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HPV 2015

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& CLINICAL AND PUBLIC HEALTH WORKSHOPS

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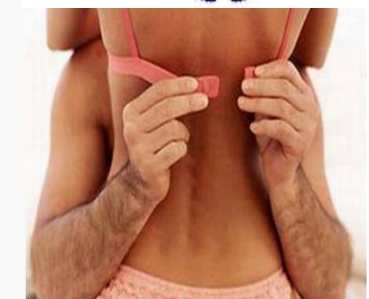
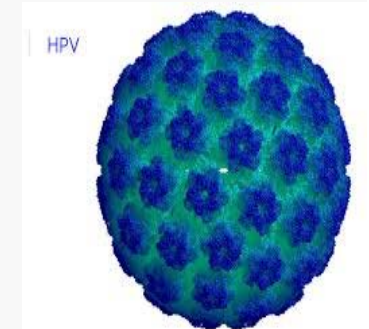
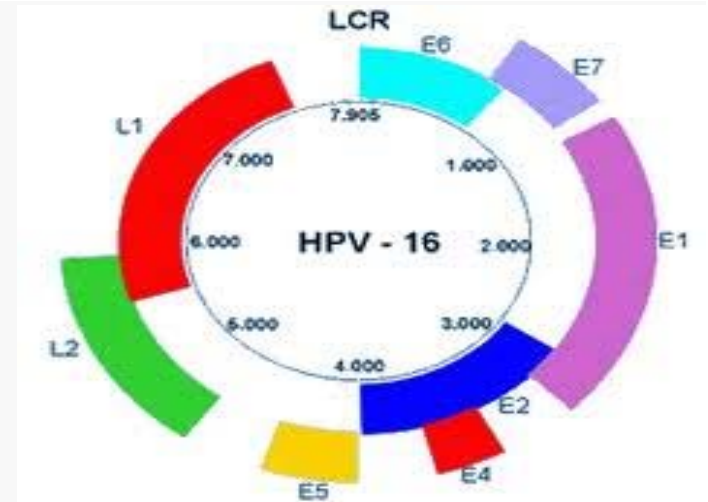
HPV

Lesões orais de comportamento essencialmente benigno

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HPV

- DNA-vírus, + de 200 subtipos,
- não cultivável
- Família *Papillomaviridae* (de Villiers, 1997)
- 55nm de diâmetro, sem envelope
- com 72 capsômeros,
- capsídeo com simetria icosaédrica
- epiteliotrópico
- transmissão sexual
- **(+) região ano-genital, (-) mucosa orofaríngea**
- - Genoma (dividido)



Vacinas contra o HPV
Reunião de Consenso Nacional
Cascais, 19 e 20 de Março de 2010



ORGANIZAÇÃO:

Secção Portuguesa de Ginecologia oncológica

Sociedade Portuguesa de Ginecologia

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2012;78(4):66-70.

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ORIGINAL ARTICLE

BJORL.org

Epidemiological study of HPV in oral mucosa through PCR

Estudo epidemiológico do HPV na mucosa oral por meio de PCR

Willys Tristão¹, Rodrigo Metzker Pereira Ribeiro¹, Camila Andrea de Oliveira², Julio Cesar Betiol³,
Jussara de Sousa Ribeiro Bettini⁴

Keywords:

mouth mucosa,
papillomavirus
infections,
polymerase chain
reaction.

Abstract

The Human Papillomavirus (HPV) belongs to the *Papillomaviridae* family and has a capsid and a single DNA strand. Its infection occurs mainly through sexual intercourse, having an important tropism for skin and mucosal cells. **Aim:** To evaluate the HPV presence in normal oral mucosa of asymptomatic subjects and; in parallel, to correlate social behavioral habits with the virus. **Materials and Methods:** Contemporary cohort cross-sectional study. The HPV was found by PCR, using general primers MY09/11 in 125 oral mucosa samples submitted to DNA extraction and PCR to search for the beta-globin gene in order to assess the quality of the extracted DNA. In parallel, we carried out a study of behavioral issues associated with the patients. **Results:** All the samples had a positive diagnosis of the beta-hemoglobin gene. HPV was diagnosed in 23.2% of the samples

“Um ano após o início da actividade sexual, quatro em cada dez mulheres são HPV positivas e dois anos após o seu início, seis em cada dez. **Estima-se que 80% da população mundial tenha um episódio de infecção por HPV ao longo da vida.**”

Stable marital relationship protects men from oral and genital HPV infections

K. M. Kero • J. Rautava • K. Syrjänen •
O. Kortekangas-Savolainen • S. Grenman • S. Syrjänen

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Abstract Human papillomavirus (HPV) infections are associated with sexual behavior. Changes in the sexual habits of couples and their impact on male genital and oral HPV infections were determined during 7 years of follow-up (FU). At baseline and 7 years FU, urethral, semen/penile, and oral samples were collected from 46 men and cervical and oral samples of their spouses for HPV DNA detection. Demographic data and risk factors of spouses were recorded by questionnaire at both time points and analyzed for concordance. HPV genotyping was done with the Multimetrix® kit. At baseline, 29.5 % of the male genital and 11 % of their oral samples tested positive. Incident genital HPV infection was found in 23 % and oral infection in 10.9 % of men. Genotype-specific persistence was detected in one man (HPV53) in

status ($p=0.001$; 95 % CI 0.000–0.002) increased the risk of incident genital HPV infections. The overall outcome of genital HPV disease in men was linked to the frequency of sexual intercourse ($p=0.023$; 95 % CI 0.019–0.026) and changes in marital status ($p=0.022$; 95 % CI 0.019–0.026), while oral HPV infections were associated with the number of sexual partners ($p=0.047$; 95 % CI 0.041–0.052). Taken together, asymptomatic genital HPV infections among the men were common. The risk of incident genital HPV infections increased among men reporting a change of sexual partner during FU, implicating that a stable marital relationship protects against oral and genital HPV infection.

Infecção oral pelo HPV e lesões epiteliais proliferativas associadas

Primeira submissão em 26/11/10
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HPV oral infection and proliferative epithelial associated lesions

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Sílvia Paula de Oliveira³; Maria da Glória da Costa Carvalho⁴; Eliane Pedra Dias⁵

unitermos

Papilomavírus humano

Biologia

Patologia

Lesões orais

resumo

Os papilomavírus humanos (HPVs) pertencem à família *Papillomaviridae* e seu ciclo de vida é diretamente ligado à diferenciação das células epiteliais do hospedeiro. Possuem seis genes que se expressam precocemente e dois genes que se expressam tardiamente, sendo denominados respectivamente E (*early*) e L (*late*). O ácido desoxirribonucleico (DNA) viral dentro da célula do hospedeiro pode assumir duas formas: episossomal e integrada. O HPV tem como alvo as células basais de epitélios escamosos, em particular da área genital, onde está associado ao carcinoma da cérvix uterina. Na boca, o HPV está associado a papiloma escamoso oral, condiloma acuminado, verruga vulgar e hiperplasia epitelial focal. Entretanto, seu papel na carcinogênese oral é ainda controverso, sendo também identificado como agente etiológico de alguns carcinomas de células escamosas de cabeça e pescoço. A infecção pelo HPV pode agir sinergicamente com agentes carcinogênicos, como o tabaco e o álcool. Pelo menos 150 subtipos diferentes de HPV já foram identificados, sendo que 25 têm sido detectados em lesões orais. Considerando a relevância do tema para a melhor compreensão da infecção oral pelo HPV, o objetivo desta atualização é rever os aspectos relevantes da biologia do HPV, com ênfase na relação HPV-ceratinócitos, e a importância dos dados clínicos e histopatológicos na definição diagnóstica das lesões orais possivelmente associadas ao HPV.



Líquen Plano Oral

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Human papillomavirus in oral atrophic lichen planus lesions

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Mouth

SUMMARY

Objectives: Oral lichen planus (OLP) is potentially premalignant disorder in which human papillomavirus (HPV) DNA is detected more often than in normal oral mucosa. We assessed HPV-genotype distribution in atrophic OLPs as related to DNA content and repair, proliferation activity, apoptosis, cell adhesion and lymphocyte infiltration.

Materials and methods: Eighty-two OLP patients (74.4% women) with a mean follow-up-time of 62.4 months were included in the study. HPV was genotyped with Luminex-based assay detecting 24 HPV-genotypes. Data on a panel of biomarkers and static cytometry performed in these samples before were compared with HPV data.

Results: HPV DNA was found in 15.9% of OLPs with genotypes: HPV6/11/16/31/33 and one multiple-type infection. Two of the five patients who developed cancer had low-risk HPV6/11 infection while three were HPV-negative. There was a statistically significant correlation between HPV DNA in OLP and DNA content and ploidy markers determined with static cytometry: in HPV-positive samples, proliferation index was higher ($p = 0.016$), less cells were in resting state G1/G0 ($p = 0.021$) but more often in the S-phase ($p = 0.036$) than in HPV-negative lesions. HPV positivity was also related to topoisomerase II α ($p = 0.051$), caspase-3 ($p = 0.049$) and CD20 ($p = 0.010$) protein expression.

Conclusion: HPV-infection is associated with a subgroup of atrophic OLP. Static cytometry is a sensitive method to identify HPV-associated changes in DNA content and cell proliferation. Of 16 markers, only topoisomerase II α (proliferation and DNA repair), caspase-3 (apoptosis) and CD20 (B-lymphocytes) were related to HPV. None of the HR-HPVs but only LR-HPVs were associated with the lesions developed to cancer.

Oral lichen planus: malignant transformation and human papilloma virus: A review of potential clinical implications

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TEL AVIV UNIVERSITY AND UNIVERSITY OF ILLINOIS

Oral lichen planus (OLP) occurs in from 2% to 3% of the population and may have a risk of malignant transformation into squamous cell carcinoma (SCC). This risk is not necessarily associated with exposure to tobacco and alcohol. An increased awareness of a possible role of human papilloma virus (HPV) and SCC led us to review a possible association between this virus infection and malignant transformation of OLP. The possible linkage between HPV and the risk of transformation of OLP to malignancy is discussed. Furthermore, management of OLP using immunosuppressive drugs may be associated with enhanced viral replication and could theoretically affect the risk of malignant transformation. Implications for clinical care are discussed. (*Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2011;111:461-464)



Review

The human papillomavirus family and its role in carcinogenesis

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ARTICLE INFO

Keywords:

Human papillomavirus
Cancer
E6 and E7 oncoproteins
Viral persistence
Cellular transformation

ABSTRACT

Human papillomaviruses (HPVs) are a family of small double-stranded DNA viruses that have a tropism for the epithelia of the genital and upper respiratory tracts and for the skin. Approximately 150 HPV types have been discovered so far, which are classified into several genera based on their DNA sequence. Approximately 15 high-risk mucosal HPV types are clearly associated with cervical cancer; HPV16 and HPV18 are the most carcinogenic since they are responsible for approximately 50% and 20% of all cervical cancers worldwide, respectively. It is now also clear that these viruses are linked to a subset of other genital cancers, as well as head and neck cancers.

Due to their high level of carcinogenic activity, HPV16 and HPV18 are the most studied HPV types

Human Papillomavirus in the Lesions of the Oral Mucosa According to Topography

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Abstract

Background: The association between human papillomavirus (HPV) types and oral lesions has been shown in many studies. Considering the significance that HPV has in the development of malignant and potentially malignant disorders of the oral mucosa, the purpose of this study was to investigate the prevalence of HPV DNA in different oral lesions. In addition, we wanted to elucidate whether the HPV infection is associated predominantly with either the lesion or a particular anatomic site of the oral cavity.

Methodology/Principal Findings: The study included 246 subjects with different oral lesions, and 73 subjects with apparently healthy oral mucosa (controls). The oral lesions were classified according to their surface morphology and clinical diagnosis. The epithelial cells were collected with a cytobrush from different topographic sites in the oral cavity of the oral lesions and controls. The presence of HPV DNA was evaluated by consensus and type-specific primer-directed polymerase chain reaction. The HPV positivity was detected in 17.7% of oral lesions, significantly more than in apparently healthy mucosa (6.8%), with a higher presence in benign proliferative mucosal lesions (18.6%). High-risk HPV types were predominantly found in potentially malignant oral disorders (HPV16 in 4.3% and HPV31 in 3.4%), while benign proliferative lesions as well as healthy oral mucosa contained mainly undetermined HPV type (13.6 and 6.8%, respectively).

Conclusions/Significance: The distribution of positive HPV findings on the oral mucosa seems to be more associated with a

S100A7 overexpression is a predictive marker for high risk of malignant transformation in oral dysplasia

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Early detection of oral lesions (OLs) at high risk of cancer development is of utmost importance for intervention. There is an urgent unmet clinical need for biomarkers that allow identification of high-risk OLs. Recently, we identified and verified a panel of five candidate protein biomarkers namely S100A7, prothymosin alpha, 14-3-3 ζ , 14-3-3 σ and heterogeneous nuclear ribonucleoprotein K using proteomics to distinguish OLs with dysplasia and oral cancers from normal oral tissues. The objective of our study was to evaluate the potential of these candidate protein biomarkers for identification of oral dysplastic lesions at high risk of cancer development. Using immunohistochemistry, we analyzed expressions of these five candidate protein biomarkers in 110 patients with biopsy-proven oral dysplasia and known clinical outcome and determined their correlations with p16 expression and HPV 16/18 status. Kaplan–Meier survival analysis showed reduced oral cancer-free survival (OCFS) of 68.6 months ($p = 0.007$) in patients showing cytoplasmic S100A7 overexpression when compared to patients with weak or no S100A7 immunostaining in cytoplasm (mean OCFS = 122.8 months). Multivariate Cox regression analysis revealed cytoplasmic S100A7 overexpression as the most significant candidate marker associated with cancer development in dysplastic lesions ($p = 0.041$, hazard ratio identifying OLs with dysplasia at high risk of S100A7 overexpression in

Leucoplakia



Parodontites Apicais

Prevalence of several herpesviruses and human papillomavirus in acute apical abscesses

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Abstract

Ozbek SM, Ozbek A, Demiray T. Prevalence of several herpesviruses and human papillomavirus in acute apical abscesses. *International Endodontic Journal*.

Aim To investigate and compare the radiographic size of acute apical abscess lesions for the presence of Epstein-Barr virus (EBV), human cytomegalovirus (HCMV), human herpesvirus-6 (HHV-6) and human papillomaviruses (HPV) DNA by means of the real-time polymerase chain reaction (PCR) method.

Methodology According to the radiographic size of acute apical abscess lesions, 11 lesions were categorized as large (≥ 5 mm) and 10 lesions as small (< 5 mm). DNA extracts from purulent exudate aspirates of 21 cases of acute apical abscess and 10 control samples were evaluated for the presence of viral loads using real-time PCR methods following the kit protocols recommended by the manufacturers. Statistical analysis was performed using chi-squared test with Yates's correction and Fisher's exact test.

Results HCMV DNA was detected in 27% of large and in 10% of small abscess lesions. EBV was identi-

fied in 18% of large and in 10% of small abscess lesions. HPV and HHV-6 DNA were found in 9% of large abscess lesions. None of the small abscess lesions contained HPV or HHV-6 DNA. Viral coinfections were found in two samples as the pair of HCMV/EBV and HCMV/HHV-6 from large abscess lesions. No significant associations were found between any of the target viruses and size of periapical lesions. As for the healthy pulps used as noninflamed controls, no control specimens contained viral DNA.

Conclusions HCMV was the most frequent herpesvirus amongst the target viruses in samples from both large and small apical abscess lesions. In large lesions, EBV and HHV-6 tended to occur in coinfection with HCMV. Additional studies are required to elucidate the role of herpesviruses in the pathogenesis of periapical abscess.

Keywords: apical abscesses, herpesviruses, human papillomavirus.

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Presença do papilomavírus humano em lesões malignas de mucosa oral

Presence of human papillomavirus
in malignant oral lesions

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Resumo O objetivo deste estudo foi investigar a prevalência do papilomavírus humano 6/11 e 16/18 em pacientes, com lesões orais clinicamente diagnosticadas como leucoplasias, atendidas na Faculdade de Odontologia de Araraquara, UNESP, Brasil. Após a inclusão em parafina, os cortes corados com H&E, foram selecionadas 30 biópsias e separadas em 3 grupos: lesões sem displasia (n=10), lesões com diferentes graus de displasia (n=10) e carcinoma espinocelular invasivo (n=10). As lesões que apresentaram displasia epitelial foram classificadas de acordo com os critérios histopatológicos propostos por Van Der Waal. As lesões foram investigadas para a presença de HPV por hibridização in situ com sondas biotiniladas de amplo espectro, 6/11 e 16/18. HPV 16/18 foi detectado em 20% (n=2) das biópsias com displasia severa. A presença de HPV 16/18 em lesões malignas sugere sua importância como fator de risco na carcinogênese oral.

Palavras-chaves: Papilomavírus Humano. Oral. Leucoplasia. Carcinoma espinocelular invasivo. Hibridização in situ.

The prevalence of human papillomavirus in oral premalignant lesions and squamous cell carcinoma in comparison to cervical lesions used as a positive control

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Katsuyuki Aozasa · Mikihiko Kogo · Satoru Toyosawa

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Abstract

Background Previous reports concerning the prevalence of human papillomavirus (HPV) in oral squamous cell carcinoma (OSCC) have observed varied results. The aim of this study was to evaluate the prevalence of HPV in oral premalignant lesions (OPL) and OSCC. For accurate HPV detection in oral lesions, comparative analysis was performed on cervical lesions as positive controls.

Methods Fifty-seven cases with OPL and 50 with OSCC were selected. Twenty-nine control cases were selected from cervical lesions. The HPV infection rate was analysed by consensus polymerase chain reaction (PCR) using the My09/

OPL and three cases (6.0%) of OSCC were positive by genotyping. The total HPV-positive rate in oral lesions was 22.4% (26.3% of OPL and 18.0% of OSCC). In cervical lesions, immunohistochemistry of p16^{INK4a} identified 27 cases (93.1%) as positive. Fifteen cases (26.3%) of OPL and eight cases (16.0%) of OSCC were positive for p16^{INK4a}.

Conclusions The HPV infection and p16^{INK4a}-positive rates in oral lesions are lower than previously reported. This suggests that HPV may not play a major role in oral lesions although its involvement cannot completely be ruled out.

Review

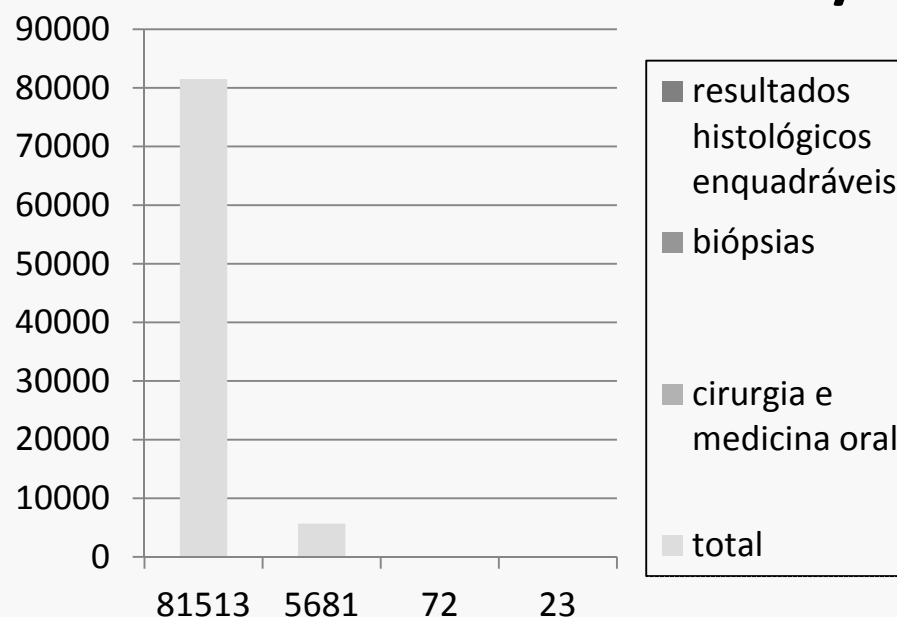
Do high-risk human papillomaviruses cause oral cavity squamous cell carcinoma?

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either suffered from significant site misclassification or has lacked adequate site separation to allow accurate conclusions to be drawn. For instance, some studies have grouped base of tongue cancers with mobile tongue cancers as OCSCC even though the base of tongue belongs to the oropharynx subsite [33]. Such confusion has probably falsely increased the rate of HPV-DNA identification in OCSCC. Most recent publications have resolved this problem, but these issues should be considered when reviewing and interpreting existing data. Secondly, the use of PCR-based techniques to identify HPV DNA leads to several problems. PCR is a very sensitive tool, but it can provide false positive results as it lacks specificity. Despite the use of stringent proce-

potentially contaminate negative specimens. Moreover, there is no tissue context. The result is either positive or negative and it is not possible to determine if viral DNA arises from the population of cancer cells, or the surrounding non-neoplastic tissue. Indeed, analyses of healthy oral and oropharyngeal mucosa have shown HPV infection in at least 5–15% of cases, but rates exceeding 50% have also been reported [34]. Finally, even if the viral DNA that was amplified and detected comes from the tumor itself, this does not necessarily support a causal role in tumorigenesis, which is the key question. HPV DNA detection by PCR does not distinguish

Desempenho Clínico da Clínica Universitária do ISCSEM, Monte da Caparica , Almada Ano Letivo 2013/14



Dados da consulta de Cirurgia e Medicina Oral:

- **5681** consultas (**6,96%**), correspondendo a **1833** doentes
- **72** biópsias realizadas (**3,92%** do total de doentes em tratamento cirúrgico)
- **23** resultados histológicos enquadráveis numa correlação com infeção por HPV (**31,9% do total de biópsias**)

Obrigado

JSM