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Research Article

Diagnostic Concordance between Cytology, Colposcopy and Biopsy in Cervical Cancer in Chihuahua, Mexico

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Abstract

Background: Cervical cancer is the second leading cause of death in women worldwide and the first in developing countries. In Mexico, it is the leading cause of cancer death in women over 35 years of age. Cytology, colposcopy and biopsy are complementary systems for the study of patients with cervical pathology and are diagnostic methods that must be evaluated continuously. Early identification through screening is key to prognosis and treatment since it is curable in primary stages.

Aim: So the purpose of this study is to know the diagnostic concordance between cytology, colposcopy and biopsy in patients with cervical cancer in Chihuahua, Mexico.

Design and Setting: Comparative cross-sectional study.

Methods: A total of 74 records were reviewed and women with cervical cancer diagnosed with cytology, colposcopy and biopsy were identified at the Gynecology and obstetrics hospital #15 in the year 2014. The Kappa coefficient was used for concordance between diagnostic tests, sensitivity and positive predictive value of cytology and colposcopy were calculated compared to biopsy (gold standard).

Results: poor concordance was found between cytology-biopsy findings (K=0.08) and between colposcopy-biopsy (K=0.06), however, moderate concordance was found between citology-colposcopy (K=0.504, p=0.001).

Conclusion: Cytology and colposcopy as diagnostic methods for cervical cancer have low sensitivity and high positive predictive values, their level of concordance compared to the gold standard is also low according to the Kappa coefficient; however, the degree of concordance between cytology and colposcopy is moderate with a significant Kappa coefficient.

Keywords: Cervical Cancer; Cervical Biopsy; Cytology; Colposcopy

Introduction

Cervical cancer is the second most common cancer in women and more than 270,000 die each year from this cancer, 85% of these deaths occur in low and middle-income countries. According to the Pan-American Health Organization in 2008, more than 80,000 women were diagnosed with cervical cancer and nearly 36,000 died from this disease in Latin American countries [1]. It is estimated that there are currently more than 2 million women in the world who have cervical cancer. Each year 490,000 new cases are diagnosed, that is more than 1350 new cases per day, 650 women die daily from cervical cancer, this gives an approximate of 237,000 deaths in a year and this is for not performing a screening test in women with risk factors. For this reason it is important for women to know about cervical cancer and how to prevent [2].

In Mexico, cervical cancer was the leading cause of death from malignant tumors in women until 2005; thereafter, breast cancer is the one with the highest rate. Currently the most appropriate way to prevent this disease is sought; one of these strategies is the development of effective vaccines against the human papillomavirus and the existence of new methods of viral DNA detection. Mexico is located in the first places of mortality due to cervical cancer; despite the existence of prevention and detection programs that focus efforts on cytological screening, it has not been possible to incorporate a culture of prevention, a situation that has an impact on the health of the population. In the state of Chihuahua 130 women died in 2007 by Cervical Cancer [3].

Cervical cancer is defined as a cellular alteration that originates in the epithelium of the cervix and that manifests initially through precursor lesions of slow and progressive evolution, these can happen in stages of mild, moderate and severe dysplasia, cancer in situ (circumscribed to the epithelial surface) or invasive cancer when the lesion crosses the basement membrane [4]. The most common histological type is squamous carcinoma (80% of cases) and is frequently associated with human papillomavirus 16. Adenocarcinoma is the second most common histological type and although HPV 16 is also the most frequent, the proportion of Genotypes 18 and 45 increased significantly in this type of tumor [5].

Human Papilloma Virus is the main risk factor associated with cervical cancer. The virus produces a selective infection of the epithelium of the skin and the genital mucosa. Human papillomavirus

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Table 1: Diagnostic concordance between cytology and colposcopy.

		Colposcopy		Total	K
		With cervical cancer	Without cervical cancer		
Cytology	With cervical cancer	34 (45.9%)*	12 (16.2%)+	46 (62.2%)	0.504 (p=0.001)
	Without cervical cancer	06 (8.1%)+	22 (29.7%)*	28 (37.8%)	
	Total	40 (54.1%)	34 (45.9%)	74 (100%)	
	*Concordance rate	76%			
	+Discordance rate	24%			

%: Percentage, K: Kappa, *: concordance, +: discordance, p: Chi Square.

Table 2: Diagnostic concordance between cytology and biopsy.

		Biopsy		Total	K
		With cervical cancer	Without cervical cancer		
Cytology	With cervical cancer	46 (62.2%)*	0+	46 (62.2%)	0.087
	Without cervical cancer	26 (35.1%)+	2 (2.7%)*	28 (37.8%)	
	Total	72 (97.3%)	2 (2.7%)	74 (100%)	
	*Concordance rate	65%			
	+Discordance rate	35%			

%: Percentage, K: Kappa, *: concordance, +: discordance.

Table 3: Diagnostic concordance between colposcopy and biopsy.

		Biopsy		Total	K
		With cervical cancer	Without cervical cancer		
Colposcopy	With cervical cancer	40 (54.1%)*	0+	40 (54.1%)	0.063
	Without cervical cancer	32 (43.2%)+	2 (2.7%)*	34 (45.9%)	
	Total	72 (97.3%)	2 (2.7%)	74 (100%)	
	*Concordance rate	57%			
	+Discordance rate	43%			

%: Percentage, K: Kappa, *: concordance, +: discordance.

infection in the cervix can cause abnormalities in the squamous cells that are most frequently detected by Papanicolaou screening; most human papillomavirus genital infections are transmitted through direct sexual contact without evidence of injury [6]. Factors that influence the persistence of the virus are viral, genetic and behavioral co-factors related to women's or environmental factors. Among the environmental factors that favor persistent infection are other sexually transmitted infections, multiparity, sexual promiscuity, and couples who have or have had numerous sexual partners. [7-8].

Since the introduction of cervical screening (cytology) in 1960, incidence and mortality from cervical cancer have declined by about 75%; however, this reduction is not uniform worldwide [9]. Women with abnormal cervical cytology undergo colposcopy, a procedure that generally clarifies the nature of abnormalities found in cytology [10]. Colposcopy has a sensitivity of 95% and specificity of 98%, as it is possible to perform a systematic assessment of the cervix and biopsy under direct vision of areas suspected of malignancy [11]. However, it is frequently the incorrect diagnosis by cytology and colposcopy; Therefore, these methods should be comparable and evaluated with histological findings (gold standard).

Cytology, colposcopy and biopsy have become complementary systems for patients with cervical pathology. Cervical cytology is a diagnostic aid method for detecting intraepithelial squamous lesions as well as invasive carcinomas; should be complemented with correlation studies such as colposcopy and biopsy to increase diagnostic certainty [12]. Cytology and colposcopy have been used over the years to diagnose premalignant and malignant conditions of the uterine cervix; however, the histological study is conclusive in order to establish the diagnosis. This can be done by a punch biopsy, scalpel conization and with a diathermic loop [13]. Based on the above, the objective of the study was to establish the correlation between cytology, colposcopy and biopsy in patients with cervical carcinoma of the Gynecology and obstetrics hospital #15 of Chihuahua, Mexico.

Materials and Methods

An analytical, retrospective and cross-sectional study was carried out in the Department of Preventive Medicine of the Mexican Institute of Social Security (IMSS) in Chihuahua, Mexico, from January to December, 2014. All the medical records of patients with histological diagnosis of cervical cancer that had cytology, colposcopy and biopsy were reviewed. The cytology was read in the pathology department of the same hospital; the smears were stained with the standard Papanicolaou technique and the reading was carried out by certified pathologists or cytotechnologists. All the cytology with abnormal results were reviewed by a pathologist before a definitive result was issued. For the results, Bethesda and Richard classification (NIC) was used.

Table 4: Sensibility and positive predictive value of cytology and colposcopy.

	Sensibility	Positive Predictive Value
Cytology	64%	100%
Colposcopy	56%	100%

%: Percentage, specificity and negative predictive value were not calculated because there were not negative cytologies.

The colposcopy biopsy was also done at the IMSS hospital No. 15 and was performed by a colposcopist gynecologist, with an Ecleris colposcope model C-100FL, and the biopsy was analyzed by a certified medical pathologist. Histological diagnoses of abnormal cytology were taken from the files of pathology or medical records as well as age and waiting time between cytology and colposcopy. Histological diagnoses were made similarly to Bethesda and Richard (NIC) terminology. Cohen's Kappa coefficient was calculated, which measures the level between two categories of values, a Kappa value of 1 means a perfect concordance. Landis and Koch [14] subdivide the range 0 to 1 into five categories, namely: 0 to 0.2 = bad; 0.2 to 0.4 = low; 0.4 to 0.6 = modest; 0.6 to 0.8 = good and 0.8 to 1 = very good. Statistically Kappa measures the concordance but not the validity of the test [15]. The cytology is compared with colposcopy, cytology with biopsy and colposcopy with biopsy, following the process that is ordinarily done in the hospital. In addition to the Kappa coefficient, concordance, discordance, sensitivity and positive predictive value were calculated. Specificity and negative predictive value were not calculated because no biopsies were performed in patients with negative cytology.

The data obtained was integrated into data collection sheets and analyzed using the SPSS program version 20 in Spanish, where we applied descriptive statistics for qualitative variables use frequencies and percentages and for quantitative variables mean and standard deviation were used. It was considered a $p < 0.05$, with a 95% confidence interval. The protocol was authorized by the Local Committee of Research and Ethics in Health Research from the obstetrical and gynecological hospital #15, where the study took place.

Results

We reviewed 75 cases of patients from obstetrical and gynecological Hospital #15, Chihuahua, Mexico, from January to December of 2014, who were exclusively diagnosed with Cervical Cancer. Of the total of 75 cases, only 74 cases complied with the inclusion criteria when having cytology, colposcopy and biopsy. We analyzed a sample of 74 women, the average age was 45.4±14.3 (21-76) years, the time between the realization of cytology and colposcopy was on average 57.3±42.1 (2-210) days.

In cytology results according to Bethesda, out of the 74 patients, 4(5.4%) suffered Atypical Squamous Cells of Undetermined Significance (ASCUS), 9(12.2%) Low Grade Squamous Intraepithelial Lesion (LGSIL), 15(20.3%) High Grade Squamous Intraepithelial Lesion (HGSIL) and 46(62.2%) cervical cancer; according to Richard classification, 4(5.4%) suffered inflammatory process, 9(12.2%) cervical intraepithelial neoplasia I (CIN I), 5(6.8%) cervical intraepithelial neoplasia II (CIN II), 10(13.5%) cervical intraepithelial neoplasia III (CIN III) and 46(62.2%) cervical cancer. In colposcopy results according to Bethesda, out of the 74 patients, 2(2.7%) suffered ASCUS, 31(41.9%) LGSIL, and 41(55.4%) cervical cancer; according to Richard classification, 2(2.7%) suffered inflammatory process, 25(33.8%) CIN II, 6(8.1%) CIN III and 41(55.4%) cervical cancer. In biopsy results, 72(97.3%) suffered cervical cancer, one (1.4%) CIN I and one (1.4%) CIN II.

A concordance analysis was performed between cytology, colposcopy and biopsy; a concordance was found between cytology and colposcopy of 76% with a discordance of 24% and a Kappa coefficient of 0.504 (p=0.001) (Table 1); the concordance between cytology and biopsy was 65% with a discordance of 35% and a Kappa coefficient of 0.087 (Table 2); the sensitivity identified for cytology is 64% with a positive predictive value of 100%. The concordance between colposcopy and biopsy was 57% with a discordance of 43% and a Kappa coefficient of 0.063 (Table 3); the sensitivity identified for colposcopy is 56% with a positive predictive value of 100% (Table 4).

Discussion

As a result, the sensitivity of the cytology study was 64%, which was the same as that reported in the national and international literature, ranging from 41 to 75% [16-17]. Colposcopy had a sensitivity of 55.6%, which is lower than that reported in previous studies (83%) [16]. The cytological, colposcopic and biopsy correlation allows to evaluate the quality of interpretation using the gold standard biopsy. Buenano-Aldaz (2011) reported that there is concordance between the cytological result and the histopathological report in 58% of the cases studied [18] which is lower than reported in our study (65%). Pérez et al in Cuba (2007) reported a cytological-biopsy correlation of 63.6% which is similar to that described in our study. As for colposcopy studies by Pajtler and Mitchell, showed a sensitivity of 85% and specificity of 69%, which is higher than our results.

Conclusion

No test is completely effective in the detection of cervical cancer. The diagnosis of cervical epithelial lesions, especially cervical cáncer is based in three pillars: cytology, colposcopy and biopsy. The limitation of each method requires concordance studies of the findings to reach an accurate diagnosis. The concordance between cyto-colposcopic and histological diagnosis is a fact that should concern the physicians involved in the problem. The rates found in this study justify carrying out new concordance studies among the different institutions of the country, as well as conducting concordance studies among observers and training to reduce the factors associated with error in the different diagnostic methods.

The main objective of this research was to evaluate the cytological study and colposcopy performed at the obstetrical and gynecological hospital #15 in Chihuahua, Mexico as methods for the detection of cervical cancer, and it was determined that its sensitivity is low with high positive predictive values, their level of concordance compared to the gold standard is also low according to the Kappa coefficient; however, the degree of concordance between cytology and colposcopy is moderate with a significant Kappa coefficient (Kappa = 0.504, p = 0.001).

Recommendations

1. Concordance studies among observers should be conducted, trying to determine the causes of discrepancies in sampling or

interpretation.

2. The pathology department could conduct correlation studies to know the concordance numbers and act on the findings.

3. Cervical specimen collection techniques should be improved.

4. Improve the waiting time between each study performed in public hospitals in pathologies that represent public health problems.

5. Pathologists should periodically review their criteria and procedures, standardize them, record them, and correlate biopsies with cytology and clinical findings.

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