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Original Article

Visual inspection of cervix with acetic acid (VIA) in early diagnosis of cervical intraepithelial neoplasia (CIN) and early cancer cervix

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Abstract

Objectives: To study the place of visual inspection of cervix with acetic acid in screening for CIN and cancer cervix and to compare and correlate the efficacy of VIA with cervical cytology in early detection of cancer cervix. *Methods:* This cross sectional study took place in the Gynaecology out patient department (GGOPD) of NSCB Medical College, Jabalpur between June 2005 and September 2006. Out of the total 16,400 women who attended GOPD during this period, 750 women were screened for CIN and early cancer cervix. VIA and pap smears were done concurrently and their sensitivity and specificity compared. For ethical reasons all those who were found positive were subjected to colposcopy and further management as per standard guidelines. *Results:* Out of the 750 women screened VIA was positive in 122 (16.26%) women and cytology was positive in 39 (5.2%) cases of the true positive (27 cases). The difference between the two tests was statistically significant (P=0.000001) VIA being highly sensitive (93.1%) buy less specific than cytology. *Conclusion:* The high sensitivity of VIA shows that the test could be valuable in detection of precancerous lesions of the cervix.

Key words: cervical carcinoma, screening, VIA cytology

Introduction

Cervical cancer is the second most common cancer in women worldwide [1]. An estimated 3,71,000 new cases of cervical cancer are identified every year and accounts for about 1,90,000 deaths annually [2]. Carcinoma cervix continues to be the most common genital cancer encountered in clinical practice in India [1]. The disease is more prevalent among women living in poor conditions with a low income and indifferent education. In India approximately 90,000 new cases of cancer cervix occur every year. The incidence in India is 45 per one lakh women [3].

VIA involves naked eye examination of the 3-5% acetic acid swabbed uterine cervix without any magnification with illumination provided by a bright light source, such as a halogen lamp. A positive test is the detection of well-defined, dull acetowhite lesions on the cervix. The objective of VIA is to detect acetowhite lesions leading to the early diagnosis of high grade cervical intraepithelial neoplasia and early preclinical, asymptomatic invasive cancer. A major advantage with

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VIA is that, it is a real-time screening test, as the outcome is known immediately after the administration of the test, so that further investigations/treatment can be planned and carried out during the same visit.

Material and Methods

This cross sectional study was carried out in NSCB Medical College hospital in the out patient Department of Obstetrics and Gynecology between 1st June 2005 and 30th September 2006. Seven hundred fifty women with inclusion and exclusion criteria were screened for CIN and early cervical cancer.

The study protocol was reviewed and approved by institutional ethical committee and informed consent was obtained from each woman. Relevant obstetric and gynecological history was obtained and recorded.

Inclusion criteria

All women about 25 years of age or marital life more than 3 years were subjected for screening irrespective of the purpose of GOPD visit.

Exclusion criteria

Unmarried women, women with frank invasive cancer cervix (with visible growth on cervix), women with bleeding per vaginum, pregnancy were excluded.

Per speculum examination was done by the same observer, to observe the size and shape of the cervix, the external os identified with pinkish squamous epithelium and reddish columnar epithelium and transformation zone. pap smear was taken and two samples were taken one from ectocervix and other from endocervix. The pap smear slide was immediately fixed with 90% ethyl alcohol. Later, the slide was sent for cytology in the Department of Pathology, NSCB, Medical College Hospital, Jabalpur.

Pap smear reporting was done according to the Bethesda classification [4]. After taking pap smear, the same patients were subjected to visual inspection of the cervix with acetic acid. Using a cotton swab soaked in acetic acid for 1-2 minutes, 5% acetic acid was applied and then the cervix was carefully inspected for any acetowhite lesions, particularly in the transformation zone.

The test outcome was considered positive on the basis of the following criteria –

1. Intensity of the white color of acetowhite lesion
2. Borders and demarcation of the white lesion
3. Whether the lesion is uniformly white in color or the color intensity varies across the lesion
4. Location of the lesion
5. Size and number of the lesion

Reporting of test outcome

In the study, test was reported as positive, negative and inconclusive VIA test.

Positive test: Visualization of the dense acetowhite lesion with sharp margins located in the transformation zone, close to SCJ.

Negative test: If no acetowhite lesions were observed on the cervix polyps protruding from cervix, bluish white in color, nabothian cysts which appear as button like areas as whitish area or pimples, dot like areas present in the endocervix which were due to grape like columnar epithelium staining with acetic acid; if there were shiny pinkish white, cloudy white or bluish white, faint patchy or doubtful lesions with ill defined, indefinite margins or irregular, acetowhite lesions resembling geographical lesions away from the SCJ.

Inconclusive test: No distinct acetowhite lesion or somewhat doubtful lesions or when the cervix could not be adequately assessed.

If VIA turns out to be positive the patient was subjected to further investigations such as colposcopy and guided biopsy.

The results of visual inspection of cervix with acetic acid (VIA) were correlated with that of pap smear on the basis of sensitivity, specificity and positive predictive value.

Statistical analysis was done as follows

2x2 table was used to compare VIA and cytology and analysis was done as follows:

	VIA positive	**VIA negative**
Cytology positive	a	b
Cytology negative	c	d

Where a = true positive b = false positive
c = false negative d = true negative

1. Sensitivity = $\frac{a}{(a + c)}$ x 100

2. Specificity = $\frac{d}{(d + b)}$ x 100

3. Positive predictive value (PPV) = $\frac{a}{(a + b)}$ x 100

4. Negative predictive value (NPV) = $\frac{d}{(c + d)}$ x 100

5. Chi square test

Results

Out of the 750 women screened, VIA was positive in 122 (16.26%) women and cytology was positive in 39 (5.2%) cases of the true positive (27 cases), 25 were detected by VIA and only 20 cases were detected by pap smear. Two cases were missed by VIA and seven cases were missed by cytology.

The mean age of the population in the study group was 38.2 years and the majority was parous women belonging to the low socioeconomic status (Table 1).

On comparing the results of VIA and pap smear, 32 cases having positive cytological findings, nine as ASCUS, 15 as LSIL, seven as HSIL, one as invasive cancer were detected correctly by VIA. Only seven cases positive on cytology (five ASCUS, two LSIL) were not detected by VIA. VIA had a high detection rate (82.05%) for lesions positive on cytology (82.05%). (Table 2).

In the present study the sensitivity and specificity calculated were the assumed sensitivity and specificity as the reference standard test was not applied to all the cases.

On comparing the results of VIA and pap smear, the sensitivity of VIA (93.1%) was more than pap smear (70.02%). Hence it was more effective in screening the true positives. The specificity of VIA (86.8%) was comparable to pap smear (97.2%) whereas the positive predictive value of pap smear (51.2%) was greater than VIA (22.1%). The negative predictive value for VIA is 99% vs 97% for pap smear. (Table 3).

Sensitivity ratio of VIA with pap smear is 1.41.

In the study, there were 750 women out of which 122 (16.27%) women were VIA positive. Colposcopy was performed on 140 cases (18.67%), 122 VIA positive and the remaining women with an unhealthy looking cervix.

VIA could detect 25 out of 27 cases positive by histopathology. The sensitivity of VIA was 93.1% and the specificity was 86.86% (Table 4).

Sankaranarayanan[4] in Kerala found that out of 1,357 subjects 509 (37.7%) women were positive for VIA, 205 (15.2%) were positive on pap smear and 107 cases had an abnormal looking cervix. The sensitivity estimate was 96% vs 62% of VIA and cytology specificity was 68% vs 90% for VIA and cytology. VIA demonstrated a higher detection rate of moderate dysplasia or worse lesions than cytology. However it was significantly less specific than cytology and resulted in referral of more than one third of women for colposcopy.

Table 1. Basic characteristics.

Characteristics	Findings (%)
Age (In years)	
18-24	85 (11.3)
25-34	232 (30.9)
35-44	343 (45.7)
45-54	72 (9.6)
>54	18 (2.4)
Mean age	38.2 years ± (2)
OCCUPATION	
Unskilled	517 (68.9)
Semiskilled	69 (12.8)
Skilled	131 (17.4)
Unemployed	6 (0.8)
LOCALITY	
Rural	286
Urban	464
EDUCATION	
None	436 (58.1)
Primary	100 (13.3)
Secondary	214 (28.4)
Graduate	30 (3.9)
NUMBER OF CHILDREN	
1-2	353 (47.0)
3-4	342 (45.6)
5-6	46 (6-1)
7 and above	5 (0.6)

Table 2. Comparison and correlation of visual inspection of cervix with acetic acid with cytology.

	Pap smear Reporting							
VIA	**NILM**	**ASCUS**	**LSIL**	**HSIL**	**Invasive cancer**	**Report missing**	**Inadequate smear**	**Total**
Positive	85	9	15	7	1	5	0	122
Negative	574	5	2	0	0	31	16	628
Total	659	14	18	7	1	35	16	750

NILM – Negative for intraepithelial lesions or malignancy

ASCUS – Atypical squamous cells of undetermined significance.

LSIL – Low grade squamous intraepithelial neoplasia

HSIL – High grade squamous intraepithelial neoplasia

Table 3. Statistical comparison of VIA and cytology.

Pap smear	**VIA**		
	Positive	**Negative**	**Total**
Positive	32	7	39
Negative	90	621	711
Total	122	628	750

c^2 = 125.66, P=0.000001. *df*=1 CL=12.8 – 81

Table 4. Correlation of histopathology report, visual inspection cervix with acetic acid and pap smear.

HPR*	**VIA** Positive	**Pap smear** Negative	**Total** Positive	Negative	
Chronic cervicitis with atypical cells	1	1	2	-	2
Mild dysplasia	10	1	7	4	11
Moderate dysplasia	7	-	6	1	7
Severe dysplasia	6	-	4	2	6
Invasive cancer	1	-	1	-	1
Total	25	2	20	7	27

*HPR = Histo pathology Report ** VIA visual inspection of cervix with acetic acid.

In our study, there were 750 subjects out of which 122 (16.27%) women were VIA positive. Colposcopy was performed on 140 cases (122 VIA positive and the remaining women with an unhealthy looking cervix).

The estimated sensitivity in the present study was 93% vs 70.02% and specificity 86% vs 97% for VIA and cytology respectively.

Thus in the present study VIA had a higher detection

Table 5. Summary of VIA study results.

Reference	N	Purpose	Key statistics	Key results
Sankaranarayanan et al[4]	3000	Compare performance of VIA and cytology	Sensitivity ratio / approximate 2 Sensitivity / McNemars	Sensitivity ratio = 1.05, p=0.25, (Sensitivity estimate = 90% vs 86% for cytology) approximate specificity of VIA= 92% approximate specificity of cytology, 91% PPV 17% for VIA vs 22% for cytology; NPV 99% vs 99%.
Sankaranarayanan[4]	1351	Compare performance of VIA and cytology	Sensitivity ratio / approximate 2 specificity McNemars	Sensitivity ratio = 1.54, p<0.001 (Sensitivity estimate = 96% vs 62% for cytology) approximate specificity of VIA =68% , approximate specificity of cytology; 90%, PPV 15% for VIA vs 25% for cytology, NPV 99% vs 97%.
University of Zimbabwe JHPIEGO	10934	Test qualities of VIA	Sensitivity / Specificity	Sensitivity = 77% for VIA vs 44% for cytology / specificity = 64% for VIA vs 91% for cytology, PPV 19% vs 88%, NPV 96% vs 94%.
Present study NSCB MCH, Jabalpur	750	Compare performance of VIA and Pap smear	Sensitivity / Specificity	Estimated sensitivity for VIA 93.1 vs 70.020% for cytology, approximate specificity 86.8% for VIA vs 97% for cytology, PPV, 22.1% vs 51.2% NPV 99.1% vs 97.1%

rate of true positive cases than cytology. VIA could detect seven cases missed by cytology, and cytology was able to detect only one case, missed by VIA.

Discussion

The results of the present study were consistent with recent studies shown in table 5. As per the studies, VIA is more sensitive but usually less specific than cytology. The results of the current study and other reported studies indicate that VIA is a simple objective test. The result of this procedure positive or negative is available immediately, allowing an algorithm of further investigations to be carried out for the identification of cervical lesions. It has been shown that follow up colposcopy and treatment of preinvasive lesions can be performed immediately which not only avoids recall but also increases compliance to diagnostic investigation and treatment. The test is not expensive and it is possible to train providers to detect acetowhite lesions with the naked eye examination.

Notwithstanding the specificity (a high false positive rate) which means that many subjects will be recalled for colposcopy, it seems that the objectivity of the test can further be improved possibly by magnification.

Currently, there are three large randomized trials ongoing in India (Dindigul district, Tamil Nadu; Mumbai (Bombay) city and Osmanabad district, Maharashtra) that are addressing the efficacy of VIA:

ConclusionVIA is an attractive test in low resource settings like India. It is simple, inexpensive, low technology test that requires minimal infrastructure for use. It is comparable to cytology in detecting low as well as high grade lesions in terms of sensitivity, specificity and positive predictive value. It is a real time in the sense that the results are available immediately, making it possible to institute further diagnostic investigations for test positive women, as well as plan and offer treatment during the same visit. The reporting of pap smear is not available immediately and it is not cost effective.

The majority of women in India, who belong to the low

socio economic status, remain devoid of any screening test, as pap smear is unaffordable to them.

The time has come, to integrate VIA based screening programs at the primary care level of health services, and to downstage cancer cervix in our country

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