TRANSMISSION OF HUMAN PAPILLOMA VIRUS AMONG COUPLES: MATCH BETWEEN THE SUBTYPES AND DIFFERENT SITES OF INFECTION

Transmissão do Papilomavírus humano entre casais: concordância entre os subtipos e sítios diferentes de infecção

Andréa Gazzinelli Dantés¹, Carlos Eduardo Gazzinelli Cruz², Eduardo Batista Cândido³, Soraya Moukhaiber Zhour⁴, Myrian Fátima de Siqueira Celani⁴, Agnaldo Lopes da Silva Filho⁵

ABSTRACT

Introduction: Among the sexually transmitted diseases, the highest world incidence is infection by the human papillomavirus (HPV). It affects 65% of men and 80% of women. At the moment, it is only the viral infection associated with development of cancer. **Objective:** To review the aspects related to the transmission of the HPV in men and women, collecting studies that analyze their transmission among couples, comparing the correlation between the partners and the transmission rates among different sites. **Methods:** The study was designed based upon literature review, using medical search tools like Pubmed/Medline, with the keywords: "Human Papillomavirus"; and combinations, "Human Papillomavirus" and "couples," "HPV infection in men," "transmission of papilloma virus." The studies selected were those that included HPV detection through HPV-DNA. **Results:** The concomitance of at least one viral genotype between genders showed great variation from 2.63 to 100%, the latter being specifically related to high-grade and consistency in HIV-positive groups. **Conclusion:** Men play a decisive role in this mechanism, both as a transmitter and as a carrier, thus they should also be the focus of HPV vaccination and treatment policies .

Keywords: Papillomaviridae; sexually transmited diseases; pathogenicity.

RESUMO

Introdução: Dentre as doenças sexualmente transmissíveis, a de maior incidência mundial, é a infecção pelo Papilomavírus humano (*HumanPapillomavirus* — HPV). Atinge 65% dos homens e 80% das mulheres. No momento, é única infecção viral que está associada desenvolvimento de um câncer. **Objetivo:** Revisar os aspectos relacionados à transmissão do papilomavírus humano em homens e mulheres, reunindo estudos que analisam sua transmissão entre casais, comparam a concordância entre os parceiros e as taxas de transmissão entre sítios diferentes. **Métodos:** O estudo foi concebido a partir de revisão bibliográfica usando a ferramenta de busca médica pubmed/medline, com as palavras-chave: "papilomavírus humano"; e as combinações: "papilomavírus humano" e "casais", "infecção HPV no homem", "transmissão do papilomavírus". Foram selecionados aqueles em que a presença do HPV foi comprovada pela detecção do HPV-DNA. **Resultados:** A concomitância de pelo menos um genótipo viral entre os gêneros mostrou grande variação desde 2,63% até 100,00%, especificamente este relacionado ao alto grau e concordância em grupos HIV-positivo. **Conclusão:** O homem desempenha um papel decisivo nesse mecanismo, tanto como transmissor quanto como reservatório, devendo ser alvo também das políticas de vacinação e tratamento do HPV.

Palavras-chave: Papillomaviridae; doenças sexualmente transmissíveis; patogenicidade.

INTRODUCTION

Among the sexually transmitted diseases, the one with the highest incidence worldwide is the infection by the human papillomavirus (HPV). It affects 65% men and 80% women⁽¹⁾. It is currently the only viral infection linked with the development of cancer⁽²⁾. HPV is largely responsible for cervical neoplasia, estimated at 450,000 new cases per year worldwide⁽³⁾. It was identified in 46–100% cases of cancer of squamous cells in the anal region.

Despite affecting both genders, there are few studies concerning couples or male individuals.

The infection and transmission among men and women have distinct patterns, with significant differences in the persistence of the virus.

After a year of investigation, a Dutch study showed the persistence of the virus among women of 20% whereas only 6% among men⁽⁵⁾. In Finland, the majority of women presented an average clearance time (the capacity to eliminate the virus) of 6 years, an average of 62.5 months. However, among 75% men the average was merely 12 months^(6,7). In addition, when comparing the rate of infection and the manifested disease, higher rates of infection were found among men than women, in contrast to the rates of the disease, which are higher among women⁽⁸⁾.

The consistent findings between sexual partners are still poorly understood. They seem to depend upon the type of sexual relation,

¹Obstetrics and Gynecology Resident Doctor at Santa Casa de Misericórdia in Belo Horizonte – Belo Horizonte (MG). Brazil. ²Assistant Professor at the Department of Medicine and Nursing at the School of Medicine at the Universidade Federal de Viçosa (UFV) – Viçosa (MG). Brazil.

³Assistant Professor in the Department of Obstetrics and Gynecology at the School of Medicine at the Universidade Federal de Minas Gerais (UFMG) – Belo Horizonte (MG). Brazil.

⁴Associate Professor at the Department of Obstetrics and Gynecology at the School of Medicine at UFMG – Belo Horizonte (MG). Brazil. ⁵Full Professor at the Department of Obstetrics and Gynecology at the School of Medicine at UFMG – Belo Horizonte (MG). Brazil.

the time since the act, the subtype of HPV involved, and the site in which the virus is found⁽⁹⁾.

OBJECTIVE

Review the aspects related to the transmission of the HPV among men and women, collecting studies that analyze the transmission among couples, comparing the consistency among partners, and the rates of transmission in different sites.

METHODS

The study was designed based on a literaturereview utilizing the medical search tool Pubmed/Medline, with the keywords: "human papillomavirus"; and combinations: "human papillomavirus" and "couples," "HPV infection in men," "transmission of papillomavirus." The studies selected were those that included HPV detection through HPV-DNA. In all of them, the collection was carried out from the site of the female genitalia using the Papanicolaou test and the male by swabbing the penile regions, such as the glans, urethra, and foreskin.

RESULTS

Consistency among couples

when assessing the existence of the HPV virus in partners, we can locate corresponding characteristics in its presence or lack thereof as well as in the similarity between viral subtypes.

Huang et al. found a rate of 5.26% of concomitant presence of the virus in partners, with this being the lowest rate found among the studies. In the HIM (HPV in men) study, conducted in the USA, which assessed 88 couples, the concomitance of the viral infection was of 62.5%.

A similar rate was found by Widdice, in an assessment of 25 couples through 116 examinations, with correspondence in 77 of them (61%). Each participant was examined five times, each at distinct times after sexual intercourse. The highest rate of consistency was of 95%, with the material being collected 24 h after sexual intercourse. The rate was of 74% after 48 h of sexual intercourse. The variation found was of 61–91% in all sites and all examinations.

In Brazil, Afonso et al. conducted a study in two population groups; the first, in which the woman presented cervical intraepithelial neoplasia (CIN), presented 50% of consistency between the couples; and the second, conducted with asymptomatic couples, resulted in $15\%^{(8)}$.

When the comparison is made between African couples, specifically those who are carriers of the human immunodeficiency virus (HIV), the correspondence in the detection of HPV was of 56%, whereas in patients who were not carriers of the HIV virus, the correspondence was of $22\%^{(13)}$.

Parada et al.⁽¹⁴⁾ obtained the highest percentage (79%) among the analyzed studies, perhaps due to the sample being bigger and due to the method for collecting material in men having included numerous anatomical sites on the penis, increasing the chance for detection of $HPV^{(14)}$ (Table 1).

CONSISTENCY OF VIRAL SUBTYPE

Another assessment of the analyzed studies was carried out in relation to the consistency among couples and the subtype of the virus present in the individual, both related to oncogenic as well as non-oncogenic subtypes.

The concomitance of at least one viral genotype among the gendersreveals a great variance from 2.63%, in a Chinese study, to 100%, a value obtained in an African study, with the latter being specifically conducted on an HIV positive group.

Subtype 16 is the most common among oncogenic individuals, being found in a higher prevalence, both in the studies by Huang *et al.* as well as in the Brazilian study^(8,10).

Subtypes 31 and 89 can also be considered important as they are predominant in the HIM study, where 23.9% partners had equivalence in at least one viral genotype; another relevant finding was the total correspondence of subtypes in merely 2 of 88 couples⁽¹⁹⁾.

Subtypes 39, 54, 59, and 62, found by Parada et al.⁽¹⁴⁾, are highlighted due to their viral similarities of 61.8% and subtype 84, prevalent in the Widdice et al.⁽¹²⁾ study. This last study, unlike the others, utilized anogenital consistency among the genders, obtaining 15% rate in 116 examinations.

Despite not citing the specific subtypes of HPV involved, the Canadian study, known as HITCH, revealed that 42% couples presented at least one similar subtype⁽¹⁵⁾.

Finally, it is worth noting that the correspondence of genotype of the HPV virus was higher when the participants presented diseases such as CIN, in the Brazilian study, and HIV, in the African study^(8,13) (**Table 2**).

FACTORS RELATED TO TRANSMISSION

Some factors seem to influence the transmission of the virus and the rate of consistency.

The rate of consistency, taking the specific subtypes into consideration, was higher among couples with a similar age and who had

Table 1 – Consistency among couples in the various studies.

Study	Number of couples	Rate of consistency
Huang et al.(10)	76	5.26%
Giuliano et al.(19)	88	62.5%
Widdice et al.(12)	25	61.00%
Afonso et al. ⁽⁸⁾	60	15-50%
Vogt et al.(13)	34	22-56%
Parada et al. ⁽¹⁴⁾	504	79%

Table 2 – Consistency of viral subtypes.

Study	Subtype consistency	Most common subtype
Huang et al. ⁽¹⁰⁾	2.63%	16
Giuliano et al.(19)	23.9%	31 and 89
Widdice et al.(12)	15%	84
Afonso et al. ⁽⁸⁾	42%	
Vogt et al.(13)	61.8%	59. 62.54, and 39
Parada et al.(14)	3–26%	16

been in a relationship for less than a year⁽¹¹⁾, and in the presence of the HIV virus⁽¹³⁾.

Although not statistically significant, the presence of non-monogamous relationships seems to have a connection with the transmission of the virus, which was not found in relation to variables such as race, ethnicity, education level, and marital status⁽¹¹⁾.

The inconsistency of subtype was related to a lower number of partners for each individual during their life $(p<0.0001)^{(11)}$.

Other positive variables for the increase in the transmission of the virus are the following: men having had a higher number of partners throughout his life; the couples involved maintaining an active sex life; not using condoms; and having recently had vaginal intercourse^(14,15). It is imperative to emphasize that the main risk factor for the transmission of the virus appears to be the presence of the same partner, increasing the rate of transmission up to 5.1 times^(12,14).

RATE OF TRANSMISSION

Some authors investigated the rate of transmission between different sites of the human body. In 2013, Widdice⁽¹²⁾ assessed each partner during five examinations and obtained the following values: detection of female genital HPV on the partners had varied from 48% to 60%; in the partner's perianal area, from 48 to 60%; and in the partner's oral cavity, from 0 to 5%. The consistency between the female anal site and the male genitalia was between 56 and 76%; male hand, from 33 to 63%; male perianal area, from 13 to 38%; and the oral cavity, 0% — showing that in addition to the genitals, the hand and perianal areas are important vehicles of transmission, contrary to the oral cavity which did not present a significant role. In all the examinations, the rate of transmission of the women to men was higher than the inverse, the same occurring when non-genital sites were considered⁽¹²⁾.

A similar result was found by Burchell et al.⁽¹⁵⁾, in the HITCH study, and by Hernandez et al.⁽¹⁶⁾. The former found a rate of transmission of 4.0 from the women to the men whereas the inverse was 3.5, when a calculated variable of 100 people/months (number of events divided by the number of people exposed per month, multiplied by 100)⁽¹⁵⁾. The latter shows the transmission of women to men as approximately 3.5 times higher than the inverse; they also attempt to statistically define the main sources of transmission for each sex, verifying the penis as the main vehicle for transmission in men and the cervix as the main vehicle of transmission in women. In addition, the hand and anus of women are also relevant as they can transmit HPV to men. In the same study, self-inoculation was noted in both sexes, but mainly in men⁽¹⁶⁾.

DISCUSSION

Based on the cited studies, it can be inferred that the HPV is highly transmissible, which is corroborated by the average of consistency among 58% couples. In the study by Huang et al.⁽¹⁰⁾, which presented lower rates (5.26%), the authors believe that this fact is due to the characteristics of the couples studied, such as long-term monogamous relationships and the men over 35 years of age, which likely decreases the chance of recent contamination of the individuals. In addition, the clearance among men is more efficient and the faster elimination of the virus in men decreases its identification after a long period has passed since the sexual relationship⁽¹⁰⁾.

The finding that the HPV genotype 16 presents higher consistency among couples is in line with what had been shown in previous studies: infection by high-risk HPV, attributed to this genotype, is long-lasting and seems to have a higher potential for transmission⁽¹⁷⁾.

The presence of HIV seems to be an important cofactor in the transmission and infection of the HPV, as the African study demonstrated. People with reduced immunity, such as those infected by HIV or with transplants, present more persistent infection and a higher prevalence of cervical cancer^(13,17).

The viral difference between the men and women can be due to numerous factors. Beginning with the greater difficulty in collecting material from men, who present various sites for collection in the genitals, such as the glans, prepuce, and urethra. In case of women, there is a greater ease in detecting the virus, since cervical smear provides greater cellularity than the urethral swab, which is performed on men. There is also a relevant difference between the cervical and penile epithelium, which helps to emphasize this difference^(10,14,18).

The fact that these studies demonstrate the presence of HPV-DNA, which does not necessarily mean viral infection, is another important aspect that should be discussed. Furthermore, even stable sexual partners present low consistency of genotypes. Detection of viral DNA and the high rate of transmission may not be as significant for the infection and the diseases caused by them⁽¹²⁾.

Despite the analyzed studies had a high degree of relevant consistency, more of them should be conducted, especially those which involve more significant samples, with more heterogeneous population groups.

There is a clear barrier imposed by the difficulty in treating sexually transmitted diseases among couples that are important to emphasize. They conflict with preconceived cultural and religious notions, in addition to a lack of communication between partners and between the patient and the doctor.

CONCLUSION

Transmission of HPV involves various factors and its study can help to unveil and help its prevention.

Men play a decisive role in this mechanism, both as transmitters as well as carriers, thus they should also be the focus of HPV vaccination and treatment policies.

New studies can better clarify this relationship and contribute to the decrease in the dissemination of this virus.

Conflict of interests

The authors reported no conflict of interests.

REFERENCES

- Rocha MG, Faria FL, Gonçalves L, Souza M, Fernandes P, Fernandes AP. Prevalence of DNA-HPV in Male Sexual Partners of HPV-Infected Women and Concordance of Viral Types in Infected Couples. PLoS ONE. 2012;7(7):e40988.
- Liu M, He Z, Zhang C, Liu F, Liu Y, Li J, et al. Prevalence, Incidence, Clearance and Associated Factors of Genital Human papillomavirus Infection among Men: a population-based cohort study in rural China. Cancer Epidemiol Biomarkers Prev. 2014;23(12):2857-65.

- Bodily J, Laimins L. Persistence of human papillomavirus infections: keys to malignant progression. Trends Microbiology. 2011;19(1):33-9.
- Franceschi S, Castellsague X, Dal Maso L, Smith JS, Plummer M, Ngelangel C, et al. Prevalence and determinants of human papillomavirus genital infection in men. Br J Cancer. 2002;86(5):705-11
- Van Doomum G, Prins M, Juffermans L, Hooykaas C, Van den Hoek J, Coutinho R, et al. Regional distribution and incidence ofhuman papillomavirus infections among heterosexual men and women with multiple sexual partners: a prospective study. Genitourinary Med. 1994;70(4):240-6
- Louvanto K, Rintala MA, Syrjänen KJ, Grénman SE, Syrjänen SM. Genotype-specific persistence of genital human papillomavirus (HPV) infections in women followed for 6 years in the Finnish Family HPV Study. J Infect Dis. 2010;202(3):436-44
- Giuliano AR, Lazcano-Ponce E, Villa LL, Flores R, Salmeron J, Lee JH, et al. The Human Papillo-mavirus Infection in Men study: human papillomavirus prevalence and type distribution among men residing in Brazil, Mexico, and the United States. Cancer Epidemiol Biomarkers Prev. 2008;17(8):2036-43.
- Afonso LA, Rocha W, Carestiato F, Dobao E, Pesca L, Passos M, et al. Human papillomavirus infection among sexual partners attending a Sexually Transmitted Disease Clinic in Rio de Janeiro, Brazil. Braz J Med Biol Res. 2013;46(6):533-8
- Widdice L,Breland D,Jonte J, FarhatS,Ma Y, Leonard A, Moscicki AB. Papillomavirus (HPV) Concordance in Heterosexual Couples. Journal Adolescent Health. 2010;47(2):151-159
- Huang Y, Lin M, Luo Z, Wen-Yu Li, Zhan XF, Yang L. Low Prevalence of HPV in Male Sexual Partners of HR-HPV Infected Females and Low Concordance of Viral Types in Couples in Eastern Guangdong. Asian Pacific J Cancer Prev. 2013;14(3):1755-60.
- Nyitray AG, Menezes L, Lu B, Lin HY, Smith D, Abrahamsen M, et al. Genital Human Papillomavirus (HPV) Concordance in Heterosexual Couples. J Infect Dis. 2012;206(2):202-11.
- Widdice L, Ma Y, Jonte J, Farhat S, Breland D, Shiboski S, Moscicki AB. Concordance and transmission of human papillomavirus within heterosexual couples observed over short intervals. Journal of Infectious Disease. 2013;207(8):1286-94.
- 13. Vogt S, Gravitt P, Martinson N, Hoffmann J, D'Souza G. Concordant oral-

genital HPV infection in South Africa couples: evidence for transmission. Front Oncol. 2013;3:303.

- Parada R, Morales R 2, Giuliano A, Cruz A, Castellsagué X, Lazcano-Ponce E. Prevalence, concordance and determinants of human papillomavirus infection among heterosexual partners in a rural region in central Mexico. BMC Infect Dis. 2010;10:223.
- Burchell AN, Coutlée F, Tellier PP, Hanley J, Franco EL. Genital Transmission of Human Papillomavirus in Recently Formed Heterosexual Couples. J Infect Dis. 2011;204(11):1723-9.
- Hernandez BY, Wilkens LR, Zhu X, Thompson P, McDuffie K, Shvetsov YB, et al. Transmission of human papillomavirus in heterosexual couples. Emerg Infect Dis. 2008;14(6):888-94.
- 17. van der Snoek EM, Niesters HG, van Doornum GJ, Mulder PG, Osterhaus AD, van der Meijden WI. Acquisition and Clearance of Perianal Human Papillomavirus Infection in Relation to HIVpositivity in Men Who Have Sex with Men in the Netherlands. Acta Derm Venereol. 2005;85(5):437-43.
- Dunne EF, Nielson CM, Stone KM, Markowitz LE, Giuliano AR. Prevalence of HPV infection among men: A systematic review of the literature. J Infect Dis. 2006;194(8):1044-57.
- Giuliano AR, Lee JH, Fulp W, Villa LL, Lazcano E, Papenfuss MR, et al. Incidence and clearance of genital human papillomavirus infection in men (HIM): a cohort study. Lancet. 2011;377(9769);932-40.

Address for correspondence AGNALDO LOPES DA SILVA FILHO

Department of Obstetrics and Gynecology of the School of Medicine at theUniversidade Federal de Minas Gerais Avenida Professor Alfredo Balena, 190 – Centro Belo Horizonte (MG), Brazil CEP: 30130-100 Tel: +55 (31) 99225-0909 E-mail: agnaldo.ufmg@gmail.com

Received on: 09.12.2015 Approved on: 12.26.2015