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Original Article

Comparison of the diagnostic value of the visual inspection with acetic acid (VIA) and Pap smear in cervical cancer screening



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ABSTRACT

Objective: This study aimed to compare the diagnostic value of VIA with Pap smear in screening for cervical cancer.

Materials and methods: In this cross-sectional study, 440 women who had eligibility criteria, in Kashan city were assessed. All women underwent Pap smear test and then a visual inspection with acetic acid and colposcopy-biopsy (Gold Standard). Then, the diagnostic value indices including the specificity, sensitivity, positive and negative predictive values for the results of VIA and Pap smear were analyzed by SPSS V16 software.

Results: Finding showed that 29.9% of women had abnormal Pap smear. The false positive rate of Pap smear was 40.2%, and its false negative rate was 37.4%. For VIA, the false positive and false negative rates were 21.2% and 4.6%. The sensitivity, specificity, NPV and PPV of Pap smear was 29.7%, 85.5%, 59.8%, 62.6%, and these values for VIA was 94.6%, 81.6%, 78.8%, 95.4% respectively. Combination of Pap smear and VIA showed the sensitivity of 97.3% and 100% in low grade and high grade cervical lesions.

Conclusion: VIA has a higher sensitivity than Pap smear in detection of low and high grade cervical lesions, however, its specificity is less than Pap smears. Therefore it is recommended to use of VIA along with Pap smear to reach a higher sensitivity.

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Introduction

Cervical cancer is the fourth most common cancer in the world, and included 7.9% of all women's cancer. 90% of this cancer occurs in low-middle income countries [1]. In Iran, cervical cancer is the second cancer after ovarian cancer and consists of 32.5% of all female cancers [2]. Over the past 50 years, mortality from this malignancy has clearly dropped in developed countries, largely due to Pap smear screening test [3]. Despite this decline, the disease is still a major cause of death among women, especially in developing countries [4]. Also incidence rate of this cancer in Iran was 1.64 per 100,000 women in 2003 and increased to 2.61 per 100,000 women in 2009 [5]. One of the methods for cervical cancer screening is Pap

smear, but repeated screening for cervical cancer requires laboratories and well-trained, experienced staff and high costs, which are not available in all developing countries and in all places [6,7]. Also, the relatively long interval between doing the test and reaching the patient's result in some cases leads to a lack of follow-up by the patient. These problems has led to the development of several cheap techniques, such as the use of magnification, visual inspection with acetic acid (VIA) or visual inspection with lugol iodine (VILI), which can eliminate the barriers to screening by cytology. The basis of VIA is that cervix with CIN lesions is whitened in the presence of acetic acid. The benefits of VIA are low cost, no need for high technology, the result is immediate and is ready in 1–2 min, and can be done by health care providers in distance areas, which makes VIA an excellent alternative method for Pap smear in developing countries [8–10], but the low specificity of this method has limited it [11].

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Various studies in the world have been conducted to evaluate the diagnostic value of VIA and Pap smear in screening for cervical cancer and different results have been obtained with regard to the studied population and the methodology. In some studies, VIA has been identified as an appropriate screening method [12–17] and in others, given its low specificity, using these two methods simultaneously for cervical cancer screening has been recommended [7,10,11,18–20].

Since cervical cancer is preventable and has a longer pre-cancerous stage, so its screening is available and can be cured if detected early. Since the sensitivity of the VIA method has been very different in various studies, and according to the findings on the usefulness of VIA in screening for cervical cancer compared to pap smear, this study aimed to compare the diagnostic value of VIA and pap smear in screening for cervical cancer in women referring to Naghavi Hospital in Kashan, Iran.

Materials and methods

A cross-sectional study was performed on 440 women aged 20–65 years old in the Naghavi clinic at Kashan city in 2017. All women participating in the study after examination of the cervix underwent Pap smear test and then a visual inspection with acetic acid. In the VIA method, the cervix was first smeared with a 3% acetic acid solution for 30–60 s and then was observed under sufficient light. The observation test with acetic acid is considered to be positive when the whitening reaction (Aceto White) is clearly seen (Fig. 1). Pap smear test were reported based on Bethesda system. Positive Pap smear test refers to “unspecified abnormal squamous cell” (ASCUS) lesions and more severe lesions (1 and 17). Then, all subjects underwent colposcopy and biopsy (as a Gold Standard method) by Fellowship of Women's Oncology who was not aware of the results of VIA, if there was a suspected lesion biopsy was taken, and in the absence of aceto white random biopsy was taken from four cervical regions. If the result of the colposcopy was normal and satisfactory, it was considered negative and in the case of abnormal or unsatisfactory colposcopy for the person, biopsy or endocervical curettage (ECC) was performed and a sample was sent to the pathology department. If the report of pathology indicates a CIN lesion or higher, it was considered as positive result. All cytology slides and biopsy or ECC samples were reviewed by a pathologist.

Inclusion and exclusion criteria

Inclusion criteria were sexually active and non-pregnant women with no active disease of the cervix and no history of cervical conization, cryo or other invasive cervical cancer treatment, with no history of pre-invasive lesions or history of cervical cancer, and exclusion criteria were not cooperating with other follow-up steps.

Ethical considerations

This study was approved at the Ethics Committee of Kashan University of Medical Sciences. Before the start of the study, the consent of all individuals was obtained for participation in the study and it was assured that their information would remain confidential.

Statistical analysis

After collecting data, frequency tables and statistical indices were mapped according to the background variables. Then, the diagnostic value indices including the specificity, sensitivity, positive and negative predictive values for the results of VIA, Pap smear and combination of these two test were analyzed by SPSS V16 software. The level of significance was lower than 0.05.

Results

In this study, 440 patients referred to gynecologic clinic of Naghavi Hospital were evaluated. None of the patients were excluded from the study. Patients were between the ages of 22 and 65 with an average age of 39. From 440 patients, 79.1% had normal Pap smear. There were 77 ASCUS, 12 LSILs, 2 HSILs and 1 ASC-H. Totally, 21% of Pap smears were reported abnormal. The findings showed that 50.5% of patients were VIA positive. In 58% of patients colposcopy was normal. In 145 patients CIN1 and in 27 patients CIN2 and in 12 patients CIN3 and in one patient SCC was reported. In total, 42% of the colposcopic findings were positive.

Table 1 shows the false positive rate of VIA was 21.2% and its false negative was 4.6%.

Findings showed that of 92 patients with positive Pap smear, 55 patients had positive colposcopy and biopsy. In other words, its false positive and false negative was 40.2% and 37.4% respectively (Table 2).

Table 3 indicates that the negative results of the VIA in 85.8% of cases were in accordance with pap smear but positive results only in 27.5% of cases were matched with pap smear. The Kappa coefficient was 0.132 ($p = 0.038$).

The Sensitivity, specificity, NPV and PPV of Pap smear, VIA and combination of Pap smear and VIA in screening for cervical cancer are presented in Table 4.

Results of our data based on high grade cervical lesions (CIN II, CINIII and carcinoma) are presented at Table 5.

Discussion

In this study, all women regardless of screening test results underwent colposcopy and biopsy. Evaluation of screening tests in different settings is important because the results of these tests are valuable for screening policies.

In this study, it was found that 21% of patients had abnormal Pap smear such as ASCUS lesions and higher lesions. In one study, 53.5% of patients had an abnormal pap smear [6] that was more than the

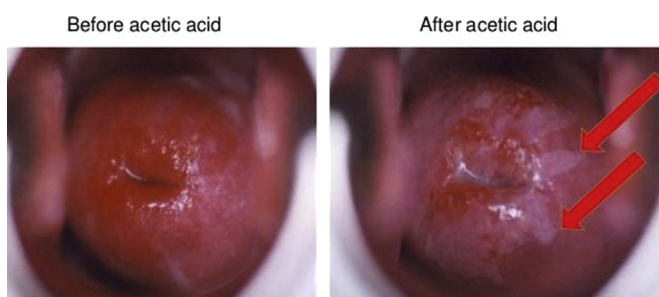


Fig. 1. VIA negative and positive pattern.

Table 1
Comparison of VIA Results and colposcopy.

VIA	Colposcopy + Biopsy*		
	Positive	Negative	Total
Positive	175 (78.8)	47 (21.2)	222 (100.0)
Negative	10 (4.6)	208 (95.4)	218 (100.0)
Total	185 (42.0)	255 (58.0)	440 (100.0)

*Data are presented as No and percent.

Table 2
Comparison of Pap smear results and colposcopy.

Pap Smear	Colposcopy + Biopsy*		
	Positive	Negative	Total
Positive	55 (59.8)	37 (40.2)	92 (100.0)
Negative	130 (37.4)	218 (62.6)	348 (100.0)
Total	185 (42.0)	255 (58.0)	440 (100.0)

*Data are presented as No and percent.

Table 3
Comparison of VIA and Pap smear results.

VIA	Pap Smear*		
	Positive	Negative	Total
Positive	61 (27.5)	161 (72.5)	222 (100.0)
Negative	31 (14.2)	187 (85.8)	218 (100.0)
Total	92 (20.9)	348 (79.1)	440 (100.0)

*Data are presented as No and percent.

Table 4
Diagnostic value of Pap smear, VIA and combination of Pap smear and VIA.

Test	Sensitivity	specificity	PPV	NPV
VIA	94.6%	81.6%	78.8%	95.4%
Pap smear	29.7%	85.5%	59.8%	62.6%
Pap smear and VIA	97.3%	71.4%	71.1%	92.4%

Table 5
Diagnostic value of Pap smear, VIA and combination of Pap smear and VIA in High grade CIN.

Test	Sensitivity	specificity	PPV	NPV
VIA	100%	54.5%	18%	100%
Pap smear	45%	81.5%	19.6%	93.7%
Pap smear and VIA	100%	46.8%	15.8%	100%

current study, and the reason is that inflammatory lesions are also considered abnormal in that study. Among the cases of abnormal Pap smear, most reported cases include ASCUS with 17% and LSIL, HSIL, ASC-H 2.7%, 0.5%, 0.2% respectively that are more than rates (13.5%) reported by recent study [6].

In 51% of pap smears, have been reported varying degrees of inflammation from mild to severe that was more than results of one study (38.5%) [6], which could be due to differences in the study population. The findings showed that VIA was positive in 50.5%. This is reported 41.5% in one study [6], but in comparison to the other studies, is higher [15,21,22], which is probably due to the use of different criteria in the positive view of VIA in these studies or the difference in the population of screened women. For example, in the study of Jeronimo et al. CIN was not considered positive or in the study of Sankaranarayanan et al. VIA divided into two groups (+) and (++), which only consider (++) as positive. But in this study both VIA + and VIA ++ are considered to be positive.

The findings of the study on colposcopy showed that 58% of subjects had normal colposcopy and other lesions including CIN1, CIN2, CIN3 and SCC were reported 33%, 6.1%, 2.7%, 0.2% respectively. In recent study [22] normal colposcopy was seen in 38% of patients and CIN1, CIN2, CIN3 and SCC were reported 28%, 19%, 10% and 5%, respectively.

The results of this study showed that the false positive rate of VIA was 21.2% and its false negative was 4.6%. The false positive rate in several studies were reported 29.4%, 67.4% and 9.1%, and false negative were reported 12%, 20% and 6.8% [6,7,11]. All of these values were different from the present study which could be

difference in the studied population. The findings show that inflammation and infection increase the false-positive VIA by up to two times [23].

In patients with positive VIA, 27.5% had positive Pap smear and 72.5% were Pap smear negative. For patients with VIA negative, 14.2% had positive Pap smear and in 85.8% of patients, Pap smear was reported negative. In one study 40% of the patients with positive VIA were positive for Pap smear and 24.5% despite having positive VIA, Pap smears were negative. 12.9% of patients with negative VIA, had positive Pap smear and at 22.5% of patients both VIA and Pap smear were reported negative [22].

In this study, the false positive rate (40.2%) of Pap smear was higher than other studies that varied from 0% to 22.2% [6,7,11]. High levels of false positives can lead to additional diagnostic and therapeutic procedures for patients. Also in this study, the false negative rate of Pap smear was 37.4%, which is lower than most of the studies that have been reported a range of 13.5%–74.2% [6,7,11]. A high false negative level can lead to a lack of early detection of patients and a delay in treatment.

The findings showed that VIA had a higher sensitivity than Pap smear, but its specificity was less than Pap smear. These values are higher than most studies in terms of sensitivity and specificity. In various studies, the sensitivity of VIA was between 62.5% and 96%, and its specificity was between 32.5% and 98.8%. Also, Pap smear sensitivity in different studies has been reported between 10% and 75% and its specificity between 42% and 100% [6,7,11,12,19,22,24,25].

In our study, Pap smear had a higher specificity than some studies, but its sensitivity was less than many studies. In all of these studies, apart from two studies, Pap smear specificity is reported more than VIA [11,19]. Overall, it can be said that in the present study, VIA has a higher sensitivity than Pap smear, but its specificity, as the same as most studies is less than Pap smear. The reason for low level of VIA specificity in the present study was that all white lesions were considered positive and that the presence of cervical polyps, inflammation and metaplasia, could also result in false positive results for VIA.

In this study, the PPV of VIA was higher than Pap smear, but the NPV for Pap smear was higher than the VIA. In various studies, the PPV of VIA has been reported between 8.3% and 90.9% [6,7,11,12,19,21,22,25,26]. In our study, PPV for VIA was similar to the Eftekhari et al. and Khan et al. studies [11,25]. The PPV of Pap smear has also been reported between 6.3% and 100% [6,7,11,12,19,21,22,25,26], that our findings are almost similar to the Gupta et al. study.

In various studies, the NPV of VIA were reported between 66.6% and 99% [6,7,11,12,19,25,26]. Our findings are lower than other studies. The NPV of the pap smear varied from 43 to 96% [6,7,11,12,19,25,26]. The NPV in our study is almost similar to Keshavarzi et al. study [12].

Combination of Pap smear and VIA showed the higher sensitivity than VIA or Pap smear alone. In one study the sensitivity of combination of VIA and Pap smear were reported 70% [11]. In that study like ours, the sensitivity of VIA was higher than Pap smear (96% and 10% respectively).

VIA was 100% sensitive for detection of high grade lesions but, Pap smear had 45% sensitivity. Combination of these two tests was resulted in 100% sensitivity for CIN II and higher. In one study the VIA sensitivity and specificity for detection of high grade lesions was 87.5% and 78.8% respectively [27].

The reason for these variations in the diagnostic value of Pap smear and VIA in different studies may be due to considering different diagnostic criteria, difference in considering the positive tests results and differences in the studied population. The findings of this study and other studies indicate that the main limitation of

VIA is its low specificity, which can lead to higher rates of referral and performing more colposcopic procedure in patients. On the other hand, it is a low cost, simpler and easier method than Pap smear, and does not require complicated laboratory facilities. Therefore it can be recommended for primary screening program in low resource settings. In a study in five low resource countries, direct cost for Pap smear was twofold of VIA and direct cost of colposcopy and biopsy was approximately 9 fold of Pap smear [28].

The strengths of this study are performing colposcopy and biopsy in all patients, which led to an accurate report of sensitivity and specificity of Pap smear and VIA. The high false negative rates of VIA limit it as a screening test. Therefore, it is advisable to design more studies with different VIA positive protocols in order to reduce the amount of colposcopy and final costs. It is recommended to reduce errors and increase the accuracy of results, more studies with higher sample size and multi-centered studies would be done.

VIA is a sensitive, practical and low-cost test in detection of low grade and high grade cervical lesion, but has a lower specificity than Pap smear. Therefore, as the test used in screening should have good sensitivity and specificity, it is more valuable to use of VIA in cervical cancer screening. Use of VIA along with Pap smear resulted a higher sensitivity for detection of cervical lesions.

Conflict of interest

The authors declare that they have no conflict of interest.

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