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Topical Zinc Oxide Nanostructures as an Immunomodulatory Component in the Therapy of Chronic Contact Dermatitis: Morphometric Dynamics of $CD68^+$ and $CD207^+$ Cells

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Abstract Objective to evaluate the effect of topical application of a cream containing zinc oxide nanowires (0.5% ZnO-NW) on cellular markers of the innate immune response in the skin (CD68 and CD207) in patients with chronic allergic contact dermatitis (CACD). Materials and methods. The study included 40 patients with clinically and histologically confirmed CACD; ten healthy volunteers served as controls. Immunohistochemical staining with antibodies to CD68 and CD207 (Langerin) was performed. The inflammatory infiltrate was quantified as the number of positive cells per mm^2 of dermis. Patients in the main group received topical therapy with a cream containing 0.5% zinc oxide nanowires (ZnO-NW) for 4 weeks. Statistical significance was assessed using ANOVA followed by Tukey's post hoc test. Results. Before treatment, CACD lesions demonstrated more than a threefold increase in the density of $CD68^+$ macrophages and $CD207^+$ dendritic cells compared with healthy skin. After 4 weeks of 0.5% ZnO-NW therapy, the number of $CD68^+$ cells decreased by 37%, and $CD207^+$ cells by 42% ($p<0.01$). Clinically, 92% of patients reported reduction of pruritus and erythema; no local adverse reactions were observed. Conclusion. The use of 0.5% ZnO-NW is associated with a marked reduction of macrophage and dendritic cell infiltration in CACD, supporting the immunomodulatory and anti-inflammatory potential of this non-steroidal topical technology.

Keywords Chronic allergic contact dermatitis, Macrophages, Dendritic cells, CD68, CD207 (Langerin), ZnO nanowires, Immunohistochemistry

1. Introduction

Introduction. Chronic allergic contact dermatitis (CACD) is a persistent inflammatory dermatosis driven by a type IV hypersensitivity reaction, that is, a delayed-type cell-mediated immune response [1,2,3,7]. Continuous exposure to low-dose sensitizing haptens activates cutaneous antigen-presenting cells, recruits memory T lymphocytes, and promotes the release of proinflammatory cytokines, leading to clinically persistent erythema, lichenification, pruritus, and relapsing course [1,4,5,6,7].

From the standpoint of cutaneous immunopathology, two cellular compartments are central: (1) tissue macrophages and cells of the monocyte–macrophage lineage, immunohistochemically identified by CD68, and (2) Langerhans and dermal dendritic cells expressing CD207 (Langerin), which capture and present antigens to T cells, thus maintaining the pathogenic T cell response [1,7].

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Increased numbers of $CD68^+$ macrophages and $CD207^+$ dendritic cells in lesional skin correlate with clinical severity in CACD [1]. Targeting these populations is therefore a rational therapeutic strategy.

Conventional topical therapy of chronic eczematous dermatoses largely relies on topical corticosteroids and calcineurin inhibitors. Although effective, long-term corticosteroid use carries risks of epidermal atrophy, telangiectasia, barrier dysfunction and local immunosuppression [8]. The search for non-steroidal agents capable of controlling chronic cutaneous inflammation is thus clinically relevant.

In recent years, nanostructured inorganic compounds — in particular zinc oxide (ZnO) — have emerged as promising topical candidates for inflammatory skin diseases [2,3,6]. One-dimensional zinc oxide nanowires (ZnO-NW), typically tens of nanometers in diameter with a very high surface-to-volume ratio, exhibit antibacterial, anti-inflammatory, barrier-protective and immunomodulatory activity [2,3,6]. Experimental data indicate that ZnO nanostructures can modulate local cytokine signaling, attenuate NF-κB and MAPK pathways, and dampen hyperactivation of innate immune effector cells in the skin [2,3,4].

Against this background, it is of specific interest to determine whether topical ZnO-NW can quantitatively reduce CD68+ macrophage and CD207+ dendritic cell infiltrates in chronic allergic contact dermatitis.

Aim of the Study. To assess changes in the density of CD68+ macrophages and CD207+ dendritic cells in the skin of patients with chronic allergic contact dermatitis after a 4-week course of topical therapy with a cream containing 0.5% zinc oxide nanowires (ZnO-NW).

Scientific Novelty

1. We demonstrate that a four-week course of a 0.5% ZnO-NW topical cream reduces lesional CD68+ and CD207+ cell density by 37% and 42%, respectively ($p<0.01$), indicating suppression of both innate-inflammatory and antigen-presenting components of CACD.
2. After treatment, CD207+ dendritic cell density in lesional skin nearly returns to the range observed in healthy controls, suggesting partial normalization of local antigen presentation and interruption of the pathogenic cycle of hapten-driven T cell reactivation [1,7].
3. Clinically, 92% of patients reported alleviation of pruritus and erythema, with no steroid-like adverse effects, supporting the feasibility of ZnO-NW as a non-steroidal anti-inflammatory platform [2-4,6,8].
4. The study proposes quantitative immunohistochemical metrics (CD68 and CD207 cells per mm ²of dermis) as objective markers for monitoring the response to ZnO-NW–based topical therapy.

2. Materials and Methods

Study design. A prospective single-center observational study was conducted. The cohort included 40 patients with chronic allergic contact dermatitis (21 women, 19 men; mean age 28 ± 7 years). The diagnosis was confirmed clinically and histologically. Exclusion criteria included the use of systemic immunosuppressive drugs within the previous two months and active purulent skin infection.

Control group. Ten practically healthy volunteers without chronic skin disease, matched by age and sex, served as controls.

Investigational product. A hydrophilic cream containing 0.5% zinc oxide nanowires (ZnO-NW) was used. The nanowires were one-dimensional crystalline ZnO structures with a diameter of approximately 20–60 nm and a length up to 0.8 μm. A biomimetic ("green") synthesis route with protein stabilizers was applied, aimed at reducing cytotoxicity and improving cutaneous biocompatibility [2,3,6]. The cream was applied twice daily to affected areas for 28 days.

Biopsy and tissue processing. Before therapy initiation and after 4 weeks of treatment, lesional skin biopsies were obtained from each patient. Specimens were fixed in 10% neutral buffered formalin, embedded in paraffin, and sectioned at 4 μm thickness.

Immunohistochemistry. Sections were stained with antibodies against CD68 (clone KP1, 1:600) and CD207/Langerin (clone SP130, 1:200), allowing identification of macrophages/ monocyte–macrophage lineage cells and Langerhans/dermal dendritic cells, respectively [1,7]. Positive cells were quantified morphometrically (ImageJ) and expressed as the number of immunopositive cells per mm ²of dermis.

Statistics. Statistical processing was performed using one-way ANOVA with the factor "skin condition" (healthy skin / CACD before treatment / CACD after ZnO-NW), followed by Tukey's post hoc test. Differences were considered significant at $p<0.05$.

3. Results

Baseline infiltrate. In healthy volunteers, the density of CD68+ macrophages were 50 ± 10 cells/mm², and the density of CD207+ dendritic cells was 40 ± 8 cells/mm². In CACD lesions prior to treatment, these values were markedly higher: CD68+, 150 ± 20 cells/mm²; CD207+, 120 ± 15 cells/mm². Thus, chronic allergic contact dermatitis was associated with a more than threefold increase in both macrophage and dendritic cell infiltrates compared with healthy skin, consistent with the pivotal role of innate and antigen-presenting cells in CACD pathogenesis.

Dynamics after ZnO-NW therapy. After 4 weeks of twice-daily application of the 0.5% ZnO-NW cream, the density of CD68+ cells decreased to 94 ± 18 cells/mm² (−37% from baseline; $p=0.002$), and the density of CD207+ cells decreased to 70 ± 12 cells/mm² (−42% from baseline; $p=0.001$). Notably, post-treatment CD207+ cell counts in lesional skin were close to the range observed in healthy controls. This suggests restoration of cutaneous antigen-presenting homeostasis and attenuation of the delayed-type hypersensitivity loop.

Clinical outcome. By week 4, 92% of patients reported subjective improvement (reduced pruritus and erythema). No local adverse reactions such as burning, irritation aggravation, epidermal atrophy or telangiectasia were recorded. No systemic side effects were observed. This safety profile aligns with published data showing that ZnO nanostructures can exert anti-inflammatory and antimicrobial effects while maintaining acceptable biocompatibility in cutaneous application].

Statistical significance. The factor "skin condition" (healthy / CACD before treatment / CACD after ZnO-NW) was highly significant for both markers: CD68: $F = 62.3$; CD207: $F = 71.6$; $p < 0.0001$ for both. Tukey's post hoc test showed no significant difference between healthy control skin and CACD after ZnO-NW with respect to CD207+ dendritic cells, indicating near-complete normalization of this compartment.

4. Discussion

The pronounced accumulation of CD68+ macrophages and CD207+ dendritic cells in lesional skin confirms that chronic

allergic contact dermatitis is maintained not only by adaptive T cell responses but also by persistent activation of innate effector cells in the skin [1,7]. The marked decline in both cell populations after four weeks of ZnO-NW treatment supports the concept that zinc oxide nanostructures can exert a steroid-sparing, immunomodulatory effect in CACD [2-4,6,8].

CD207 (Langerin) marks Langerhans and dermal dendritic cells involved in antigen capture and presentation to T lymphocytes. The near-normalization of $CD207^+$ cell density after ZnO-NW suggests disruption of the pathogenic circuit of antigen presentation and T cell reactivation that underlies delayed-type hypersensitivity in allergic contact dermatitis [1,7]. This is clinically relevant in relapsing disease driven by continual hapten exposure.

Multiple mechanisms may underlie the observed effect of ZnO-NW: (i) controlled Zn^{2+} release that modulates proinflammatory signaling pathways such as NF-κB and MAPK [2,3]; (ii) redox activity that can activate NRF2 -dependent cytoprotective programs in keratinocytes, thereby dampening the local cytokine milieu [3]; (iii) antibacterial action that limits secondary colonization of the compromised epidermal barrier [2,6]; (iv) a mild barrier-supportive physical coverage of the lesion surface [2,4].

Of particular practical importance, the anti-inflammatory effect was achieved without chronic topical corticosteroid exposure. Long-term topical steroids, especially in chronic eczematous dermatoses, are well known to induce skin atrophy, telangiectasia, and local immunosuppression [8]. No such steroid-like adverse events were recorded during ZnO-NW use in this cohort.

Study limitations include: (1) relatively small sample size and single-center design; (2) limited follow-up (4 weeks), which precludes assessment of long-term remission; (3) reliance on patient-reported symptom improvement without a standardized clinical severity score; (4) absence of a formal placebo control group. Nevertheless, the morphometric findings are internally consistent and align with current evidence that ZnO nanostructures possess anti-inflammatory and immunomodulatory potential in cutaneous inflammation [2-4,6]. These observations justify future randomized controlled trials with longer follow-up, validated pruritus/ erythema scales, and extended inflammatory panels (TNF-α, IL-1β, IL-17, IL-22).

5. Conclusions

Chronic allergic contact dermatitis is characterized by marked infiltration of lesional skin with $CD68^+$ macrophages and $CD207^+$ dendritic cells, reflecting activation of both innate inflammatory and antigen-presenting compartments [1,7].

A four-week course of a 0.5% zinc oxide nanowire (ZnO-NW) cream reduced lesional $CD68^+$ and $CD207^+$ cell density by 37% and 42%, respectively ($p<0.01$), and was associated with symptomatic improvement in 92% of patients without local adverse effects [2-4,6].

These data support the immunomodulatory potential of ZnO-NW as a non-steroidal topical platform for managing chronic allergic contact dermatitis and warrant further controlled clinical studies with extended follow-up [2-4].

REFERENCES

[1] Yamaguchi H. L., Yamaguchi Y., Peeva E. Role of innate immunity in allergic contact dermatitis: an update. International Journal of Molecular Sciences. 2023; 24(16): 12975. DOI: 10.3390/ijms241612975.

[2] Wang S., Ilves M., M ænp ää K. et al. ZnO nanoparticles as potent inducers of dermal immunosuppression in contact hypersensitivity in mice. ACS Nano. 2024; 18(43): 29479–29491. DOI: 10.1021/acsnano.4c04270.

[3] Yin Y., Peng H., Shao J. et al. NRF2 deficiency sensitizes human keratinocytes to zinc oxide nanoparticles-induced autophagy and cytotoxicity. Environmental Toxicology and Pharmacology. 2021; 87: 103721. DOI: 10.1016/j.etap.2021.103721.

[4] Kurian A. G., Singh R. K., Sagar V. et al. Nanozyme-engineered hydrogels for anti-inflammation and skin regeneration. Nano-Micro Letters. 2024; 16: 110. DOI: 10.1007/s40820-024-01323-6.

[5] Marwa K., Goldin J., Kondamudi N. P. Type IV hypersensitivity reaction. StatPearls. Treasure Island (FL): StatPearls Publishing; 2025.

[6] Sirelkhatim A., Mahmud S., Seeni A. et al. Review on zinc oxide nanoparticles: antibacterial activity and toxicity mechanism. Nano-Micro Letters. 2015; 7(3): 219–242. DOI: 10.1007/s40820-015-0040-x.

[7] Vocanson M., Hennino A., Rozi ères A., Poyet G., Nicolas J.F. Effector and regulatory mechanisms in allergic contact dermatitis. Allergy. 2009; 64(12): 1699–1714. DOI: 10.1111/j.1398-9995.2009.02147.x.

[8] Ference J. D., Last A. R. Choosing topical corticosteroids. American Family Physician. 2009; 79(2): 135–140.