



ACNE, ROSACEA, AND RELATED DISORDERS (INCLUDING HIDRADENITIS SUPPURATIVA)

## TOPICAL TREATMENT WITH IVERMECTIN INHIBITS EXPERIMENTALLY-INDUCED ACUTE SKIN INFLAMMATION

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**Background:** The physiopathology of papulopustular rosacea (PPR) is not fully understood, but recent findings suggest the involvement of an abnormal immune response. Similar inflammatory processes to those observed in PPR are seen when skin inflammation is induced by 12 O tetradecanoylphorbol-13-acetate (TPA), including neutrophil recruitment and a rapid release of prostaglandins, leukotrienes, and inflammatory cytokines. Ivermectin has anti-inflammatory properties, and phase 3 trials have demonstrated that ivermectin 1% cream is an effective treatment for the inflammatory lesions of PPR. Additional research is needed, but it is possible that the beneficial effect of ivermectin in PPR involves the anti-inflammatory properties of ivermectin.

**Objective:** Use a TPA-induced inflammation model to investigate the anti-inflammatory effects of ivermectin.

**Methods:** Topical application of TPA 0.01% was used to induce ear edema in the right ear of mice. Mice were also treated with topical vehicle or ivermectin (0.01% to 1%). Right ear thickness ( $\mu\text{m}$ ) was measured using a micrometer pre- and post-application. Neutrophil and inflammatory monocyte infiltrates were quantified using flow cytometry. Inflammatory cytokine secretion was assessed using a ProcartaPlex™ Simplex assay.

**Results:** Topical ivermectin treatment inhibited TPA induced inflammation in a dose dependent manner. Topical 0.3% ivermectin decreased ear swelling, with maximal inhibition at concentrations of 0.3 to 1%. The topical reference corticosteroid had a similar dose response. Topical ivermectin was associated with decreased pro-inflammatory cytokine levels in the skin, and an 80% decrease in the absolute number of neutrophils and inflammatory monocytes. Combination treatment using topical ivermectin (0.3 to 1%) and brimonidine (0.2%) further reduced ear edema (brimonidine topical gel, 0.33% is indicated





for the topical treatment of  
persistent facial erythema of rosacea in adults).

Summary: These data demonstrate the potent anti-inflammatory effects of ivermectin in acute skin inflammation, and suggest that the combination of ivermectin with brimonidine could be of interest for the management of PPR.

