Annals of Clinical Case Reports

Research Article
Published: 27 Jun, 2023

Oropharyngeal HPV Testing in Life Partners of Patients with Oropharyngeal Cancer: Case Series

Kofler B[1], Schnöll J[2], Laimer J[3,4], Dudas J[1] and Borena W[5]*

[1]Department of Otorhinolaryngology and Head and Neck Surgery, Medical University of Innsbruck, Austria

[2]Department of Otorhinolaryngology and Head and Neck Surgery, Medical University of Vienna, Austria

[3]University Hospital for Cranio-Maxillofacial and Oral Surgery, Medical University of Innsbruck, Austria

[4]Oral and Maxillofacial Surgery, Lana, Italy

[5]Department of Hygiene, Microbiology, Social Medicine, Institute of Virology, Medical University of Innsbruck, Austria

Abstract

Objective: Human papillomavirus is one of the most common sexually transmitted infections in the world. A persistence of an HPV infection in the oropharyngeal region can lead to an HPV-positive Oropharyngeal Cancer (OPC). Partners of patients with HPV-positive oropharyngeal cancer are probably at risk to carry an oropharyngeal HPV infection.

Methods: In partners of patients diagnosed with oropharyngeal cancer an oropharyngeal brush test from the surface of the palatine and lingual tonsil was performed and examined for an oropharyngeal HPV infection. Additionally, all partners answered a questionnaire on socio-demographic data and sexual behavior.

Results: In this study 44 patients with oropharyngeal cancer were included and 21 were positive for a high-risk HPV genotype. Overall, 25 partners were willing to participate, of which 13 were the partner of a high-risk-HPV positive patient. Most partners were female (21/25) and all partners had an HPV-DNA negative oropharyngeal surface brush test. Accordingly, none of the partners of patients with HPV-positive OPC carried an oropharyngeal hr-HPV infection.

Conclusion: In this study, all partners of OPC patients had an HPV-negative oropharyngeal brush test.

Keywords: Human papillomavirus, oropharyngeal cancer, risk factor, sexual behavior, HPV vaccination

OPEN ACCESS

Correspondence:
Barbara Kofler, Department of Otorhinolaryngology, Medical University Innsbruck, Anichstrasse 35, 6020 Innsbruck, Austria, Tel: 0043 43 50 504 23141; Fax: 0043 43 50 504 23144; E-mail: ba.kofler@triol-kliniken.at

Received Date: *06 Jun 2023*
Accepted Date: *22 Jun 2023*
Published Date: *27 Jun 2023*

Citation:
Kofler B, Schnöll J, Laimer J, Dudas J, Borena W. Oropharyngeal HPV Testing in Life Partners of Patients with Oropharyngeal Cancer: Case Series. Ann Clin Case Rep. 2023; 8: 2430.
ISSN: 2474-1655.

Introduction

Human Papillomavirus (HPV) is one of the most common sexually transmitted infections in the world. About 75% to 80% of sexually active people become infected at some time in their lives, but only a small portion of HPV infections develop cancerous lesions, caused by high-risk (hr) HPV types, such as HPV16 and HPV18. Most common HPV-related cancers are female genital cancers, including cervical, vulvar and vaginal cancers. HPV associated Oropharyngeal Cancer (OPC) is more frequent in male patients. Patients with HPV-positive OPC are characterized by younger age and less alcohol and nicotine consumption compared to patients with HPV-negative OPC [1-3].

Several studies reported that patients with HPV-positive OPC are associated with a higher number of passionate kissing partners, lifetime oral sex partners and a higher number of oral sex partners [1,4,5]. In multivariate analysis from 2,116 men and 2,140 women, gender, age, and race were significant predictors for oral sexual behavior and oral sexual behavior was the primary predictor of an oral HPV16 infection [6]. There is only little data about the risk of an oropharyngeal HPV transmission for the partner from patients with HPV-positive OPC. Recently, in a case report of a female patient treated for an HPV-positive OPC was described that her husband presented with the same diagnosis 3 years later, also HPV-positive [7]. D'Souza et al. collected oral rinses from 164 patients with OPC and 93 of their partners. The patients were primarily men (90%), not-smokers (51%) and had performed oral sex (97%), the median age was 56 years. In this study 61% of the patients were HPV-positive and an oral HPV detection in the female partners was found in 1.2%. Among the six male partners, no oncogenic oral HPV infections was detected. No OPC was

identified during partner oral cancer screening examinations. The authors concluded that oral HPV16 DNA is not commonly detected among the partners of patients with HPV-positive OPC. Partners of patients with HPV-positive OPC do not seem to have an increased risk for oral HPV infection compared with the general population [8].

In a previous publication, we reported that surface brushings from oropharyngeal cancer reliably detect HPV-DNA [9-12]. In this study, we examined whether oropharyngeal HPV infection is present in the partners of patients with OPC by brush test of the oropharynx and if life style characteristics like smoking, alcohol and sexual behavior are a risk factor for an oropharyngeal HPV infection. We compared the results with samples from healthy volunteers as control group.

Methods

All patients with histological confirmed oropharyngeal cancer and their partner were invited to participate. All patients with OPC were treated at the Department of Otorhinolaryngology – Head & Neck Surgery, Medical University of Innsbruck or Medical University of Vienna, Austria between February 2018 and October 2019 according to the recommendation of the interdisciplinary tumor board. A positive IRB vote for this investigator-initiated study had been obtained. The respective reference number was 1260/2017. For the control group healthy participants presenting for dentoalveolar procedures at the outpatient clinic of Oral and Maxillofacial Surgery, Medical University Innsbruck, Austria was recruited.

Specimen harvest and handling

On patients with OPC and their partners an oropharyngeal brush test was performed (Digene® HC2 DNA Collection Device, Qiagen, Hilden, Germany). The brush test was taken from the tumor surface during panendoscopy in the patients and then kept in a sterile container in 0.05% sodium azide and sent to the Division of Virology of the Medical University of Innsbruck. The partner´s brush test and the brush test of the healthy volunteers was taken from the surface of the base of tongue and both tonsils. Additionally, the patient´s partner answered a validated questionnaire on socio-demographic data and sexual behavior.

Processing of brush specimens

Brush samples were purified in a fully automated manner (NucliSens® easyMAG®, Biomerieux). We did DNA amplification and genotyping using a commercial test kit (AmpliQuality HPV-TYPE EXPRESS, AB Analitica®, Padova, Italy). The kit amplifies the L1 Open Reading Frames (ORF). As a second step PCR products were denatured and hybridized on nitrocellulose membrane strips that harbor about 40 genotype- specific probes. The house-keeping gene beta-globin was used as an internal control.

Results

Oropharyngeal cancer patients and brush test

During the study period, 44 patients with OPC were enrolled. The mean age of was 65 years. Eight patients were female (18%), and 36 were male (82%). Most patient had UICC stage IV (n=20, 45%) (Table 1). HPV DNA of all patients was available, of which 21 patients were hr-HPV positive. The most common genotype was HPV16 (n=19, 43%), other genotypes were HPV18 and HPV33 (Table 2).

Partner and brush test

Twenty-five partners could be included. Thirteen partners (52%) were in a relationship with an HPV-positive OPC patient. The reasons why in 20 patients no oropharyngeal brush of the partner was taken was no current partner (n=9), separation (n=4), no interest (n=5) and other (n=2). The majority of the partners were female (n=21, 84%), the mean age was 62 years. None of them had a previous HPV vaccination. All oropharyngeal brush tests of the partners were HPV negative (Table 3).

Table 1: Patient characteristics.

	Number of patients (%)
Sex	
Female	8 (18%)
Male	36 (82%)
Tumor site	
Oropharynx	44 (100%)
Histology	
Squamous cell carcinoma	44 (100%)
UICC-stage	
Stage I	13 (30%)
Stage II	4 (9%)
Stage III	7 (16%)
Stage IV	20 (45%)

Table 2: HPV genotypes.

HPV genotypes	Number of patients (%)
HPV 16	19 (43%)
HPV 18	1 (2.5%)
HPV 33	1 (2.5%)
HPV neg.	23 (52%)

Table 3: Partner characteristics.

	Number of patients (%)
Sex	
Male	4 (16%)
Female	21 (84%)
Oropharyngeal HPV brush test	
HPV neg.	25 (100%)
HPV vaccination	
Yes	0
No	25 (100%)
Number oral sex partner	
0-3	22 (88%)
>3	3 (12%)
Alcohol	
Not daily	21 (84%)
Daily	4 (16%)

Partner´s lifestyle characteristics

The questionnaire on sociodemographic and sexual behavior gave the following information, the first sex was performed with a mean age of 18 years. Three of the partners (12%) had oral sex with more than 3 different sex partners. Seven partners (28%) were smoking ≥ 20 PY and 4 partners (12%) reported to drink alcohol daily (Table 3). The mean BMI was 24 kg/m^2 and the mean sportive activity was 3 times per week.

Healthy control group

In total 112 healthy participants served as the control group. The median age of the participants was 62.1 years and most participants were male (83% versus 17%). In 2/112 participants low-risk HPV genotypes were detected in the oropharynx.

Discussion

In this study, we questioned whether the partners of patients with hr-HPV-positive OPC are at risk of an oropharyngeal HPV infection. Additionally, we collected socio-demographic data from the partners and examined if there is a higher risk of oropharyngeal HPV infection in partners performing oral sex with more than 3 different people. From the 44 patients with OPC, 21 were hr-HPV positive. This is in line with the current hr-HPV prevalence in OPC patients in Central Europe [13,14]. Twenty-five partners of OPC patients participated in the study and all of them were HPV-negative in the oropharyngeal brush test. Regarding the low number of participating partners this study is not representative but the results are in line with previous studies. Uken et al. performed HPV testing of the uterine cervix and the tonsillar region in women with cervical dysplasia. In addition, sexual partners received an oral HPV testing. In this study 101 women were tested HPV-positive in the cervix and only 3/101 (3%) were tested HPV-positive in the oropharynx. In 60/101 women also the sexual partner could be tested for an oral HPV infection. The HPV test was positive in 3/60 (5%) partners. The study group concluded that an HPV transmission to the oropharynx by oral-genital sex or by autoinoculation is a rare and an unlikely event with low HPV concordance [15]. As described before D'Souza et al. also reported in their study that OPC patients were primarily male and the female partners did not have a higher oncogenic oral HPV prevalence compared with members of the general population of the same age [8].

In our study healthy participants, who are not in a relationship with an OPC patient, were tested for an oropharyngeal HPV infection and served as a control group reflecting the general population. In our control group 2/112 (1.8%) harvested a low-grade oropharyngeal HPV infection, which is in line with previous studies. Ilmarinen et al. reported a low HPV prevalence in nonmalignant tonsils, 5/477 (1.0%) patients receiving tonsillectomy because of chronic tonsillitis were tested positive for HPV [16].

In our study 3/25 (12%) partners reported to have performed oral sex with more than 3 different sex partners. People who practiced oral sex with multiple partners are at possible risk for developing oropharyngeal cancer [17]. Emmett et al. reported a strong association between oral sex behaviors and HPV-positive oropharyngeal tumors [4].

As reported in other studies [18,19] also our patient-population consists mainly of men. Faraji et al. reported in their study with 20,886 patients the prevalence of HPV-positive OPC to be higher among men than women. There was no association between sex and race with survival among patients with HPV-positive OPC. In contrast, for patients with HPV-negative OPC, the risk of death was significantly higher for women versus men and black versus white patients [20].

Limitations of this study are that the number of participating partners of OPC patients was low. The reasons why it was not possible to collect a brush test in all OPC patients was no current partner, separation, no interest and other. Further limitations are that the group of healthy volunteers was not asked to answer the questionnaire on sociodemographic data and sexual behavior. So, we do not have any information of oral sex behavior in this group, the volunteers were also not asked if their partners have or had an OPC.

Conclusion

In this study, all partners of OPC patients were HPV negative in the oropharyngeal surface brushing. Also, other studies reported a low rate of oropharyngeal HPV infection in partners. Due to a low number of participating partners further studies are needed.

References

1. De Santis S, Spinosi MC, Cambi J, Bengala C, Boccuzzi S. Oropharyngeal squamous cell carcinoma and HPV. Systematic review on overall management. J Stomatol Oral Maxillofac Surg. 2017;118(2):103-8.
2. Kofler B, Uecker FC, Muenscher A, Knecht R. [New aspects of HPV-positive head and neck cancer. Highlights from the 2011 ASCO Congress]. HNO. 2012;60(5):404-7.
3. Kofler B, Laban S, Busch CJ, Lorincz B, Knecht R. New treatment strategies for HPV-positive head and neck cancer. Eur Arch Otorhinolaryngol. 2014;271(7):1861-7.
4. Emmett S, Boros S, Whiteman DC, Porceddu SV, Panizza BJ, Antonsson A. Sexual behaviour, HPV status and p16 (INK4a) expression in oropharyngeal and oral cavity squamous cell carcinomas: A case-case comparison study. J Gen Virol. 2018;99(6):783-9.
5. Dalla Torre D, Burtscher D, Soelder E, Offermanns V, Rasse M, Puelacher W. Human papillomavirus prevalence in a Mid-European oral squamous cell cancer population: A cohort study. Oral Dis. 2018;24(6):948-56.
6. D'Souza G, Cullen K, Bowie J, Thorpe R, Fakhry C. Differences in oral sexual behaviors by gender, age, and race explain observed differences in prevalence of oral human papillomavirus infection. PloS One. 2014;9(1):e86023.
7. Vahl JM, Hoffmann TK. [HPV-positive oropharyngeal cancer-risk for the partner?]. HNO. 2019;67(2):126-8.
8. D'Souza G, Gross ND, Pai SI, Haddad R, Anderson KS, Rajan S, et al. Oral Human Papillomavirus (HPV) infection in HPV-positive patients with oropharyngeal cancer and their partners. J Clin Oncol. 2014;32(23):2408-15.
9. Kofler B, Borena W, Manzl C, Dudas J, Wegscheider AS, Jansen-Durr P, et al. Sensitivity of tumor surface brushings to detect human papilloma virus DNA in head and neck cancer. Oral oncol. 2017;67:103-8.
10. Kofler B, Borena W, Dudas J, Innerhofer V, Dejaco D, Steinbichler TB, et al. Post-treatment HPV surface brushings and risk of relapse in oropharyngeal carcinoma. Cancers. 2020;12(5):1069.
11. Kofler B, Laimer J, Bruckmoser E, Steinbichler TB, Runge A, Schartinger VH, et al. The Role of HPV and non-HPV sexually transmitted infections in patients with oropharyngeal carcinoma: A case control study. Cancers. 2020;12(5):1192.
12. Borena W, Schartinger VH, Dudas J, Ingruber J, Greier MC, Steinbichler TB, et al. HPV-induced oropharyngeal cancer and the role of the E7 Oncoprotein detection via brush test. Cancers. 2020;12(9):2388.
13. Wittekindt C, Wagner S, Bushnak A, Prigge ES, von Knebel Doeberitz M, Wurdemann N, et al. Increasing incidence rates of oropharyngeal squamous cell carcinoma in Germany and significance of disease burden attributed to human papillomavirus. Cancer Prev Res (Phila). 2019;12(6):375-82.
14. Ndiaye C, Mena M, Alemany L, Arbyn M, Castellsague X, Laporte L, et al. HPV DNA, E6/E7 mRNA, and p16INK4a detection in head and neck cancers: A systematic review and meta-analysis. Lancet Oncol. 2014;15(12):1319-31.

15. Uken RB, Brummer O, von Schubert-Bayer C, Brodegger T, Teudt IU. Oral HPV prevalence in women positive for cervical HPV infection and their sexual partners: A German screening study. Eur Arch Otorhinolaryngol. 2016;273(7):1933-42.

16. Ilmarinen T, Munne P, Hagstrom J, Haglund C, Auvinen E, Virtanen EI, et al. Prevalence of high-risk human papillomavirus infection and cancer gene mutations in nonmalignant tonsils. Oral Oncol. 2017;73:77-82.

17. Nguyen NP, Nguyen LM, Thomas S, Hong-Ly B, Chi A, Vos P, et al. Oral sex and oropharyngeal cancer: The role of the primary care physicians. Medicine (Baltimore). 2016;95(28):e4228.

18. Xu L, Dahlstrom KR, Lairson DR, Sturgis EM. Projected oropharyngeal carcinoma incidence among middle-aged US men. Head Neck. 2019;41(9):3226-34.

19. Pytynia KB, Dahlstrom KR, Sturgis EM. Epidemiology of HPV-associated oropharyngeal cancer. Oral oncology. 2014;50(5):380-6.

20. Faraji F, Rettig EM, Tsai HL, El Asmar M, Fung N, Eisele DW, et al. The prevalence of human papillomavirus in oropharyngeal cancer is increasing regardless of sex or race, and the influence of sex and race on survival is modified by human papillomavirus tumor status. Cancer. 2019;125(5):761-9.