Visual Inspection using Acetic Acid for Cervical Cancer in Low Resource Settings

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Introduction

Cervical cancer is a major public health problem in developing countries, with India itself accounting for one-fifth of the global burden of the disease. Approximately 1,30,000 new cases of cervical cancer are being detected in the country each year. India's cervical cancer age-standardised incidence rate of 30.7 per 100,000 and age-standardised mortality rate of 17.4 per 100,000 are the highest in South Central Asia [1]. While the ultimate option for reducing the prevalence of cervical cancer is vaccination, the costs are prohibitive. Though cytology (Pap smear) is reliable, the laboratory infrastructure and logistics including technical expertise may not be available in low-resource countries. The cost factor in testing for human papillomavirus (HPV) using DNA testing, coupled with requirement of trained manpower makes this option non-viable for developing countries [2], thus accentuating the need for alternative screening procedures.

Visual inspection using acetic acid (VIA) has emerged as a promising, cost effective, non-cytology based, "see and treat" alternative for economically underprivileged geographic regions [3].

Basis of VIA

VIA is based on the premise that the majority of pre-invasive and invasive cervical lesions are visible by 'naked-eye' examination following application of acetic acid. It involves insertion of a vaginal speculum and application of 3-5% acetic acid solution using a cotton swab, followed by inspection of the cervix with a halogen lamp after a waiting period of one minute. The results of the test may be interpreted as positive when an acetowhitening is present (VIA-positive) and negative when there is no acetowhitening (VIA-negative). The normal squamous epithelium of the cervix is pink. On application of acetic acid, cervical intraepithelial neoplasia (CIN) lesions take on a white colour; due to the increased nuclear proteins and cytokeratins in the cervical epithelium [4].

Efficacy and Effectiveness

A seven year (2000 to 2006) cluster sampling based randomised controlled trial conducted in Tamil Nadu to assess the efficacy of VIA screening in reducing cervical cancer incidence and associated mortality has demonstrated that the test is highly effective in low resource settings [5]. These clusters were randomly assigned into two equal groups; one getting VIA and the other getting existing care; and the results compared (Table 1). On follow up, it was observed that women who received VIA screening were 25% less likely to be diagnosed with cervical cancer later in life than those who did not and were 35% less likely to die from it as

Table 1

Results of a seven year followup after VIA in a cluster based study at Tamil Nadu (2000-2006)

	Intervention group	Control group
No of subjects observed	31 343	30958
Test Done	VIA	Existing care only
Positive on VIA	3088 (9.9%)	-
Diagnosed with precancerous lesions following VIA	1874 women (6.0%)	-
Person-years of observation	274 430	178 781
Cervical cancer cases	167 (0.61 per 1000 person years)	158 (0.88 per 1000 person years)
Cervical cancer deaths	83 (0.30 per 1000 person years)	92 (0.51 per 1000 person years)
Incidence hazard ratio	0.75 (95% CI: 0.55–0.95)	
Mortality hazard ratio	0.65 (95% CI: 0.47–0.89)	

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compared to the control group. However, of the 9.9% subjects who were screened as VIA-positive, only 6.2% actually had CIN or cancer, thus leading to over treatment of about 27% of the subjects.

In another Indian hospital based study comparing Pap smear, VIA and colposcopy for screening CIN involving 400 women, the sensitivity of VIA (96.7%) was much higher than that of the Pap smear (50%), and almost as high as that of colposcopy (100%). The specificity of VIA (36.4%) was lower than that of the Pap smear (97%) and colposcopy (96.9%), resulting in high false-positive rates for VIA. Two cases of endocervical lesions were also missed by VIA [6].

In an Iranian study [7], cytology and VIA was performed on all women attending a gynaecological clinic. Of these women, 100 subjects with a positive VIA test and 100 with a negative VIA test were selected randomly and colposcopy was performed for all 200 cases. Biopsies were obtained from subjects having abnormal colposcopic findings. Only those subjects with a final diagnosis of cervix dysplasia confirmed by colposcopy were considered positive cases for estimation of validity. The results (Table 2) showed that VIA had a higher sensitivity, but lower specificity than the Pap smear for detection of cervical dysplasia.

Validity

The sensitivity of VIA ranges from 63-77%, which is much higher than that of cytology (range 30-77%). The specificity of VIA is however low; being 44-73% in contrast to 99-99.8% specificity of cytology [6]. Though useful as a screening modality, VIA does not enjoy the status of a confirmatory test due to its low specificity when compared to cytology. Specificity may be improved by following up women having positive results following VIA with HPV testing or cytology. The positive predictive value of in VIA in various studies has ranged from 10-20%; while the negative predictive value has ranged from 92-100% [8].

Table 2

Performance of the VIA in comparison to pap smear in detecting cervical dysplasia in Iran (2005)

Screening test	Sensitivity (%)	Specificity (%)	PPV## (%)	NPV** (%)
VIA	96	44	71	88
Pap Smear	10	42	70	43
VIA+ Pap Smear	70	91	77	88

#Positive predictive value; **Negative predictive value

Advantages

The test is inexpensive, costing Rs 22.00 per examination vis-a–vis cytology; which costs Rs 47.00 per examination [9]. VIA can be performed with minimal infrastructure and may be done even in field conditions by the auxiliary health workers. The same has been demonstrated in a study to evaluate test performance of VIA by gynaecologists as compared to paramedical workers [10]. The results showed that VIA done by paramedical workers had a higher sensitivity (100% versus 87.5%), but lower specificity (53% versus 63%) than VIA done by the gynaecologists. There was moderate agreement (kappa=0.56) between the VIA findings of the paramedical workers and the gynaecologists (Table 3).

Besides, as the results are available immediately, multiple visits to the health facility are avoided, thereby reducing the percentage of dropouts. The training period required to acquire the skills of VIA is short. A course of 5 - 10 days is adequate, even for paramedical workers [11]; though it depends on the baseline skill level of the trainee and the amount of clinical practice available during training.

Limitations

The main limitation of the "see and treat" strategy of VIA is low specificity, which may lead to overtreatment; alongwith accompanying health and cost implications [5]. Although VIA is a sensitive screening test for detection of cervical dysplasia, it can not be used by itself. Applying VIA along with secondary triage procedures like HPV testing, Pap smear and colposcopy helps in detecting a higher number of cases with cancer precursor lesions. VIA may be less effective for elderly patients, because of the tendency of the transformation zone, and thus, any lesions within it, to recede into the

Table 3

Test performance of VIA conducted by gynaecologists and paramedical workers vis-a-vis the gold standard (cervical biopsy) (2004)

	Pos*	Neg@	TP#	TN+	Sens#	Spec~	PPV##	NPV**	DA++
Gold Standard	8	92	-	-	-	-	-	-	-
VIA by Gynaecologist	-	-	7	58	87.5 (47.3-93.6)	63.0 (52.3-72.8)	17.0 (7.1-32.0)	98.3 (90.9-99.9)	65.0 (54.8-72.2)
VIA by paramedical worker	-	-	8	49	100	53.3 (42.8-63.7)	15.7 (7.0-28.5)	100	58 (46.7-66.8)

* Positive; @ Negative; #True positive;+ True negative; #Sensitivity; ~ Specificity; ##Positive predictive value; **Negative predictive value; ++Diagnostic accuracy. Diagnostic accuracy = (TP+TN/ TP+FP+TN+FN) x 100. Figures in brackets indicate 95% confidence intervals

endocervical canal [12]. VIA results are subject to observer bias, making quality control in remote settings difficult. The other problem with VIA is the subjective nature of the test; which can be circumvented by the addition of Lugol's iodine staining to improve upon the sensitivity and specificity [13].

Conclusion

Although VIA is a useful alternative to cytology in low-resource settings, the test positivity and the detection rate of lesions has to be carefully monitored to maintain satisfactory performance. Regular training of health care providers is an important component; initial training being the most vital aspect. In majority of the studies, the assessment of the cervix and decisions on case management by freshly trained providers agreed with those of their trainers [11]. Follow-up assessments in Thailand and Ghana showed that the level of skills of the providers remained high regardless of the amount of time elapsed since the initial training [14].

As VIA is an entirely provider-dependent screening method, definitive standards need to be set for identifying precancerous lesions requiring therapeutic intervention. Mechanisms also need to be incorporated for effective supervision and continuous quality improvement. As VIA is a relatively new public health approach, evidence-based training materials including didactic training augmented by clinical practice need to be incorporated [11]; therby making it plausible to amalgamate VIA screening into primary health care services.

Conflicts of Interest

None identified

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