Assessing alternate technique Visual inspection with acetic acid (VIA) for screening of Carcinoma of cervix in Situ for low resource countries like India.

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Abstract—Background and Objective: A Clinic initiated community oriented cross sectional study to assess efficacy of VIA Technique in Screening of Carcinoma of cervix in Situ was conducted by department of Tahaffuzi-wa-Samaji Tib (Preventive and Social Medicine), Jamia Hamdard, New Delhi. The General Objective of the study was to evaluate accuracy of VIA technique (visual inspection with acetic acid) as a screening tool for carcinoma in situ. Methods: After informed consent had been obtained from the subjects, the eligible subjects were first laid in lithotmy position and Pap smear was taken by scraping cervix with Ayer's spatula. Then 5% acetic acid was applied on cervix and findings were noted after one minute. Definite acetowhite lesions near the transformation zone were regarded as positive. Relative sensitivity, specificity, Positive predictive value and negative predictive value of VIA relative to Pap smear was calculated. McNemar's test was applied for test of significance of effectiveness of VIA by group comparison of paired samples. Results: Relative sensitivity of VIA was 62.5%.Relative Specificity of VIA was 85.5%.Relative Positive predictive value of VIA was 27.7%.Relative negative predictive value of VIA was 96.25%. Conclusion: VIA was found to be more effective in detecting Cervical Intraepithelial Lesion (CIN) than Pap smear and the difference was statistically significant (Mc Nemar's χ 2 =6.25; Mc Nemar's with Yates's Correction χ2=5.06, both statistically significant at d.f 1 and C.I 95%).Relative negative predictive value being high ,it can be used in low resource settings like India at primary care level and will play important role in prevention of Carcinoma of cervix in situ.

Index Terms— VIA, cervical cancer, prevention.

INTRODUCTION

Globally, cancer cervix is the second most common cancer in women following breast cancer. 493 thousand new women suffer from cervical cancer and 274 thousand women die of this disease annually. Eighty percent of them are diagnosed in developing countries.1 It is found that cervical cancer is an important women's health problem, especially in developing countries, where an estimated 190,000 women die from the disease each year. In developing countries, mortality rates are reported at 11.2 per million/year women on an average, almost three times the rate of developed countries.2 In India Cervical cancer is the most common malignancy affecting female population. An estimated 132 thousand new cases, or more than one-fourth of the worldwide total, are reported annually.3 The estimated number of women diagnosed with cancer each year is 3,000,000 of women. Among them approximately one third have cervical cancer. According to the data compiled by Indian council of Medical Research (2005) from the cancer registries cervical cancer ranks first among cancers in women.4 Although cervical cancer can be prevented or treated effectively if detected early. More than 70% of all cancers in India are found when the disease is so advanced that treatment is much less effective.4

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Cytology is the accepted method for screening of early stages of carcinoma of the uterine cervix all over the world. However, while the test has achieved tremendous success in industrialized countries that offer periodic, high-quality screening. One of the reason for lack of effective screening is that the favored screening technique of Pap smear requires technical capabilities, system for transportation, follow up and training that is beyond the capability of health care infrastructure in most of the developing countries. It is a major reason for the sharply higher cervical cancer rates in developing countries. Pap smear programs are complex and costly to run and have failed to reach a significant proportion of women in countries where health systems and infrastructure are poor.[5] For low-resource settings, there is particular interest in the accuracy and acceptability of visual screening as a means of detecting cervical dysplasia or cancer.[6,7] This type of screening may reduce the cost and complexity of Pap smear screening, and holds the potential for screening and treatment in the same visit.[8] Visual inspection with acetic acid (VIA) may be suitable for developing countries because it is cheap; requires materials which are locally available; needs less expertise and even trained paramedicos can perform it. VIA has potential advantage over feedback of the test and results.[9,10] With this background the current study was envisaged as one for evaluation of a technique that has proven to be effective in other developing countries and in some centers of India as well. If the results are encouraging it can be the screening method of choice in the Indian rural setting as an alternative to cytology. The General Objective of the study was to evaluate accuracy of VIA technique (visual inspection with acetic acid) as a screening tool for carcinoma in situ.

MATERIAL AND METHODS

Study Design

The study was conducted during September 2004 to June 2006, and was a clinic initiated community oriented cross sectional study. Study was carried out in urban slums of South Delhi covering Khanpur, Tigri, Sangam Vihar, Tughlakabad and Vasant kunj.

Study population

The study participants were apparently healthy, asymptomatic women who were aged between 30 and 60 years of age with intact uterus and with no past history of cervical neoplasia attending Surjit wasu charitable dispensary Khanpur and Global cancer Concern India (GCCI), health centre, Vasant Kunj in South Delhi (Vide Annexure I).

Study Unit ,Sample size & Sampling technique

On the basis of eligibility for the study subjects attending Vasant Kunj Health Centre and Surjit wasu Memorial Trust were taken using random number technique and screened. Out of 2230 female subjects who attended Surjit wasu memorial Trust and Vasant Kunj Health Centre in South Delhi, 419 (18.78%) were found eligible for screening. Out of them 189 (45% of eligible subjects or 8% of the total subjects) agreed to participate in the study. One hundred were located in the community. Further 2 more subjects were lost due to attrition, so 98 (4.4%) subjects formed the final sample set. Sample size was kept as 98 due to resource limitations. Analysis of Pap smear and VIA with personal attributes and observational results was done by Chi Square test. Relative sensitivity, specificity, Positive predictive value and negative predictive value of VIA relative to Pap smear was calculated. McNemar's test was applied for test of significance of effectiveness of VIA by group comparison of paired samples. Ninety eight eligible women were included in the study.

Technique of study

Screening test with Pap smear and VIA at the clinic followed by Personal oral interview of each eligible woman in the community was taken. Steps of the technique were explained and an informed consent was obtained. The woman was reassured that the procedure is painless, and every effort was made to ensure that she is fully relaxed and remains at ease during testing. An unlubricated bivalve speculum was inserted in the vagina of the subject and then Pap smear was collected by Ayres's spatula by scraping cervix around entire transformation zone under direct vision.The smear was spread onto the glass slide and fixed immediately with 100% alcohol to preserve cells.After Pap smear was taken and specimen preserved, the procedure of VIA was started. Cotton-tipped applicator soaked in 4% acetic acid was applied to the cervix. After one minute, with the aid of a common spotlight used for out patient gynaecological examination, the cervix was visualized and findings recorded according to the following categories.

VIA findings were categorized as **negative** when any of the following findings were observed:-

- No aceto white lesion or faint, ill defined bluish white or doubtful lesion.
- Aceto whitening on cervical polyp.
- Dull or strike like aceto whitening on cervix.
- Angular acetowhite lesion away from SCJ.

VIA findings were categorized as **positive** when any of the following were observed:-

- Well defined, opaque aceto white lesion touching the squamocolumnar junction or the external Os if the SCJ was not visible.
- A large circumferential acetowhite lesion surrounding the whole external Os.
- Pre-existing leukoplakia or wart turning intensely white on application of acetic acid.
- Ulceroproliferative growth turning densely acetowhite after application of acetic acid.

Statistical analysis

1. Analysis of Pap smear and VIA with personal attributes and observational results was done by Chi Square test. Result was calculated correct upto two decimal places.
2. The performances of VIA was done by following parameters:

- Relative sensitivity, specificity, Positive predictive value and negative predictive value of VIA to pap smear was calculated.
- McNemar's test was applied for test of significance of effectiveness of VIA. Mc Nemar's χ^2 was calculated by the following formula

RESULTS

Of 98 women, 5 had well defined; opaque aceto white lesion touching the squamocolumnar junction or the whole external Os on VIA and 5 had rich degree of cellularity, with suspicious looking cells with open hyper chromatin and open chromatin on Pap smear. That is 5 (5.1%) were positive on both VIA and Pap smear. Twelve had well defined, opaque aceto white lesion touching the squamocolumnar junction or the whole external Os and one had Pre existing leukoplakia turning intensely white on application of acetic acid that is 13 (13.26%) were positive on VIA only and 3 (3.06%) were positive on Pap smear only. Seventy-seven (78.57%) had no aceto white lesion or faint, ill defined bluish white or doubtful lesion on VIA and had normal or inflammatory smear on Pap smear. That is 77 (78.57%) were negative on both tests. Thus 18.36% had aceto white lesions on naked eye inspection and 8.16% had HSIL on Pap smear. Of 9 women who were referred to colposcopy and colposcopy guided biopsy 2 HSIL and 2LSIL were confirmed (See table1).

1. Relative sensitivity of VIA was 62.5%.Relative Specificity of VIA was 85.5%.Relative Positive predictive value of VIA was 27.7%.Relative negative predictive value of VIA was 96.25% (Seee table 2).
2. VIA was found to be more effective in detecting CIN than Pap smear and the difference was statistically significant (Mc Nemar's χ 2 =6.25; Mc Nemar's with Yates's Correction χ2=5.06, both statistically significant at d.f 1 and C.I 95%)(See table 3).
3. Compared to Pap smear examination VIA has the advantage of higher sensitivity and comparable specificity.

DISCUSSIONS

In other studies evaluating VIA, Eftikhar found Sensitivity of 95.7 %, Tayyeb found Sensitivity to be 93.9%, JHIPEGO study found Sensitivity of 76.6%, Londhe study found Sensitivity of 72.4 %, and Denny found Sensitivity of 58.3%. The current study statistic of relative sensitivity of VIA at 62.5% was comparable. Similarly, for specificity of VIA, Denny found Specificity of 83.5%, JHIPEGO study found Specificity of 64.1%, Londhe study found Specificity of 54 %, Efekahar found Specificity of 44.1 % and Tayyeb found Specificity to be 30.4%. Current study statistic for relative specificity of VIA at 85.5 % was comparable.[11-18] Relative negative predictive value being high ,it can be used in low resource settings like India at primary care level and will play important role in prevention of Carcinoma of cervix in situ.Being easy to adopt in the Indian setting, feasible even in rural areas with simple clinic level infrastructure like examination table and light. The test can be performed by medical practioners with simple training. On the basis of observations of this study it is recommended that a larger study with statistically determined sample size and stratified design may be conducted to reach conclusions that can be extrapolated to the Indian population in general. In the mean time on the basis of the current study that generally lead to similar conclusion as other studies on the same subject in Indian setting, the practioners may be encouraged to use VIA as an important adjunct to their decision tree for screening of Cervical cancer in the high risk group in a resource poor setting. Further studies can be conducted on skill training of nurses, Para medical staff and grass root level health functionaries to perform VIA in the community setting.

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TABLE 1. : TEST RESULTS OF VIA AND PAP SMEAR (DESCRIPTIVE) N=*98.*

VIA	PAP SMEAR	TOTAL
Positive	Positive	5
Positive	Negative	13
Negative	Positive	3
Negative	Negative	77
TOTAL		98

TABLE 2 : RELATIVE SENSITIVITY AND SPECIFICITY OF VIA N=98

Screening test VIA	Pap Smear		*Total*
	Positive	Negative	
Positive	5	13	*18*
Negative	3	77	*80*
Total	8	90	*98*

Inference: Relative sensitivity of VIA was 62.5%.

- Relative Specificity of VIA was 85.5%.
- Relative Positive predictive value of VIA was 27.7%.
- Relative Negative predictive vakue if VIA was 96.25%.

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TABLE 3 : APPLYING MCNEMARS TEST

Screening test VIA	Pap Smear		*Total*
	Positive	Negative	
Positive	5	13	*18*
Negative	3	77	*80*
Total	8	90	*98*

Note: Mc Nemar's $\chi 2$ = 6.25; Applying Yates's correction $\chi 2$=5.06

Inference: VIA was found to be more effective in detecting CIN than pap smear and the difference was statistically significant (Mc Nemar's $\chi 2$ =6.25; Mc Nemar's with Yates's Correction $\chi 2$=5.06, both statistically significant at d.f 1 and C.I 95%).