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Review Paper: A narrative review for evaluation of muscarinic receptor type-3 (MR3) in oral lichen planus patients

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ABSTRACT

Introduction: Oral lichen planus (OLP) is a persistent, inflammatory, mucocutaneous skin condition that often affects the oral cavity. The purpose of this narrative review research was to investigate muscarinic receptor type-3 (MR3) in OLP patients.

Materials and Methods: In order to perform this research, papers and scientific reports pertinent to the subject at hand were searched for utilizing specialized keywords in national and worldwide databases. The requisite final papers were then analyzed using the inclusion and exclusion criteria, and their findings were retrieved.

Results: The amount of stimulated and unstimulated salivary flow, as well as the levels of MR3, were significantly reduced in patients with OLP compared to healthy persons. In addition, the data demonstrated that the prevalence of xerostomia in OLP patients was more than in healthy people.

Conclusion: Based on the results, it can be concluded that OLP patients have low salivary flow rate and lower level of MR3 and these patients suffer from xerostomia.

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Introduction

Oral lichen planus (OLP) is a chronic inflammatory mucosal skin disease that often affects the oral cavity and mostly affects women among the ages of 30 and 70.(1) Its prevalence in various populations has been observed to range between 0.5% and 2.3%.(2) In 28% of OLP patients, skin lesions consisting of smooth vesicular papule with a scaly surface are also found. Unlike oral lesions, these lesions heal on their own within a year or less. Oral lesions may develop anywhere on the oral mucosa, although the most common sites are the buccal mucosa, sublingual surface of the tongue, and gums.(3) Lichen planus often manifests as symmetrical and bilateral lesions involving many regions of the oral mucosa.(4) This disease's origin has not yet been thoroughly established. Lesions resembling lichen planus occur in a variety of systemic disorders and autoimmune diseases owing to the use of medicines and exposure to a variety of chemicals and infections; however, the precise link between all of these variables and the development of lesions is yet unknown. Although it is known that an alter immune responses has a role in the development of the illness (5,6), the exact mechanism remains unknown. The risk of malignant transformations is an essential aspect of this illness that has been debated for many years. Although substantial study has been conducted in this sector and a particular lesion has been found and presented as a premalignant, it remains uncertain whether the lesion is benign or malignantly predisposed .(6)The majority of patients referred to departments of oral and maxillofacial medicine with oral lesions are ultimately diagnosed with OLP. However, medication usage, viral antigens, chemical factors, genetics, and immunological variables may all have a role in the development of this illness.(7) OLP is characterized by its great occurrence in the oral mucosa, its symptomatology even in mesh instances (roughness), the absence of a definite therapy, and its vulnerability to malignant development. Moreover, this issue is associated with dry mouth, which has made the assessment of this illness one of the most important areas of dental study (8-10) Salivary glands produce and release saliva, a multifunctional fluid that lubricates the oral mucosa, and plays a crucial role in oral homeostasis. Salivary glands contain electrolytes and antibacterial activity that protects the mucosal and tooth surfaces (through enzyme activity) and maintain oral hydration.(11) On the basis of genetic and pharmacological properties(12,13), muscarinic acetylcholine receptors are divided into five subgroups (M1-M5). The vast majority of salivary gland receptors are M1 and M3 muscarinic receptors. In salivary glands, M3 receptors are the predominant muscarinic receptors.(14) Xerostomia is the mental complaint of a patient with dry mouth; this condition is more prevalent in women and its incidence rises with age. Patients with xerostomia report difficulties with swallowing, eating, and speaking, as well as an unpleasant taste in the mouth. Additionally, this issue is related with foul breath, altered taste perception, dry and sticky buccal mucosa, and tooth decay despite regular dental care. This difficulty may even result in a restriction in social contact, a decline in self-esteem, and a rise in psychological stress, therfore diminishing life quality.(15, 16) Considering the significance of dry mouth and the need for a better understanding of the pathogenesis of dry mouth in OLP, the purpose of this narrative review study was to evaluate and compare the level of muscarinic receptor type-3 (MR3) in the minor salivary glands of OLP patients and healthy individuals.

Materials and Methods

Search strategy

This research surveyed the association between heavy metals exposure and an autism spectrum disorder. For this objective, systematic searches of internationally available databases, including Web of Science, Science Direct, Scopus, PubMed, and Google Scholar, were performed from 1982-2022. Systematic review applying Mesh terms "lichen planus", "oral", "Muscarinic cholinergic receptors", "xerostomia", "dentistry", "maxillofacial medicine departments", "oral lesions", "salivary glands", "oral homeostasis", "inflammatory disease", "oral homeostasis", "oral mucosa",

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"salivary gland receptors" and "oral infection", were performed. For other databases, the same mesh terms were used similarly.Unofficial reports, articles in a letters to editors format, and unpublished articles and content posted on internet sites were removed from the final selected articles.

Data selection

After conducting an electronic search of all databases, the authors divided the screening process into three distinct steps to assess the eligibility of the studies: phases I, II, and III. In phase I, article titles and abstracts were examined, and in phase II, studies with irrelevant titles or dosages that did not meet the inclusion crieteria were eliminated. In step III, the final full-text publications chosen were analyzed in order to extract considered findings. In addition, the references of full-text papers were rigorously examined to ensure that no relevant articles were omitted from the research (reference checking). In addition, the full-text article citations were examined (citation tracking) to ensure that the search was exhaustive and fruitful.

In overall, 37 published publications were evaluated for this study.

Results And Discussion

Based on their pharmacological and genetic properties,(17, 18) five subgroups of muscarinic acetylcholine receptors (MR1-MR5) have been discovered. Exocrine glands express MR3 and it plays a key role in exocrine secretion.(19) Acetylcholine binds to MR3 in salivary gland cells, activates it, and increases intracellular Ca^{2+} ions via inositol 1,4,5-triphosphate. An increase in intracellular Ca^{2+} concentration activates apical membrane channels and induces saliva secretion.(20,19) MR3 is thus the primary muscarinic acetylcholine receptor in the salivary glands. The relevance of these receptors in salivary secretion has been established in animal experiments, demonstrating that disruption of MR3 signaling in salivary glands results in reduced salivary secretion.(21) Since the pathophysiology of OLP has not yet been completely understood, numerous symptomatic treatments have been recommended for this condition. The most common consern with OLP is the possibility of malignant development into squamous cell carcinoma (SCC).(22–25)

In the research done by Agha-Hosseini et al. (2016), patients with OLP had substantially reduced stimulated and unstimulated salivary flow rates and levels of M3 muscarinic receptors. According to the study's findings, the average MR3 concentration in the non-stimulated saliva of OLP patients and healthy individuals is 0.25 0.14 and 0.34 0.12 ng/mL, respectively. Besides, in OLP patient's stimulated saliva and healthy group, the average MR3 was 0.25 ± 0.15 and 0.34 ± 0.24 ng/mL, respectively.(12) In this regard, Agha-Hosseini et al. (2016) reported that the degree of xerostomia in OLP patients (23.9 ± 1.21) was significantly higher compared to healthy subjects (17.42 ± 0.91). According to the findings of the aforementioned research, salivary MR3 is low in OLP patients, who also suffer from dry mouth and a reduced saliva ry flow rate.(12)In another study with 40 OLP patients and 22 healthy subjects, Agha-Hosseini et al. (2020) found that both the unstimulated and stimulated saliva flow rates were considerably lower in OLP patients. In addition, the findings of the research indicated that the OLP group scored much higher on the xerostomia questionnaire than the healthy group. In addition, the amount of MR3 in OLP patients' minor salivary glands was substantially greater than that of the control group.(26) In a separate investigation, Lundstrom et al. (1982) found that salivary gland function is impaired in certain OLP patients. In their research, 39 individuals with OLP in patient, aged between 32 to 82 years old had their stimulated and unstimulated saliva flow rates determined. The findings of their investigation revealed that 87 percent of OLP patients had low or extremely low levels of unstimulated saliva, whereas their stimulated saliva flow was normal.(27) Kho et al. (2013) found that the quantity of stimulated and unstimulated salivary flow in patients with OLP is significantly lower than in the control group (28), which is similar with the findings of Agha-Hosseini et al. (2016).(12)

Several theories have been put forth to explain the pathogenesis of OLP, including the first cause being an antigen-specific cell-mediated immune response, the second being non-specific mechanisms, and the third being T-cell-mediated autoimmune responses that cause epithelial cells to undergo apoptosis and the beginning of inflammation.(22)

OLP does not have a universal etiology or pathophysiology, hence a number of therapeutic approaches, most of which are symptomatic, have been suggested for treating it. Asymptomatic instances of OLP are often left untreated. The most often recommended medications to treat this condition are systemic and topical corticosteroids. in resistance case , additional medications such as azathioprine, cyclosporine (a calcineurin inhibitor), retinoids, mycophenolate mofetil, and hydroxychloroquine are often utilized.(29) OLP patients may have an increased risk of oral cancer despite the fact that treatment-induced immunosuppression at first seemed to be advantageous for OLP.(30, 12) This immunosuppression may also decrease the antitumor immune response. In comparison to other parts of the body, the oral cavity has a faster wound healing process and produces less scars. Saliva plays a significant role in the healing process because it fosters a moist environment that enhances the survival and activity of inflammatory cells, which are crucial for wound healing. Additionally, saliva includes a variety of proteins that are crucial for the different phases of oral ulcer healing. Epithelial cells proliferate as a result of growth factors in saliva, particularly epidermal growth factor (EGF).(12) Secretory leukocyte protease inhibitor, according to Brand and Veerman (2013), facilitates wound healing. Salivary histatins also promote cell migration, which leads to wound closure.(31) In light of the aforem aforementioned data

entioned , it seems that reduced salivary flow in OLP patients may cause delayed oral ulcer healing and may be the cause of these patients' recurrent OLP ulcers.(12,26)OLP is regarded as an autoimmune disease, and many autoimmunity characteristics of OLP, such as its chronicity, adult onset, higher prevalence in women, association with other autoimmune conditions, reduced immunosuppressive activity, and the presence of self-cytotoxic T cell clones in OLP, support the role of autoimmunity in the pathogenesis of this disease.(32) In comparison to the general population, OLP patients had a greater frequency of autoimmune illnesses, according to prior research. A few other autoimmune disorders, such as Sjogren's syndrome, Hashimoto's thyroiditis, and pernicious anemia, may coexist with OLP, for this reason.(33) These receptors have been the subject of certain investigations on Sjogren's syndrome. According to a study by Reina et al. (2011), pro-inflammatory mediators are produced as a result of the interaction between antibodies and muscarinic acetylcholine receptors, which leads to the inflammation and destruction of the salivary glands, which are frequently associated with Sjogren's syndrome .(34) In their 2010 research, Lizuka et al. examined the pathogenic significance of the immunological response to MR3 in Sjogren's disease patients. In the aforementioned investigation, autoantibodies against MR3 were found in the blood of 14% of Sjogren's disease patients. Additionally, they stated that certain Sjogren's disease patients have autoreactive T cells against MR3.(35) Additionally, Kim et al. (2015) noted that early Sjogren's disease is associated with an increase in anti-muscarinic autoantibodies.(36) Both plasma membrane proteins and intracellular proteins may be autoantigens. In reaction to immunological and environmental stimuli, apoptotic cell death and disruption of membrane traffic may play a significant role in the discovery of isolated autoantibodies and novel surface epitopes. MR3 have been identified as autoantigens in Sjogren syndrome and are mostly limited to target tissues. Some Sjogren's syndrome individuals with serum autoantibodies against MR3 may also have autonomic problems. The pathophysiology of primary Sjogren's syndrome is significantly influenced by apoptotic cell death. One of the hypothesized reasons for this condition is an increase in the rate of ductal epithelial cell death, which results in a reduction in salivary flow.(12,26) The parasympathetic nervous system, which

regulates exocrine secretion, and autonomic sensitivity in general may be to blame for glandular malfunction, which results in decreased saliva and tears. Lacrimal and salivary glands mostly contain M3 muscarinic receptors, one of the most distinct five types. Lowered salivary flow is thought to be caused by particular antibodies blocking receptors.(37)

Conclusion

Based on the findings of the current investigation, it can be deduced that patients with OLP had lower levels of salivary muscarinic M3 receptors than healthy people, greater levels of xerostomia, and decreased saliva ry flow rates.

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None

Authors'contributions

Mina Khayamzadeh: Conceptualization, Methodology, Writing - Review & Editing Mahsa Koochaki: Writing - Original Draft, Data Curation, Supervision

Conflict of Interests

The authors declare no conflict of interest.

Ethical declarations

Not applicable

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None

Availability of data and material

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request

References

1. Eisen D, Carrozzo M, Bagan Sebastian JV, Thongprasom K. Number V Oral lichen planus: clinical features and management. Oral Dis 2005; 11(6):338-49.https://doi.org/10.1111/j.1601-0825.2005.01142.x

2. Thanakun S, Musikasukont P. Psychological profile in a group of Thai patient with oral lichen planus. J Mahidol Dent 2006; 26:219-6.

3. Martin S, Greenberg M, Glick M, Ship J. Burket's Oral Medicine. Diagnosis and Treatment. 11th ed Hamilton: B.C. Inc; Decker 2008: P.191-206.

4. Ismail SB, Kumar SK, Zain RB. Oral lichen planus and lichenoid reactions: Etiopathogenesis, diagnosis, management and malignant transformation. J Oral Sci 2007; 49(2): 89-106. https://doi.org/10.2334/josnusd.49.89

5. Van Belle TL, Gysemans C, Mathieu C. Vitamin D in autoimmune, infectious and allergic diseases: A vital player? Best Pract Res Clin Endocrin Metabolism 2011; 25(4): 617-32.https://doi.org/10.1016/j.beem.2011.04.009

6. Seif S, Jafari-Ashkavandi Z, Mardani M, Hamidizadeh N. Evaluation of serum vitamin D level in oral lichen planus patients. Journal of Mashhad Dental School. 2018;42(1):58-49.

7. Lukács J, Schliemann S, Elsner P. Lichen planus and lichenoid reactions as a systemic disease. Clinics in dermatology. 2015 Sep 1;33(5):512-9 https://doi.org/10.1016/j.clindermatol.2015.05.001

8. Agha-Hosseini F, Sheykhbahaei N, SadrZadeh-Afshar MS. Evaluation of potential risk factors that contribute to malignant transformation of oral lichen planus: a literature review. J Contemp Dent Pract. 2016 Aug 1;17(8):692-701.https://doi.org/10.5005/jp-journals-10024-1914

9. Agha-Hosseini F, Imanpour M, Mirzaii-Dizgah I, Moosavi MS. Mucin 5B in saliva and serum of patients with oral lichen planus. Scientific reports. 2017 Sep 21;7(1):1-6. https://doi.org/10.1038/s41598-017-12157-1

10. Dudhia BB, Dudhia SB, Patel PS, Jani YV. Oral lichen planus to oral lichenoid lesions: Evolution or revolution. Journal of oral and maxillofacial pathology: JOMFP. 2015 Sep;19(3):364. https://doi.org/10.4103/0973-029X.174632

11. de Paula F, Teshima TH, Hsieh R, Souza MM, Nico MM, Lourenco SV. Overview of human salivary glands: highlights of morphology and developing processes. The Anatomical Record. 2017 Jul;300(7):1180-8. https://doi.org/10.1002/ar.23569

12. Agha-Hosseini F, Mirzaii-Dizgah I, Mohammadpour N. Muscarinic cholinergic receptors (MR3) in saliva of patients with oral lichen planus. Archives of dermatological research. 2016 Sep;308(7):481-6.https://doi.org/10.1007/s00403-016-1670-7

13. Haga T. Molecular properties of muscarinic acetylcholine receptors. Proceedings of the Japan Academy, Series B. 2013 Jun 11;89(6):226-56.https://doi.org/10.2183/pjab.89.226

14. Sumida T, Tsuboi H, Iizuka M, Hirota T, Asashima H, Matsumoto I. The role of M3 muscarinic acetylcholine receptor reactive T cells in Sjögren's syndrome: a critical review. Journal of autoimmunity. 2014 Jun 1;51:44-50. https://doi.org/10.1016/j.jaut.2013.12.012

15. Millsop JW, Wang EA, Fazel N. Etiology, evaluation, and management of xerostomia. Clinics in dermatology. 2017 Sep 1;35(5):468-76.https://doi.org/10.1016/j.clindermatol.2017.06.010

16. Villa A, Connell CL, Abati S. Diagnosis and management of xerostomia and hyposalivation. Therapeutics and clinical risk management. 2015;11:45.https://doi.

org/10.2147/TCRM.S76282

17. Ito Y, Oyunzul L, Yoshida A, Fujino T, Noguchi Y, Yuyama H, Ohtake A, Suzuki M, Sasamata M, Matsui M, Yamada S. Comparison of muscarinic receptor selectivity of solifenacin and oxybutynin in the bladder and submandibular gland of muscarinic receptor knockout mice. European journal of pharmacology. 2009 Aug 1;615(1-3):201-6.https://doi.org/10.1016/j.ejphar.2009.04.068

18. Yamada S, Maruyama S, Takagi Y, Uchida S, Oki T. In vivo demonstration of M3 muscarinic receptor subtype selectivity of darifenacin in mice. Life sciences. 2006 Dec 14;80(2):127-32.https://doi.org/10.1016/j.lfs.2006.08.028

19. Tsuboi H, Matsumoto I, Wakamatsu E, Nakamura Y, Iizuka M, Hayashi T, Goto D, Ito S, Sumida T. New epitopes and function of anti-M3 muscarinic acetylcholine receptor antibodies in patients with Sjögren's syndrome. Clinical & Experimental Immunology. 2010 Oct;162(1):53-61.https://doi.org/10.1111/j.1365-2249.2010.04188.x

20. Jin M, Hwang SM, Davies AJ, Shin Y, Bae JS, Lee JH, Lee EB, Song YW, Park K. Autoantibodies in primary Sjögren's syndrome patients induce internalization of muscarinic type 3 receptors. Biochimica et Biophysica Acta (BBA)-Molecular Basis of Disease. 2012 Feb 1;1822(2):161-7.https://doi.org/10.1016/j.bbadis.2011.11.012

21. Iizuka M, Wakamatsu E, Tsuboi H, Nakamura Y, Hayashi T, Matsui M, Goto D, Ito S, Matsumoto I, Sumida T. Pathogenic role of immune response to M3 muscarinic acetylcholine receptor in Sjögren's syndrome-like sialoadenitis. Journal of autoimmunity. 2010 Dec 1;35(4):383-9.https://doi.org/10.1016/j.jaut.2010.08.004

22. Aghahosseini F, Arbabi-Kalati F, Fashtami LA, Djavid GE, Fateh M, Beitollahi JM. Methylene blue-mediated photodynamic therapy: A possible alternative treatment for oral lichen planus. Lasers in Surgery and Medicine: The Official Journal of the American Society for Laser Medicine and Surgery. 2006 Jan;38(1):33-8. https://doi.org/10.1002/lsm.20278

23. Agha-Hosseini F, Mirzaii-Dizgah I, Abdollahi M, Akbari-Gillani N. Efficacy of IMOD in the treatment of oral lichen planus. Open J Stomatol. 2011 Jun;1(1):13-7. https://doi.org/10.4236/ojst.2011.12003

24. Agha-Hosseini F, Mirzaii-Dizgah I, Farmanbar N, Abdollahi M. Oxidative stress status and DNA damage in saliva of human subjects with oral lichen planus and oral squamous cell carcinoma. Journal of Oral Pathology & Medicine. 2012 Nov;41(10):736-40.https://doi.org/10.1111/j.1600-0714.2012.01172.x

25. Agha-Hosseini F, Mirzaii-Dizgah I, Mikaili S, Abdollahi M. Increased salivary lipid peroxidation in human subjects with oral lichen planus. International journal of dental hygiene. 2009 Nov;7(4):246-50.https://doi.org/10.1111/j.1601-5037.2009.00365.x

26. Agha-Hosseini F, Moosavi MS, Mirzaii-Dizgah I, Samami M. Muscarinic cholinergic receptors in minor salivary gland tissues of patients with oral lichen planus: A case-control study. Journal of Oral Pathology & Medicine. 2020 Sep;49(8):816-21.https://doi.org/10.1111/jop.13094

27. Lundström IC, Göran K, Anneroth B, Bergstedt HF. Salivary gland function and changes in patients with oral lichen planus. European Journal of Oral Sciences. 1982 Dec;90(6):443-58.https://doi.org/10.1111/j.1600-0722.1982.tb00761.x

28. Kho HS, Chang JY, Kim YY, Kim Y. MUC1 and Toll-like receptor-2 expression in burning mouth syndrome and oral lichen planus. Archives of Oral Biology. 2013 Jul 1;58(7):837-42.https://doi.org/10.1016/j.archoralbio.2013.01.008

29. Richter I, Andabak-Rogulj A, Vučićević-Boras V, Brailo V. Oral lichen planus-Retrospective study of 563 Croatian patients. Med Oral Patol Oral Cir Bucal. 2014 May;19(3):e255.https://doi.org/10.4317/medoral.18940

30. Sugerman P, Savage NW, Walsh LJ, Zhao ZZ, Zhou XJ, Khan A, Seymour GJ, Bigby M. The pathogenesis of oral lichen planus. Critical Reviews in Oral Biology & Medicine. 2002 Jul;13(4):350-65.https://doi.org/10.1177/154411130201300405

31. Brand HS, Veerman EC. Saliva and wound healing. The Chinese Journal of Dental Research: the Official Journal of the Scientific Section of the Chinese Stomatological Association (CSA). 2013 Jan 1;16(1):7-12.

32. Roopashree MR, Gondhalekar RV, Shashikanth MC, George J, Thippeswamy SH, Shukla A. Pathogenesis of oral lichen planus-a review. Journal of Oral Pathology & Medicine. 2010 Nov;39(10):729-34.https://doi.org/10.1111/j.1600-0714.2010.00946.x

33. López-Jornet P, Parra-Perez F, Pons-Fuster A. Association of autoimmune diseases with oral lichen planus: a cross-sectional, clinical study. Journal of the European Academy of Dermatology and Venereology. 2014 Jul;28(7):895-9.https://doi.org/10.1111/jdv.12202

34. Reina S, Sterin-Borda L, Passafaro D, Borda E. Anti-M3 muscarinic cholinergic autoantibodies from patients with primary Sjögren's syndrome trigger production of matrix metalloproteinase-3 (MMP-3) and prostaglandin E2 (PGE2) from the submandibular glands. archives of oral biology. 2011 May 1;56(5):413-20. https://doi.org/10.1016/j.archoralbio.2010.08.017

35. Iizuka M, Wakamatsu E, Tsuboi H, Nakamura Y, Hayashi T, Matsui M, Goto D, Ito S, Matsumoto I, Sumida T. Pathogenic role of immune response to M3 muscarinic acetylcholine receptor in Sjögren's syndrome-like sialoadenitis. Journal of autoimmunity. 2010 Dec 1;35(4):383-9.https://doi.org/10.1016/j.jaut.2010.08.004

36. Kim N, Shin Y, Choi S, Namkoong E, Kim M, Lee J, Song Y, Park K. Effect of antimuscarinic autoantibodies in primary Sjögren's syndrome. Journal of Dental Research. 2015 May;94(5):722-8.https://doi.org/10.1177/0022034515577813

37. Agarwal P. Immunopathogenesis of Sjo¨gren's syndrome. J Indian Rheumatol Assoc. 2003, 11(3):71-75