

Category: Clinical Research

Title: Curcumin Promotes Regression of HPV-Associated anogenital HSIL through Immunomodulatory and Anti-Inflammatory Effects

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Abstract

Background: Persistent human papillomavirus (HPV) infection is the principal driver of anogenital cancers and their premalignant precursors, including high-grade squamous intraepithelial lesions (HSIL). Despite the risk of malignant progression, therapeutic options for HPV-associated disease remain limited. Curcumin, the bioactive compound of *Curcuma longa* (turmeric), possesses anti-inflammatory and anti-tumor properties. This study evaluates the immunomodulatory and anti-inflammatory effects of curcumin in HPV-associated disease using patient biopsy samples and complementary in vitro models.

Methods: Tissue biopsy samples were collected from 17 participants with biopsy-proven HPV-positive anogenital HSIL (aHSIL). Biopsies obtained before and after a 2-week course of topical curcumin were evaluated for lesion progression and inflammatory markers. For mechanistic insight, peripheral blood mononuclear cells (PBMCs) from healthy donors were cultured in vitro with curcumin-loaded solid lipid nanoparticles (SLNs) or free curcumin, in the presence or absence of T-cell receptor (TCR) stimulation. Immune cell populations were analyzed by flow cytometry, and cytokines were measured using the Meso Scale Discovery (MSD) platform. Additionally, CaSki cells, an HPV-positive cancer cell line, were treated with increasing concentrations of curcumin and analyzed by multiplex flow cytometry to assess cytokine expression profiles.

Results: In patient samples, topical curcumin treatment was associated with measurable regression of aHSIL and reduced expression of the inflammatory marker IL-1 α in post-treatment biopsies. In vitro, curcumin treatment of human PBMCs promoted activation and expansion of innate immune populations (monocytes, neutrophils, and myeloid dendritic cells). Concurrently, curcumin decreased the frequency of immunosuppressive polymorphonuclear myeloid-derived suppressor cells (PMN-MDSCs) and reduced PD-L1 expression on monocytes and MDSCs. Curcumin exposure also reduced several pro-inflammatory cytokines (IFN- γ , TNF- α , IL-2, IL-17A, IL-1 α , IL-12p70, and IL-6) while increasing the anti-inflammatory cytokine TGF- β 1. Consistent with these findings, curcumin treatment of CaSki cells also produced dose-dependent reductions in pro-inflammatory cytokines IL-6 and IL-8.

Conclusion: Curcumin demonstrates immunomodulatory effects characterized by activation of innate immune populations, reduction of immunosuppressive PMN-MDSCs and PD-L1 expression, and decreased pro-inflammatory cytokine signaling. Importantly, topical curcumin treatment was associated with regression of aHSIL lesions. Collectively, these findings suggest that curcumin may represent a promising topical therapeutic strategy for HPV-associated lesions by promoting anti-neoplastic activity while limiting inflammation.

References

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