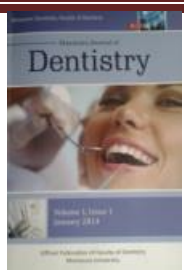


Immunohistochemical Expression of Claudin-1, in Oral epithelial dysplasia of Qat Chewers.

Essam Taher Gaballah[1], Naglaa Mahmoud Salama[2], Ayed Dahan[3]

1Professor of Oral Pathology, Faculty of Dentistry, Mansoura University.

2Assistant Professor of Oral Pathology, Faculty of Dentistry, Mansoura University.

3B.D.S, M.D.S, PhD candidate, Faculty of Dentistry, Taiz University, Yemen.

Abstract:

Qat is planted in Yemen and greatest of the republics of East Africa as a normal stimulating from the Catha edulis plant(1)(2)**.** However, Qat chewing spread approximately to totally parts of the world due to improvements in passage and bulk travel of people. Qat naturally accompanying or associated with oral white lesions which arise in the area in the buccal mucosa where the Qat is sited during chewing. Certain of these lesions demonstrate epithelial cytological alterations as acanthosis, hyperkeratosis and mild dysplasia, the danger for emerging white lesions was especially great between Qat chewers who also used tobacco products(3). So this study was conducted to compare the immunohistochemical expression of CLDN1 in different grade of epithelial dysplasia in site of Qat position at buccal mucosa.

Material and methods: the study was carried out in 40 individuals of Qat chewers. The individuals had a mean age of 38.28 years (range 19-65 years). The group comprised 3 females and 37 males. Dysplasia were categorized to (12 mild, 17 moderate, and 11 severe). The mean and standard deviation of area percent of IHC staining was evaluated, ($P < 0.05$) was considered statistically significant.

RESULTS: CLDN1 the greatest mean area of immunoexpression was recorded in the mild dysplasia, whereas the least value was recorded in severe dysplasia. (ANOVA) test exposed that the variance was statistically significant ($P<0.000$).

Introduction

In certain situations, the carcinoma recognized at the identical position of Qat bolus was sited during chewing. oral cancer(4) and also plasma-cell gingivitis(5) also described in association with Qat chewing. The Toxigenicity of Qat ingredients has been displayed by a time dependent initiation of micronuclei in the buccal mucosal cells between Qat employers (6).Tight junctions (TJs), demonstration a foremost part for signaling cascades that regulator cell growing and differentiation (7)**.** TJs are supposed to perform essential roles in the neoplastic procedure (8)**.** CLDN1 as the TJs protein is an essential portion of the epithelial and endothelial TJs complex, which achieves signal transduction pathways and cellular passage roles (9)**.** CLDN-1 is a protein of TJs that has been revealed to be comprised in carcinogenesis and cancer advancement in numerous kinds of solid cancer (10)**.**

Materials and methods:

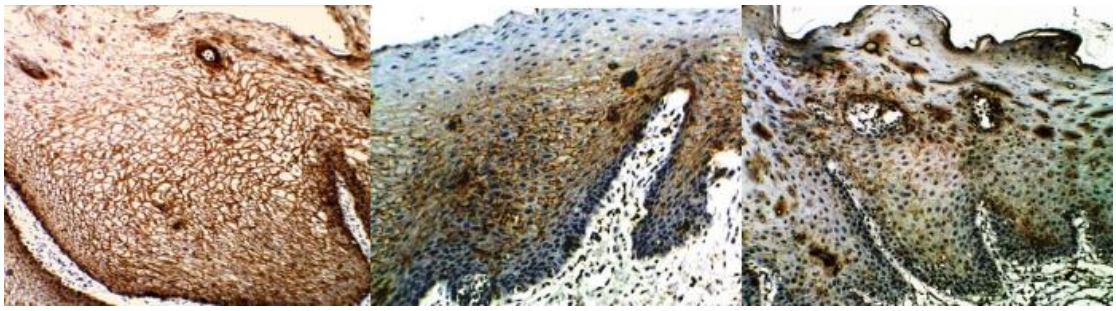
forty sectioned tissues, biopsies taken from Qat chewing individuals, prepared for IHC

staining using the Biotin-Streptavidin immunoperoxidase technique anti- CLDN1 antibody: (Thermo Scientific RB-9209, USA). Quantification of CLDN1 positivity was performed using an image analyser computer system which measuring the area percentage of CLDN1 immunoreactivity. The positive immunoreactions of CLDN1 were detected as a brownish colour in the stained tissues.

RESULTS:

the entire specimens revealed a positive reaction for the CLDN1 in the tissues, the level of CLDN1 expression in relation to grades of epithelial dysplasia showing membranous pattern immunoexpression and the greatest expression at mild dysplasia and decrease with increase severity of dysplasia (fig.1).

Statistical analysis Comparing different grades of oral ED in this group, the greatest mean area of immunoexpression was recorded in the mild ED, followed by the moderately type and the severe type. ANOVA test exposed that the difference was statistically significant ($P<0.000$).



(Figure 1): In mild dysplasia, the strong membranous immunopositivity involving the full thickness of epithelium, the nucleus negative staining left picture. In moderate dysplasia, loss of cell membrane staining of CLDN1 in lower third thickness of epithelium and –ve nuclear staining middle picture. Severe dysplasia, showing sporadic immunoreaction of cell membrane CLDN1 in upper third of epithelium thickness and losing the reaction in lower third and –ve nuclear staining right picture.

Discussion:

The results of this work demonstrated that showed strong positive membranous CLDN1 immunoreactivity. Similar findings were detected by Lee et al., (2005)(9) ,the expressions mainly as membranous staining. CLDN1 expression was mainly cell membrane in the most of the squamous cell carcinomas, while weak to strong cytoplasmic reaction was also seen in certain cases (12). In the existing study, the level of CLDN1 expression in relation to grades of epithelial dysplasia showing greatest expression at mild dysplasia and decrease with increase severity of dysplasia.

Immunoexpression of CLDN1 was reported by many studies in different body organs showed decreased in some and increased in the others, the decrease reaction of CLDN1 was detected in breast Cancer (13) and prostate Cancer (14), conversely, a larger amount of further cancers comprising gastric, pancreatic (15), urothelial (16) and cervical cancers exhibited elevation CLDN1 reaction(11). Evidence proposed that CLDNs may be included in tumour advancement through the multifarious interaction with numerous extracellular matrix components (17).

CONCLUSION:

there are significant differences between different grades of epithelial dysplasia in expression of CLDN1, CLDN1 may perform a function in OED development in Qat chewers and could be assist as a prognostic markers of progressive lesion.

References

1. Ageely HM. Harm Reduction Journal Prevalence of Khat chewing in college and secondary (high) school students of Jazan region, Saudi Arabia.

2. Wabe NT, Mohammed MA. What science says about khat (Catha edulis Forsk) Overview of chemistry , toxicology and pharmacology. J Exp Integr Med. 2012;2(1):29–37.

3. Ali AA, Al-Sharabi AK, Aguirre JM, Nahas R. A study of 342 oral keratotic white lesions induced by qat chewing among 2500 Yemeni. J oral Pathol Med. 2004;33(6):368–72.

4. Fasanmade, Adekunmi EK& LN. Oral squamous cell carcinoma associated with khat chewing. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2007;104:e53–5.

5. Marker P, Krogdahl A. Plasma cell gingivitis apparently related to the use of khat : report of a case. Br Dent Journa. 2002;192(6):311–3.

6. Kassie F, Darroudi F, Kundi M, Schulte-Hermann R, Knasmüller S. Khat (Catha edulis) consumption causes genotoxic effects in humans. Int J Cancer. 2001;92(3):329–32.

7. Tsukita S, Furuse M. Overcoming barriers in the study of tight junction functions: From occludin to claudin. Genes to Cells. 1998;3(9):569–73.

8. Ding L, Lu Z, Lu Q, Chen Y. The claudin famili of proteins in human malignacy: a clinical perspective. Cancer Manag Res. 2013;5:367–75.

9. Kominsky SL. Claudins: emerging targets for cancer therapy. Expert Rev Mol Med. 2006;8(18):1–11.

10. Hoellen F, Waldmann A, Banz‐Jansen C, Holtrich U, Karn T, Oberlander M, et al. Claudin‐1 expression in cervical cancer. Mol Clin Oncol. 2017;7:880–4.

11. Lee JW, Lee SJ, Seo JW, Song SY, Ahn G, Park CS, et al. Increased expressions of claudin-1 and claudin-7 during the progression of cervical neoplasia. Gynecol Oncol. 2005;97(1):53–9.

12. Ouban A, Ahmed A. Analysis of the distribution and expression of claudin-1 tight junction protein in the oral cavity. Appl Immunohistochem Mol Morphol AIMM. 2015;23(6):444–8.

13. Morohashi S, Kusumi T, Sato F, Odagiri H, Chiba H, Yoshihara S, et al. Decreased expression of claudin-1 correlates with recurrence status in breast cancer. Int J Mol Med. 2007;20(2):139–43.

14. Seo KW, Kwon YK, Kim BH, Kim C Il, Chang HS, Choe MS, et al. Correlation between Claudins expression and prognostic factors in prostate cancer. Korean J Urol. 2010;51(4):239–44.

15. Resnick MB, Gavilanez M, Newton E, Konkin T, Bhattacharya B, Britt DE, et al. Claudin expression in gastric adenocarcinomas: A tissue microarray study with prognostic correlation. Hum Pathol. 2005;36(8):886–92.

16. Nakanishi K, Ogata S, Hiroi S, Tominaga S, Aida S, Kawai T. Expression of occludin and claudins 1, 3, 4, and 7 in urothelial carcinoma of the upper urinary tract. Am J Clin Pathol. 2008;130(1):43–9.

17. Miyamori H, Takino T, Kobayashi Y, Tokai H, Itoh Y, Seiki M, et al. Claudin Promotes Activation of Pro-matrix Metalloproteinase-2 Mediated by Membrane-type Matrix Metalloproteinases. J Biol Chem. 2001;276(30):28204–11.