue Province: City of Hue (at An Hoa, An Cuu, An Dong, and Phuong Duc Communes), Nam Dong District (at Khe Tre, Huong Loc, and Huong Huu Communes), and Phu Vang District (at Phu Mau, Vinh Ha, Phu Dien, and Vinh Thanh Communes). One hundred women in the eligible age group from each commune were randomly selected, and 66 women were excluded according to exclusion criteria, resulting in the final sample size of 1034 women.

All individuals enrolled in the study were subjected to gynecologic examination and conventional Pap smear, followed by visual inspection with acetic acid, as described elsewhere (World Health Organization, 2014). The abnormal cytologic results include ASC-US/-H, AGUS, LSIL, HSIL, and invasive cancer.

Women who had abnormal VIA and/or had a positive cytology result were invited for a second visit at the Hue University Hospital for colposcopy. If there was lesion classified as abnormal or suspicious for invasive cancer according to the nomenclature of 2002 International Federation of Colposcopy and Cervical Pathology, a biopsy was performed (Bornstein et al., 2012). Histopathological results were assessed according to the WHO classification. Histologic confirmed CIN2+ served as gold standards for diagnostic values analysis.

Data were entered and statistical analysis was performed using the software SPSS 19.0. Ethical approval for study protocol was obtained from the Ethic Committee for Biomedical Researches of Hue University of Medicine and Pharmacy.

3. Results

3.1. General characteristics of study sample

From the 1034 women included into the final evaluation, there were 87 women having VIA+, and 48 women having ACS-US+ cytologic findings. General characteristics of study sample were described in Table 1.

3.2. Diagnostic value of VIA

In total, 123 subjects were positive from VIA and/or cervical cytology and/or HPV DNA testing and were invited for colposcopy examination and biopsy. CIN2+ lesions were identified from 69 subjects, which resulted in a biopsy confirmed rate of 56.1%. Abnormal VIA results were recorded in 87 cases (7.7%). Table 2 describes the distribution of VIA findings according to histopathological results. Using histologic confirmed CIN2+ as a gold standard, the sensitivity, specificity, accuracy, positive predictive value (PPV), and negative predictive value (NPV) of VIA were 88.8%, 43.8%, 63.4%, 51.2% and 83.3%, respectively.

3.3. Diagnostic value of Pap smear

Among 69 cases having CIN2+; 40 out of 48 cases presented with abnormal Pap smear, accounting for 83.3%. Diagnostic match rate between cytologic LSIL and HSIL and histopathology was 100% (see Table 3).

From Table 4, diagnostic values of Pap smear were 58.0%, 85.2%, 69.9%, 83.3% and 61.3% for its sensitivity, specificity, accuracy, PPV and NPV, respectively.

Table 1
General characteristics of study sample.

Characteristics	n = 1132	%
Age		
18–19	2	0.2
20–29	176	15.5
30–39	484	42.8
40–49	470	41.5
Level of literacy		
Illiteracy	128	11.3
Primary to high school	876	77.4
College/university	128	11.3
Occupation		
Farmer	311	27.5
Trader	322	28.4
Officials	134	11.8
Housewife	215	19.0
Others	150	13.3
Current number of children		
0	9	0.8
1–2	575	50.8
≥3	548	48.4

Table 2
VIA and histopathological results.

Histologic VIA	CIN 2	CIN 3	Negative	Total
VIA (+)	25	14	48	87
VIA (−)	27	3	6	36
Total	52	17	54	123

P < 0.001.

Table 3
Distribution of Pap smear and pathology results.

PAP	n	Pathology		Diagnostic match rate between Pap and pathology (%)
		Benign changes	CIN2+	
Normal/Benign change	75	46	29	61.3
ASCUS/H	28	5	23	82.1
AGUS	11	3	8	72.7
LSIL	7	0	7	100
HSIL	2	0	2	100
Cancer	0	0	0	100
Total	**123**	**48**	**69**	

Table 4
Results of Pap smear and pathology.

	Pathology (+)	Pathology (−)	Total
Pap (+)	40	8	**48**
Pap (−)	29	46	**75**
Total	**69**	**54**	**123**

P < 0.001.

4. Discussion

This study sample is geographically representative of urban,

mountainous and coastal regions of the Thua Thien Hue Province, Vietnam. The pelvic examination, HPV, cytologic sampling, and VIA were performed at the Commune Health Centers, the lowest-level health facility within the health system of Vietnam. Thereafter samples were sent back to Hue University Hospital for processing and interpretation. Therefore, the study setting reflected the real-world environment of cytologic testing, especially the performance of VIA at the grass-roots level.

Diagnostic values of Pap smear were 58.0%, 85.2%, 69.9%, 83.3% and 61.3% for its sensitivity, specificity, accuracy, PPV and NPV, respectively. This means that Pap smears are needed on VIA+ patients because VIA is very sensitive, but with a lower PPV. Pap smear has a high PPV which can determine who truly had CIN2+. VIA from this data also has a good NPV.

Diagnostic values of Pap smear were in expected range as reported by other authors. Its sensitivity for cervical lesion detection seems to be much lower than those of VIA, which was confirmed by many previous studies.

A study on 2199 women in Harare, Zimbabwe, used VIA, Pap smear, and HPV as cervical screening tests, with HGSIL/CIN II-III as the reference threshold of disease. The net sensitivity and specificity of VIA and HPV when used sequentially were 63.6 and 81.9%, respectively, compared to 43.3 and 91%, respectively, when Pap smears were followed by HPV testing. VIA followed by the Pap smear yielded a net sensitivity of 37.5% and net specificity of 94.3%. The authors concluded that the use of VIA followed by HPV could yield fewer false positives than the use of VIA alone (Blumenthal et al., 2001).

In other studies, the combination of PAP smear and HPV testing offers clear advantages over single cytology with SE of 90.0%, SP 50.0%, PPV 52.9% and NPV 88.9% at first follow-up, and 100% SE and 100% NPV at the second follow-up visit (Costa et al., 2007). In 2008, Chao et al. also evaluated the complementary value of HPV testing to Pap smear in Taiwan and concluded that the combination of two methods improved the sensitivity by 15.3% (Chao et al., 2008). Another study in Kenya on 653 women showed a sensitivity for CIN2 or higher and specificity were 83.3% and 94.6%, respectively, for Pap smear; 73.3% and 80.0% for VIA; and up to 94.4% and 73.9% for high-risk HPV testing (De Vuyst et al., 2005).

To the best of our knowledge, this study is among the rare field studies from Vietnam to test the feasibility and validity of VIA performed after cervical sampling for Pap smear. It showed that even after being cytologically sampled, the cervix is still suitable for implementing VIA with the purpose of cervical screening, if the of mucus and blood removal step before applying acetic acid is observed. This finding has been long confirmed in the 2003 Pan American Health Organization's critical review on the validity of VIA (Pan American Health Organization, 2003).

The limitations of this study include the rather small number of subjects involved, and due to the limited resources, colposcopy has been carried out only on subjects having abnormal cytologic and/or VIA findings, and not among those having negative screening results for a better quality assurance.

In conclusion, VIA yielded high sensitivity, but its accuracy is limited during cervical cancer screening for pre-cancerous lesions. The Pap smear has acceptable sensitivity and specificity, but its false-negative rate is high. Based on this finding, screening at community settings in Vietnam should include a combination of VIA, followed by confirmatory Pap test to increase the efficiency of screening.

Conflict of interest

The authors whose names are listed above certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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