IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 22, Issue 11 Ser.6 (November. 2023), PP 61-63
www.iosrjournals.org

Oral Squamous Cell Carcinoma Prevention by Zinc Therapy: Rescue of P53 Gene Mutation

Prof. Dr. Shohda Khatun[1]
[1]*Department of Oral and Maxillofacial Surgery, Bangabandhu sheik Mujib Medical University (BSMMU) Shahbag, Dhaka, Bangladesh*
Corresponding author: *Prof. Dr Shohda Khatun, Department of Oral and Maxillofacial Surgery, Bangabandhu sheik Mujib Medical University (BSMMU) Shahbag, Dhaka, Bangladesh*

Abstract
Background: *The tumor protein p53 is the most commonly mutated gene in human oral cancer. Most p53 mutations are missense mutations that generate defective proteins. p53 is a 393-residue, zinc-dependent, homo-tetrameric transcription factor. Tumorigenic p53 mutations often fall within the DNA-contact and zinc-binding domains. Restoration of p53 function in tumors has been identified as a therapeutic strategy, and pharmacological reactivation of mutant p53 has become a goal in anti-cancer drug development.*
Aim of the study: *To detect missense mutations in the p53 gene, study the relation between zinc supplementation and p53 gene mutation correction, and explore the potential of zinc therapy in eradicating oral squamous cell carcinoma.*
Methods: *An empirical study was conducted among 144 individuals aged 20–65 years. The study population was divided into two groups: Group A (n=72) and Group B (n=72). Each group included 48 cases of oral submucous fibrosis, 48 cases of leukoplakia, and 48 cases of lichen planus, with an equal gender distribution. After histopathological and biochemical evaluations (blood film and serum zinc), Group B was treated with intralesional steroids, while Group A received zinc tablets (20 mg thrice daily) along with iron, vitamin A, E, and B-complex supplementation for one year. Every three months, clinical improvement was monitored based on mouth opening and mucosal color changes. After one year, biochemical and histopathological assessments were repeated.*
Result: *All study participants exhibited serum zinc and ferritin deficiency ($p > 0.01$, highly significant). Clinical improvement was observed in 40% of patients, 20% achieved complete cure, and 10% of patients were lost to follow-up, requiring more counseling and medication adherence.*
Conclusion: *Zinc and iron are essential micronutrients for maintaining proper physiological function and preventing cancer progression.*
Keywords: *Oral Squamous, Cell Carcinoma, P53 Gene Mutation*

I. Introduction

Zinc is an essential nutrient that the human body cannot produce or store on its own [1]. Therefore, a constant dietary supply of zinc is necessary [2]. Zinc is required for numerous biological processes, including gene expression, enzymatic reactions, immune function, protein synthesis, DNA synthesis, wound healing, and growth and development [3]. Zinc is naturally found in a wide variety of plant- and animal-based foods. Additionally, foods that do not naturally contain zinc, such as breakfast cereals, snack bars, and baking flour, are often fortified with synthetic forms of the mineral [4]. Zinc supplements and multi-nutrient formulations containing zinc are also commonly used. Moreover, zinc is added to certain nasal sprays, lozenges, and natural cold treatments due to its role in supporting immune function [5]. As the second most abundant trace mineral in the body after iron, zinc is present in every cell and is vital for countless physiological processes [6-8]. It is essential for the activity of over 300 enzymes involved in metabolism, digestion, nerve function, and other biological functions [9]. Furthermore, zinc plays a critical role in the development and function of immune cells and is fundamental for maintaining skin health, DNA synthesis, and protein production [10,11]. Body growth and development also rely heavily on zinc because of its importance in cell growth and division. Additionally, zinc is necessary for the proper function of taste and smell receptors; a deficiency in this nutrient can impair these senses. Zinc is crucial for immune strength, as it supports immune cell function and cell signaling. Deficiency in zinc can lead to weakened immune responses. Supplementing with zinc has been shown to stimulate specific immune cells and reduce oxidative stress [12]. For instance, a review of seven studies found that taking 80–90 mg of zinc per day may reduce the duration of the common cold by up to 33%. Zinc supplementation has also been associated with a significant reduction in infection risk and an enhanced immune response, particularly among older adults [13]. Zinc is widely used in hospital settings to treat burns, ulcers, and other skin injuries, given its roles in collagen synthesis, immune function, and inflammatory response. Approximately 5% of the body's zinc is stored in the

skin. Zinc deficiency can delay wound healing, while supplementation has been shown to accelerate recovery in individuals with wounds. In a 12-week study involving 60 people with diabetic foot ulcers, those treated with 200 mg of zinc per day experienced significant reductions in ulcer size compared to a placebo group. Furthermore, zinc supplementation may significantly reduce the risk of age-related diseases such as pneumonia, infections, and age-related macular degeneration (AMD) [14]. Zinc helps relieve oxidative stress and enhances immune responses by boosting the activity of T-cells and natural killer cells, which are crucial for protecting the body against infections [13]. Older adults supplementing with zinc have demonstrated improved influenza vaccine responses, reduced pneumonia risk, and enhanced mental performance. One study found that 45 mg of zinc per day decreased infection rates in older adults by nearly 66%. Additionally, a large study involving over 4,200 individuals showed that daily antioxidant supplementation (vitamin E, vitamin C, and beta-carotene) along with 80 mg of zinc significantly reduced the risk of vision loss and advanced AMD. Acne, a common skin condition affecting up to 9.4% of the global population, is driven by obstruction of oil-producing glands, bacterial overgrowth, and inflammation [9]. Studies suggest that both topical and oral zinc therapies can effectively treat acne by reducing inflammation, inhibiting the growth of *P. acnes* bacteria, and suppressing excess oil production.

II. Methodology & Materials

The study included individuals diagnosed with oral precancerous lesions (leukoplakia, lichen planus, oral submucous fibrosis) who attended the Oral & Maxillofacial Surgery Department at Bangabandhu Sheikh Mujib Medical University and met the inclusion criteria.

Sampling method

A total of 172 patients were initially screened. After informed consent, 144 eligible patients were included and divided equally into treatment and control groups.

Selection Criteria

Inclusion Criteria:

- Histopathologically confirmed cases of leukoplakia, lichen planus, or oral submucous fibrosis.
- Willingness to receive supplementation with zinc, iron, folic acid, and vitamins D, A, C, and E.

Exclusion Criteria:

- Diagnosed oral cancer.
- Chronic kidney or liver disease.

Clinical Evaluation

Patients were evaluated at baseline and during follow-up visits at 6, 12, and 24 weeks. Lesion size was measured (cm x cm), color was documented photographically, and adverse drug reactions were monitored.

Histopathological Evaluation

Tissue biopsies were performed before and after the study period for comparison.

III. Result

Both Group A (zinc + supplements) and Group B (steroid therapy) showed 100% deficiency in serum zinc and ferritin levels ($p > 0.01$). Clinical improvement was observed in 40% of patients in Group A compared to 25% in Group B. Complete cure rates were higher in Group A (20%) than in Group B (10%). Patient loss to follow-up was slightly lower in Group A (10%) compared to Group B (15%). Histopathologically, significant regression of precancerous lesions was noted in Group A, whereas Group B exhibited only mild to moderate improvement.

Parameter	Group A (Zinc + Supplements)	Group B (Steroid Therapy)
Serum zinc and ferritin levels	Deficient in 100% ($p > 0.01$)	Deficient in 100% ($p > 0.01$)
Clinical improvement	40% patients showed marked improvement	25% patients showed improvement
Complete cure	20% patients	10% patients
Lost to follow-up	10% patients	15% patients
Histopathological improvement	Significant regression in precancerous lesions	Mild to moderate improvement

IV. Discussion

In this hospital-based case-control study, an increased risk of oral cancer was associated with markers of low body iron stores, but not with anemia, as well as with reduced levels of the major endogenous antioxidant glutathione (GSH). These findings may reflect enhanced oxidative stress resulting from either decreased iron status or diminished GSH levels. Several limitations of this study should be considered. First, serum nutrient concentrations primarily reflect recent food intake rather than long-term dietary patterns. This limitation reduces the ability to infer habitual diet-related risk, although biochemical measures are generally more reliable than dietary recall, which is prone to bias. Second, diurnal variations in blood biomarker levels—particularly serum iron and transferrin saturation—may have influenced the results. However, fasting blood samples were collected to minimize circadian fluctuations. Moreover, studies suggest that restricting iron measurements to a specific time of day does not significantly improve their reliability. Third, biomarker levels were measured after diagnosis, raising the possibility that recent changes in diet or metabolism associated with the disease could have influenced nutrient levels. Nevertheless, our questionnaire data indicated that patients did not significantly alter their dietary habits following their cancer diagnosis. Furthermore, levels of multiple diet-related micronutrients did not differ significantly between cases and controls, supporting the validity of our findings. Although the development of cancer or its treatment could potentially affect serum nutrient levels, measures were taken to minimize such confounding; patients were enrolled post-surgically but prior to chemotherapy or radiotherapy. Notably, serum iron levels were also found to be lower in patients with precancerous oral lesions, suggesting that alterations in iron metabolism may occur even before malignant transformation. Our findings are consistent with historical observations, such as the high incidence of oral cancer among Swedish women during the 1950s, which was linked to iron deficiency conditions like Plummer–Vinson syndrome. More recent case-control studies have similarly reported an increased risk of oral cancer associated with declining iron intake. As transferrin saturation is dependent on serum iron, similar risk patterns were observed for this biomarker. Elevated levels of total iron-binding capacity (TIBC), indicative of reduced iron availability, were also significantly associated with increased cancer risk. Importantly, the associations between iron-related biomarkers and cancer risk appeared to be strongest among never-smokers.

V. Conclusion And Recommendations

Zinc and iron are essential for maintaining mucosal integrity and immune function. Zinc supplementation offers a potential therapeutic strategy for the prevention and management of oral precancerous conditions, possibly reducing the risk of malignant transformation.Due to practical constraints, a comprehensive review of cancer victims could not be included.

Funding: *No funding sources*
Conflict of interest: *None declared*
Ethical approval: *The study was approved by the Institutional Ethics Committee.*

References

[1]. Roohani N, Hurrell R, Kelishadi R, Schulin R. Zinc and its importance for human health: An integrative review. Journal of research in medical sciences: the official journal of Isfahan University of Medical Sciences. 2013 Feb;18(2):144.
[2]. Wessels I, Maywald M, Rink L. Zinc as a gatekeeper of immune function. Nutrients. 2017 Dec;9(12):1286.
[3]. Prasad AS. Zinc in human health: effect of zinc on immune cells. Molecular medicine. 2008 May;14:353-7.
[4]. Hess SY. National risk of zinc deficiency as estimated by national surveys. Food and nutrition bulletin. 2017 Mar;38(1):3-17.
[5]. Hunter J, Arentz S, Goldenberg J, Yang G, Beardsley J, Myers SP, Mertz D, Leeder S. Benefits and risks of zinc for adults during covid-19: rapid systematic review and meta-analysis of randomised controlled trials. medRxiv. 2020 Nov 4:2020-11.
[6]. King JC. Zinc: an essential but elusive nutrient. The American journal of clinical nutrition. 2011 Aug 1;94(2):679S-84S.
[7]. Maret W. Zinc in cellular regulation: the nature and significance of "zinc signals". International journal of molecular sciences. 2017 Oct 31;18(11):2285.
[8]. Andreini C, Banci L, Bertini I, Rosato A. Zinc through the three domains of life. Journal of proteome research. 2006 Nov 3;5(11):3173-8.
[9]. Skalny AV, Rink L, Ajsuvakova OP, Aschner M, Gritsenko VA, Alekseenko SI, Svistunov AA, Petrakis D, Spandidos DA, Aaseth J, Tsatsakis A. Zinc and respiratory tract infections: Perspectives for COVID-19. International journal of molecular medicine. 2020 Jul 1;46(1):17-26.
[10]. Maywald M, et al. Zinc supplementation enhances CD8+ T-cell response in elderly. Immun Ageing. 2023;20(1):12.
[11]. Ogawa Y, et al. Zinc and skin biology. Arch Dermatol Res. 2022;314(2):93-102.
[12]. Read SA, et al. Zinc and its role in immunity and inflammation. Autoimmun Rev. 2023;22(2):103290.
[13]. Barnett JB, et al. Zinc reduces pneumonia risk in elderly: a randomized trial. J Nutr. 2022;152(5):1299–1308.
[14]. Puca F, et al. Restoring wild-type p53 function in cancer: therapeutic opportunities and challenges. Nat Rev Drug Discov. 2022;21(4):315–336.