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IMMUNOHISTOCHEMICAL EXPRESSION OF P16 AND CYCLIN D1 IN ORAL LESIONS

Expressão imuno-histoquímica de P16 e ciclina D1 em lesões orais

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ABSTRACT

Aim: To evaluate the immunohistochemical expression of p16, cyclin D1 and Ki67 in oral lesions (fibroepithelial hyperplasia, squamous papilloma and epidermoid carcinoma). **Study type:** This is a retrospective, quantitative and cross-sectional study, carried out by the survey of paraffin blocks in the Oral

Pathology Laboratory of the Dentistry course of the Federal University of Ceará, from 2008 to 2014. **Methods:** A total of 89 samples were selected, grouped into: 25 fibroepithelialhyperplasias (FHE); 16 oral squamous papillomas (OP); 28 oral squamous cell carcinomas (SCC), subdivided between patients below 50 years (SCC-50) and above 50 years (SCC+50). Twenty cases of oral mucosa without microscopic changes were used as the control group (CTL). **Main outcome measures:** Morphological evaluation through hematoxylin-eosin staining; Quantitative and dichotomous immunoexpression by streptavidin-biotin technique (P16, cyclin D1 and Ki67). **Results:** All evaluated groups, except for SCC+50 and CTL, presented a significantly higher frequency of cytological changes consistent with koilocytosis (p <0.001). The benign oral lesions (FHE and OP) and the SCC-50 group showed high immunostaining for p16 and cyclin D1, being statistically significant in relation to the control group (p <0.001). The quantitative expression of Ki67 was higher in SCC-50 than in the CTL group, with statistical significance (p <0.001). **Conclusion:** Oral lesions (OP, FHE and SCC-50) showed, together, koilocytosis and significant positivity for p16 and cyclin D1. Further studies should be conducted to clarify the possible relationship between cytopathic changes and p16 expression.

Key words: Mouth Neoplasms; p16; Cyclin D1 gene and Ki-67 Antigen.

RESUMO

Objetivo: Avaliar a expressão imuno-histoquímica de P16, ciclina D1 e Ki67 em lesões orais (hiperplasia fibroepitelial, papiloma escamoso e carcinoma epidermóide). **Tipo de estudo**: Trata-se de um estudo retrospectivo, quantitativo e transversal, realizado pelo levantamento de blocos de parafina no Laboratório de Patologia Bucal do curso de Odontologia da Universidade Federal do Ceará, no período de 2008 a 2014. **Métodos**: Total de 89 amostras foram selecionadas e agrupadas em: 25 hiperplasias fibroepiteliais (FHE); 16 papilomas escamosos orais (OP); 28 carcinomas espinocelulares (CEC) orais, subdivididos entre pacientes abaixo de 50 anos (CEC-50) e acima de 50 anos (CEC+50). Vinte casos de mucosa oral sem alterações microscópicas foram utilizados como grupo controle (CTL). **Principais medidas de resultados:** Avaliação morfológica através da coloração com hematoxilina-eosina; Imunoexpressão quantitativa e dicotômica pela técnica de estreptavidina-biotina (P16, ciclina D1 e Ki67). Resultados: Todos os grupos avaliados, exceto CEC+50 e CTL, apresentaram frequência significativamente maior de alterações citológicas consistentes com coilocitose (p<0,001). As lesões orais benignas (FHE e OP) e o grupo SCC-50 apresentaram elevada imunomarcação para p16 e ciclina D1, sendo estatisticamente significativo em relação ao grupo controle (p<0,001). A

expressão quantitativa do Ki67 foi maior no grupo SCC-50 do que no grupo CTL, com significância estatística (p<0,001). **Conclusão**: As lesões orais (OP, FHE e SCC-50) apresentaram, em conjunto, coilocitose e positividade significativa para p16 e ciclina D1. Mais estudos devem ser realizados para esclarecer a possível relação entre alterações citopáticas e expressão de p16.

Palavras-chave: Neoplasias Bucais. P16. Gene da ciclina D1. Antígeno Ki-67.

INTRODUÇÃO

The oral cavity may present lesions of inflammatory, reactive, infectious, cystic and neoplastic nature. Among those related to microorganisms, we highlight the viral lesions, of which we can highlight those that have an association with the human papillomavirus (HPV). The main mouth lesions associated with human papillomavirus (HPV) are oral squamous papilloma, verruca vulgaris, focal epithelial hyperplasia (multifocal papilloma) and condyloma acuminatum. There are manyseveral viral subtypes responsible for these clinical forms of presentation and the biological behavior, although mostly benign, is variable.In some cases, cancer may develop from those pre-existing HPV lesions [1].

The human papillomavirus is a non-enveloped deoxyribonucleic acid (DNA) virus belonging to the Papillomaviridae Family, which infects squamous epithelial cells [1]. In histopathological examination, koilocytosis is the morphological aspect most suggestive of the presence of the virus. However, this and other changes are only indicative of viral infection [2].

HPV is directly associated with p16 protein detection and is often used as an indirect marker linked to viral oncoproteins (E5, E6 and E7). This immunostaining helps to differentiate active lesions from those in latent forms, since immunoexpression of this protein occurs only in the active form of HPV [3].

P16 is a tumor suppressor gene that specifically binds to cyclin-dependent kinases (CDKs) CDK4 and CDK6. These kinases are the major catalytic partners for the cyclins D. In the presence of active HPV, hypophosphorylated retinoblastoma protein (pRb) binds to the E7 oncoprotein, allowing the

transcription of the activating factor E2F and stopping the negative feedback in p16. Therefore, the molecule accumulates intracellularly without being able to exercise its function adequately [4].

Cyclin D1 has also been used as a marker of tumor lesions. This protein belongs to a highly conserved cyclin family whose members are characterized by increasing their concentration ranges throughout the cell cycle. Cyclins work as regulators of CDKs [5]. In this context of cell proliferation, anti-Ki67 monoclonal antibody has been showing correlations with the histological degree of anaplasia and the biological behavior of tumors, suggesting that the expression of this marker provides prognostic information in some types of skin carcinomas and mucous membranes, such as squamous cell carcinoma [6,7,8].

This study aimed to analyze the immunohistochemical expression of p16, cyclin D1 and Ki67 in malignant neoplasias (squamous cell carcinoma), benign (squamous papillomas) and reactive lesions (fibroepithelial hyperplasias), with the presence of koilocytosis detected in routine histopathological examination.

MATERIAIS E MÉTODOS

Sample selection

Paraffin blocks were selected from benign oral lesions with microscopic presence of koilocytosis, and oral cancer registered in the Oral Pathology Laboratory of the Dentistry course of the Federal University of Ceará (Campus of Fortaleza).

The group of benign lesions consisted of oral squamous papilloma (OP) (16 cases) and fibroepithelial hyperplasia with cytological indications of viral infection described in the histopathological report (FHE) (24 cases); Malignant lesions comprised squamous cell carcinomas, separated in two subgroups (14 cases each): patients who were older than 50 years (SCC+50), for which only the smokers were selected, and patients with age under 50 (SCC-50), for which only non-smokers were included.

Fragments of oral mucosa without microscopic evidence of koilocytosis (20 cases) were used as control for comparative purposes.

Lesions located in the oropharynx, and those with incomplete biopsy records (clinical diagnosis and anatomical location) were excluded. In addition, all cases which blocks were not located, or were not in good condition were excluded from the sample.

Histological Analysis (Hematoxylin-Eosin)

Hematoxylin-eosin stained slides, corresponding to each lesion group, were reviewed by an experienced oral pathologist. For the purposes of microscopic diagnosis suggestive of viral infection, parameters already described in the literature were considered as strong indicators of HPV infection: kylocytosis (epithelial cell with clear peri-nuclear halo, nuclear irregularity and nuclear hyperchromasia, with or without binucleation), papillomatosis, hyperkeratosis, acanthosis, and prominent ceratohyaline granules. Among these characteristics, koilocytosis stands out as a strongly suggestive sign of infection by this virus. Nuclear alterations were classified by assigning scores, and lesions that had a sum of at least four points were considered positive for koilocytosis [9].

Immunohistochemical expression

Tissue fragments with 3μm were obtained from paraffin blocks and arranged on silanized slides to perform immunohistochemical reaction using antibodies against p16 and cyclin D1. In addition, Ki67 was used only in SCC-50 group, in fibroepithelial hyperplasias that presented koilocytosis and simultaneous immunostaining for p16 and cyclin D1, and in the control group. The antigenic recovery of the specimens was performed with EZ prepared solution (ROCHE®) for 60 minutes for cyclin D1, and 30 minutes for p16 and Ki67. The primary antibodies used had the following dilutions: p16 (Dako®) (1: 100), Cyclin D1 (Dako®) (1:300) and Ki-67 (Dako®) (1:50). The indirect SABC (streptoavidin /

biotin / immunoperoxidase) complex was revealed by the XT Ultraview DAB (chromogen diaminobenzidine) detection system. Posteriorly, the slides were counterstained with Harris hematoxylin. External positive controls of the reaction were used individually on each slide. High grade cervical lesion was used for p16 antibody, small intestine for cyclin D1 and lymph nodes for Ki67. The internal negative control was performed by suppressing the primary antibody in each reaction [Table 1].

Capturing Digital Images

Digital images of histological preparations were captured using na optical microscope (Olympus CX 31, Olympus Corporation, Japan) equipped with a digital camera (Sony 10.1 megapixels, Sony Corporation, Japan). Cell count was performed through the software MBF Image J. The density of keratinocytes in each field was determined by counting cells stained in brown of the surface epithelium. Immunoexpression was considered as diffuse and / or focal, in nucleus and / or cytoplasm. The number of stained cells, and also the intensity of staining were described. The basal layer of epithelium on benign lesions was excluded because its high rate of keratinocytes mitosis, which is able to express the proteins used (p16, cyclin D1 and Ki67). The marking was categorized in a dichotomous way (positive and negative)considering positive those whose ratio between cells stained on the total field was ≥ 10%, calculated by the average of ten fields per sample. Additionally, the quantitative profile of cellular immunostaining was evaluated [9]. Malignant lesions were separately considered for counting of the 10 (ten) peritumoral and intratumoral fields (for p16 and cyclin D1).

Statistical analysis

Data were tabulated in Microsoft Excel (version 2013) and exported to Statistical Packing for Social Sciences (SPSS) version 17.0 for Windows, in which all

analyzes were performed considering a 95% confidence index. Kolmogorov-Smirnov test was used to evaluate the distribution pattern of the quantitative variables (percentage of immunopositive cells) and Kruskall-Wallis test followed by Dunn post-test (non-parametric data) and Mann- Whitney for comparison between groups. Moreover, Fisher or Chi-square tests were used for the dichotomous variables.

Ethical aspects

This research was approved by Human Research Ethics Committee of the Faculty of Medicine (Federal University of Ceara), under protocol 255.612 / 14.

RESULTADOS

Coilocytes related at least with three changes suggestive of HPV infection were observed in histological analysis. In cases of oral papilloma (OP), koilocytosis was associated with paraceratosis, followed by disceratosis and sometimes granulosis. In fibroepithelial hyperplasias (FHE) group, koilocytosis, paraaceratosis and granulosis were seen simultaneously. The analysis of perilesional zones of non-neoplastic epithelial tissue revealed coylocytes (associated with paraceratosis, disceratosis and granulosis) only in cases of SCC below 50 years (SCC-50), except for one specimen of SCC group above 50 years (SCC+50), where disceratosis was detected and followed by parakeratosis and granulosis. OPgroup presented an85.71% positive frequency for koilocytosis; FHE 100%; SCC-50, 92.31% and SCC+50, 6.7%. In control group (CTL), microscopic criteria of viral infection were not visualized. All groups were individually compared to CTL and in all of them a statistically significant difference was found in the analysis of this variable ($p < 0.001$) [Table 1].

Frame 1: Primary antibody types, clones, dilutions, incubation periods and antigen retrieval procedures used in the sample.

PRIMARY ANTIBODY	CLONE	DILUTION	ANTIGEN RETRIEVAL	INCUBATION PERIOD
p16	SP4	1:100	EZ solution prep.(ROCHE®), for 60 minutes	16 minutes
Ciclina D1	DCS-6	1:300	EZ solution prep.(ROCHE®), for 30 minutes	32 minutes
Ki67	MIB-1	1:50	EZ solution prep.(ROCHE®), for 30 minutes	30 minutes

(Dako®, Denmark A/S.)

Table 1: Absolute and relative frequency data of histological review considering the presence of koilocytosis of 89 oral lesions (p <0.001).

Group	Positive	Negative	
FHE	25*	0	<0.001
	100%	0%	
OP	13*	3	
	81.25%	18.75%	
SCC-50	12*	2	
	92.31%	7.69%	
SCC+50	1*	13	
	6.7%	93.3%	
CTL	0	20	
	0.0%	100.0%	

*p<0.05, Chi-square (n, %)

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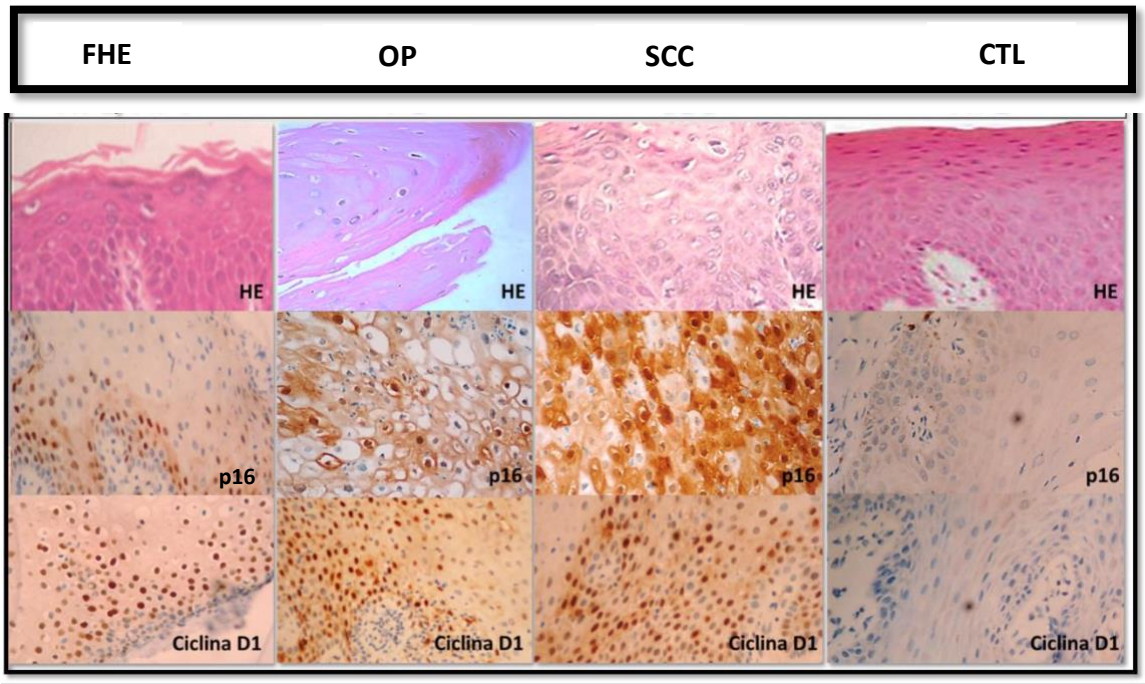
Immunostaining for p16 was visualized, mainly in the nucleus (although not limited to it), being diffuse and focal. In SCC-50 group positive samples for p16, the immunostaining was high, intense and diffuse, being able to be identified in nucleus and / or cytoplasm. The only case of SCC + 50 group that showed koilocytosis also presented a diffuse and intense nuclear marking pattern for p16. The other cases of SCC + 50 presented predominantly negative immunostaining. In benign lesions (FHE and OP), however, the expression of p16 was predominantly focal and did not always exhibit simultaneous nuclear and / or cytoplasmic staining [Figure 1].

Figure 1: Photomicrography of FHE, OP, ECC and CTL stained by HE and respective immunohistochemical expression of p16 and cyclin D1 (400x).



Dichotomous immunostaining profile (positive and negative) for p16 showed high expression in FHE (80%), OP (68.75%) and SCC-50 (92.9%) groups. Differences were observed in SCC + 50 (7.1%) and CTL (20%) groups, with a statistically

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significant difference for this variable in the first three groups compared to the control group (p <0.001) [Table 2].

Table 2: Dichotomic immunostaining of p16 and cyclin D1 from 89 oral lesions with microscopic evidence of koilocytosis (p<0.001).

	p16		Cyclin D1		
Group	-	+	-	+	**p-Value**
FHE	5	20*	8	17*	<0.001
	20.0%	80.0%	33.3%	66,7%	
OP	5	11	6	10	
	31.25%	68.75%	37.5%	62,%	
SCC-50	1	13*	2	12	
	7.1%	92,9%	14.28%	85,72%	
SCC+50	13	1	11	3	
	92.9%	7.1%	78.57%	21,43%	
CTL	16	4	16	4	
	80%	20%	80%	20%	

*p<0.05, Chi-square.

Regarding the evaluation of the percentage of p16 immunostained cells, a high mean ratio was observed in SCC-50 group, followed by FHE and OP. In control group, however, this ratio was low. In p16 expression profile analysis, there was a significant difference in SCC-50 group in relation to the control group (p <0.001) [Table 3].

Table 3: Quantitative evaluation of p16 and cyclin D1 positive cells from 89 oral lesions with microscopic evidence of koilocytosis (p<0.001).

	Group	Mean±SD	Median (Minimum - Maximum)	p-Value
p16	**CTL**	10.1±21.2	14.0 (0.0 – 23.0)	<0.001
	FHE	20.6±12.2	24.0 (3.0 - 37.0)	
	OP	24.9±6.4	23.0 (12.0 - 37.0)	
	SCC-50†	65.7±13.0	61.0 (32.0 - 78.0)	
	SCC+50	5.9±13.0	1.0 (0.0 - 51.0)	
Cyclin D1	**CTL**	11.0±17.0	12.0 (0.0 – 18.0)	0.501
	FHE	13.6±9.5	16.0 (0.0 - 28.0)	
	OP	18.0±5.5	18.0 (10.0 - 30.0)	
	SCC-50	35.5±20.0	37.0 (3.0 - 32.0)	
	SCC+50	3.4±8.7	1.0 (0.0 - 34.0)	

*p<0.05 compared with other groups; †p<0.05 compared with other groups (Kruskal-Wallis/Dunn, data expressed as mean percentage of positive cells).

Cyclin D1 expression, dichotomically categorized, was positive in FHE, OP and SCC-50 groups, presenting statistical significance (p <0.001) in relation to CTL [Table 2]. Diffuse and homogeneous marking pattern was observed in all groups of benign lesions and in SCC-50. However, in carcinomas, the staining intensity was often increased, contrasting with the groups of benign lesions. Furthermore, immunostaining was predominantly suprabasal and rarely exceeded the spinous layer [Figure 1]. Regarding the quantitative analysis of cyclin D1 immunostained cells, there was high expression in SCC-50, FHE and OP groups, but without statistical significance (p = 0.501) [Table 3].

Ki67 immunoexpression in FHE group extended to the middle portion of the spinous layer. In a few samples from control group there was positivity for Ki67, considering the same cell layers. In SCC-50, immunoblotting was frequently observed throughout the spinous layer [Figure 2]. FHE and SCC-50 groups did

not present a statistically significant difference in immunostaining profile (dichotomic cases), when compared to the control group (p = 0.789) [Table 4].

Table 4: Dichotomic immunostaining profile for Ki67 from 59 oral lesions.

	Ki67		
Group	**-**	**+**	**p-Value**
FHE	9	16	1.000
	36%	64%	
CTL	7	13	
	35%	65%	
SCC-50	4	10	
	28,57%	71,43%	

*p<0.05, Chi-square

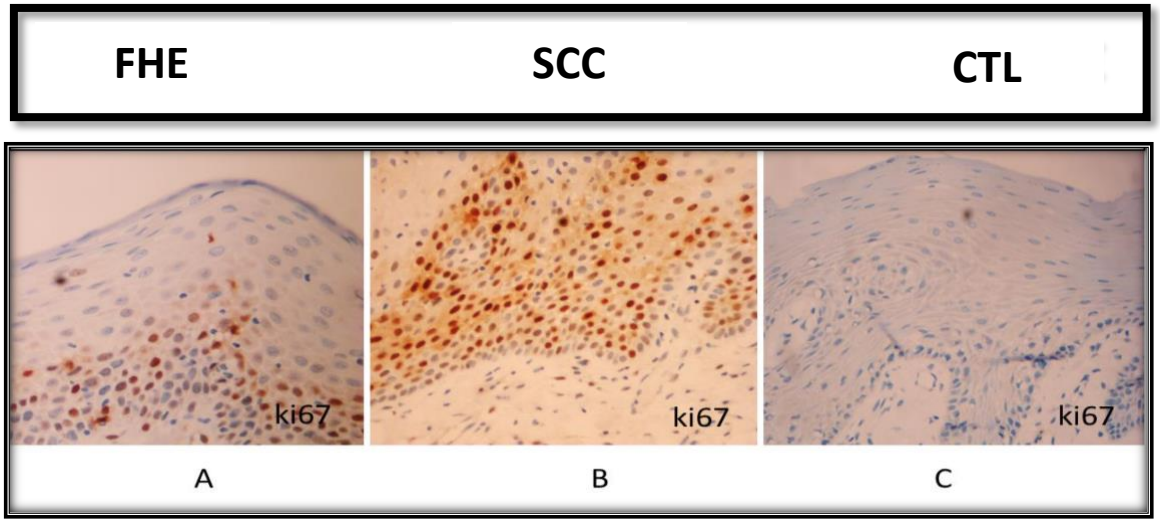
Immunostaining for Ki67 showed statistically increased values of mean and median in SCC-50 group, in relation to control group (p <0.005), with values 60.6 and 65.5, respectively [Table 5].

Table 5: Quantitative evaluation of Ki67 immunostaining cell profile from 59 oral lesions.

	Ki67		
Group	**Mean±SD**	**Median (Minimum - Maximum)**	**p<value**
FHE	27.2±12.6	24 (08 - 56)	0.005
CTL	23.8±9.1	25 (05 - 12)	
SCC-50	60.6±25.0*	65.5 (17 - 95)*	

*p<0.05 in relation to the negative control (Kruskal-Wallis / Dunn, data expressed as mean percentage of positive cells).

Figure 2: Photomicrography of FHE (A), SCC-50 (B) and CTL (C) groups, immunolabeled by Ki67 (400x).



DISCUSSÃO

P16 is directly related to increased expression of viral proteins E6 and E7. In epithelial cells with HPV infection, regulation of Rb-E2F is altered by E7 and the modulation of this pathway by activation of p16 lacks the desired regulatory effect. As a result, p16 is overexpressed and accumulates in cells, but without function. These properties make p16 an excellent biomarker for HPV-related cancers [3,10].

The most recent studies on oral cancer shows HPV as a possible participant in the pathogenesis of oral squamous cell carcinoma. Due to the presence of cytological alterations consistent with viral infection in tumor adjacent areas, the researchers try to confirm the presence of this virus by submitting their samples to tests such as PCR, hybrid capture and immunohistochemistry, in order to identify and quantify the high risk subtypes, as well as guide the diagnosis [11].

In evaluated sample, koilocytosis was frequently found in the epithelium adjacent of the SCC group below 50 years, as well as intense and diffuse positivity of p16 marker, which is overexpressed in HPV-infected cells [12].

Some authors have demonstrated a strong correlation between PCR positivity in HPV-associated head and neck malignancies and simultaneous immunohistochemical expression of p16, with 47.2% of the cases showing positive p16 immunolabeling [13,14].

It has already been observed in samples of oral SCCs with cytological evidence suggestive of viral infection (compared to normal mucosa or reactive lesions), that 60% of cases had expressed p16, whereas in the control the immunostaining was less than 15% [3]. The findings of the present study corroborate with these data, in which cytopathological changes (mainly koilocytosis), combined with the immunohistochemical expression of p16, were present in oral lesions (benign and malignant) with a probable viral association, whereas in the control group none of these parameters was observed.

Smoking is the main factor correlated to oral cancer. However, the presence of cytopathologic alterations of viral infection in samples without smoking associationraises the hypothesis HPV participation in its etiopathogenesis. Based on changes in nuclear chromatin (koilocytosis), researchers associate the expression of p16 to PCR or ISH to check for the presence of HPV, and if they correspond to active lesions [15,16,17]. PCR is not yet a reality in the diagnostic routine of most pathology laboratories, and is generally inaccessible from a public health point of view. In this context, p16 could appear as a more accessible option for screening cases with subsequent confirmation of HPV. It is emphasized, however, that immunohistochemistry does not have the same sensitivity and specificity as PCR.

The positive correlation between the simultaneous immunoexpression of cyclin D1 and p16 in mouth lesions has been reported in several studies [18,19]. When compared to the present study, they are concordant since p16 and cyclin D1 immunopositivitywas strong in oral mucosa of FHE and SCC-50 groups.

Other authors observed low positivity for cyclin D1 immunostaining in oral SCCs (less than 10%) when cytological alterations suggestive of viral infection were also absent. The results of this research corroborate with these data, in which the detection of cyclin D1 in SCC+50 group (without microscopic presence of koilocytosis) was low. It should be noted that in the methodology of the author, he evaluated only perilesional zones for cell counting (immunoexpression) and there was no subdivision of the sample by age [19,20].

The presence or absence of HPV is not always associated with a greater or lesser expression of Ki67 [21,22]. Previous studies have evaluated the proliferative activity of oral squamous cell carcinomas using Ki67, considering HPV-positive (with p16 immunoexpression) and HPV-negative (no p16 expression) groups. At the end of the study, however, they found no statistically significant difference [21]. In the current research, Ki67 immunoexpression (when dichotomously described) was also not significant.

The quantitative expression (percentage) of cell marking for Ki67 in oral SCCs associated with the cytopathic effects suggestive of viral infection has been reported in the literature [21]. Other studies also demonstrated a significant difference in cell marking rate (Ki67 by immunohistochemistry) in samples of HPV positive lesions confirmed by real-time PCR [22]. These results are consistent with those of the present study where a higher percentage of Ki67 cell markers was visualized through immunohistochemistry in C16-positive group for p16. Furthermore, simultaneous cyclin D1 and Ki67 staining was shown primarily in FHE and SCC-50 groups. This immunopositivity seems to reflect the relationship between proliferative action and HPV protein expression.

CONCLUSÃO(ÕES)

Oral lesions represented by FHE, SCC-50 and OP, in which koilocytes were identified, were positive for p16, suggesting a possible presence of human papillomavirus. In these same groups, high expression of cyclin D1 was observed. In the future, these data may constitute a complementary element in

the evaluation of the biological behavior of these lesions, and suggest p16 as a possible screening antibody for subsequent confirmation of HPV infection.

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ANNEXES - ETHICAL APPROVAL

UNIVERSIDADE FEDERAL DO CEARÁ/ PROPESQ

PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: ESTUDO CLÍNICO PATOLÓGICO E EXPRESSÃO IMUNOISTOQUÍMICA DE P16, CICLINA D1 E KI67 EM LESÕES ORAIS ASSOCIADAS AO PAPILOMAVÍRUS HUMANO

Pesquisador: Ana Paula Negreiros Nunes Alves

Área Temática:

Versão: 1

CAAE: 12559413.0.0000.5054

Instituição Proponente: UNIVERSIDADE FEDERAL DO CEARÁ

Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 255.612

Data da Relatoria: 25/02/2014

Apresentação do Projeto:

Serão selecionados pacientes portadores de lesões orais benignas associadas ao HPV e carcinoma de células escamosas orais cadastrados no Serviço de Biópsia do laboratório de Patologia Bucal do curso de Odontologia *campus* Fortaleza. Fragmentos de mucosa normal catalogados no banco de dados como hiperplasia fibroepitelial associadas a outras lesões serão utilizados como grupo controle. Dados do diagnóstico histopatológico referentes à localização anatômica da lesão, o sexo e a idade serão retirados dos laudos de biópsias dos pacientes. As lâminas correspondentes a cada lesão serão separadas e revistas por um patologista oral experiente. O tamanho da Amostra no Brasil: 72.

Serão realizados exames específicos para identificação da associação desses tumores com HPV.

Objetivo da Pesquisa:

PRIMÁRIO

Realizar um estudo clínico-patológico e expressão imunoistoquímica de p16, cilcina D1 e Ki67 em lesões orais associadas à infecção por HPV. Objetivos Secundários: Determinar a prevalência de lesões benignas e malignas em boca com provável associação com HPV, catalogar as lesões associadas ao papilomavírus humano encontradas em boca segundo as variáveis de sexo, idade e sítio anatômico, descrever os aspectos microscópicos sugestivos de infecção por HPV e comparar com a positividade do teste de imunoistoquímica para p16, correlacionar o aparecimento do câncer de boca com a positividade de p16 e possível presença de HPV, sugerir o diagnóstico de lesões com positividade simultânea para p16, ciclina D1 e Ki67.

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Avaliação dos Riscos e Benefícios:

Riscos

Não haverá riscos, tendo em vista que o estudo de caráter retrospectivo, utilizará material de biópsias parafinadas não havendo participação direta dos indivíduos na pesquisa.

Benefícios

A perspectiva, comprovada a hipótese do trabalho, será de contribuir para uma maior atenção as infecções do HPV em cavidade oral, principalmente aquelas com potencial de transformação maligna, tendo em vista que o grupo mais sucetível, segundo a literatura científica atual, envolve pacientes jovens e do sexo feminino quando associado o Carcinoma de Células Escamosas (CEC) de Cavidade Oral e o HPV. Este perfil é discordante quando se estuda isoladamente o CEC, onde o mesmo é visto como mais incidente em indivíduos do sexo masculino, acima de 40 anos com histórico de consumo de drogas lícitas (fumo e álcool). Sabe-se também que as práticas sexuais contemporâneas sem o uso do preservativo contribuem para a disseminação das infecções do HPV em mucosa oral, genital e anal. Medidas de controle de infecção, portanto, são válidas e tema intenção de prevenir o contágio e consequentemente o aparecimento dessas lesões. Diante do exposto vemos que o HPV se apresenta como uma infecção viral comum em indivíduos com vida sexual ativa, sabendo-se que a diversidade de lesões associadas ao vírus pode ter desde um comportamento inócuo como podem contribuir para o surgimento do câncer, medidas de controle desta infecção devem ser adotadas, principalmente para os grupos que forem considerados vulneráveis.

Comentários e Considerações sobre a Pesquisa:

O PROJETO É RELEVANTE, A METODOLOGIA É ADEQUADA E ATENDE AO QUE ESTÁ POSTO NA RES. 96/96 E CORRELATAS.

Considerações sobre os Termos de apresentação obrigatória:

ORÇAMENTO FINANCEIRO, FOLHA DE ROSTO, AUTORIZAÇÃO DA CHEFIA DO LABORATORIO DE PATOLOGIA, TERMO DE DISPENSA DO TCLE, TERMO DE FIEL DEPOSITÁRIO, OFICIO DE ENCAMINHAMENTO E CURRICULUM VITAE foram devidamente apresentados.

Recomendações:

Não há recomendação especifica.

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