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ORIGINAL ARTICLE

Diagnostic Value of VIA Comparing with Conventional Pap Smear in the Detection of Colposcopic Biopsy Proved CIN

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Abstract

Aim: A study to assess the role of visual inspection with acetic acid VIA as an alternative to Pap smear in screening program for cervical cancer in low resource settings.

Method: Two hundred and twenty five women in reproductive age group attending the Gynecology department at K.S Hegde Charitable Hospital were enrolled in the study. A Papanicolaou smear and visual inspection of the cervix with acetic acid was done. All women then underwent colposcopy using the video colposcope. All patients who tested positive on screening then underwent colposcopy guided biopsy. Pap smear of Low grade squamous intraepithelial lesion (LSIL) and above was taken as abnormal. The statistical test used was chi square test and results were computed using Statistical Package for the Social Sciences (SPSS) version 12.0.

Results: Out of 225 patients, VIA was positive in 27(12%) patients and Pap smear was abnormal in 26(11.7%). There were 15 LSIL, 6 high Grade Squamous intraepithelial lesions (HSIL) and 5 were squamous cell carcinoma. On biopsy, there were 15 mild dysplasia, 2 moderate dysplasia, 4 severe dysplasia and 3 squamous cancers. Pap smear had a sensitivity of 83%, specificity of 98%, and positive predictive value of 80 % and negative predictive value of 97.9%. VIA had a sensitivity of 70.8%, specificity of 95%, and positive predictive value of 62.9 % and negative predictive value of 96.5%.

Conclusion: Since diagnostic values of VIA is comparable to Pap smear, and it performs well in detecting high grade lesion we conclude that VIA can be used as a screening modality for cervical cancer in low resource settings.

Keywords: Cervical cancer in low resource settings, Pap smear- colposcopy, visual inspection with acetic acid

Introduction

Cervical cancer is the leading malignancy among Indian women accounting for 26.1- 43.8% of all cancers in Indian women.[1] Conventional cervical cytology is the most widely used cervical cancer screening test in the world and cytology screening programmes in several developed countries have been associated with impressive reduction in cervical cancer burden.[2] Papanicolaou (PAP) smear is a simple, safe, non-invasive and effective method for detection of pre-cancerous, cancerous and non-cancerous changes in the cervix and vagina.[3] Colposcopy is a worldwide accepted method for detection of early cervical neoplasia.[4] Common problems encountered in colposcopy are inadequate expertise, interpretation difficulties, disagreements and failure to follow standard diagnostic protocol.[5]

The use of acetic acid during visual examination of the cervix, termed visual inspection with acetic acid (VIA), has been advocated as an alternative screening method to PAP smears in developing countries.[6] The attractive features of VIA include low cost, simple administration, real time screening, of results and accuracy comparable to good quality PAP smears.[7,

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[8] In a developing nation like India VIA would be a possible alternative screening tool for early detection of cervical cancer. Our study was intended to evaluate whether VIA was a suitable alternative to Pap smear in a low resource setting.

Methods

In this prospective study 225 women of age group between 20-50 years of age group attending the gynecology department at K.S. Hegde Charitable Hospital from November 2008 to June 2010 with their consent were included .Unmarried or pregnant women and women with active vaginal bleeding or frank growth of cervix were exclude from the study. A complete history of the patient pertaining to complaints, any white discharge per vagina, post coital bleeding , previous Pap smears obstetric history, menstrual history, contraception history is obtained. Informed written consent is taken. Detailed clinical data was obtained and noted on a structured proforma. Per speculum examination of cervix and vagina was done. The squamocolumnar junction was visualized, with the hooked end of Ayer's spatula, squamocolumnar junction was scraped gently throughout its circumference and material was transferred to glass slides. Two such smears were fixed with 95% alcohol immediately and stained by Papanicolaou stain.

A solution of 5% acetic acid was then applied to cervix using a cotton swab. The cervix was then examined under 1-2 minutes under an adequate light source. The detection of any distinct acetowhite area was considered positive result. If no acetowhite areas were recorded, or if a whitish appearance is doubtful, the test result was considered negative.

All women then underwent colposcopy using the videocolposcope COL PRO 222 DX [PRO MIS]. All patients who tested positive on screening underwent colposcopy guided biopsy.

In colposcopy saline was used initially to clean the surface and then vascular lesions and surface lesions are assessed. Abnormal vessels are examined with the aid of green filter, 5% acetic acid is then applied to mucosal epithelium and it causes disappearance of cervical mucus. If any acetowhite lesions are noted, their intensity, speed of appearance and disappearance are noted. On colposcopy, findings such as dense acetowhite epithelium, sharply bordered acetowhite epithelium, dilated caliber, irregular shaped or coiled vessels, coarse punctuation, mosaic appearance, atypical vessels and irregular surface contour indicate imminent cancer. Biopsy was done using a punch biopsy forceps from abnormal areas detected by under colposcopic guidance. A test after visual inspection of cervix with acetic acid is considered positive if cervical epithelium becomes white and opaque with distinct margins within the transformation zone. For Pap smear a finding of LSIL [low grade squamous intraepithelial lesion] and above was considered positive. If Pap smear was positive and VIA /colposcopy is negative in the first setting, biopsy is taken at a later visit.

Results were then compiled and analyzed. Sensitivity, specificity, positive predictive value negative predictive value was then calculated for Pap smear, visual inspection with acetic acid, colposcopy or colposcopy with the histopathology results as the gold standard. The statistical test used was chi square test and results were computed using Statistical Package for the Social Sciences (SPSS) version 12.

Results

Of the 225 women screened for precancerous lesions of the cervix in the department of Obstetrics and gynecology 56.6% belonged to the 41-50 year age group and 68.5% belonged to the lower middle group. Of the 225 women examined using the VIA 27 (12%) were positive. A sum total of 26 Pap smears were abnormal (Figure 1). Colposcopic examination revealed 35 patients (11.5%) had abnormal findings and 190 (84.4%) were normal. In 34.5% of cases, biopsy report was normal or cervicitis. Majority of the cases had mild dysplasia (41.7%). Squamous cell carcinoma and moderate dysplasia were reported in 8.3% and 5.5% respectively**.** Colposcopy or colposcopy guided cervical biopsy wherever available was taken as gold standard. The major presenting complaint was menstrual irregularities in 92 women (40.8%). Twenty-nine women had complaints of white discharge per vagina forming 12.9%. After further questioning, it was found that 22 women also had white discharge per vagina with other complaints. White discharge per vagina was the most common presenting complaint where in precancerous and malignant lesions were detected.

There was an increased incidence of precancerous lesions in the age group of 41-50 years reflecting that cervical cancer has a long latent phase of progression. This pattern of age distribution was observed in both screening techniques ie VIA and Pap smear (Table 1 and 2). On comparing the results of Pap smear with colposcopy/colposcopy guide biopsy it was found that Pap smear missed 2 cases of mild dysplasia. One report of ASCUS was detected to be moderate dysplasia on biopsy. Three cases of HSIL were found to be mild dysplasia on biopsy. There were 5 false positive cases (Table 3). When results of VIA were compared that of colposcopy/colposcopy guide biopsy it was found that with VIA did not detect 6 cases of mild dysplasia. However it detected all the cases of moderate and

severe dysplasia. Two cases of mild dysplasia and one case of severe dysplasia not detected by Pap smear were detected by VIA. There were eleven cases of false positives (Table 4). Six cases of moderate and severe dysplasia were detected by biopsy. VIA performs better in diagnosing moderate and severe dysplasia which are true precursors of cervical cancer. VIA and Pap smear detected all the cases of squamous cell cancer which were micro invasive (Table 5). On comparison of the diagnostic values of Pap smear with VIA, VIA seems to have relatively lower sensitivity, specificity positive and negative predictive values (Table 6).

Discussion

In our study, 225 women who attended Department of Obstetrics and Gynecology in Justice K.S. Hegde Charitable Hospital with various presenting symptoms were included in the study. Similar hospital based study was first performed in 1982.[9] Recent studies that were performed using hospital based population were conducted in 2005 involving 400 patients and in 2007 involving 300 women.[10, 11] Similar studies were performed at corporate hospital.[12] In 1997, University of Zimbabwe / JHPIEGO Cervical Cancer Project

Table 1. Age wise Distribution of squamous intraepithelial lesions by Pap smear report

Age	No	LSIL	HSIL	Squamous cell cancer	Total SIL	%
21-30	15	0	0	0	0	-
31-40	83	3	1	3	7	3.1
41-50	127	12	5	2	19	8.4
Total	**225**	**15**	**6**	**5**	**26**	**11.5**

Table 2. Age wise distribution of VIA results

Age	No	VIA positive	%
21-30	15	2	1
31-40	83	10	4.4
41-50	127	15	6.6
Total	**225**	**27**	**12**

Fig 1. Showing results of Pap smear examination.

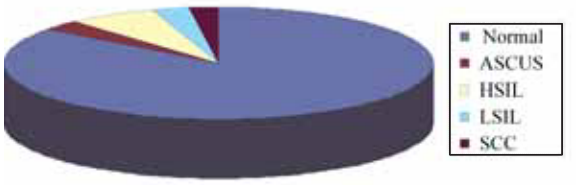

Table 3. Agreement between Pap smear and result of colposcopy guided biopsy

Histopathology of colposcopy guided biopsy	Pap smear results				
	Normal	ASCUS	LSIL	HSIL	Squamous cancer
Normal	2	2	2		
Chronic cervicitis	1	3	3		
Mild dysplasia	2		9	3	
Moderate dysplasia				1	1
Severe dysplasia		1		2	1
Squamous cancer					3

Table 4. Agreement of VIA and colposcopy guided biopsy result

VIA	Histopathology report						
	Normal	Chronic cervicitis	Mild dysplasia	Moderate dysplasia	Severe dysplasia	Squamous cancer	Total
Positive	4	7	7	2	4	3	27
Negative	2		6				8
Total	**6**	**7**	**13**	**2**	**4**	**3**	**35**

Table 5. The detection rate of moderate and severe dysplasia by VIA and Pap smears

Screening test	Moderate and severe dysplasia	Total no of patients	Percentage %
Pap smear	4	225	1.7%
VIA	5	225	2.2%

(1997) involved around 8,731 women screened by VIA.[6]

Women in the age group of 20-50 years were involved in our study. In study done by Goel A et al most subjects belonged to age group of 30 to 34 years [10].Whereas Khan S et al (2007) studied this screening method in the age range of 25 to 65 years [11].Denny L conducted a screening programme in the age group 35 to 65 years in South African women [7].

In our study VIA was performed by gynecologist. In studies conducted by Slawson et al , Bharani B and Phatak S, Goel A et al and Khan S et al gynecologists performed the procedure [10,11,12,13].However in another study done six oncologists performed the procedure [14]. In contrast trained nurses and midwives were involved in few studies [6,7,15].

Our study compared VIA with Pap smear with colposcopy or colposcopy guided biopsy being considered as gold standard. In our study colposcopy was done for all patients and biopsy taken if positive findings were present on Pap smear, VIA or colposcopy. Goel et al used similar methods; however they did LLETZ (large loop excision of transformation zone) instead of biopsy [10]. Few studies used VIA and cytology to screen patients and if positive screening test or clinical suspicion invited women for colposcopy and did colposcopy guided biopsy if necessary[14,15]. In one study researchers chose to do only VIA and if VIA was positive did colposcopy with biopsy being done in patients with abnormal colposcopic findings [12]. Khan S et al (VILI) Visual inspection with Lugols Iodine in addition to VIA and cytology and patients with positive findings were scheduled for colposcopy guided biopsies [11].

VIA positive rate in our study was 12%. Goel et al had a similar rate of 12.5% of VIA[10]. There was a wide variation in VIA positive rate that has been reported so far. Cecchini S et al reported positive VIA in 25.4% in their study[16]. Whereas Slawson et al and Megevand E et al reported a incidence of abnormal VIA of 4.2 and 3.13% in their study [13,15]. The wide range is due to difference in interpretation since few studies used nurses or paramedical workers to do the test. It also depends on the study population since few studies were done on symptomatic hospital based population and others as a mass screening test

It was noted that 11.7% of Pap smear in our study was abnormal considering LSIL and above as abnormal. Denny L reported a incidence of abnormal Pap smear as 8.2% [7]. University of Zimbabwe/JHPIEGO Cervical Cancer Project found that 14.6% of the women in their study had an abnormal Pap smear.

Megevand E et al noted an abnormal Pap smear in 13% of their study population. However Cecchini S et al could detect abnormal Pap smear only in 1% of their study population[16]. All these studies considered Pap smear of LSIL and above as abnormal. A study done by Slawson et al (1992) considered Pap smear of ASCUS and above as abnormal and found abnormal Pap smear in 7.1% of the women in their study.

The incidence of biopsy confirmed dysplasia in our study was 10.5%. Goel et al a dysplasia rate confirmed on histopathology in 7.5% of their population.

Table 6. Comparison of diagnostic values of VIA and Pap smear by other studies

Study	Screening Test	Sensitivity %	Specificity %	PPV %	NPV %
Present study	VIA	70.8	95	96.5	62.9
	Pap Smear	83	98	97.9	80
Shankarnarayanan et al (2001)	VIA	90.2	92.2	17.0	99
	Pap Smear	86	91	22	99
Goel et al (2005)	VIA	96.7	36.4	58	99.7
	Pap Smear	50	97	97.5	96.09
Singh K N, et al (2010)	VIA	93.1	86.8	22.1	99
	Pap Smear	70.02	97.2	51.2	97
Bhatla N, et al (2007)	VIA	100	53.3	15.7	100
	Pap Smear	50	98.9	80	95.8

Jeronimo J et al and Singh K N et al had a dysplasia rate of 2.49% and 3.6% respectively [8,14]. Since these studies involved larger number of patients, their incidence of dysplasia was less in comparison to ours

The results of test accuracy in cross-sectional study settings indicate that the sensitivity of VIA to detect high-grade precancerous lesions ranges from 66–96 % (median 84%); the specificity varied from 64–98% (median 82%); the positive predictive value ranged from 10–20% and the negative predictive value ranged from 92–97%._

The wide variation in results lies in the number of screeners, including different paramedical workers, and in the lack of uniform criteria used. Despite different study settings, providers, study protocols and definitions of positive tests, the estimates of VIA sensitivity cluster around a mean value of 76%.

There is general agreement that high quality cytology is a highly specific screening test, with estimates of the order of 98-99%. There is less agreement on the sensitivity of the test; cross-sectional studies have suggested sensitivity in the order of 50% in some circumstances. However, studies that have been able to assess sensitivity longitudinally have produced estimates that approximate to 75%.

Our study finds that VIA is comparable to Pap smear in sensitivity and specificity. It performs better in detection of moderate and severe dysplasia which are true precursors of cervical cancer.

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