

MICHAEL R. RICH, MD
Division of Cardiovascular
Diseases
Department of Internal Medicine
Mayo Clinic College of Medicine
Rochester, Minnesota

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DOWN-REGULATION OF ATOPIC DERMATITIS-ASSOCIATED SERUM CHEMOKINES BY WET-WRAP TREATMENT: A PILOT STUDY

The treatment for severe atopic dermatitis (AD) can be challenging because many patients do not respond to the conventional therapy of topical anti-inflammatory medications and moisturizers. Wet-wrap treatment (WWT) has been shown to be relatively safe for the treatment of severe AD, but its efficacy remains controversial because of a lack of large prospective studies and objective efficacy parameters.¹ To evaluate the efficacy of WWT in AD more objectively, we performed a pilot study to investigate the serum levels of 38 chemokines in 6 children with severe AD before and after WWT. Patients' ages ranged from 3 to 13 years. No patient had received any systemic corticosteroid, immunosuppressant, UV light treatment, or topical or systemic antibiotics at least 4 weeks before the study. Their mean $\pm$ SD total serum IgE level was $14,213 \pm 15,229$ IU/mL, and their mean $\pm$ SD

AD severity, as measured by objective SCORing AD (SCORAD), was 48.2 ± 3.9 . These patients underwent WWT based on a double-layer wet-wrap technique.² Briefly, the patients were bathed for 15 minutes and patted dry; 0.05% fluticasone propionate cream was applied on the active lesions and petrolatum ointment on the unaffected areas. A set of cotton long-sleeved sweatshirt, pants, and socks were soaked in warm water, squeezed dry, and worn by the patients. This set of damp clothing was overlaid with a second, dry set of cotton clothing and socks. The patients underwent WWT for 2 hours, twice a day, for 7 days. The study was approved by the hospital's institutional review board. Serum chemokine levels were measured at a core laboratory using a 38-chemokine array (http://www.raybiotech.com/map/human_chemokine_map.pdf). The relative levels of proteins obtained with this method have correlated well with enzyme-linked immunosorbent assay.³ The data were analyzed using RayBio analysis software. The ratio of relative expression (densitometric ratio) was established after subtraction of the background intensity and comparison with the positive spots available in the membrane. The objective SCORAD and chemokine levels before and after the treatment were analyzed by the Wilcoxon matched-pairs signed-ranks test and the 2-tailed paired *t* test, respectively. $P \leq .05$ was considered statistically significant.

After WWT, all patients showed significant clinical improvement as measured by objective SCORAD scores, which decreased from 48.2 ± 3.9 to 9.5 ± 6.1 ($P = .03$). Of the 38 serum chemokines analyzed, 7 showed significant decrease after WWT (Figure 1). These chemokines were macrophage

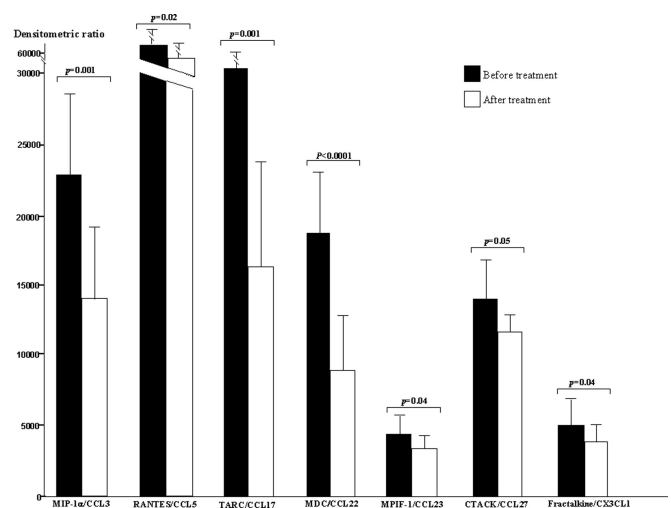


Figure 1. Serum chemokine levels after wet-wrap treatment in patients with severe atopic dermatitis. Chemokines were macrophage inflammatory protein 1α (MIP-1α/CCL3); regulated on activation, normal T cells expressed and secreted (RANTES/CCL5); thymus- and activation-regulated chemokine (TARC/CCL17); monocyte-derived chemokine (MDC/CCL22); myeloid progenitor inhibitory factor 1 (MPIF-1/CCL23); cutaneous T-cell-activating chemokine (CTACK/CCL27); and fractalkine (fractalkine/CX3CL1).

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To date, 6 chemokines are known to be potential serum markers for the disease activity of AD.⁴ These chemokines are eotaxin/CCL11, TARC/CCL17, MDC/CCL22, eotaxin-3/CCL26, CTACK/CCL27, and fractalkine/CX3CL1.⁴ Our results confirmed a significant decrease in 4 of these 6 serum chemokines after WWT (ie, TARC/CCL17, MDC/CCL22, CTACK/CCL27, and fractalkine/CX3CL1). Of interest, we found that serum TARC/CCL17 and MDC/CCL22 had the largest fold decrease after WWT (1.9- and 2.0-fold decrease, respectively). These 2 chemokines interact with the CCR4 receptor, which is preferentially expressed on T_H2 cells.⁵ When activated, T_H2 cells express high levels of interleukin 4 and interleukin 13, both of which are associated with the production of IgE and acute AD lesions.⁴ Not only do these chemokines play an important role in the pathogenesis of AD, but also their serum levels have consistently been shown to correlate with the severity and disease activity of AD in multiple studies.^{4,6} CTACK/CCL27 attracts a mixture of CCR10⁺ T_H1/T_H2 cells that are characteristics of subacute AD lesions.⁴ Fractalkine/CX3CL1 also contributes to the pathogenesis of AD lesions by attracting T cells with the CX3CR1 receptor.⁴ MIP-1 α /CCL3 attracts monocytes and T cells that express CCR1 and/or CCR5 receptors,⁷ whereas RANTES/CCL5 attracts eosinophils and T cells with CCR1, CCR3, or CCR5 receptors to AD lesions.⁴ The potential role of MPIF-1/CCL23 in the pathogenesis of AD has recently been shown.⁸ This chemokine is produced by monocytes and may attract dendritic cells with the CCR1 receptor to AD lesions.⁸

In summary, the current study showed significant down-regulation of AD-associated serum chemokines after WWT. The results provide laboratory support for the efficacy of WWT in severe AD. Since the serum chemokine changes should reflect the chemokine changes in the AD skin lesions after WWT, we are currently extending our study to include skin biopsy analysis and to compare that to a control group of patients with severe AD receiving conventional treatment with topical fluticasone cream and petrolatum ointment.

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PECK Y. ONG, MD

RONALD M. FERDMAN, MD

THERESA DUNAWAY, RN

JOSEPH A. CHURCH, MD

Division of Clinical Immunology and Allergy

Children's Hospital Los Angeles

Department of Pediatrics

Keck School of Medicine

University of Southern California

Los Angeles, California

CLARK B. INDERLIED, PhD

Department of Pathology and Laboratory Medicine

Children's Hospital Los Angeles

Los Angeles, California

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