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Research Article

Comparison of E-cadherin Marker Expression Between Lichen Planus, Leukoplakia and Oral Squamous Cell Carcinoma

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Abstract

Objective: E-cadherin is a membranous glycoprotein that acts as an adhesive agent in intercellular communication, this marker level decreases in dysplastic condition, the aim of the present study is to evaluate the expression level of the mentioned marker on Oral Lichen Planus (OLP), Oral Leukoplakia (OL) and Oral Squamous Cell Carcinoma (OSCC) lesions. *Methods*: In this in-vitro study was conducted on 60 pararhyme blocks of patients with OL, OLP, and OSCC (n = 20) using Immunohistochemically (IHC) staining diagnosis were classified as follows: Code 0: Not painted Code 1: Less than 25% staining, Code 2: 25% - 50% staining, Code 3: 50% - 75% staining, Code 4: More than 75% staining and reported as proportional score and data were compared according to gender and lesion type using SPSS 22.0 Software and significance level of $p < 0.05$). *Results*: 60 blocks of 60 patients (30 males and 30 females) were included in the study. E-cadherin marker expression on IHC code I (< 25% staining) and code II (25% < 50%) was the most in OSCC (25%) and OL (30%) respectively and the least in OLP (10 and 20% respectively). In IHC code 3 (50% < 75%) and code IV (< 75%) was the most in OLP (40% and 30% respectively) and the least in OSCC (20% and 30% respectively).. There was no significant difference in marker expression according to gender and lesion type ($p > 0.05$). *Conclusion*: The results of this study show that changes in cadherin expression in leukoplakia and lichen planus compared to squamous cell carcinoma can be considered as an important factor in the expression of dysplasia changes.

Keywords

Oral Leukoplakia, Oral Lichen Planus, Oral Squamous Cell Carcinoma, E-cadherin, Preneoplastic Lesions

1. Introduction

Oral cancer ranks eleventh among various neoplasms in terms of prevalence and sixth in terms of mortality. Iran is one of the countries with the highest prevalence in terms of (OSCC) [1]. Most oral malignancies are transformed from precancerous lesions. Studies have shown that the risk of malignant precancerous lesions such as oral leukoplakia within 1 to 30 years is 1 to 20%, while lesions such as oral lichen planus and submucosal fibrosis within 7 to 13 years have a 0.2% chance of conversion [2].

Transformation of these precancerous lesions into carci-

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nomas is a multistage process in which the sequence of these steps is programmed by the cellular genome. Numerous studies have suggested the role of genetic mutations in the development of carcinomas [3].

But oral lichen planus and leukoplakia are common lesions in the oral cavity with a white appearance. Both of these lesions are pre-malignant lesions that, if not diagnosed early, are more likely to become malignant. Given all this, early detection of these two lesions is very important in preventing them from becoming malignant [4].

Given that the prognosis of treatment decreases with the further spread of a carcinogenic lesion, early detection of an abnormality is essential to effectively control and treat the abnormality [3].

Recently, the role of cellular markers in the diagnosis of the pathogenic process has been the focus of attention, the most important of which are intercellular adhesion molecules [5].

The E-Cad tumor suppressor gene is expressed in epithelial tissue. Glycoprotein E-Cad, 120 kDa is a calcium-dependent cell surface adhesion molecule that promotes intercellular adhesion of epithelial tissue and also induces signals that control cellular events such as polarity, differentiation, growth, and cell migration [6]. In addition, E-Cad has the ability to inhibit the proliferation of cellular proteins by expressing p27 protein through epidermal growth factor receptors and is a known biomarker of tumor growth inhibitors. This biomarker is expressed by the CDHI gene on chromosome 16-q-22 and its removal has been linked to the progression of cancer [7].

E-Cadherin has been associated with the incidence of many neoplasms of the head and neck, esophagus, stomach, intestine, and uterus, and decreased expression has been reported with high proliferation, invasion, metastasis, and a mild prognosis of head and neck neoplasms [5].

Some researchers have hypothesized that E-Cad expression decreases with increasing degrees of dysplasia [8]. Therefore, this marker can be used as a predictor of the rate of invasion and the incidence of precancerous lesions such as leukoplakia and lichen planus and malignant lesions such as squamous cell carcinoma of the oral mucosa. Therefore, this marker can play a role in determining the prognosis of treatment of carcinomas and malignancies [3, 5].

In this study, by measuring the expression of E-cad marker in lichen planus, leukoplakia and OSCC lesions, we try to investigate its role in the pathogenesis and malignancy of these lesions.

2. Material and Methods

In the present in-vitro study, 60 blocks of patients with OL, OLP, and OSCC (n = 20) were included in the study. The sample size was calculated according to previous studies with a statistical power of 80% and a 95% confidence interval. Figure 1.

After selecting the files, all the required information such as the location of the lesion and microscopic diagnosis of the lesion were recorded in tables, and then the sample blocks were selected and specific staining was performed to determine the staining rate of the cell adhesion marker. Incomplete records were excluded in terms of patient information and definitive diagnosis of the lesion.

Because in the normal group the expression of E-cad is 100%, The authors excluded the normal group from the study and divide it into 3 groups.

1. Mucus with OLP 20 blocks
2. Mucus with OSCC lesion 20 blocks
3. Mucus with OL lesion 20 blocks

The existing smears stained by H&E were first examined by a pathologist and the smears will be diagnosed with OL, but OLP and OSCC, then the smear blocks were collected. The blocks were evaluated for the amount of tissue required for immunohistochemical (IHC) staining.

By E-CADHERIN antibody kit (Envision kit, Dako, Denmark and Dako, Carpinteria CA, (USA). The blocks were stained and then 5-micron slices will be cut and new slides will be stained with IHC, by an oral pathologist and the general pathologist will be evaluated with a light microscope.

The following codes are defined to evaluate the intensity of staining (16): Code 0: Not painted Code 1: Less than 25% staining Code 2: 25% - 50% staining Code 3: 50% - 75% staining Code 4: More than 75% staining.

Data were obtained using descriptive statistical methods (mean ± standard deviation) for quantitative variables and frequencies and percentages for qualitative variables. Mann U Whitney test was used to examine the relationship between qualitative variables in more depth. All analyzes were performed using STATA 16 software. In this study, the value probability less than 0.05 was considered statistically significant.

3. Results

60 blocks of 60 patients (30 males and 30 females) participated in the study. Based on the intensity of staining, four codes have been used, which is code 1 (less than 25% of staining) in Oral lichen Planus 10%, in Oral leukoplakia 15%, and in Oral Squamous cell carcinoma. Code 2 (25% to 50% immunoreactivity) is 20% in Oral lichen Planus, 30% in Oral leukoplakia, and 25% in Oral Squamous cell carcinoma. The results showed that code 3 (50% to 75% immunoreactivity) is 40% in Oral lichen Planus, 30% in Oral leukoplakia, and 30% in Oral Squamous cell carcinoma. Finally, code 4 (more than 75% immunoreactivity) is 30% in Oral lichen Planus, 25% in Oral leukoplakia, and 20% in Oral Squamous cell carcinoma. The results are detailed in Tables 1 & 2, Figure 1.

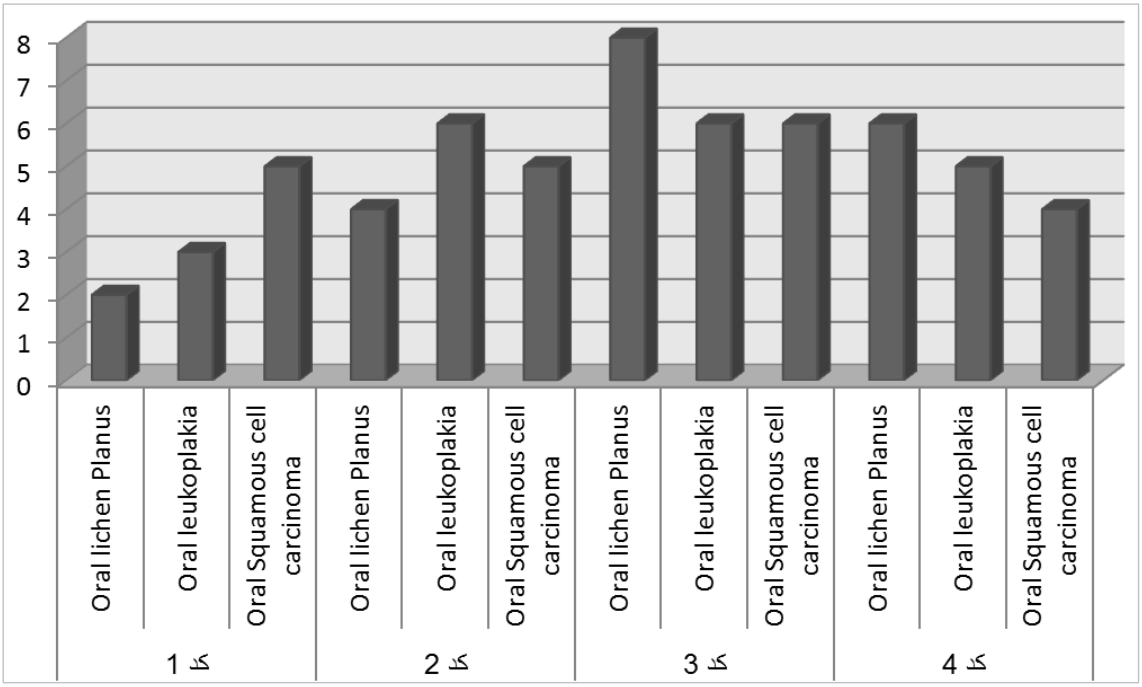

Figure 1. *Difference in E-cadherin expression between different groups and codes.*

Table 1. *Frequency of staining intensity in different groups and codes.*

Code	Group	Frequency	Percent	P-value *
1	OLP	3	10	0.112
	OL	3	15	
	OSCC	5	25	
2	OLP	4	20	0.208
	OL	6	30	
	OSCC	5	25	
3	OLP	8	40	0.672
	OL	6	30	
	OSCC	6	30	
4	OLP	6	30	0.308
	OL	5	25	
	OSCC	4	20	

Kruskal Wallis test.

The results of the Table 1 revealed that there was no difference between different lesions and codes according to E-cadherin expression level.

To examine the role of gender in marker level, the Mann U Whitney test was used according to different genders the results were illustrated in Table 2.

Microscopic views of H&E and IHC staining (OLP, OL, SCC) are presented in Figures 2 and 3.

Table 2. *Difference in E-cadherin expression according to gender.*

Group	Number and mean			Z	p-value*
OL	Male	7	11.57	- 0.595	0.595
	Female	13	9.92		
OLP	Male	12	9.92	- 0.54	0.589
	Female	8	11.58		
OSCC	Male	11	8.91	- 1.332	0.183
	Female	9	12.24		

Mann U Whitney test

According to above table findings there was no significant difference between two genders in terms of E-cadherin expression.

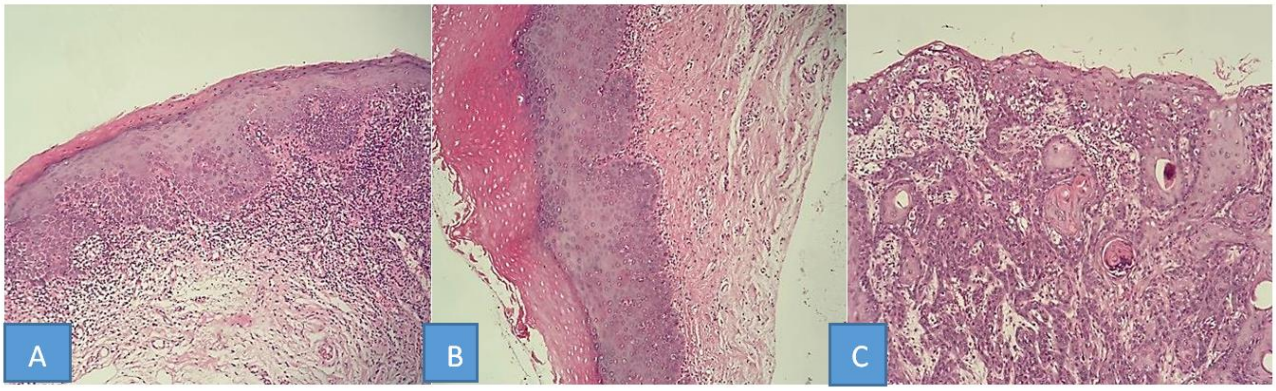

Figure 2. *Hematoxcilim eosin (H&E) in studied groups. oral lichen planus, ×10 magnification (A), leukoplakia ×10 magnification (B), squamous cell carcinoma ×10 magnification (C).*

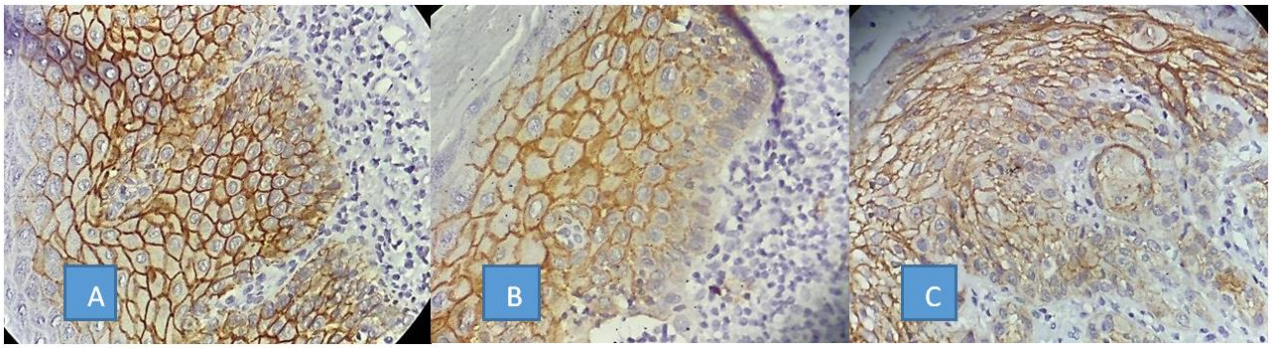

Figure 3. *E-cadherin immunostaining in studied groups. CD44 expression in oral lichen planus, ×40 magnification (A), leukoplakia ×40 magnification (B), squamous cell carcinoma ×40 magnification (C).*

4. Discussion

Cellular adhesion molecules and proteins are located on the cell membrane surface and their main function is to adhere cells together and to the extracellular matrix. These proteins are located both intramembranous and extra membranous these adhesion molecules are categorized according to their dependence oncalcium into calcium-dependent and non-calcium-dependent. Cadherin is among calcium-dependent surface adhesive molecules [5]. Cadherin plays a vital role in calcium-binding to the cell surface [3]. Nowadays we have more than 15 different cadherin molecules which all are unique in their structure and histological location. One of the main sources of difference in these molecules is their expression in different situations. Since disintegrates in cellular attachment are crucial findings of neoplastic changes, these factors could be used as a predictor marker in neoplastic changes [9].

E-cadherin is one of the most important members of the cadherinfamily which is located on the membrane of epithelial cells and its gene is located on 16. q 22.1 position of chromosomes. This protein functions exclusively and E-cadherin in cell surface only attaches to E-cadherin on other cells [10]. In this process, cells expressing E-cadherin, have domains which activated by calcium and binds to other E-cadherin cells through the Zonula adherence junction [8]. E-cadherin expression can reflect developmental changes in tissue especially tissue cells migration to the epithelium. Cell-cell attachment disintegrates in epithelial injury can induce E-cadherin cells to start tissue regeneration [11]. Also, the E-cadherin attachment axis is a hallmark for tumor growth and morphology change. There was a significant correlation between E-cadherin expression and tissue dysplasia in the oral epithelium [12].

In the present study, 80, 60, and 85 percent of OL, OLP, and OSCC samples showed more than 25 to 75% expression of E-cadherin which was consistence with findings of Sridevi et al [13] which showed that more than 80% of all three groups has mild to moderate E-cadherin expression. The study conducted by Canto et al [14] showed that code II OLP E-cadherin expression was mostly in specimens with and without dysplasia. Whereas, another study conducted by Silva et al [15] suggested that mild (code I) was mostly reported in specimen with OL, El-handawy et l. showed that E-cadherin expression in OL was mostly low in comparison with OSCC and OLP which was not in consistence with our findings. The reason for the discrepancyshould be related to the difference

in measurement tools. In this study, there was no significant difference in E-cadherin expression in OLP lesions in comparison to other groups which was constant with previous studies [12, 13].

Also in the present study, there was no difference in E-cadherin expression between OSCC and other lesions, the studies revealed that a decrease in E-cadherin level was a hallmark of carcinoma cell invasion [8, 14]. No significant difference in E-cadherin expression in tumor cells in comparison to other tissues can be a hallmark in tumor recurrence [8, 13] which can be a justification for high recurrence of OSCC following surgery and radiotherapy. Lower the E-cadherin expression is, the tumor is more invasive and the prognosis is poorer [16].

Also, there was no difference in OL E-cadherin expression in comparison to other groups which was consistent with other studies [9, 13, 15]. Decrease in E-cadherin expression shifts cells through collagen deposition to EGF-R expression which susceptible tissue to pre-neoplastic changes including oral leukoplakia, whereas this fact was not consistent with our findings The reason could be related to the neoplastic stage of studied OL lesions in two studies [3, 8].

In the present study, there was no difference in E-cadherin expression between the two genders, which was consistent with with the findings of Du et al (14) for OLP.

5. Conclusion

The results of this study show that changes in cadherin expression in leukoplakia and lichen planus compared to squamous cell carcinoma can be considered as an important factor in the expression of dysplasia changes.

Abbreviations

OSCC	Oral Squamous Cell Carcinoma
OLP	Oral Lichen Planus
E-cad	E-cadherin
OL	Oral Leukoplakia

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Author Contributions

Fariba Abdal: Conceptualization, Project administration, Supervision, Writing – original draft

Samira Mostafazadeh: Data curation, Resources, Software, Supervision, Validation, Writing – review & editing

Conflicts of Interest

No potential conflict of interest was reported by the authors.

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