



CLINICAL ARTICLE

Visual inspection of the cervix with acetic acid for cervical intraepithelial lesions

A. Goel*, G. Gandhi, S. Batra, S. Bhambhani, V. Zutshi, P. Sachdeva

Department of Obstetrics and Gynecology, Maulana Azad Medical College, New Delhi, India

Received 17 March 2004; received in revised form 24 September 2004; accepted 27 September 2004

KEYWORDS

Cervical intraepithelial neoplasia;
Screening;
Papanicolaou smear;
Acetic acid

Abstract

Objective: Evaluation of visual inspection of the cervix with acetic acid (VIA) for screening cervical intraepithelial neoplasia. **Methods:** In this prospective study, 400 women were screened using the Papanicolaou (PAP) smear, VIA and colposcopy. Those who had positive results with any of the screening methods underwent large loop excision of the transformation zone (LLETZ). The sensitivity and specificity of each of the screening methods was analyzed. **Results:** 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 missed with VIA. **Conclusion:** Visual inspection of the cervix with acetic acid is very sensitive for ectocervical lesions. The advantages of the VIA method are its low cost and ease of use (it can be used by paramedical workers), its high sensitivity and its immediate results (it is possible to “see and treat” at the first visit). Its main limitation is a high rate of false-positive results, which may lead to overtreatment if a “see and treat” policy is applied.

© 2004 International Federation of Gynecology and Obstetrics. Published by Elsevier Ireland Ltd.

1. Introduction

Cancer of the cervix is a major health problem in India, which accounts for 26.1–43.8% of all cancers

in Indian women [1,2]. Therefore, screening and early detection of precancerous lesions is a priority in our country. A screening test is a simple, cost-effective and sensitive test that can be applied to large numbers of apparently healthy individuals; a diagnostic test, on the other hand, confirms a disease in symptomatic individuals or in individuals at high risk.

* Corresponding author. B-50 Preet Vihar, Delhi-110092, India. Tel.: +91 93 13770706; fax: +91 11 28122041.

E-mail address: dr_anjugoel@yahoo.co.in (A. Goel).

The main method of screening has been cytologic evaluation of the cervix (Papanicolaou [Pap] smear). The Pap smear has several limitations. These include low sensitivity, a need for trained personnel and laboratory facilities, and patients' compliance with follow-up. Thus, alternative strategies are being investigated [3].

One alternative strategy is screening by visual inspection of the cervix after application of acetic acid (VIA) [4–9]. The application of a 3–5% solution of acetic acid to the cervix causes cervical intraepithelial lesions to become white. This aceto whitening, which is visible to the naked eye, constitutes a positive result to the VIA test. Initial studies have shown VIA sensitivity to be similar to or higher than that of the Pap smear; however, more studies are required to confirm the utility of VIA as a primary screening method.

The aim of this prospective clinical study was to screen symptomatic women of reproductive age with the Pap smear, VIA and colposcopy. Those who had positive results with any screening method underwent large loop excision of the transformation zone (LLETZ).

2. Materials and methods

The study was carried out in the Department of Obstetrics and Gynecology of Maulana Azad Medical College (MAMC) and its associated hospital, Lok Nayak Hospital New Delhi, India, from March 2001 to February 2002. All Pap smears and cervical tissue specimens obtained with the LLETZ method were processed and diagnosed in the Cytopathology Division of the Institute of Preventive Oncology of the MAMC New Delhi. The study, which included 400 patients of reproductive age attending the gynecological outpatient department, was approved by the institutional research and ethics committee.

A detailed history was taken from all the women, followed by a general and gynecological examination. Those who were nulliparous or pregnant, with active vaginal bleeding or who had a frank growth on the cervix, were excluded from the study. Informed consent was obtained from all. The procedure included a speculum examination of the cervix followed by a Pap smear, VIA and colposcopy.

After taking a Pap smear, a 5% solution of acetic acid was applied to the cervix using a cotton swab. The cervix was examined after

1–2 min under an adequate light source. The detection of any distinct aceto-white areas was considered a positive result. The area and distribution of aceto-white lesions was recorded diagrammatically. If no aceto-white areas were detected, or if a whitish appearance was doubtful, the test result was considered negative. A review of the literature indicated that performing the cytologic smear first has no impact on VIA.

Colposcopy was performed in all women using the videocolposcope CT14FE (Sometch Model No. RS400). Scoring was done using the Reid combined colposcopic index [10] and a Reid score greater than 2 was considered positive. All patients who tested positive on screening underwent LLETZ and the tissue obtained was sent for histopathologic evaluation.

Large loop excision of the transformation zone was performed under local anesthesia as an outpatient procedure. A Divlabs electrosurgical unit was used (Divlabs Model RS400). The lesions found mildly dysplastic or worse on histopathologic evaluation of the LLETZ specimen were considered true-positive cases.

All results were compiled and analyzed. The sensitivity and specificity, the predictive value for positive test results and for negative test results, and the percentages of false-positive results and false-negative results were calculated for Pap smears, VIA and colposcopy, with histopathologic results as the gold standard.

3. Results

Most women belonged were aged between 30 and 34 years, with a mean age of 32.6 years. Mean age at first coitus was 21 years and 80% of the women had their first coitus before 22 years. Mean parity was 2.7.

Cytologic evaluation of the Pap smear revealed that 384 (86%) of the 400 women evaluated had a normal or inflammatory Pap smear and 16 (4%) had an abnormal Pap smear (Table 1). The result of the cytologic evaluation was considered positive if it revealed mild, moderate or severe dysplasia, carcinoma in situ (CIS), atypical endocervical cells or invasive cancer. Among the 16 abnormal cases, there were five cases of mild dysplasia (1.3%), three cases of moderate dysplasia (0.8%), four cases of severe dysplasia (1%), one case of carcinoma in situ (0.3%), one case of suspicious malignancy (0.3%) and two cases of atypical endocervical cells (0.5%).

Table 1 Results of cytological examination in 400 women

Cytological diagnosis	No. (%)
Normal	128 (32%)
Inflammation	195 (48.7%)
Inflammation with associated infection ^a	61 (15.3%)
Mild dysplasia	5 (1.2%)
Moderate dysplasia	3 (0.8%)
Severe dysplasia	4 (1%)
Carcinoma in situ	1 (0.3%)
Atypical endocervical cells	2 (0.5%)
Suspicion of malignancy	1 (0.3%)
Total	400 (100%)

^a Associated infections were human papilloma virus, *Trichomonas vaginalis*, *Gardnerella vaginalis*, *Candida* and shifting vaginal flora.

On VIA, 350 women (87.5%) were found to have a normal cervix and 50 (12.5%) had a positive result (Table 2).

On colposcopy, 337 women (84.3%) were found to have a normal cervix and 61 (15.3%) to have a positive result. Two women (0.5%) had unsatisfactory colposcopy (Table 3). Among the 61 colposcopies with abnormal results, 30 had a Reid score greater than 2, which was considered positive.

Large loop excision of the transformation zone was performed in the 63 women who tested positive on any of the 3 screening methods. Of the 63 (47.6%) biopsy specimens evaluated, 33 (52.4%) were negative and 30 were positive (Table 4). The 30 positive biopsy samples included 17 mild dysplasias, 4 moderate dysplasias, 5 severe dysplasias, 3 carcinomas in situ and 1 malignancy.

The three screening tests were analyzed with reference to biopsy results.

3.1. Cytologic evaluation correlated with biopsy results

Of 400 women, 16 had a Pap smear positive for mild dysplasia or worse (Table 5) and, of these 16 positive pap smears, 15 were also positive on biopsy, showing a high specificity of 97% for cytologic evaluation. One case of abnormal Pap smear had a

Table 2 Results of VIA in 400 women

Result	No. (%)
Negative	350 (87.5)
Positive	50 (12.5)
Total	400 (100)

Table 3 Results of colposcopy in 400 women

Result	No. (%)
Normal	337 (84.3%)
Abnormal	61 (15.2%)
Colposcopy unsatisfactory	2 (5%)
Total	400 (100%)

negative biopsy result. However, 15 other cases that were positive on biopsy (12 of mild, 2 of moderate and 1 of severe dysplasia) were missed on cytologic evaluation of the Pap smear, thus showing a low sensitivity of 50%. These cases had been detected on VIA.

3.2. VIA correlated with biopsy

The results of VIA were positive in 50 of the 400 women. On biopsy, 21 (42%) of the 50 tissue specimens had benign histologic changes, which included chronic cervicitis and chronic cervicitis with condylomatous changes, and 29 (58%) were found positive on biopsy (Table 6). The sensitivity of VIA to diagnose mild dysplasia or worse was 96.7% and the percentage of false-negatives was only 3.3%. The specificity of VIA, however, was only 36.4%, giving a large percentage (63.6%) of false-positive results.

One case of severe dysplasia, which was endocervical, was missed on VIA, showing that, although VIA is very sensitive for lesions of the ectocervix, it can miss endocervical lesions. The Pap smear had detected this lesion.

The sensitivity of colposcopy to diagnose mild dysplasia or worse was 100% when colposcopy was satisfactory. There were no false-negative results. Specificity was also very high (96.9%) and false-positive results were only 3.1%. Colposcopy was unsatisfactory in 2 women, both of whom had atypical endocervical cells on cytologic

Table 4 Results of LLETZ biopsy in 63 women

Histopathologic evaluation	No.	% (n=63)	% (n=400)
Chronic cervicitis	10	15.8%	2.5%
Chronic cervicitis with condylomatous changes	23	36.5%	5.8%
Mild dysplasia	9	14.3%	2.3%
Mild dysplasia with condylomatous changes	8	12.7%	2%
Moderate dysplasia	4	6.3%	1%
Severe dysplasia	5	7.9%	1.3%
Carcinoma in situ	3	4.8%	0.8%
Malignancy	1	1.6%	0.3%
Total	63	100%	15.8%

Table 5 Agreement between the diagnosis of the PAP test and biopsy (n=63)

		Biopsy								Total
		CHR. CER.	CHR. CER. and CONDYL	Mild DYSPL	Mild DYSPL and CONDYL	Mod DYSPL	Sev DYSPL	Ca in situ	Malig	
Pap test	Normal	1	3							4
	Inflam	6	13	5	1	2	1			28
	INFL and INFEC	2	7	1	5					15
	Mild DYSPL			3	1	1				5
	Mod DYSPL				1	1	1			3
	Sev DYSPL						2	2		4
	Carcinoma in situ							1		1
	Atypical endocer. cells	1					1			2
	Malignancy								1	1
Total	10	23	9	8	4	5	3	1	63	

evaluation (one was found to have severe dysplasia on biopsy).

4. Discussion

Cervical cancer continues to be a major public health problem in India, where 70% of the affected patients present late and, also, because screening programs have not been effective in detecting preinvasive lesions and early cancer [1,2,3].

4.1. The Pap smear

In India, screening by Pap smear has not significantly decreased the incidence of cervical cancer owing to several limitations:

1. Inadequate coverage of a large population, specially the rural and underdeveloped sections of society.
2. Lack of adequate infrastructure, including medical and paramedical staff, laboratory and transport facilities, and trained cytotechnicians and cytopathologists.
3. Poor compliance with follow-up visits.
4. The low sensitivity of the Pap smear.

As a screening test, the Pap smear has been found to have a low sensitivity, between 50% and 80%, resulting in a high false-negative rate of 9–40% [11–13]. The sensitivity of the Pap smear has

been found to be even lower in developing countries. The possible reason for this may be the large percentage of cervicitis and inflammatory smears, which mask mild dysplasia [14].

In our study, the sensitivity (50%) was even lower and the false-negative rate was higher (50%) than in other studies. There were 15 cases of dysplasia underdiagnosed as inflammation. These included 12 cases of mild, 2 of moderate and 1 of severe dysplasia (Table 5).

The specificity of cytologic evaluation, however, is high. The 97% specificity found in our study is similar to findings from other studies, in which the specificity ranges from 99% to 99.8%, with a low false-positive rate of only 0.2% to 1% [11–13].

4.2. VIA

Because of the limitations of the Pap smear, alternative strategies such as VIA have been studied. Various studies have shown VIA to be positive in 3–27% of cases [4–9]. In our study, 50 (12.5%) of 400 women had a positive result and 350 (87.5%) had a negative result on VIA. Since we screened a hospital-based symptomatic population, our VIA positivity rate of 12.5% was slightly higher than that found in other studies [4–8]. If this test had been done among the general population, we may have obtained lower positive rates. The wide variation in rates in various studies is due to the different criteria used for screening and the different population

Table 6 Agreement between the diagnosis of VIA and biopsy

		Biopsy								Total
		CHR. CER.	CHR. CER. and CONDYL	Mild DYSPL	Mild DYSPL and CONDYL	Mod DYSPL	Sev DYSPL	Ca in situ	Malig	
VIA	Positive	7	14	9	8	4	4	3	1	50
	Negative	3	9				1			13
	Total	10	23	9	8	4	5	3	1	63

of women screened. In a study from South Africa by Megavand et al. [4], only 3.1% of the women screened were positive on VIA. The authors found a lower rate of positive results on VIA because only distinct aceto-white areas were considered positive. In an Indian study by Shankaranarayanan [5] in which distinct aceto-white areas were considered positive, 9.8% of the women screened were found to have a positive result. In a recent study by Belinson et al. [9], the percentage of positive results on VIA (28%) was higher. This was because all grades of aceto-whiteness were taken as positive.

4.2.1. Sensitivity of VIA

The sensitivity of VIA to detect mild dysplasia or worse, as shown in various studies, ranges from 63% to 77% [4–9]. In our study, there were 30 biopsies with positive results and 29 of these were detected on VIA, giving VIA a high sensitivity of 96.7%. The only lesion missed on VIA was endocervical and it was detected by cytologic evaluation. Our study showed a higher sensitivity (96.7%) than in previous studies [4–9], probably because the screening was performed by the same two observers using uniform criteria.

4.2.2. Specificity of VIA

The specificity was low (36.4%) in our study. Other studies have shown a specificity ranging from 44% to 73% [4–9]. The wide variation in the results lies in the number of screeners, including different paramedical workers, and in the lack of uniformity of the criteria used.

The low specificity of VIA in our study could also be due to a large number of inflammatory smears (64% of the total population), as it is well known that inflammatory lesions becomes aceto-white [14].

Several variables affect the performance of VIA: (1) the light source, which should be white and condensed; (2) the training and experience of the observer; and (3) the presence of inflammation, infection and metaplasia.

5. Comparison of VIA with the Pap smear

In our study, VIA was more sensitive (96.7%) than the Pap smear (50%) for the detection of dysplasia. However, the specificity of VIA was much lower (36.4%) than that of the Pap smear (97%). Since we screened the same population with both modalities, the selection bias does not affect the sensitivity rates of VIA relative to cytology. Although colposcopy has a higher sensitivity and specificity than

VIA, it cannot be used for large-scale screening because of the equipment and expertise required.

6. Conclusions

In developing countries, adequate coverage of the entire female population by cytology-based screening programs is not at present feasible. Also, women are often not compliant regarding follow-up visits. In such a situation, VIA is a suitable primary screening alternative for a large population.

The advantages of VIA over the Pap smear include higher sensitivity, low costs, and immediate results. The availability of immediate results overcomes the problem of “loss to follow-up” that occurs in cytology-based programs.

However, the low specificity of VIA would lead to overtreatment of nonneoplastic lesions if a “screen and treat” policy is used. Thus, alternative strategies, including the two-stage screening process, have been investigated to improve the specificity of VIA [15,16]. A review of the literature reveals that a sequential testing of women having positive results with VIA, who would then receive human papillomavirus or Pap smear testing, would improve the specificity from 70–77% to 80–96%. However, the sensitivity falls from 75–90% to 50–80% [15,16].

The treatment of women found positive with VIA using inexpensive methods such as cryosurgery is being investigated [7]. If all cases found positive with VIA were treated by cryosurgery at the first visit, the following point should be kept in mind: all grades of dysplasia can take an aceto-white appearance. In our study, 12 of 50 cases found positive with VIA were moderate or severe dysplasia. The ideal treatment of high-grade lesions is excisional and not ablative. Cryosurgery is suitable only for low-grade lesions involving less than two quadrants; therefore, cases of moderate and high-grade dysplasias would have inadequate treatment.

Therefore, VIA is a good screening modality but needs to be combined with secondary triage procedures like human papillomavirus testing, Pap smear testing and colposcopy before the correct treatment can be instituted.

References

- [1] Cervical cancer control in developing countries: Memorandum from a WHO meeting. *Bulletin of WHO* 1996;74: 345–51.

- [2] Parkin DM, Bray F, Ferlay J. Estimating the world cancer burden: Globocan 2000. *Int J Cancer* 2001;94:153–6.
- [3] WHO J. National Cancer Control Programme. Policies and Managerial Guidelines.
- [4] Megavand E, Denny L, Dehaeck K, Soeters R, Bloch B. Acetic acid visualization of the cervix: an alternative to cytologic screening. *Obstet Gynecol* 1996;88:383–5.
- [5] Sankaranarayanan R, Wesley R, Somanathan T, et al. Visual inspection of the uterine cervix after application of acetic acid in the detection of cervical carcinoma and its precursors. *Cancer* 1998;83:2150–6.
- [6] Denny L, Kuhn L, Pollack A, Wright TC. Direct visual inspection for cervical cancer screening: an analysis of factors influencing test performance. *Cancer* 2002;94:1699–707.
- [7] Wright TC, Denny L, Kuhn L, Goldie S. Use of visual screening methods for cervical cancer screening. *Obstet Gynecol Clin North Am* 2002;29:701–34.
- [8] University of Zimbabwe/HPIEGO Cervical Cancer Project S. Visual inspection with acetic acid for cervical cancer screening: test qualities in a primary-care setting. *Lancet* 1999;353:869–73.
- [9] Belinson J, Pretorius R, Zhange W, Wu LY, Qiao Y, Elson P. Cervical cancer screening by simple visual inspection after acetic acid. *Obs Gynecol* 2001;98:441–4.
- [10] Reid R, Scalzi P. Genital warts and cancer: an improved colposcopic index for differentiating benign papilloma viral infection from high-grade cervical intraepithelial neoplasia. *Am J Obstet Gynecol* 1985;153:611–8.
- [11] Di Bonito L, Falconieri G, Tomasic G, Colautti I, Bonifacio D, Dudine S. Cervical cytopathology: an evaluation of its accuracy based on cytolohistologic comparison. *Cancer* 1993;72:3002–6.
- [12] Fahey MT, Irwig L, Macaskill P. Metanalysis of Pap test accuracy. *Am J Epidemiol* 1995;141:680.
- [13] McCrory DC, Matchar BB, Bastain L. Evaluation of Cervical Cytology: Evidence Report Technology Assessment. No. 5. AHCPR Publication No. 99-E10. Rockville, MD: Agency for Health Care Policy and Research; 1999.
- [14] Schwebke JR, Zajackowski ME. Effect of concurrent lower genital infection and cervical cancer screening. *Genitourin Med* 1997;73:383.
- [15] Denny L, Kuhn L, Risi L. Two-stage cervical cancer screening: an alternative for resource-poor settings. *Am J Obstet Gynecol* 2000;183:383–8.
- [16] Blumenthal PD, Gaffikin L, Chirenje ZM, Mcrath J, Womack S, Shah K. Adjuvant testing for cervical cancer in lower resource settings with visual inspection, HPV and the Pap smear. *Int J Gynecol Obstet* 2001;72:47–53.