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Comparative study of visual inspection with acetic acid (VIA), Pap smear and biopsy for cervical cytology

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Abstract

Introduction: Cervical lesions are generally screened[(1)] with Pap smear test. However, the procedure is quite intensive and takes time. An effective alternate method is proposed by WHO with visual inspection of acetowhite areas in acetic acid test, which can be used in developing countries as it is cheap and results can be given immediately. Biopsy is considered confirmative test for same cervical lesions. Study was conducted to compare all these methods for diagnosis of cervical lesions and study the effectiveness of acetic acid (VIA) test.

Materials and Method: A total number of 543 cases of Women with unhealthy cervix, aged between 20 to 70 years who fulfill the selection criteria were included in the study. Pap smear and VIA were done in these cases. Cervical biopsy was done in positive cases. All these methods were compared.

Results: A total of 543 women between age groups 20- 70 years were included in the study. Out of 543 women 29 (5.34%) found to be positive with acetic acid test (VIA).

Conclusion: The acetic acid test found to be 93.5% accurate when compared with Pap smear, so acetic acid test can be used effectively for screening the cervical lesions. For further diagnosis, Pap smear shall be used. However, biopsy is confirmative.

Keywords: Women, Cervix, VIA, Pap smear, Biopsy.

Introduction

The cervix is the most common site for genital tract infections and a target for viral, chemical carcinogens, which leads to invasive carcinoma. Infections constitute one of the most common complaints in gynecological practice. As age advances malignant diseases becoming important cause of death. All over the world, cervical carcinoma is the second most common cancer in women after breast cancer, 80% of cancer cervix seen in developing countries, where it is the commonest cancer in woman.[(1)] Incidence is very high in rural areas where cancer cervix accounts for more than half of cancers among women. In India it accounts for 25 to 50% of all malignancies and every year 1,00,000 new cases of cervical cancers are registered, mostly in late stages. There are approximately 130000 new cases of cervical cancer in India per year and the disease is reported to be responsible for almost 20% of all female deaths.[(2)]

According to WHO Cancer cervix is a preventable disease.[(3)] Unfortunately more than 80% of the cases are diagnosed at an advanced clinical stage when the five year survival rates are less than 40%. Keeping this in mind, increased emphasis is being laid on the early detection of cervical intraepithelial changes, and hence the development of a reliable and cost effective screening method for cervical cancer.

Global evidence demonstrates that the key to reducing cervical cancer morbidity and mortality is early detection coupled with timely treatment of cervical precancerous lesions.[(4)] Cervical cytology often referred to as Pap smear is perhaps the most known of available screening methods.[(5,6)] although performing a pap test may seem relatively simple, a large number of steps are required to take an adequate smear, process and analyze the specimen and inform patients of the results. If any of these steps are unreliable or logistically burdensome, the entire screening program could breakdown.

The other method is visual inspection of acetowhite areas.[(7)] The cervix is washed with acetic acid and then inspected by eye for evidence of disease. This has potential advantages over traditional screening technique "pap test" in resource limited settings does not require a second person for interpretation of results and a second visit by the patient is also not required to collect the report.

Materials and Method

In this prospective study 543 women of age group between 20 and 70 years presenting to the Obstetrics and Gynecology Department of GEMS Medical College, Srikakulam, between January 2014 to December 2015 with various complaints such as post coital bleeding, leucorrhoea, intermenstrual bleeding or cervicalerosion/ cervical irregularities on examination were included. An informed consent was obtained. The study was carried out after obtaining Institute's ethical committee approval.

Exclusion criteria:

- Women undergone hysterectomy.
- Women in the menstrual phase of their cycle.
- Pregnant women.
- Women with vaginal medications, vaginal contraceptives or douches.

- Women in puerperium.

After taking patient consent, unaided visual inspection of the cervix is performed under good illumination and normal /abnormal features noted. The Instruments Sterile speculum, Cusco's Vulsellum, Ayre's spatula, numbered glass slides, Coplin jars with fixative, Alcohols, stains, Sterile rubber gloves and 3-5% acetic acid.

The cervix is visualized with a speculum. Smears were taken using Ayer's spatula for cytological examination. The specimen is immediately spread evenly onto a previously marked glass slide which is immediately fixed in a coplin jar filled with 95% Isopropyl alcohol. In some cases aerosol fixative spray was used. After obtaining the Pap smear the cervix is painted with 3 - 5% freshly prepared acetic acid solution using sterile cotton swabs. The cervix is inspected after 1 minute and the results are noted as either positive if there are distinct "acetowhite" areas or negative if no "acetowhite" areas are seen (Shown in Fig. 1). Later the results are analyzed for correlation. The Fig. 2 shows the normal smear and squamous cell carcinoma. All patients with Pap smear findings of LSIS and above were recorded as Pap positive for malignancy. All VIA or Pap positive patients were subjected to a cervical biopsy, the histopathological findings of which were taken as gold standard in this study.

Fig. 1: "Acetowhite" positive

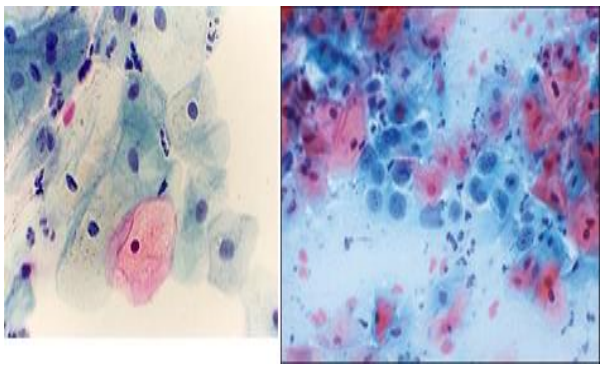

Fig. 2: Normal and Squamous cell carcinoma

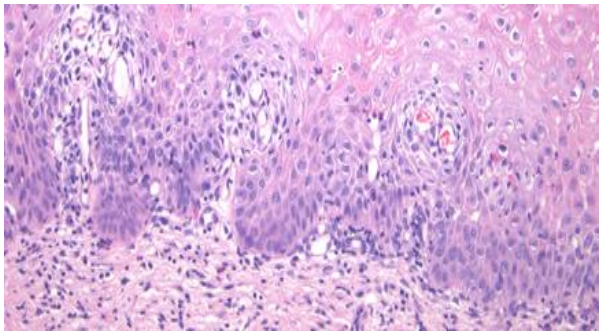

Fig. 3: CIN1

Results

A total of 543 women between age groups 20- 70 years were included in the study. Out of 543 women 29 (5.34%) found to be positive with acetic acid test (VIA). Majority of the positive women were in the age group 50-60 years (13.89%) followed by 60-70 age group (13.04%). (Table 1)

Table 1: Age-wise distribution of Visual inspection with acetic acid test (VIA)

Age	No. of cases	No of positive cases with acetic acid test	% of positive cases
20-30	50	2	4.00%
30-40	267	8	3.00%
40-50	167	11	6.59%
50-60	36	5	13.89%
60-70	23	3	13.04%
Total	543	29	5.34%

Pap test was positive among 417 women (76.8%). Majority of the women were in the age – group 40-50 years (80.84%). (Table 2)

Table 2: Age-wise distribution of Pap smear test results

Age	No. of cases	Pap Normal	Pap abnormal	Pap Abnormal %
20-30	50	13	37	74.00%
30-40	267	62	205	76.78%
40-50	167	32	135	80.84%
50-60	36	11	25	69.44%
60-70	23	8	15	65.22%
Total	543	126	417	76.80%

Pap smear test showed – inflammatory in 382 (91.6%), ASCUS – 4 (0.95%) and carcinoma in 4 (0.95%) (Table 3). Pap smear abnormality was found in 7.8% of the cases considering LSIL and above as the cut-off.

Table 3: Pap smear test details

Age	No. of positive cases with Pap smear test	No. of Inflammatory smear cases	ASCUS	AGUS	LSIL	HSIL	Carcinoma
20-30	37	34	1	0	2	0	0
30-40	205	195	1	0	8	1	0
40-50	135	122	1	0	8	2	2
50-60	25	19	1	0	2	1	2
60-70	15	12	0	0	2	1	0
Total	417	382	4	0	22	5	4

Note: ASCUS - atypical squamous cell carcinoma of undetermined significance, AGUS- atypical glandular cells not otherwise specified, LSIL – low grade squamous intra epithelial lesion, HSIL – high grade squamous intra epithelial lesion.

Biopsy study was done for pre-malignant and malignant smears (31 cases), out of which 2 found to have non-specific cervicitis, 25 are pre-malignant (CIN1, CIN2 and CIN3) and 4 are malignant as shown in Table 4.

Table 4: Biopsy test results

Age	No of abnormal (LSIL, HSIL and CARICINOMA) with Pap smear test	Non-specific cervicitis	CIN1	CIN2	CIN3	Carcinoma
20-30	2	1	1	0	0	0
30-40	9	0	8	1	0	0
40-50	12	1	7	1	1	2
50-60	5	0	2	0	1	2
60-70	3	0	2	1	0	0
Total	31	2	20	3	2	4

Biopsy results are strongly co-related to Pap and acetic acid tests. Table 5 shows the co-relation between acetic acid, Pap smear and corresponding Biopsy results.

Table 5: Correlation between acetic acid, Pap smear and Biopsy tests

Age	No of positive cases with acetic acid test	No of abnormal (LSIL, HSIL and CARICINOMA) with Pap smear test	Biopsy (CIN1+CIN2+CIN3+Carcinoma)
20-30	2	2	1
30-40	8	9	9
40-50	11	12	11
50-60	5	5	5
60-70	3	3	3
Total	29	31	29

Acetic acid tests are 96.88% reliable when compared with Pap smear tests and 84.3% reliable when compared with biopsy. Pap smear tests are 87.09% reliable when compared with biopsy. Biopsy results are strongly co-related to Pap and acetic acid tests. Many cases found to have inflammatory smear i.e. though the results were negative with acetic acid test (VIA). 3 cases which were negative and 1 case which was positive with acetic acid test (VIA) were found to be ASCUS in Pap smear test. Sensitivity of acetic acid (VIA) test with biopsy is 84.38% and specificity is 99.42%. Sensitivity of Pap smear test with biopsy is 87.10% and specificity is 100% (As biopsy was not done for the normal and inflammatory smears).

Discussion

Women in the age group of 20–70 years were involved in this study. Khan et al studied this screening method in the age range of 25–65years.[8] Denny conducted a screening program in the age group of 35–65 years in South African women.[9]

In this study VIA was performed by gynecologist. In studies conducted by Khan et al, Goel et al Bharani and Phatak, gynecologists performed the procedure.[8,10,11] However in another study done six oncologists performed the procedure.[12] In contrast, trained nurses and midwives were involved in few studies.[9,13,14]

Our study compared VIA with Pap smear with cervical biopsy being considered as the gold standard. In our study biopsy was taken if positive findings were

present on Pap smear, VIA. Goel et al. used similar methods; however they did LLETZ (large loop excision of transformation zone) instead of a biopsy.[10] Few studies used VIA and cytology to screen patients and in case of a positive screening test or clinical suspicion women were subjected to colposcopy and a colposcopy-guided biopsy if necessary. Few researchers chose to do only VIA and if VIA was positive did colposcopy and biopsy was done in patients with abnormal findings. In Khan et al. study visual inspection with Lugols iodine (VILI) was done in addition to VIA and cytology.[8]

The VIA-positive rate in our study was 5.8%. Goel et al. had a rate of 12.5% of VIA.[8] Cecchini et al. reported positive VIA in 25.4% in their study, 15 whereas Megevand et al. and Slawson et al. reported an abnormal VIA rate of 3.13% and 4.2% respectively.[14,16] this wide variation was due to the 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 a symptomatic hospital-based population and others as a mass screening test. The VIA test is also affected by the quality of and concentration of the acetic acid, lighting, and visualization.

It was noted that 7.4% of Pap smear was abnormal in this study which was close to study conducted by Denny et al who reported an incidence of abnormal Pap smear as 8.2%. University of Zimbabwe/JHPIEGO Cervical Cancer Project reported 14.6%[13] and Megevand et al. noted an abnormal Pap smear in 13% of their study population.[14] However Cecchini et al. could detect abnormal pap smear in only 1% of their study population.[15] 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 involved.[16]

The results of test accuracy in cross-sectional study settings indicate that the sensitivity of VIA to detect high-grade Pre-cancerous lesions ranges from 66% to 96% (median 84%); the specificity varied from 64% to 98% (median 82%).

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 on the order of 50% in some circumstances. However, studies that have been able to assess sensitivity longitudinally have produced estimates that approximate to 75%.

Though Pap smear had a better sensitivity and specificity than VIA, VIA is comparable to Pap smear in sensitivity and specificity. It performs better in detection of moderate and severe dysplasia which is true precursor of cervical cancer.

Most of the women who undergo screening with Pap smear in developing countries do not come for follow-up or do not collect their report on time thereby leading to delay in diagnosis and treatment. The advantage of VIA is that it is a real-time screening test where results are immediately known and appropriate counseling and referral for treatment can be given.

Conclusion

Based on the above results the following conclusions can be made:

- The acetic acid test found to be 93.5% accurate when compared with Pap smear, so acetic acid test can be used effectively for screening the cervical lesions.
- For further diagnosis, Pap smear shall be used. However, biopsy is confirmative.

At present, cytology is the standard screening of cervical cancer. However in countries with low resource settings where cytology-based screening programs are not available, VIA is a promising alternative. The advantages of VIA are that it is simple, rapid, easy to administer, does not require much infrastructure, cost-effective, and its result is available immediately. If the test result is positive, in the same setting further investigations can be carried out and treatment can be planned out. Healthcare workers can be appropriately trained and can use VIA to screen patients. In countries with high incidence of cervical cancer and with no cytology-based screening programs, additional cases of dysplasia can be detected at minimal cost.

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