Original Article

Performance of a low cost magnifying device, magnivisualizer, versus colposcope for detection of pre-cancer and cancerous lesions of uterine cervix

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See accompanying editorial by Sankaranarayanan on page 263.

Objective: To assess the performance of a low cost magnifying device (Magnivisualizer) compared to a standard optical colposcope for detection of precancerous and cancerous lesions of the uterine cervix.

Methods: A total of 659 consecutive symptomatic women attending a gynecologic outpatient clinic underwent unaided visual inspection followed by cytology, visual inspection of the cervix using 5% acetic acid (VIA), and VIA under magnification (VIAM) with the Magnivisualizer. All women, independently of test results, were referred for colposcopic examination. Colposcopic-directed biopsies were obtained from all positive lesions and compared to positive VIAM cases.

Results: The detection rate for VIA positive lesions was 12% (134/659), while it was 29% for VIAM positive lesions (191/659). The sensitivities of detection of cervical intraepithelial neoplasia (CIN) 2 and higher lesions were 61.7% for VIA, 88.3% for VIAM, and 86.7% for colposcopy, with a specificity of 58.5% for VIA, 55.8% for VIAM, and 90.4% for colposcopy. The performance of colposcopy and VIAM was moderate (κ, 0.48; 95% confidence interval [CI], 0.41 to 0.54) for detection of CIN 1 and higher lesions and excellent (κ, 0.87; 95% CI, 0.82 to 0.94) for detection of CIN 2 and higher lesions.

Conclusion: In low resource settings, where colposcopic facilities are not available at the community level, a simple low-cost, handheld Magnivisualizer can be considered a valid option for detection of cervical precancerous and cancerous lesions. However, it cannot replace traditional colposcopy because it has a low specificity that results in many unnecessary biopsies.

Keywords: Ambulatory care facilities, Colposcopy, Sensitivity and Specificity, Uterine cervical dysplasia, Uterine cervical neoplasms

INTRODUCTION

Cervical cancer is a leading malignancy among women in developing countries, although screening programs can reduce both morbidity and mortality. Several screening options are available in developing countries, including cytology, visual inspection with acetic acid, and detection of high risk Human papillomavirus DNA [1,2]. The abnormalities detected by screening modalities must be further evaluated by colposcopic examination and biopsy. Keeping in mind the high cost of a colposcope, and problems with its portability in remote rural and tribal areas, along with the requirement of a trained colposcopist, there is thus an objective need for alternative screening methods. A published report has suggested that the Magnivisualizer can be used for this purpose [3]. The

present study assessed the comparative performance of the Magnivisualizer device versus a standard optical colposcope.

MATERIALS AND METHODS

1. Clinical setting and study subjects

The study was carried out in the gynecology outpatient clinic of a teaching hospital in New Delhi over a period of 1.5 years. The hospital serves the surrounding areas of the walled city where the majority of the population is illiterate and of a lower socioeconomic status. The study included a total of 659 consecutive symptomatic women attending one of the units of gynecology outpatient clinic. The most common complaints of these women were white discharge, foul-smelling discharge, blood-stained discharge, postcoital bleeding, intermenstrual bleeding, and postmenopausal bleeding.

2. Procedures

The general screening procedures are shown in the flow chart in **Fig. 1**. All women underwent sequential examinations using different screening modalities at the same sitting. First, unaided visual inspection was carried out. Subsequently, visual inspec-

659 General examination

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659 Speculum-unaided visual examination

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659 Pap smear sampling

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659 VIA (visual inspection of cervix after application of 5% acetic acid)

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659 VIAM (VIA using magnification: Magnivisualizer)

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659 Colposcopy in all cases

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320 Colposcopic-directed biopsy and endocervical curettage as needed

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320 Follow-up after 15 days for any postbiopsy complaints and collection of biopsy report for further management

Fig. 1. Flow chart of study.

tion of the cervix was performed using 5% acetic acid (VIA) followed by visual inspection of the cervix under magnification (VIAM). All these screening tests were carried out by trained physicians at the gynecology outpatient unit. All women, independently of test results, were referred to a trained colposcopist (VS) who examined them without knowledge of screening results. Coppelson's colposcopic grading system was adopted for reporting purposes [4]. Colposcopic-directed biopsies were taken from abnormal areas in VIAM positive cases when the colposcopy results were negative.

3. Instruments

The Magnivisualizer is an illuminated magnifying device developed in our institute [5]. This instrument has an inbuilt source providing white light (full visible spectrum of light and temperature 5,500°K to 6,000°K) with an interchangeable magnification ($\times 2$ to $\times 5$) that was used for VIAM [3]. The instrument is portable, uses a rechargeable battery, and is designed so that it can be used in the field by both physicians and paramedicals. It costs only US $160 and is ideal for settings with low resources. A Carl Zeiss optical colposcope was used for colposcopy and colposcopic-directed biopsies.

4. Histopathologic examination and analysis

The following reporting system was used for VIA and VIAM: a distinct aceto-white lesion within the transformation zone was considered positive and the patient was referred for evaluation by colposcopy. The reporting system for colposcopy was as follows: any atypical lesions within the transformation zone were subjected to colposcopic-directed biopsy. Histopathology was considered as the gold standard. Biopsies revealing cervical intraepithelial neoplasia (CIN) 2 or higher lesions were considered as positive, whereas CIN 1, chronic cervicitis with koilocytotic changes, or metaplasia were considered negative.

SPSS ver. 13.0 (SPSS Inc., Chicago, IL, USA) and Epi-6 software was used for data analysis. For agreement analysis, Cohen's un-weighted kappa (κ) was calculated with 95% confidence interval (CI). Cohen's kappa is a statistical measure of inter-rater agreement for qualitative (between two methods of judgments). It is thought to be a more robust measure than a simple present agreement calculation.

RESULTS

A total of 659 women were studied using three modalities: VIA, VIAM, and colposcopy. The mean age of subjects was 37.5 ±10.6 years (range, 26 to 75 years) with a mean parity of 2.9 ±1.2 (range, 1 to 9). The detection rates for grade II lesions
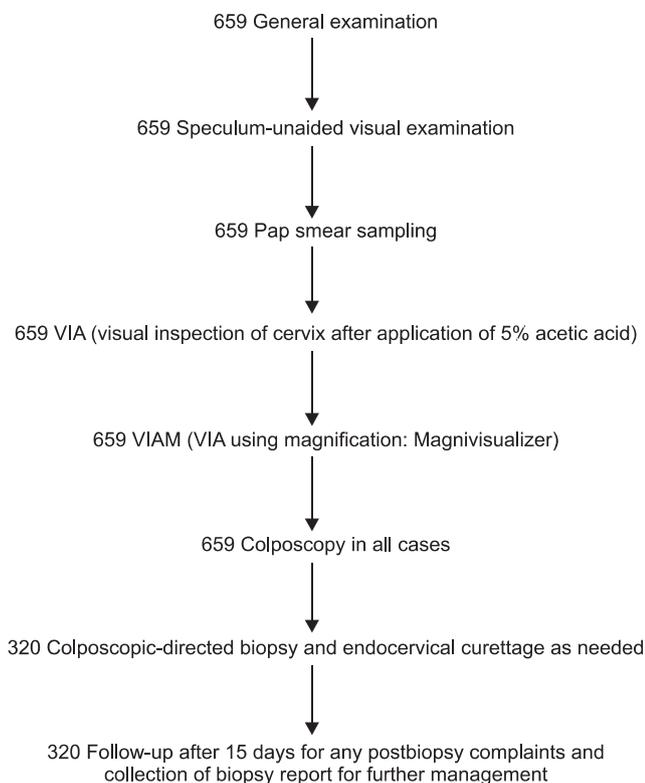
varied between colposcopy (n=79, 12%), VIAM (n=191, 29.0%), and VIA (n=134, 20.3%). The comparative performance of VIA, VIAM, and colposcopy is shown in **Table 1**. The frequency of aceto-white lesions significantly increased with higher grade of colposcopic lesions; chi-square for trends for both VIA and VIAM were significant (p<0.001). Biopsies were obtained in 320 women; 303 were colposcopic-directed; and 17 were positive by VIA or VIAM, but negative on colposcopy.

Agreements between biopsy-proven VIAM and the results of VIA are reported in **Table 2**. In 152 cases with negative VIAM, 81 (53.2%) CIN 2 and 7 (4.6%) CIN 3 were confirmed by histology. In 168 cases with positive VIAM, 53 (31.5%) and 70 (41.6%) were histopathologically diagnosed as CIN 2 or higher and CIN 1, respectively. In the remaining 45 cases (26.7%) with positive VIAM, biopsy failed to confirm any atypical lesions. In 145 cases with positive VIA lesions, analysis of the biopsy confirmed CIN 2 or higher lesions in 37 cases (25.5%) and CIN 1 lesions in 44 cases (30.3%). In the remaining 64 cases (44.1%) with positive VIA, biopsy failed to confirm any atypical lesions.

On the other hand, VIA did not detect positive lesions in 23 cases (13.1%), where biopsy showed CIN 2 or higher lesions. Agreement between VIAM and histopathology was good (κ, 0.67; 95% CI, 0.60 to 0.75), although there was poor agreement between VIA and histopathology (κ, 0.13; 95% CI, 0.04 to 0.22).

Table 3 shows the correlation between colposcopic diagnosis and histological results. Agreement between colposcopy and histopathology was good (κ, 0.695; 95% CI, 0.59 to 0.79). Of 659 cases, biopsy was carried out in 320 (48.6%), including 17 patients (5.3%) with normal/negative colposcopy but positive VIA or VIAM. Incidentally, 5.9% (1/17) of these showed a CIN 3 lesion by biopsy. In addition, 67.5% (52/77) of cases with grade II or higher colposcopic findings were histopathologically diagnosed as CIN 2 or higher lesions, while only 19.5% (59/303) of cases with grade I colposcopic findings were diagnosed as CIN 1.

The sensitivity of VIA, VIAM, and colposcopy for detection of CIN 2 or higher lesions was 61.7%, 88.3%, and 86.7%, respec-

Table 1. Comparison of uterine cervical lesions detected by colposcopy, VIA, and VIAM

Lesions detected by colposcopy	VIA-positive lesions	Magnivisualizer-positive lesions
Normal/inflammatory colposcopy (n=163)	2 (1.3)	2 (1.3)
Metaplasia grades I & II (n=135)	4 (2.9)	3 (2.2)
Grade I (n=282)	71(25.2)*	119 (42.2)[†]
Grade II (n=49)	30 (61.2)[†]	39 (79.5)[§]
Grade III (n=9)	8 (88.9)[†]	9 (100)[§]
Suspicious for malignancy (n=21)	19 (90.4)[†]	19 (90.4)[§]
Total (n=659)	134	191

Values are presented as number (%).
CI, confidence interval; VIA, visual Inspection with acetic acid; VIAM, visual inspection with acetic acid under magnification with Magnivisualizer.
*Agreement for VIA: κ, 0.31; 95% CI, 0.26–0.36 for detection of grade I and higher lesions. [†] Agreement for VIAM: κ, 0.48; 95% CI, 0.41–0.54 for detection of grade I and higher lesions. [†] Agreement for VIA: κ, 0.45; 95% CI, 0.36–0.54 for detection of grade II and higher lesions. [§] Agreement for VIAM: κ, 0.87; 95% CI, 0.82–0.94 for detection of grade II and higher lesions.

Table 2. Agreement between VIA, VIAM, and histopathology

Lesions diagnosed by VIA, VIAM	Histopathology				
	Negative (cervicitis) metaplasia/condylomatous changes	CIN 1	CIN 2	CIN 3	Cancer
VIAM negative (n=152)	64 (42.1)	81 (53.2)	–	7 (4.6)	–
VIAM positive* (n=168)	45 (26.7)	70 (41.6)	8 (4.7)	26 (15.4)	19 (11.3)
VIA negative (n=175)	45 (25.7)	107 (61.1)	5 (2.8)	14 (8.0)	4 (2.3)
VIA positive[†] (n=145)	64 (44.1)	44 (30.3)	3 (2.1)	19 (13.1)	15 (10.3)

Values are presented as number (%).
CI, confidence interval; CIN, cervical intraepithelial neoplasia; VIA, visual Inspection with acetic acid; VIAM, visual inspection with acetic acid under magnification with Magnivisualizer.
*κ, 0.67; 95% CI, 0.60–0.75 for detection of grade II and higher lesions by VIAM. [†]κ, 0.13; 95% CI, 0.04–0.22 for detection of grade II and higher lesions by VIA.

Table 3. Agreement between colposcopy and histopathology of colposcopic-directed biopsies

Colposcopy	Histopathology*				
	Negative (cervicitis) metaplasia/ condylomatous changes	CIN 1	CIN 2	CIN 3	Cancer
Normal including squamous metaplasia of all grades (n=17)	11 (16.7)	5 (29.4)	–	1 (5.8)	–
Grade I (n=226)	84 (37.1)	135 (59.7)	–	6 (2.6)	1 (0.4)
Grade II (n=49)	12 (24.4)	10 (20.4)	8 (16.3)	18 (36.7)	1 (2.0)
Grade III (n=9)	–	–	–	6 (66.6)	3 (33.3)
Suspicious for cancer (n=19)	2 (10.5)	1 (5.2)	–	2 (10.5)	14 (73.6)
Total (n=320)	109	151	8	33	19

Values are presented as number (%).
CI, confidence interval; CIN, cervical intraepithelial neoplasia.
*κ, 0.695; 95% CI, 0.59–0.79 for detection of grade II and higher lesions.

Table 4. Results of VIA, VIAM, and colposcopy for detection of CIN 2 and higher lesions

Modality	Sensitivity	Specificity	PPV	NPV
VIA	61.7 (48.2–73.6)	58.5 (52.2–64.5)	25.5 (18.8–33.5)	86.8 (80.7–91.3)
VIAM	88.3 (77.8–94.2)	55.8 (49.7–61.7)	31.5 (25.0–38.9)	95.4 (90.8–97.8)
Colposcopy	86.7 (75.8–93.1)	90.4 (86.2–93.4)	67.5 (56.5–76.9)	96.7 (93.6–98.3)

Values are presented as percentage (95% CI).
CI, confidence interval; CIN, cervical intraepithelial neoplasia; NPV, negative predictive value; PPV, positive predictive value; VIA, visual Inspection with acetic acid; VIAM, visual inspection with acetic acid under magnification with Magnivisualizer.

tively, whereas the specificity was 58.5%, 55.8%, and 90.4%, respectively (**Table 4**).

DISCUSSION

Variable results have been reported for the sensitivity (34% to 74%) and specificity (63% to 90%) of VIAM in the detection of precancerous lesions of the uterine cervix by VIAM [3,6-10]. In the present study, the rate of detection for VIA positive lesions was 12% (134/659), while it was 29% (191/659) for VIAM positive lesions. Herein, it was clearly demonstrated that detection of lesions was significantly higher by VIAM with increasing grades of lesions detected by colposcopy (i.e., 42.1% for grade I lesions, 79.5% for grade II lesions, 100% for grade III lesions, and 90.4% for suspicious of cancerous lesions; chi-square for trend test p<0.001). A good correlation (87.3% agreement) was also observed between VIAM positive and colposcopic grade II and higher lesions. In case of normal/ inflammatory and metaplastic lesions detected by colposcopy, VIAM also showed negative lesions in 98.3% cases. The overall agreement between colposcopy and VIAM was very good (κ, 0.87; 95% CI, 0.82 to 0.94) for detection of CIN 2 and higher lesions.

The present study found a comparable sensitivity of VIAM

for detection of CIN 2 and above lesions, i.e., 88.3% with our earlier studies and other studies cited in the literature [3,9]. However, the specificity was lower, i.e., 55.8%, compared to these previous studies. The lower specificity seen herein may be related to the fact that the results of VIAM were compared with cytology in the previous study [3], whereas they were compared with colposcopy in the present study. Secondly, in the present study, colposcopy was performed in all cases independently of the results of VIAM, and more specific CIN 2 lesions were detected by colposcopy and confirmed by biopsy.

A variable sensitivity (62% to 100%) and specificity (48% to 99%) has also been reported for colposcopy in early detection of cervical lesions. The present study found a sensitivity of 86.7% and specificity of 90.4%, in agreement with previous studies [9-13]. The large variation in the results among different studies may be attributed to the different grading systems adopted for colposcopic findings.

The Magnivisualizer is a simple, handheld, user friendly, low cost device (produced by the Indian Council of Medical Research). The cost of the instrument is only US $160 and is powered by a portable battery that lasts for 2 years. The screening cost per patient is around US $0.40 [3]. A colposcope costs more than US $15,000 and requires expertise to

handle the equipment and interpret the results, which further increases operating costs. The present study clearly demonstrated that the Magnivisualizer can be used satisfactorily in place of colposcopy in settings where resources are limited, although it cannot replace colposcopic examination as a diagnostic tool.

In low resource settings, where colposcopic facilities are not available at the community level, a simple and cost effective, handheld device (i.e., Magnivisualizer) is an alternative option in the absence of standard colposcopy for early diagnosis of precancerous and cancerous lesions of the cervix. It cannot replace colposcopy because of its low specificity, resulting in a large number of unnecessary biopsies. Thus, early detection using a cost-effective tool, especially in low resource settings, holds promise to reduce cancer burden through early diagnosis [14]. Even a "see and treat" approach can be offered using this technique at the community level, which undoubtedly reduces the cancer load in more specialized tertiary cancer centers. However, larger multicenter studies are needed to further evaluate the efficacy of the Magnivisualizer in the general population.

CONFLICT OF INTEREST

ACKNOWLEDGMENTS

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