Can Visual Inspection with Acetic Acid and Lugol's Iodine be used Instead of Colposcopy in Low Resource Settings?

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ABSTRACT

Objective: The purpose of this study is to estimate the diagnostic efficacy of VIA (Visual Inspection after Acetic Acid) and VILI (Visual Inspection with Lugol's Iodine) and to investigate the strength of the correlation between VIA, VILI, and colposcopic examination using Reid Colposcopic Index (RCI) and histopathology.

Methods: Two-hundred women aged 19-72 who underwent colposcopy because of abnormal pap-smear, were included in the study. All women underwent cervical examination, VIA and VILI practices and colposcopy, respectively. Primarily, the first gynecologist (N.V.T) used both VIA and VILI to take samples from visually abnormal areas. Then, the second gynecologist (F.K) who was blinded to the results of first exam performed colposcopy and took biopsy samples from the suspicious areas on colposcopy. Four-quadrant biopsies were taken when there were no abnormal findings on the colposcopic examination.

Results: There were 72 (36%) histopathologically abnormal sample in 200 biopsies. The sensitivity and specificity of VIA test for predicting abnormal cervical biopsies were 51.4% and 57% and 59.7% and 63.3% for VILI test, respectively. When these two methods were combined, the sensitivity and specificity were 71% and 47% respectively.

Conclusion: Although the sensitivity and the specificity of VIA and VILI in our study were lower than previous studies we think that these tests can be used as an alternative when colposcopy is unavailable. In addition, it can be convenient alternative method that is inexpensive and easy to apply and even suitable for "See and Treat" approach.

Keywords: Colposcopy, Reid Colposcopic Index, VIA, VILI

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INTRODUCTION

Cervical cancer is the most frequent type of gynecologic cancers in the developing and undeveloped countries (1). Early diagnosis is crucial for successful treatment of the cervical cancer. With early treatment, five-year survival rate for cervical cancer is 75% to 90% (2). Conventional Pap smear is the most common way of screening but currently use of liquid based cytology is increasing. In developing countries not only cytologist but also colposcopists, and colposcopy equipment are limited which are essential for effective cervical cancer screening. In this study we tried to investigate whether VIA and VILI tests can be used instead of colposcopy in low resource settings.

Material and Methods

The present study was carried out in Etlik Zubeyde Hanım Women's Health Teaching and Research Hospital. A total of 200 patients with abnormal pap-smear were enrolled in the study. We explained the procedure to all patients and took informed consent from all patients. The institute's ethics committee approved the study protocol.

After detailed obstetric and medical history, general physical examination was performed. A green filtered binocular Leica 150 CLS colposcopy device (Leica Micro systems Ltd, Heerbrugg, Switzerland) was used for colposcopy. First gynecologist (N.V.T) inspected, the cervix with naked eye .VIA was performed with 3% acetic acid and any distinct aceto-white area in the transformation zone was considered as VIA positive. After 1-2 minutes of VIA, saline was applied to cervix and visual inspection after application of Lugol's iodine (VILI) was performed. Areas of no uptake were considered as VILI positive while areas of partial uptake and positive uptake were considered as VILI negative. After visual inspection of the cervix and VIA, VILI applications biopsy was taken from the areas VIA or VILI positive parts of the cervix. Second gynecologist (F.K) assessed the cervix with colposcopy six weeks after the first examination. She was blinded to the results of first

examination findings. The lesions were evaluated regarding to the Reid colposcopic index. Four-quadrant (2, 4, 8 and 10 clockwise position) biopsy was taken in patients who did not have any lesion on colposcopy. Low-grade squamous intraepithelial lesion (LSIL), high-grade squamous intraepithelial lesion (HSIL) and invasive cancer were considered as positive biopsy and chronic cervicitis, metaplasia, epithelial hyperplasia, and Nabothian cysts were considered as negative biopsy. Regarding the screening tests; the patients who had a positive CVS but a negative biopsy results (no lesion or benign changes) were considered as false-positive. Histopathologically confirmed LSIL and high grade lesions were consideredas true-positive cases.

The Statistical Package for Social Sciences (version 17.0; SPSS, Chicago, IL) was used for statistical analysis. The Shapiro-Wilk test was used to assess the conformity of the continuous variables to normal distribution. The Spearman correlation analysis was used for determining the relations between the histopathology and VIA, VILI and the Reid index. The Logistic Regression Analysis was performed to assess the risk of abnormal biopsy result by demographical and clinical features of study population. Cross-tabs were used for calculating sensitivity, specificity, positive predictive value and negative predictive value. P value of 0.05 was considered to indicate statistical significance.

RESULTS

The study was carried out with 200 women aged 19-72 with a mean age of 42.5±10.2 years. 13.5% of the women were single. The average length of marriage was 21.8±11.5 years. The women, who stated that they smoke, have been smoking for at least 2, and for a maximum of 30 years. Number of cigarettes smoked per day is at least 1, at most 45, and the median is 9.0 (IQR = 6.5). While 12 of the patients (6.0%) have never been pregnant before, the percentage

of women who have been pregnant 5 times or more was 23% (n=43). The withdrawal method is the most commonly reported method among all birth control methods (n=55, 31.8%).

There were 83 patients (41.5%) who was VIA and VILI negative. Among these patients 71.1% (n = 59) of them had normal biopsy results. In 28.9% (n=24) of them there were abnormality in histopathologic examination. In patients who were VIA and VILI positive (n = 64) there were 32 patients (50%) with abnormal biopsies.

Abnormal findings were observed in 45.4% of the patients who were VIA positive and in 45% who were VILI positive. The distribution of VIA and VILI examination of the patients according to the biopsy results are shown in Table 1.

Regarding the result of the pathological examination, chronic cervicitis was observed in 118 women (59.0%), LSIL was observed in 47 women (23.5%) and HSIL was observed in 22 women (11.0%) respectively. Metaplasia (n=2, 1%), HPV effect (n=3, 1.5%) and squamous cell carcinoma (n=3, 1.5%) were the least common biopsy results.

The distribution of VIA and VILI examination was investigated according to the Pap smear results. The results are shown in Table 2.

The sensitivity and the specificity of VIA test for predicting abnormal cervical biopsies were 51.4% (37/72) and 57.8% (74/128), respectively. The positive predictive value (PPV) and the negative predictive value (NPV) for abnormal cervical biopsies were calculated as 40.6%, and 67.9%, respectively. The association between abnormal biopsy results and VIA was not statistically significant (r = 0089; p = 0.212).

The sensitivity and specificity of VILI were 59.7% (43/72) and 63.3% (81/128), respectively. PPV and NPV were calculated as 47.8% and 73.6%, respectively. The association between pathology results and VILI was statistically significant (r = 0.222; p = 0.002).

When the VIA and VILI methods were evaluated together, the sensitivity and specificity were 67% and 46%, respectively. PPV and NPV were calculated as 41% and 71% respectively.

Assuming all other factors remained constant; it was observed that the probability of obtaining a abnormal pathological result from the patients who had the Reid index higher than 2 was 5.9 times higher than the patients who had the Reid index less than or equal to 2 [OR = 5.9 (3.1 – 11 95% CI)].

In logistic regression model following variables were taken as the initial variables that were thought to have an impact on the pathology: smoking, age of first coitus, the weekly frequency of sexual intercourse, parity, type of delivery, number of marriages, contraceptive method used, employment status and the partner's occupation. None of the variables examined had a significant effect on the positive result of pathology in terms of increasing the risk or protection ($p > 0.05$).

DISCUSSION

The slow progression of cervical cancer emphasizes the importance of screening methods for early diagnosis of dysplastic lesions to prevent progression to invasive cancer. The extensive use of the Papanicolaou (Pap) smear has dramatically reduced the incidence of invasive cervical cancer. In developed countries having sufficient technical equipment and well-trained human resources Pap smear is efficient and satisfactory. However in underdeveloped or developing countries there is shortness in both. At this point major difficulty is the absence of adequate number of cytologist to evaluate Pap smears. There is something else which is also as important as Pap smear. If an abnormality is detected in the screening tests the following

problem that the physicians are usually faced is the need of a competent colposcopy examination.

Satisfactory colposcopy requires two major elements. First one is a good working colposcope and the second is a well-trained certified colposcopist. In developing and underdeveloped countries there is an insufficiency in both of these parameters. Warranting both of these parameters increases the cost. Garcia et al. reported that the cost of colposcopy without biopsy is 39.80 (31.84-47.76) USD and 69.01 (55.21-82.81) USD for colposcopy with biopsy per patient (3).

In this study, we investigated whether VIA and VILI tests have a reliable sensitivity and specificity to guide clinicians when they are deciding to make cervical biopsies and if so choosing the appropriate points for these biopsies. In our series, of the 143 (71.5%) patients with ASCUS there were 42 (29.5%) patients who had low-grade squamous intraepithelial lesions (LSIL) or higher-grade lesions on biopsy. In the literature the sensitivity and specificity of VIA were varies between 66–96% and 64–98%, respectively (4-6). Belinson et al. reported similar results regarding the sensitivity of colposcopy and inspection alone. They concluded that the visual inspection with acetic acid (VIA) method was convenient in many countries because of its diagnostic and single-session therapy features (7). Puntachai et al. compared the detection of cervical lesions in 164 patients using VIA plus a random cervical biopsy plus endocervical curettage (ECC) versus a colposcopic biopsy plus ECC. They found that while the sensitivity of VIA was 85.6%, VIA plus random cervical biopsy plus ECC and a colposcopic biopsy plus ECC had similar sensitivities. Consequently, they stated that VIA plus random cervical biopsy plus ECC can be used when colposcopy is unavailable (8). There is a debate on the additional benefit of colposcopy over random cervical biopsies. Pretorius et al. reported that although there was an increase in the number of abnormal biopsies (≥LSIL) obtained through colposcopy, still the results were statistically significant (57.1% vs. 42.9%)

(9). Mousavi et al. examined the correlation between the Reid colposcopic index (RCI) and histopathology and found that the RCI had a sensitivity, specificiy, PPV, and negative predictive value (NPV) of 63.8, 88.8, 89.3, and 62.5%, respectively (10). In our study the values were 65.2% (47/72), 75.8% (97/128), 60.2%, and 79.5%, respectively. Cervico-vaginal cytology screening has been hailed as a successful method for the early detection of cervical cancer. However, it must be noted that the smear test is used for cervical screening. The VIA and VILI are inexpensive, easy-to-learn methods that give results in a single session. The sensitivity of the VIA and VILI in our series were similar to reported values, whereas the specificity was lower, perhaps because we included patients with abnormal Pap smears.

In conclusion, although the sensitivity and the specificity of VIA and VILI in our study were lower than previous studies we think that these tests can be used as an alternative when colposcopy is unavailable. In addition, it can be a convenient alternative method that is inexpensive and easy to apply and even suitable for “See and Treat” approach. Further prospective studies are needed.

Declaration of interest: The authors have no relation with the companies and products mentioned in this study and declare no conflict of interest.

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Table 1: The distribution of VIA and VILI examination according to the biopsy results

Cervical Biopsy Result	**VIA +** n (%)	**VIA -** n (%)	**VILI +** n (%)	**VILI -** n (%)
Normal ectocervix	0 (0)	5 (2.5)	1 (0.5)	4 (2.0)
Chronic cervicitis	54 (27)	64 (32)	45 (22.5)	73 (36.5)
Metaplasia	0 (0)	2 (1)	0 (0)	2 (1)
HPV effect	0 (0)	3 (1.5)	1 (0.5)	2 (1)
LSIL	20 (10)	27 (13.5)	22 (11)	25 (12.5)
HSIL	14 (7)	8 (4)	19 (9.5)	3 (1.5)
Squamous cell carcinoma	3 (1.5)	0 (0)	2 (1)	1 (0.5)
Total	**91 (45.5)**	**109 (54.5)**	**90 (45)**	**110 (55)**

Table 2: The distribution of VIA and VILI examination according to the Pap smear results

Smear Result	**VIA (–), VILI (–)** n (%)	**VIA (+), VILI (–)** n (%)	**VIA (–), VILI (+)** n (%)	**VIA (+), VILI (+)** n (%)
ASCUS	66 (46.2)	20 (14.0)	18 (12.6)	39 (27.39
ASCH	3 (30.0)	2 (20.0)	3 (30.0)	2 (20.0)
LSIL	8 (27.6)	3 (10.3)	4 (13.8)	14 (48.3)
HSIL	4 (33.3)	0 (0.0)	1 (8.3)	7 (58.3)
HPV effect	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)
AGC-NOS	1 (25.0)	2 (50.0)	0 (0.0)	1 (25.0)
Cancer	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)
Total	**83 (41.5)**	**27 (13.5)**	**26 (13.0)**	**64 (32.0)**