A prospective, randomized, open-label trial comparing the safety, efficacy, and tolerability of an acne treatment regimen with and without a probiotic supplement and minocycline in subjects with mild to moderate acne

(Poster reference number 5322)

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Background: Although systemic antibiotics are an effective treatment for acne vulgaris, intolerable side effects from such medications may invariably occur. Through its demonstrated health benefits, probiotics may reduce the adverse effects imposed by antibiotics while complimenting its clinical effect.

Objective: The objective of this study was to determine whether probiotics reduce the side effects imparted by systemic antibiotics while working synergistically with the latter in treating inflammatory acne.

Methods: Forty-five female patients, 18 to 35 years of age, with Fitzpatrick skin types I to III and mild to moderate acne were enrolled in a prospective, randomized, open-label study. Subjects were randomly assigned to one of three groups. Group A received only probiotic supplementation, while group B received only minocycline. Group C was treated with both probiotic and minocycline. Clinical and subjective assessments were completed at baseline and during the 2-, 4-, 8-, and 12-week follow-up visits.

Results: All three study arms demonstrated a significant improvement in total lesion count 4 weeks after treatment initiation ($P < .001$) with continued improvement seen with each subsequent follow-up visit ($P < .001$). However, only the minocycline-probiotic arm demonstrated a significant decrease in inflamed lesions at 4 weeks ($P < .001$), while the other two groups did not achieve this result until 8 weeks. At the 8- and 12-week follow-up visits, group C had a significant decrease in total lesion count versus groups A ($P < .001$) and B ($P < .001$). Two patients (13%) from the minocycline-only arm failed to complete the study secondary to vaginal candidiasis.

Conclusion: This preliminary study supports a potential role of probiotics in acne treatment by providing a synergistic effect with systemic antibiotics while also reducing potential adverse events secondary to chronic antibiotic use.

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Therapeutic effect and immunomodulation induced by Su-An-Bo mineral water on a model of atopic dermatitis in Nc/Nga mice

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Background: Atopic dermatitis (AD) is a chronic, allergic inflammatory skin disease that often cannot be adequately controlled with topical agents. The continuous use of current systemic therapies for AD is limited by end-organ toxicities. Balneotherapy is widely used as an important treatment modality for AD. Although the clinical benefit of some mineral waters has been established, their mechanisms of action alleviating AD remain completely unclear.

Objective: This study examined clinical modification induced by bathing in the mineral water. We then investigated whether bathing in the Su-An-Bo mineral water has active immune modulating effect on T_H1, T_H2- cytokine and regulatory T cell (Tregs) production using spleens from Nc/Nga mice, AD animal model.

Methods: To induce AD-like skin lesions, Nc/Nga mice were housed under air-unregulated conventional room and *Dermatophagoides farinae* body extract ointment was applied to the back of the rostral area 3-4 times a week for up to 2 weeks. Nc/Nga mice were randomly distributed into the mineral water group (MWG, n = 10) and distilled water group (DWG, n = 6). Each of group had a bath in the mineral and distilled water every day for 2 weeks. Therapeutic effects of mice with AD and healthy controls (HCs, n = 6) were evaluated using modified SCORAD index. The skin hydration, the skin pH and transepidermal water loss (TEWL) were also measured to investigate the changes of the skin barrier function. H&E staining was used to evaluate histologic changes in the skin. We also assessed T_H1, T_H2, Tregs cell profile in spleen of both group and HCs using flow cytometry.

Results: The modified SCORAD index scores of MWG significantly decreased compared with the DWG ($P < .001$). Among the factors of the skin barrier function, TEWL decreased in the MWG more than in the DWG ($P < .05$). Compared to baseline, skin hydration improved in the MWG ($P < .05$), but not in the DWG. Tregs cell expression increased in the MWG more than DWG and HCs. H&E staining of the skin of MWG revealed normal epidermal differentiation and less periadnexal inflammatoy cell infiltration than DWG. The mineral water improved skin barrier function, enhanced stratum corneum hydration, and reduced skin inflammation.

Conclusion: These results suggest that the favorable effects of bathing in the mineral water are likely related to the increased Tregs. Tregs might not only enhance permeability barrier repair by influencing epidermal proliferation and differentiation, but also reduce inflammatory cell infiltration.

Commercial support: None identified.

A pilot study of an oral phosphodiesterase inhibitor (apremilast) for atopic dermatitis

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There are currently no FDA-approved systemic therapies for atopic dermatitis (AD), and current systemic immunosuppressants used in this population are limited by toxicities with long-term use. Monocytes from patients with atopic dermatitis (AD) display elevated cyclic AMP phosphodiesterase (PDE) activity leading to immune responses skewed towards a T_H2 profile. We aimed to gather preliminary safety and efficacy data of a novel oral PDE-4 inhibitor, apremilast, in a small cohort of adults with AD. We performed an open-label prospective trial of apremilast at 20 mg BID in 6 subjects (cohort 1) for 12 weeks and 30 mg BID in 10 subjects (cohort 2) for 24 weeks. The primary outcome was incidence of adverse events (AEs), with secondary outcomes focusing on disease severity measures and peripheral whole blood gene expression changes. Efficacy of apremilast was assessed at each study visit using the Eczema Area Severity Index (EASI), Dermatology Life Quality Index (DLQI), and the Visual Analog Scale (VAS) for pruritus. Nausea was the most common AE and appeared to be dose-related (33% cohort 1, 90% cohort 2). In all subjects, the nausea was rated as mild and improved over the course of the study. Other AEs included headache, fatigue, loose stools, bloating, and vomiting, were rated as mild and improved over the course of the study. One subject developed herpes zoster and was discontinued from the study. Intent to treat analyses performed at 3 months revealed significant improvement in VAS and DLQI in cohort 1 ($P < .021$ and $P < .003$, respectively) and EASI and DLQI in cohort 2 ($P < .008$ and $P < .012$, respectively). Combined data from both cohorts showed statistically significant improvement in all outcomes. EASI reduced from a mean baseline of 24.8 to 16.2 ($P < .002$), VAS reduced from a mean baseline of 52 to 31.7 ($P < .003$) and DLQI reduced from a mean baseline of 11.6 to 4.7 ($P < .001$). In addition, statistically significant improvement was seen in all outcomes at 6 months in the 30 mg BID group. Gene expression data revealed highly significant differential expression of the cAMP response element binding pathway, BAD phosphorylation pathway, IL-12 signaling, and regulation of immune complex clearing by monocytes and macrophages. Apremilast demonstrated an acceptable tolerability profile in subjects with AD. Our preliminary data indicate that apremilast significantly improves inflammation, pruritus and quality of life in AD.

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Results of patch test with hairdressing series in Korean patients with allergic contact dermatitis to para-phenylenediamine

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Background: Hair dye is one of the most common causes in allergic contact dermatitis (ACD), and its main allergen is para-phenylenediamine (PPDA). The patients with PPDA-induced contact dermatitis are often worried about the use of hairdressings and usually asked about any safe alternative hair dye without PPDA or safety in using any hairdressing agents such as permanent waving agents, shampoos, or bleaching agents. However, there are no reports for these answers.

Purpose: To investigate the positivity on the patch test of hair-related allergens in the patients with PPDA-induced allergic reaction.

Methods: The patients who had a history of ACD to hair dye and positive reaction to PPDA on patch test with Korean standard series were enrolled as study group. In all patients, filling out questionnaire was requested and patch tests with hairdressing series were performed. The results were interpreted according to the International Contact Dermatitis Research Group Guidelines.

Results: Twenty-four patients participated, and 20 patients finished the study. Ten patients were female (50.0%), the mean age was 58.2 ± 9.87 years, and the mean duration from initial use of hair dye to the onset of ACD was 2.3 ± 2.2 years. The frequency of positivity (n = 20) except PPDA ranked as follows: toluene-2,5-diamine sulfate (n = 3, 15.0%), balsam of Peru (n = 3, 15.0%), m-aminophenol (n = 2, 10.0%), 2-nitro-4-phenylenediamine (n = 1, 5.0%), resorcinol (n = 1, 5.0%), 4-aminophenol (n = 1, 5.0%), ammonium thioglycolate (n = 1, 5.0%), hydroquinone (n = 1, 5.0%), and formaldehyde (n = 1, 5.0%).

Conclusion: This study provides the first results of positivity of each allergen in hairdressing series on Korean patients with PPDA induced allergic reaction. This could be useful to reduce allergic reaction due to hair dye and to make hypoallergenic hair dye products.

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