Lactoferrin as Potential Treatment Oral Submucous Fibrosis: A Review Article

Gofur NRP1*, Gofur ARP2, Soesilaningtyas3, Gofur RNRP4, Kahdina M4 and Putri HM4

1Department of Health, Faculty of Vocational Studies, Universitas Airlangga, Surabaya, Indonesia
2Faculty of Dental Medicine, Universitas Airlangga, Surabaya, Indonesia
3Department of Dental Nursing, Poltekkes Kemenkes, Surabaya, Indonesia
4Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

*Corresponding author:
Nanda Rachmad Putra Gofur,
Department of Health, Faculty of Vocational Studies,
Universitas Airlangga,
Surabaya, Indonesia,
E-mail: nanda.rachmad.gofur@vokasi.unair.ac.id;
nanda.gofur@gmail.com

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1. Abstract

1.1. Background: Oral submucous fibrosis (OSMF) is a chronic disease of oral mucosa characterized by inflammation and progressive fibrosis of lamina propria and deeper connective tissues, followed by stiffening of an otherwise yielding mucosa resulting in difficulty in opening the mouth. Etiology of OSMF was excessive use of areca nut and its flavored formulations disrupts the hemostatic equilibrium between synthesis and degeneration. The copper ion in areca nut increases the activity of lysyl oxidase leading to unregulated collagen production, thereby causing oral fibrosis. Lactoferrin, could reducing the total cell numbers and their metabolic activity in smokeless tobacco users and areca nut.

1.2. Objectives: purpose of this study is to explaining lactoferrin as potential treatment for OSMF.

1.3. Problem Statement: Potential mechanism lactoferrin as potential treatment for OSMF.

1.4. Discussion: Recent studies have suggested that lactoferrin holds promise as a treatment agent for many disease. Lactoferrin treatment reduces colonic carcinogenesis in rats, and decreases solid tumor growth and metastases in mice. Previously published data on the effect of lactoferrin on head and neck squamous cell carcinoma demonstrating tumor inhibition by intravenous, oral, and intratumoral dosing. In murine model, lactoferrin induced growth inhibition of OSMF.

1.5. Conclusion: Lactoferrin is a potential treatment for OSMF. The compound is not only immune modulating, resulting in increased antiviral and antibacterial activity of intestinal mucosa, but improves cancer surveillance and has anti-inflammatory effects, especially for OSMF.

2. Introduction

Oral submucous fibrosis (OSMF) is a chronic disease of oral mucosa characterized by inflammation and progressive fibrosis of lamina propria and deeper connective tissues, followed by stiffening of an otherwise yielding mucosa resulting in difficulty in opening the mouth. The diagnosis of OSMF is based on features such as burning sensation, difficulty in taking spicy foods, paleness, blanching of the mucosa, palpable fibrotic bands in the buccal and labial mucosa and progressive reduction in opening the mouth. OSMF has been reported almost exclusively among Indians living in India and among other Asian with a reported prevalence ranging up to 0.4% in Indian rural population [5].

According to World Health Organization the prevalence of tobacco habits in India is high with 34% using bidis, 31% cigarettes, 19% smokeless tobacco, 9% hookah, and 7% other forms, respectively. The cancer patients aid association of India revealed the prevalence of cigarette usage as 20%, bidis 40%, and chewable tobacco...
immunomodulation by lactoferrin are related to immune activation and defense, anti-inflammatory activity, and cancer protection. Many iron regulation, cellular growth and differentiation, antimicrobial activity, and cancer protection. Many iron regulation, cellular growth and differentiation, antimicrobial activity, and cancer protection. Lactoferrin has multiple known biologic activities including iron regulation, cellular growth and differentiation, antimicrobial activity, and cancer protection. Lactoferrin is an 80 kDa member of the transferrin family of iron-binding glycoproteins. The protein is naturally occurring and is present in mammalian exocrine secretions, including breast milk, tears, nasal and bronchial mucus, cervical mucus and seminal fluid. Lactoferrin has multiple known biologic activities including iron regulation, cellular growth and differentiation, antimicrobial activity, anti-inflammatory activity, and cancer protection. Many of the functions of lactoferrin are related to immune activation and modulation. It is hypothesized that immunomodulation by lactoferrin contributes to the lower rate of respiratory infections and malignancies in breastfed infants, but the exact mechanism of action of lactoferrin on the immune system is not currently understood. Specifically, the relative impact of lactoferrin on intrinsic cellular proliferation as well as immunomodulatory response is unknown.

Direct inhibition of cellular growth is one mechanism by which lactoferrin may inhibit OSMF. Recent data has shown that lactoferrin induces direct cell cycle, can decrease cellular release of the proinflammatory cytokines including Interleukin-1 (IL-1), IL-6, IL-4, and TNF-α, recognized for their import in maintaining cellular viability and a malignant phenotype. Finally, lactoferrin decreases the activity of the transcription factor NF-κB. NF-κB is constitutively activated in OSMF and inhibition of this activation decreases cellular viability. Despite such well defined mechanisms for direct lactoferrin inhibition of tumor growth in vitro, the specific mechanism of growth inhibition in vivo is not understood.

2.1. Objectives
Purpose of this study is to explaining lactoferrin as potential treatment for OSMF.

2.2. Problem Statement
Potential mechanism lactoferrin as potential treatment for OSMF.

3. Discussion
Recent studies have suggested that lactoferrin holds promise as a treatment agent for many disease. Lactoferrin treatment reduces colonic carcinogenesis in rats, and decreases solid tumor growth and metastases in mice. Previously published data on the effect of lactoferrin on head and neck squamous cell carcinoma demonstrating tumor inhibition by intravenous, oral, and intratumoral dosing. In murine model, lactoferrin induced growth inhibition of OSMF. The mechanism of this tumor inhibition remains to be discerned, but oral lactoferrin dosing was associated with increases in gut release of IL-18, NK activation and quantity of serum CD8+ cells.

The lactoferrin receptor (LFR) is expressed in many mammalian tissues including intestine, heart, spleen, liver, monocytes, lymphocytes, platelets, salivary glands and mucosa. The lactoferrin receptors found in the intestinal epithelium overlying peyrs patches have the highest specific binding capability when compared to LFR at other sites. The murine lactoferrin receptor has 87% homology with the human receptor and demonstrates binding specific for human, mouse, and bovine lactoferrin. Recent data has shown the presence of the lactoferrin receptor on carcinoma cell lines.

Iron-independent lactoferrin-induced dose-dependent cellular inhibition is associated with decreases in Cyclin D1 and increases in P19. Lactoferrin also reduces the cellular production of key...
proinflammatory and prometastatic cytokines. Bovine lactoferrin (BLf) is endocytosed through lipoprotein receptor-related protein-1 (LRP1) and bound to endogenous TRAF6 to inhibit TRAF6-dependent activation of the NF-κB signaling pathway. In this study, the existence and the substantial level of LRP1 Recently, increasing number of publications focusing on contributive roles of the CXC chemokine receptor 4 (CXCR4) on growth and cell cycle of OSCC and esophageal carcinoma using PI3/Akt were reported. In addition, CXCR4 was also demonstrated to be one of receptors of bLF driving for intracellular responses via PI3K/Akt pathway in human keratinocytes HaCaT and human intestinal cells Caco-2. According to the relationship and functions of CXCR4 and bLF, the study on roles of CXCR4 and its ligand bLF in OSCC cells should be considered for further studies [4].

HSC3 cells in OSMF constitutively expressed activated Akt and p65. bLF treatment downregulated the levels of p-p65 and p-Akt in HSC3 cells, eventually leading to cell growth inhibition and induction of apoptosis via modulation of Akt-related signaling. On the other hand, since RT7 cells have low expression of both p-Akt and p-p65, therefore, bLF could not exert its inhibitory effects. Based on our further investigation in molecular levels, under bLF treatment no significant changes in p53, caspase cascades, and related molecules of G1/S cell cycle progression were seen in RT7 cells. In addition, bLF did not also have any inhibitory effects on regulation of mTOR/S6K pathway, one of an important pathways driving for OSCC cells survival. Nevertheless, bLF regulated neither SOCS3 nor its negative mediators JAK2/STAT3 in normal keratinocyte RT7 cells. These observations suggest that inhibitory action of bLF depends on the status of activated NF-κB, which is reduced by the inhibition of polyubiquitination of endogenous TRAF6. The reduction of NF-κB signaling may further contribute to the downregulation of Akt as the result of feedback regulation between NF-κB and Akt. As a consequence, bLF selectively suppresses proliferation in OSMF but not in normal mucosal cells [2].

4. Conclusion

Lactoferrin is a potential treatment for OSMF. The compound is not only immune modulating, resulting in increased antiviral and antibacterial activity of intestinal mucosa, but improves cancer surveillance and has anti-inflammatory effects, especially for OSMF.

References


