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HPV and Cervical Conization in Menopausal and Pre-Menopausal Women. What Happens after Two Years of Follow Up?

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Abstract

Introduction: *HPV represent the most frequent sexual transmitted disease in women, with the maximum prevalence between the ages of 25-29. Studies show a reactivation of previously acquired HVP during menopause.*

Methods: *A retrospective study was conducted in a tertiary center with women with a conization from December 2013 to December 2014. We collected clinical data, histological analyses, treatment and follow-up variables, and compared them according to their menopausal status.*

Results: *190 cases were collected, 19 of them were post-menopausal women (10%) and 171 were pre-menopausal women (90%). Among menopausal patients L- SIL was the most frequent cytology clesion (33,3%). The most common HPV in menopausal patients was the high risk (HR) genotype no 16/18 (47,4 %). Pre-menopausal patients presented similar HPV genotype: 44,4% of HR no 16/18, 16(28,7%) and 18 (2,3%). The definitive histological analysis in menopausal conizations revealed HSIL in 68,4% of thepatients and LSIL in 21,1%; 1 in situ carcinoma was diagnosed. In a menopausal group a consecutive operation was necessary in five women (33,3%).*

After two years of follow-up only a menopausal woman presented an ASC-H conization. The analysis of the neutralization of the virus revealed similar results in both groups: 69,2% of menopausal women Vs. 53,6% of the pre-menopausal.

Conclusions: *Menopausal women are a minority group of patients with conization. The cytologyc lesions and the prevalence of the VPH genotype is similar in menopausal women and no menopausal women. In histological analysis, premenopausal patients have more H-SIL. Results after two years of monitoring are similar in both groups.*

Keywords: *HPV, cervix cancer, menopausal, prevention, cervix neoplasms/epidemiology; risk factors; cervix neoplasms/prevention & control.*

Introduction

HPV affects around the 80 % of the sexual-active population, both men and women. It is the most frequent sexual transmitted disease in women, with the maximum peak of prevalence between the ages of 25-29. In the Spanish population it represents 18.147.440 sexual-active infected women over 18 years-old[1]. Although it appears as a youth-related infection, certain studies prove that a reactivation of HVP previously acquired in the youth exists during menopause[2]. Therefore, this is the main cause of developing cervical cancer in menopausal women.

Untreated high grade CIN significantly increases the risk of invasive cancer. Conducting a cone is currently one of the main treatments of cervical precancerous lesions, which plays both diagnostic and therapeutic roles[3]. The loop electrosurgical excisional procedure (LEEP) tends to be the most common strategy[4].

Recent studies have shown the potential of HPV DNA testing for primary screening of women and its maintained high sensitivity in comparison to cytology in postmenopausal women [5]. Older age is associated with higher risk of low-grade and high-grade squamous intraepithelial lesions (LSIL and HSIL) and invasive carcinoma[6].

The aim of the study is to describe the association of HPV with H-SIL cervical lesions diagnosed in menopausal groups and to compare such women with premenopausal ones. Further more, we analyze the persistence of HPV infection after surgical treatment in both groups.

Methods

We included all patients who have had a conization in the Gynecology department of one tertiary referral hospital in Spain (Hospital Universitario Miguel Servet of Zaragoza) between December 2013 and December 2014. We sub-classified them into menopausal and premenopausal women. Exclusion criteria included incomplete, inconclusive or missing definitive pathological analysis of the cone, inconsistent follow-up of the patient and surveillance in other medical centers.

The study was approved by the local Ethics Committee and confidential information was preserved.

The diagnosis, treatment and follow-up decisions were based on the cancer practice guidelines created by the Spanish Society of Gynecologist and Obstetrics (SEGO).[7,8] Every patient included in the hospital area who has an abnormal cytology is derived to a specific consulting room where the follow up is conducted. VPH sampling and colposcopy are performed when necessary. If an ectocervical or endocervical sample are informed as HSIL, aconizationis conducted after having given a complete information to the patient. A close monitoring is planned after the conization regarding the mentioned guidelines. A gynecological expert pathologist analyzes the cone sample, and when controversy exists, a second pathologist checks the sample.

Demographical and clinical variables are collected from hospital's databases and all information about treatment and follow-up are compiled in the gynecology medical history. Histological outcomes are shown in the hospital's electronic program.

Statistical Analysis

Data analysis was performed using SPSS 22.0 version software (v.22, SPSS Inc., Chicago, IL, USA). Continuous variables were presented as mean +- standard deviation (SD) or median (range). Categorical variables were presented as rate (%) and compared using the Chi-square test or Fisher's exact test as appropriate.

A *p*-value of <0,05 was considered statistically significant.

Results

From December 2013 through December 2014 a total of 201 patients met the inclusion criteria. Eleven of them were lost in the follow-up. Finally, 190 patiens were included in the final analysis. Among those, 19 were post-menopausal women (10%) and 171 were pre-menopausal women (90%).

Base line characteristics of the study population are shown in Table 1. Initial cytologyc lesion, office biopsy and definitive histologycal analysis after conization are described in Table 2.

Focusing on HPV subtypes, the coexistence of 16 and 18 was present in 5,3% of menopausal patients. With respect of the rest of subtypes no difference between menopausal women and not menopausal women were found (*p=0,808*). Figure 1.

In the menopausal group a consecutive operation was necessary in five women (33,3%). A hysterectomy was conducted on one of them because of the presence of an in situ carcinoma and the other four were re-conizated. Only one of them presented residual lesion in the final analysis. By contrast, a second surgery was necessary in 21% of the cases of pre-menopausal patients; nine hysterectomies and 15 re-conizations were developed.

In two years of follow-up only a menopausal woman presented an ASC-H cytological lesion, remaining the rest of menopausal patients free of disease. The analysis of the neutralization of the virus was 69,2% in menopausal women and 53,6% of the pre-menopausal ones.

Table 1. *Demographic and clinical parameters.*

	Premenopausal (n=171)	Menopausal (n= 19)
Age (years)	35 (34-36)	57 (54-59)
Smoking (%)	36,1	58,8
Always use preservative (%)	31,1	0
Hormonal contracepcive (%)	24,4	6,3
Age offirst sexual relation(years)	17 (16-18)	22(18-26)
VPH vaccunations (%)	1,2	0

Data are expressed as mean (standard deviation), number (%) or median (range)

Table 2. *Histological lesions, biopsy and definitive histological analysis post conization.*

		PREMENOPAUSAL (n=171)	MENOPAUSAL (n=19)	*P*
Histological lesion	LSIL	20,6	33,3	*NS*
	HSIL	42,9	22,2	*NS*
	ASCUS	9,4	0	*NS*
	AGUS	1,8	16,7	*NS*
	ASC-H	0	27,8	*NS*
Biopsy	LSIL	28,13	47.4	*0.043*
	HSIL	53,2	36,8	*NS*
	Endocervix HSIL	9,9	10,5	*NS*
	Situ carcinoma	8,19	5,3	*NS*
	Adenocarcinoma	0,58	0	*NS*
Definitive histological analysis	Without lesion	13,68	5,27	*NS*
	LSIL	4,67	21,1	*0,016*
	HSIL	80,1	68,4	*NS*
	Situ carcinoma	9,36	5,27	*NS*
	Adenocarcinoma	0,58	0	*NS*

Data are expressed as number (%)

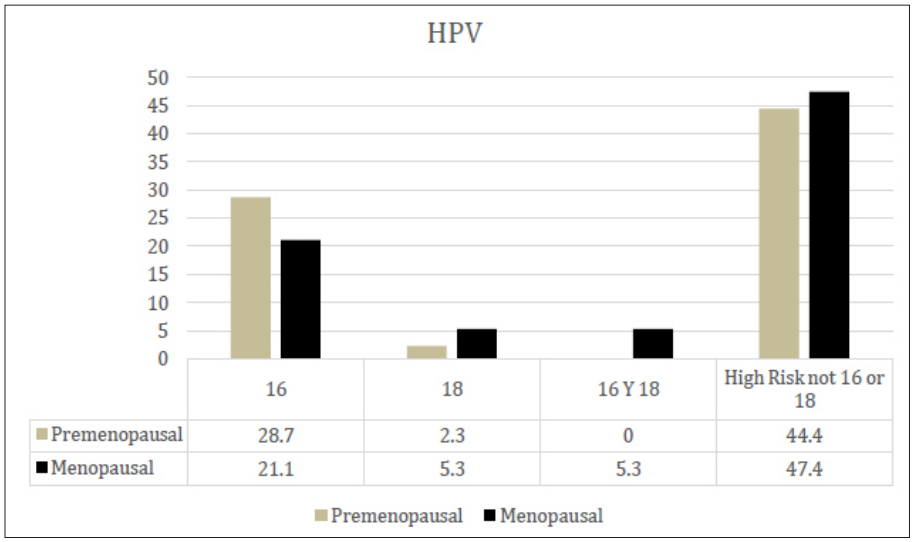

Fig 1. *VPH subtypes*
Dates are expressed as number (%)

Discussion

Our study found that the prevalence of HPV infection in HSIL cervical lesions is comparable in both premenopausal and postmenopausal women. The persistence of infection after surgical treatment is also similar between both groups.

Human papillomavirus (HPV) is now understood to be necessary, but insufficient for the development of cervical cancer. [9]Nowadays, more than 200 HPV-types are well characterized.[10] Depending on their oncogenic capacity, HPVs are classified as high risk or low risk genotypes. The International Agency of Research on Cancer (IARC) classifies HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 and 66 as High Rirsk VPH (HPV-HR) and others like 6 and 11 as Low Risk HPV(HPV-LR).[11] HPV-16 is the most prevalent HPV-type In abnormal cervical samples.[12,13]

European studies where the overall HPV prevalence shows two ages related peaks, one in the twenties and the other in the forties.[14,15] This second peak of higher prevalence of HPV was also observed with HR-HPV-types after the age of 60 and it probably might correspond to HPV-HR that tends to persist in the older women.[15] Vaginal atrophy and local immunity could play an important role in this respect. It is certain that menopausal women remain susceptible to oncogenic HPV infection.[17]

Sexual habits change with age. This could suggest the association between the HPV-geno types and cervical lesions could be different between pre and postmenopausal women. However, other previous studies have shown similar distribution of HPV-HR according to patient age.[18-20]

Persistent HPV-HR infection is strongly and consistently associated with high-grade cervical intraepithelial neoplasia and is considered essential for the progression of cervical precancer to invasive cervicalcancer.[21] A proportion of women remain infected with HPV-HR even after treatment. [22] In our study, the rates of persistent HPV-HR infection post conization were similar among menopausal and premenopausal women. Other recent studies had showed that patients with menopause are at increased risk of HPV-HR persistence after treatment for HSIL.[23] Others factors like HPV-type, detection method, treatment method, and minimum HPV post-treatment testing interval could explain these differences. [24]

The main limitation to our study is the small number of cases that does not allow to draw definitive conclusions between the possible differences among genotypes HPV-HR depending on the menopause status in general population.

Conclusions

Menopausal women represent a minority group of patients who need a conization.

In our population, the prevalence of the VPH-HR genotype in HSIL lesion is similar between the two groups. Results of virus neutralization in the two years follow-up after surgical treatment are similar depending on the menopause status.

References

[1] Alemany L, Bayas JM, Borruel N, Campins M, Castellsagué X, Curran A, et al. AEPCC-Guía: Vacunación selectiva frente al virus del papiloma humano en poblaciones de riesgo elevado. Publicaciones AEPCC. 2016: 1-46.

[2] Castle PE, Jeronimo J, Schiffman M, et al. Age-related changes of the cervix influence human papillomavirus type distribution. Cancer Res 2006; 66:1218–24.

[3] Kyrgiou M, Tsoumpou I, Vrekoussis T, et al. The up-to-date evidence on colposcopy practice and treatment of cervical intraepithelial neoplasia: the Cochrane colposcopy & cervical cytopathology collaborative group (C5 group) approach. Cancer Treat Rev 2006; 32: 516–23.

[4] Sadler L, Saftlas A, Wang W, et al. Treatment for cervical intraepithelial neoplasia and risk of preterm delivery. JAMA 2004; 291: 2100–6.

[5] Gyllensten U, Gustavsson I, Lindell M, et al. Pri-mary high-risk HPV screening for cervical cancerin post-menopausal women. Gynecol Oncol 2012; 125: 343–345.

[6] Ansari M, Mehdi G, Arif SH, et al. Smear pat-terns and spectrum of premalignant and malig-nant cervical epithelial lesions in postmenopausal Indian women: a hospital-based study. Diagn Cytopathol2012; 40: 976–83.

[7] Oncoguía SEGO. Prevención del Cáncer de Cuello de Útero SEGO. 2014. Available in: https://sego.es/Guias_de_Asistencia_Practica#oncologia.

[8] Guía de cribado del cáncer de cuello de útero en España. AEPCC. 2014. Available in: http://www.aepcc.org/aepcc-guias/

[9] Doorbar J, Quint W, Banks L, Bravo IG, Stoler M, Broker TR, et al. The Biology and Life-Cycle of HumanPapillomaviruses. Vaccine.2012;30:F55–70.

[10] Bzhalava D, Eklund C, Dillner J. International standardization and classification of human papillomavirus types. Virology.2015;476:341–344.

[11] Bouvard V, Baan R, Straif K, Grosse Y, Secretan B,El Ghissassi F, et al. Special Report: Policy A reviewof human carcinogens — Part B: biological agents.Lancet Oncol. 2009;10(4):321–2.

[12] De Vuyst H, Clifford G, Li N, Franceschi S. HPV infection in Europe. Eur J Cancer. 2009; 45: 2632–2639.

[13] Guan P, Howell-Jones R, Li N, Bruni L, de Sanjose´ S, Franceschi S, et al. Human papillomavirus types in 115,789 HPV-positive women: a meta-analysis from cervical infection to cancer. Int J Cancer. 2012; 131: 2349–2359

[14] Tachezy R, Smahelova J, Kaspirkova J, Salakova M. Human Papillomavirus Type-Specific Prevalence in the Cervical Cancer Screening Population of Czech Women. PLOS ONE. 2013; 8: e79156

[15] Arbyn M, Benoy I, Simoens C, Bogers J, Beutels P, Depuydt C. Prevaccination distribution of human papillomavirus types in women attending at cervical cancer screening in Belgium. Cancer Epidemiol Biomarkers Prev. 2009; 18: 321.

[16] Blanks RG, Moss SM, Addou S, Coleman DA, Swerdlow AJ. Risk of cervical abnormality after age 50 in women with previously negative smears. Br J Cancer. 2009; 100: 1832–1836.

[17] Castle PE, Schiffman M, Herrero R, et al. A prospective study of age trends in cervical human papillomavirus acquisition and persistence in Guanacaste, Costa Rica. J Infect Dis. 2005; 191 (11): 1808–1816.

[18] Coupe´ VMH, Berkhof J, Bulkmans NWJ, Snijders PJF, Meijer CJLM. Age-dependent prevalence of 14 high-risk HPV types in the Netherlands: implications for prophylactic vaccination and screening. Br JCancer. 2008; 98: 646–651.

[19] Sabol I, MilutinGasperov N, Matovina M, Bozinović K, Grubisić G, Fistonić I, et al. Cervical HPV type-specific pre-vaccination prevalence and age distribution in Croatia.PLoSONE. 2017; 12(7).

[20] de Villiers EM, Fauquet C, Broker TR, Bernard HU, zurHausen H. Classification of papillomaviruses. Virology. 2004; 324: 17–27.

[21] Schiffman M, Castle PE, Jeronimo J, et al. Human papillomavirus and cervical cancer. Lancet.2007; 370: 890–907.

[22] Massad LS, Einstein MH, Huh WK, et al. 2012 updated consensus guidelines for the management of abnormal cervical cancer screening tests and cancer precursors. Obstet Gynecol. 2013; 121: 829–46.

[23] So KA, Lee IH, Kim TJ, Lee K. HRisk factors of persistent HPV infection after treatment for high-grade squamous intraepithelial lesion. Arch Gynecol Obstet. 2019 Jan; 299 (1): 223-227.

[24] Hoffman SR, Le T, Lockhart A, Sanusi A, Dal Santo L, Davis M, et al.Patterns of persistent HPV infection after treatment for cervical intraepithelial neoplasia (CIN): A systematic review.Int J Cancer. 2017 Jul 1; 141 (1): 8-23.

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