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# Zinc therapy in dermatology: A Review and Update

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## Abstract

Zinc is a micronutrient used over the years for many dermatological conditions such as infections, inflammatory dermatoses, pigmentary disorders, neoplasias, etc. It is used in both elemental as well as salt form, either in topical or in oral form as a therapy. An average adult weighing 70 kg has a body zinc content of 1.4–2.3 gm. The role of zinc in deficiency disorders like acrodermatitis enteropathica is already established and used widely as treatment. Zinc has been identified as effective in the treatment of various disorders, but it cannot be used as the replacement for proven first-line treatment. Zinc can be used as an adjuvant therapy in many dermatological disorders. This is a narrative review where the various uses of zinc as therapy in dermatological disorders is highlighted.

**Key words:** Acrodermatitis Enteropathica; Micrconutrient; Zinc

## Introduction

Zinc(Zn) is an essential micronutrient for humans and its importance can be highlighted from the fact that it is an essential component of more than 300 metallo-enzymes and over 2000 transcription factors that are needed for the regulation of lipid, protein and nucleic acid metabolism, and gene transcription.[1] Its role in biology can be grouped into three general functional classes, namely catalytic, structural and regulatory functions.[2] An average adult weighing 70 kg has a body zinc content of 1.4–2.3 gm. The recommended daily allowance of zinc for an average adult male is 11 mg and the requirement increases from 8 mg/d to up to 12 mg/d in females during pregnancy and lactation. It is absorbed from the proximal jejunum and distal duodenum and helped by the presence of zinc binding ligands. It is excreted mainly through feces and in small amounts in urine and sweat.[3]

## Zinc as a therapy

Various forms of zinc have been used as a mode of therapy either in topical or oral forms. Topical preparations like zinc oxide, calamine, or zinc pyrithione have been in use as photoprotecting, soothing agents or as an active ingredient of antidandruff shampoos. The use of zinc is well established in acrodermatitis enteropathica, but over the years use of zinc has been expanded in various disorders. [4] In this article we have highlighted the various dermatological uses of zinc therapy.

Acrodermatitis Enteropathica: It is a rare congenital form of zinc deficiency. The clinical manifestations of this disease usually start following weaning from breast feeding, when the protective effect of the Zn binding ligand from the mother's milk is no longer present. They include growth retardation, diarrhea, alopecia, and characteristic cutaneous lesions involving acral, periorificial, and anogenital areas,[5] treatment with oral zinc (2-3 mg/kg/day) will cure all clinical manifestations within 1-2 weeks and needs to be continued up to adulthood for continuous supplementation and favorable long-term prognosis.[4]

Wart: Zinc can be used in both oral and topical form in treating warts without significant adverse effects.

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Moniem et al. conducted a study in 50 people divided into two groups, one with oral zinc supplementation 10 mg/kg up to 600 mg maximum daily dose for 1 month and the second group did not receive any treatment. The significant increase in serum zinc level in group I was associated with more clinical improvement in the warts.[6] Mohamed et al. demonstrated that lesions treated with intralesional injection of 2% zinc sulfate solution. Among the 225 warts injected, 135 warts (60%) cured from the first session, 51 warts (22.67%) cured from the second session, and 12 warts (5.33%) cured from the third session[7]

Cutaneous Lesihmaniasis: Bafghi et al. assessed the sensitivity of two parasite agents in cutaneous leishmaniasis: *Leishmania major* and *L. tropica* to zinc sulphate *in vitro.* Both parasite species showed sensitivity to zinc sulphate in vitro and in comparison, with the control group, their numbers were reduced.[8] Sharquie et al. used oral zinc sulphate in doses of 2.5, 5, and 10 mg/kg/day for 45 days among 104 patients with cutaneous leishmaniasis and observed cure rates of 83.9%, 93.1%, and 96.9% for the 2.5 mg/kg, 5 mg/kg, and 10 mg/kg treatment groups, respectively, without significant adverse effects. [9]

Leprosy: Zinc is found to stimulate the production of IL-2 and induces a shift from Th2 to Th1 response. It has also been demonstrated to decrease the serum levels of TNF-$\alpha$ and inhibit the TNF-$\alpha$ induced apoptosis of peripheral blood mononuclear cells that helps in controlling the disease activity and reactional state.[10] In a study comprising patients with recurrent erythema nodosum leprosum additionally receiving zinc, steroids could be tapered off completely and the duration and severity of reaction were also reduced. [11] Addition of oral zinc to antileprosy treatment too has been shown to improve therapeutic outcome. Oral zinc when given as an adjuvant to dapsone in lepromatous leprosy induced rapid lepromin conversion and bacterial clearance in the patients compared to the control group. The clinical improvement was also faster in patients receiving zinc as an adjuvant along with standard MDT.[12]

Herpes Simplex: In a study, 30 patients each group applied topical $ZnSO_4$ in concentrations of 1%, 2%, and 4%, respectively, for 3 months. Ten patients of group 1 (1% $ZnSO_4$) showed recurrence, 6 patients in group 2 (2% ZnSO4), and only one patient in group 3 (4% $ZnSO_4$) showed recurrence.[13] Ranjbar et al. stated that there was signifcant relationship between zinc level and recovery period in the recurrent herpes labialis patients. The lower the serum zinc level, the higher the duration of recovery.[14]

Dermatophytoses: Al Janabi et al. observed xerogel nanoparticles composed of ZnO had antidermatophytic action in specific concentrations. [15] In the study, 30 patients with tinea corporis received topical 10% zinc sulfate solution twice daily for two months, complete cure response was observed in 13 (43.33%) patients, partial response in 7 (23.34%) patients and no response in 10 (33.33%) patients while in placebo group the clinical response was two (6.67 %) patients with partial improvement and 28 (93.33%) patients with no improvement.[16]

Bromhidrosis: Foot odor is a common sociomedical problem that affects the feet of human beings of different etiological factors. Owing to its antibacterial action, topical zinc sulphate has been tried and found effective in the management of axillary bromhidrosis and plantar malodor. Sharquie et al. in a single blinded placebo controlled therapeutic trial studied the efficacy of 15% zinc sulphate solution for foot malodor. Zinc sulfate solution 15% was applied to the sole and toe webs once daily for two weeks, three times per week for the next two weeks and followed by single application weekly as maintenance after clearance of odor for two months. Fifty-eight patients received zinc sulphate solution while the other 50 patients received a placebo solution. Thirty-five of the 50 (70%) patients who completed the study showed complete clearance of foot odor compared to only 1 (2%) subject in the placebo group and the difference was statistically significant.[17]

Pityriasis Versicolor: Pityriasis versicolor (PV), also known as tinea versicolor, is a chronic and benign superficial fungal skin infection caused by *Malassezia* yeasts. Zinc pyrithione 1% is a proven treatment modality for pityriasis versicolor. Zinc pyrithione increases copper influx, which inactivates the fungi. [18] Sharquie et al. observed in a study of 30 patients complete clinical and mycological cure after 3 weeks' treatment with once daily application of 15% topical zinc sulphate in patients with pityriasis versicolor while no patient in the placebo group showed any response.[19]

Acne Vulgaris: Zinc is an effective treatment of acne.[20] Yee et al. observed that the patients who were treated with zinc had a significant improvement in mean inflammatory papule count compared to those who were not treated with zinc. There was no significant difference in the incidence of side effects of zinc supplementation vs comparators. Acne patients also have decreased serum zinc levels. [21] Sayyafan et al. observed that erythromycin 2% with zinc acetate 1.2% as 'topical gel' and erythromycin 2% gel alone

erythromycin treatment with zinc acetate was more effective than erythromycin alone with respect to reducing the number of acne lesions and severity grade of acne.[22] In a study, lactoferrin with vitamin E and zinc was more effective than placebo.[23]

Rosasea: Rosacea is an inflammatory facial dermatosis with varied clinical features.[24] In a randomized control trial, significant improvement was seen in 19 patients who received zinc sulfate 100 mg orally thrice daily compared to placebo in total 25 patients[25], while the other study did not show any significant advantage over placebo when zinc sulfate 220 mg twice daily for 3 months in 44 patients.[26]

Uremic Pruritus: Uremic pruritus is a common and burdensome symptom for patients with kidney failure, affecting up to 46% of hemodialysis patients. [27] Najafabadi et al. observed that zinc sulfate 440 mg/ day for 3months is more effective than placebo for the relief of pruritus in patients under maintenance hemodialysis in a study of 40 people.[28]

Psoriasis: Zinc has been used for the management of psoriasis and psoriatic arthritis as well. Sadeghian et al. found a topical 0.25% zinc pyrithione cream, applied twice daily, effective for localized plaque psoriasis in a randomized double-blind controlled trial. The benefit was attributed to the antiproliferative effect of zinc pyrithione.[29]

Eczema: Zinc plays a central role in skin integrity via barrier and immune mechanisms and may also be relevant in the pathogenesis of atopic dermatitis. [30] Kim et al. randomized children with AD and low hair zinc levels to receive oral zinc oxide supplementation or no zinc supplementation. The zinc supplementation group had a significant increase in hair zinc levels, as well as a significant improvement in the extent and severity of AD.[31]

Seborrheic Dermatitis: Zinc has many properties that affect inflammatory processes, the immune system, and epithelial differentiation, and it has antifungal properties and antiandrogenic effects, all of which also contribute to the pathogenesis of SD. Gray et al. revealed lower zinc levels in SD patients compared with controls.[32] The zinc salt of L-pyrrolidone carboxylate (zinc PCA) has long been used for its astringent and antifungal properties. It also has antioxidative and anti-inflammatory effects. Zinc PCA is a good option for patients with mild exudative seborrheic dermatitis.[33]

Molluscum Contagiosum: Safa and Darrieux showed that Zn oxide cream containing colloidal oatmeal extract was effective in the treatment of this viral infection. It has been demonstrated that oat extract has inhibitory effects on eicosanoid formation, expression of cytosolic phospholipase A2, and arachidonic acid mobilization in human keratinocytes.[34]

Melasma: Sharquie et al. revealed the efficacy of 10% Zn sulphate solution in the treatment of melasma. They reported that its effect was statistically significant (P<.0005), and most of the patients maintained this improvement 3 months after cessation of therapy. It is likely that Zn is effective in the treatment of melasma due to its roles as anti-inflammatory, anti-oxidant, peeling, sun-screening, and healing agent.[35]

Vitiligo: Yaghoobi et al. suggested oral Zn sulphate as a new therapeutic option for vitiligo. They compared the efficacy of topical corticosteroids with and without oral Zn sulphate in the treatment of this disorder. Their study showed that the combination of topical corticosteroid and oral Zn was more effective than the topical steroid alone, but this difference was not statistically significant. Zinc in combination with other micronutrients plays an important role in the process of melanogenesis.[36]

Lichen Planus: The study concluded that oral zinc acetatae 50mg 2 times a day for 8 weeks therapy was associated with significant reduction in burning sensation and size of the lesion in symptomatic oral lichen planus.[37] Mehdipour et al. compared 0.2% zinc mouthwash in combination with fluocinolone with a plain fluocinolone mouthwash in 20 patients with erosive lichen planus. It was observed that pain, irritation, and lesion surface area decreased in both groups. But the decrease in surface area with zinc mouthwash with fluocinolone was statistically more significant than that with fluocinolone alone.[38]

Premalignant and Malignant disorder: Sharquie et al. found a statistically significant response in the form of clearance of lesions with 25% topical zinc sulphate applied twice daily over the lesions for 12 weeks in 14 of 18 patients.[39] Sharquie et al. observed improvement in skin lesions, including softening and lightening of the skin color, and clearance of solar keratosis and small malignancies were observed in 15 patients who continued the study during monthly follow up over a follow-up period of 2 years when 20% topical zinc sulphate was used in 19 patients with xeroderma pigmentosa.[40]

Ulcers and wound healing: Many studies have shown that zinc deficiency increases oxidative stress. Oxidative damage is a major cause of tissue

injury and redox regulation plays a prominent role in wound repair.[41] Meta-analysis of topical zinc therapy with zinc oxide paste-medicated dressings containing zinc concentration between 6–15% for chronic venous leg ulcers showed improved healing, although the authors point out that the studies were small and of sub-optimal quality.[42]

Bechets Disease: Sharquie et al. in a randomized, controlled, double-blind crossover trial comprising 30 subjects found oral zinc sulphate, 100 mg given thrice daily for three months, to be an effective treatment modality for Behcet's disease without any major adverse effects.[43]

Alopecias: Lower serum zinc levels in patients with AA compared to controls have been identified.[44] Sharquie et al. in a randomized placebo-controlled, double-blinded crossover study used zinc sulphate in a dose of 5 mg/kg/day in three divided doses for a period of six months and observed a visible clinical response in 62% of patients with alopecia areata.[45] In a study 30 mg zinc gluconate + sulfur amino acids + vitamin D / day for at least 1 year results progressive hair growth at 3–5 months.[46] Hair count results show a modest and sustained improvement in hair growth with daily use of 1% pyrithione zinc shampoo over a 26-week treatment period.[47]

## Conclusion

Over many years, zinc has been used as therapeutic modalities in various dermatological disorders. Efficacy of zinc therapy is the most studied topic for the treatment of acne but there are many variables and results. Although zinc has been identified as effective in the treatment of various disorder, but it cannot be used as the replacement for proven 1st line treatment. Thus, Zinc can be used as an adjuvant therapy in many dermatological disorders either in topical and systemic form.

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