Visual Inspection after Acetic Acid (Via) as an Alternative Screening Tool for Cancer Cervix

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Abstract

Objective: The aim of this cross-sectional study was to assess the role of visual inspection with acetic acid VIA as an alternative cost effective tool to Pap smear in screening for cancer cervix in low resource settings.

Material and methods: 3298 women attended the obstetrics and gynecology Department in Benha University Hospital from May 2012 till August 2015 were screened by Pap smear and VIA. Colposcopy was done for all women. Positive cases on any screening test were subjected to cervical biopsy. All women with a positive VIA (200 including 124 Pap -ve), abnormal Cytology (40 were VIA -ve), or those with abnormal colposcopy (70 were Pap -ve and VIA -ve) were subjected to cervical biopsy and were included in our study. Thus a total of 310 cases from whom cervical biopsy were taken were included.

Results: Of the women screened, VIA was positive in 200 (6%) and 164 (5%) were positive on Papanicolaou smear. Cervical biopsy was done on 310 cases. 191 (62%) biopsies were positive and 119 (38%) were negative. Of the 191 positive biopsies there were 87 CIN I, 59 CIN II, 29 CIN III and 16 invasive carcinoma. The sensitivity, specificity, positive predictive value and negative predictive value of VIA were 84%, 67%, 80.5% and 73% respectively. While the Pap smears had a sensitivity of 72%, specificity of 78%, and positive predictive value of 84% and negative predictive value of 64%.

Conclusion: VIA has the advantage of easy learning, inexpensiveness, high sensitivity in comparison to Pap smear and immediate availability to assess results. Thus, VIA represents a good method of cervical cancer screening in many parts of the world especially in poorly resourced locations.

Keywords: Pap smear; VIA; Cancer cervix

Introduction

Cervical cancer is the second most common cancer in women throughout the world, and it is the leading cause of cancer death among women in underdeveloped countries. The incidence and mortality rate of cervical cancer have markedly decreased in developed countries since cytological cervical cancer screening was introduced more than 50 years ago. In many underdeveloped countries, a substantial number of women are still dying of cervical cancer, because of limited access to cytopathology [1].

Both primary prevention and early detection can prevent cervical cancer. The decreasing incidence of cervical cancer in developed countries is due to screening, early detection and treatment. However in developing countries, 80% of cervical cancers are incurable at the time of detection [2].

Screening programs based on Papanicolaou smear require technical capabilities, trained personnel, and financial resources that are beyond the capacity of health care infrastructure in most underdeveloped countries. An alternative of Pap smear, a low cost test, visual inspection using acetic acid (VIA), has emerged for use in low-resource settings where it can be performed by trained health professionals [3].

Visual inspection of the cervix after 3-5% acetic acid (VIA) technique is a cheap, simple and easy to learn method of cervical cancer screening. On exposure to this solution, abnormal cells of the cervical epithelium temporarily turn white and reveal aceto-white epithelium of the abnormal transformation zone. Several studies showed the advantages of VIA, including its simplicity, high sensitivity and instant results [4-7]. VIA as a visual screening test does not depend on laboratory services would be a possible and promising alternative screening tool for early detection of cervical cancer [4]. This study was designed to evaluate the clinical performance of visual inspection with acetic acid (VIA) as a simple test and if it is a suitable alternative to PAP smear for early detection of cervical cancer.

Patients and Methods

We conducted a cross-sectional study at Department of Obstetrics and Gynecology and Gynaecology outpatient clinic, Benha University Hospital, since May 2012 till August 2015, after approval of the study protocol by the Local Ethical Committee. A written informed consent was obtained from eligible women before doing the procedure.

In this study 3289 eligible women of age group 20-50 years were screened but only 310 cases were included and women with Pregnancy, Vaginal bleeding, History of cervical pathologies or its treatment, Use of COC, Immunosuppression, During menstruation and Women with amputated cervix, total hysterectomy or with apparent cervical pathology were excluded.

All selected women are subjected to, History taking in a special...
data entry sheet. General examination (Including vital signs, breast examination, ascites or decreased breath sounds with lung auscultation), Local pelvic examination (Inspection of the cervix with the naked eye to detect any visible lesion using Cusco’s vaginal speculum in the lithotomy position).

The squamocolumnar junction was visualized and scraped gently throughout its circumference, with the hooked end of Ayer’s spatula, and material was transferred to glass slides. The smears were fixed with 95% alcohol immediately and stained by Papanicolaou stain. Cytology was considered abnormal (positive) if it included atypical squamous cells of undetermined significance (ASCUS), low-grade intraepithelial lesion (LSIL), high-grade intraepithelial lesion (HSIL), or invasive cancer.

A cotton swab soaked with solution of 5% acetic acid was then applied to cervix using. The cervix was then examined 1-2 minutes under an adequate light source. The detection of any distinct aceto-white area was considered positive result, a single biopsy is taken from the impressive site in the aceto-white areas after VIA (most white, most thick and most sharp borders) and any bleeding is stopped by Ag NO3 application. If no aceto-white areas were recorded the test result was considered negative.

The women were screened using Pap smear and VIA while colposcopy was done for all women. Cervical biopsies were taken from Positive cases on any screening test. All women with a positive VIA (200) (124 of them are +ve VIA and Pap while other 76 are +ve VIA only), abnormal Cytology (40 are –ve VIA), or those with abnormal colposcopy (70 are VIA –ve and Pap –ve) were subjected to cervical biopsy and were included in our study. Thus a total of 310 cases from whom cervical biopsy were taken were included.

The statistical test used was the Fischer exact test and results were computed using statistical package for social sciences (SPSS) version 12.

**Results**

In our study 3298 women were screened and only 310 of them were enrolled. The percentage of included women was 9.4%. Of the women screened, VIA was positive in 200 (6%) and 164 (5%) were positive on Papanicolaou smear (ASCUS or worse lesions). Of the included 310 women the mean age of the participants was 36.1 years, the mean period of marriage was 17.3 years and the mean of parity was 1.8 (Table 1).

Pelvic pain was the most common presenting symptom (58%). Abnormal vaginal discharge was the second most common presenting complaint (23%) (Table 2).

The majority of the women were married after 20 years of age (71%). There was a significant association between early age of marriage and positive VIA (Fischer exact P=0.004) but no significant association between early age of marriage and positive Pap smear (Fischer exact P=0.38) (Table 3). The majority of the included women had abnormal Pap smear 164/310 (53%) of which 77% (n=124) showed a positive VIA.

In (Table 4) the histopathology results of the biopsy are summarized. Biopsy revealed 191 true-positive cases, VIA detected 161 of them, yielding a sensitivity of 84%, specificity of 67%, positive predictive value (PPV) of 80.5% and negative predictive value (NPV) of 73%. VIA had detected 100% (16 of 16) of invasive carcinomas, 93% (27/29) of CIN III, 85% (50/59) of CIN II, and 78% (68/87) of CIN I. While the sensitivity, specificity, PPV and NPV of cytology (PAP) were 72, 78, 84 and 64%, respectively. Cytology detected 81% (13 of 16) of invasive carcinomas, 86% of CIN III (25 of 29), 68% (40 of 59) of CIN II, and 69% (60 of 87) of CIN I.

**Discussion**

Our study showed VIA positive rate in 6%. While Goel et al. [6] had a higher rate of 12.5% of VIA. Whereas positive VIA extends from 2.8% in a study by Dhaubhadel, [8] to 41% by Sankaranarayanan et al. [9]. The wide variation in rates in various studies is due to the different criteria used for screening and the different population of women screened.

It was noted that 5% of Pap smear in our study was abnormal considering ASCUS and above as abnormal. It was reported by Denny et al. [10] an incidence of abnormal Pap smear of 8.2%.

Visual inspection with acetic acid was abnormal in 254 (12.6%); Pap smear showed atypical squamous cells of undetermined significance or worse in 3% in a study conducted by Elit et al. [11]. They aimed to evaluate the test parameters of visual inspection with acetic acid (VIA) and cervical cytology in Mongolia. Two thousand nine women underwent both tests.

In 1999, a large-scale (10934 women) study in Zimbabwe VIA was assessed to be used as an alternative to cytology in screening for cervical cancer in poorly resourced locations. They tested the sensitivity, specificity, and predictive value of VIA done by nurse-midwives in a

<table>
<thead>
<tr>
<th>Mean ± SD</th>
<th>Age</th>
<th>36.1 ± 5.6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parity</td>
<td>1.8 ± 2.1</td>
<td></td>
</tr>
<tr>
<td>Period of marriage</td>
<td>17.3 ± 6.7</td>
<td></td>
</tr>
</tbody>
</table>

**Table 1: Demographic criteria of the patients.**

<table>
<thead>
<tr>
<th>Chief complaint</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pelvic pain</td>
<td>181</td>
<td>58%</td>
</tr>
<tr>
<td>Abnormal discharge P/V</td>
<td>70</td>
<td>23%</td>
</tr>
<tr>
<td>Intermenstrual bleeding</td>
<td>30</td>
<td>10%</td>
</tr>
<tr>
<td>Postcoital bleeding</td>
<td>16</td>
<td>5%</td>
</tr>
<tr>
<td>Post-menopausal bleeding</td>
<td>7</td>
<td>2%</td>
</tr>
<tr>
<td>Urinary symptoms</td>
<td>6</td>
<td>2%</td>
</tr>
<tr>
<td>total</td>
<td>310</td>
<td>100%</td>
</tr>
</tbody>
</table>

**Table 2: Complaints of patients.**

<table>
<thead>
<tr>
<th>Age at Marriage</th>
<th>Number</th>
<th>%</th>
<th>VIA +ve</th>
<th>Fischer exact p value</th>
<th>PAP +ve</th>
<th>Fischer exact p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 20 years</td>
<td>90</td>
<td>16%</td>
<td>69</td>
<td>0.004</td>
<td>44</td>
<td>0.38</td>
</tr>
<tr>
<td>≥ 20 years</td>
<td>220</td>
<td>84%</td>
<td>131</td>
<td>0.004</td>
<td>120</td>
<td>0.38</td>
</tr>
<tr>
<td>Total</td>
<td>310</td>
<td>100%</td>
<td>200</td>
<td>164</td>
<td>164</td>
<td>100%</td>
</tr>
</tbody>
</table>

**Table 3: Screening results in relation to age at marriage.**

<table>
<thead>
<tr>
<th>Histopathological findings</th>
<th>VIA +ve PAP +ve</th>
<th>VIA +ve PAP -ve</th>
<th>VIA +ve PAP +ve</th>
<th>VIA +ve PAP -ve</th>
<th>VIA -ve PAP +ve</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative biopsy</td>
<td>Normal or inflammatory</td>
<td>11</td>
<td>28</td>
<td>15</td>
<td>65</td>
<td>119</td>
<td>38%</td>
</tr>
<tr>
<td>CIN I</td>
<td>44</td>
<td>24</td>
<td>16</td>
<td>3</td>
<td>87</td>
<td>28%</td>
<td></td>
</tr>
<tr>
<td>CIN II</td>
<td>32</td>
<td>18</td>
<td>8</td>
<td>1</td>
<td>59</td>
<td>19%</td>
<td></td>
</tr>
<tr>
<td>CIN III</td>
<td>24</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>29</td>
<td>10%</td>
<td></td>
</tr>
<tr>
<td>Invasive carcinoma</td>
<td>13</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>16</td>
<td>5%</td>
<td></td>
</tr>
<tr>
<td>total</td>
<td>124</td>
<td>76</td>
<td>40</td>
<td>70</td>
<td>310</td>
<td>100%</td>
<td></td>
</tr>
</tbody>
</table>

**Table 4: Distribution of histopathological findings based on screen test findings.**

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less-developed country. Sensitivity was 76.7% for VIA and 44.3% for cytology. Specificity was 64.1% for VIA and 90.6% for cytology [12].

The study done by Sankaranarayanan et al. [9] reported better results with visual inspection. They detected sensitivity of 90.1% and specificity of 92.2%. Our results showed 80.5% of PPV for VIA and 84% for cytology. Which are higher than the values reported by Sankaranarayanan et al. (17% of PPV for VIA and 17.2% for cytology)

The study done by Doh et al. [13] in Cameroon, Africa detected a sensitivity of 70.4% for VIA while for PAP it was 47.7%. Specificities were 77.6%, 94.2% for VIA and PAP respectively. PPV of VIA was 44% and NPV 91.3%. They concluded that, although PAP has slightly better testing qualities, VIA has acceptable test qualities and may in low resource settings be implemented as a large scale screening method.

In India Goel et al. [6] found a sensitivity of 96.7% for VIA, much higher than that of a Pap smear, which was 50%. The specificity of VIA, however, was much lower than the Pap smear, 36.4% vs 97%.

Eftekhar et al. [14] conducted a study to evaluate the accuracy of visual inspection with 5% acetic acid (VIA) when used to detect cervical cancer and its precursors. One hundred with a positive VIA test and 100 women with a negative VIA test were randomly selected for this study. They reported VIA test sensitivity and specificity were 95.7% and 44.0% respectively, while they were 10% and 92% for cytology tests.

In Egypt, Abdel-Hady et al. [15] conducted a study to assess the performance of VIA as screening test for detection of cervical carcinoma. Diluted acetic acid (5%) was applied to the cervix during routine gynecologic examination. Women with positive results were referred for colposcopy. Among the 5,000 women who were screened using VIA, 409 were referred for colposcopy. The sensitivity and negative predictive value of the VIA screening test was 97%.

In a study done by Gravitt et al. [16] a population-based sample of 5603 women in India were invited to participate in a study comparing Pap cytology, VIA, and HPV DNA screening for the detection of CIN3 and cancer. HPV testing had a higher sensitivity (100%) and specificity (90.6%) compared to Pap cytology (sensitivity =78.2%; specificity=86.0%) and VIA (sensitivity=31.6%; specificity=87.5%).

At the Ege University clinic Ardahan and Temel, [17] conducted a study addressed the validity of VIA in cervical cancer screening by comparing results with colposcopy findings. Of 350 women screened using the Papanicolaou test, colposcopy and VIA. When VIA findings were compared with Papanicolaou test findings, the sensitivity of VIA was 82%, specificity was 50%, (PPV) was 67.6%, and (NPV) was 68.8%.

The study done by Nessa et al. [1] compared the efficacy of VIA and cytology-based primary methods for cervical cancer screening in Bangladesh. 650 women were included, were VIA was +ve in 74 (11.4%) and 8 (1.2%) had abnormalities in their Pap smear reports. VIA had a sensitivity of 88.9% and specificity of 52.1%. While the PPV and NPV were 41.0%, and 92.6% respectively. In Pap smear the sensitivity, specificity, PPV and NPV were of 33.3%, 95.8%, 75.0% and 79.3%, respectively.

The study done by Saleh, [2] in Egypt reported that VIA had a sensitivity of 90%, specificity of 37%, and positive predictive value of 52% and negative predictive value of 81%. While the Pap smear had a sensitivity of 50.1%, specificity of 93.1%, and positive predictive value of 89.3% and negative predictive value of 65.6%.

It is nearly accepted by all the previous studies that VIA is an easy alternative screening test for cancer cervix. The results of our study were compatible with the previous studies in showing that the sensitivity, specificity, positive predictive value, and negative predictive value of VIA were 84%,67%, 80.5% and 73% respectively and that of Pap smear 72%, 78%, 84%, and 64% respectively. Thus we concluded that VIA as compared to Pap smear can be a better screening test due to its ease of use and low cost.

Accordingly, we concluded that we can effectively screen most of the cases with cervical pre-cancer and cancer through VIA. The rate of detection of cervical dysplasia in both VIA and the Pap smear was equal in our study. The VIA has better sensitivity and negative predictive value than that of the Pap smear but a lower specificity than that of Pap smear.

Conclusion
VIA has the advantage of easy learning, inexpensiveness, high sensitivity in comparison to Pap smear and immediate availability to assess results. Thus, VIA represents a good method of cervical cancer screening in many parts of the world especially in poorly resourced locations.

Limitations of the Study
The main limitation of VIA strategy is low specificity which may lead to overtreatment. Also colposcopy was used as a confirmatory test (final diagnosis) in this study, rather than histology, because of the ethical pitfalls of subjecting VIA-negative women to surgical procedures like cervical biopsy.

References


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