Atopic Dermatitis Treatments Go Outside the Box

BY PATRICE WENDLING
Chicago Bureau

CHICAGO — Despite bone-chilling temperatures and the risk of frostbite, patients who underwent experimental whole-body cryotherapy for atopic dermatitis said they were willing to do it again.

This Finnish experience with whole-body cryotherapy was just one of three "outside-the-box" treatments for atopic dermatitis to emerge in recent months and was highlighted by Dr. Albert C. Yan, chief of the dermatology section at Children's Hospital of Philadelphia, during an atopic dermatitis symposium at the American Academy of Dermatology Academy 2008 summer meeting.

► **Whole-body cryotherapy.** This therapy has been used to treat rheumatic inflammation and pain since the 1970s. The rationale for the therapy in atopic dermatitis is based on reports that very cold air increases the body's antioxidative capacity and reduces the conduction velocity of peripheral nerves and the nerve ganglia capacity to synthesize acetylcholine, which is considered a neurotransmitter in atopic pruritus, according to Dr. Yan.

Investigators at the Skin and Allergy Hospital in Helsinki applied whole-body cryotherapy to 18 adults with mild to moderate atopic dermatitis three times a week for 4 weeks, followed by an 8-week follow-up period.

Topical anti-inflammatory preparations or systemic antihistamines were not allowed for 1 week before or at any time during the study, and there was a 6-week washout period for systemic therapy and phototherapy.

The Univers Cryo-Combi whole-body cryotherapy device (Oy MJG Univers Ab, Helsinki) consists of two precooling chambers set at –30° C and –60° C, where patients remained for a very short time, and a third chamber that reaches –110° C, where patients remained for 1 to 3 minutes wearing a bathing suit or trunks, with acral parts covered.

The study's primary end point of change in the Scoring of Atopic Dermatitis (SCORAD) index (scale 0-103) decreased almost 20% from 38.7 to 31.1 (Arch. Dermatol. 2008; 144:806-8).

Pruritus, sleep loss, and SCORAD rating tended to improve after the 4 weeks of treatment.

Three patients had treatment-related adverse events, all mild acral frostbite. Sixteen of the 18 patients completed therapy, an average of 11 sessions (range from 9 to 12 sessions).

One patient left the study because of worsening dermatitis, and another left because of work schedule. All patients were willing to undergo further treatment.

The device used in the study is the first to use both liquid nitrogen and compressor technology to produce cold air. This maintains an optimal oxygen level of 22% in the chamber that allows even patients with asthma to undergo the treatment, according to lead author Dr. Taras Klimenko and colleagues, who reported no conflicts of interest.

The study was supported by grants from The Finnish Society of Dermatology and The Finnish Society of Dermatopathology.

Rosiglitazone may serve as a 'good alternative to current systemic immunosuppressants used for severe AD,' the investigators suggested.

► **Vitamin D supplementation.** Supplements of vitamin D helped improve wintertime onset or exacerbation of atopic dermatitis in children aged 2-13 years who were randomized to oral ergocalciferol 1000 IU in a double-blind, pilot study (Br. J. Dermatol. 2008;159:245-7).

The Investigator's Global Assessment—based on six categories, ranging from clear (1) to very severe (6)—improved by one category in four (80%) of five children on vitamin D versus one (17%) of six children on placebo. Similar improvements were seen in Eczema Area and Severity Index scores.

Lead author Dr. Robert Sidbury of Children's Hospital Boston and his associates suggested that the favorable impact of vitamin D on atopic dermatitis is biologically plausible.

The active form of vitamin D, 1,25-dihydroxyvitamin D_3, induces expression of antimicrobial peptides that help prevent skin infection and possess immunosuppressive properties in the skin. Recent research also has drawn attention to the connection between vitamin D–mediated activation of toll-like receptors, production of the antimicrobial peptide cathelicidin, and human susceptibility to bacterial infection.

"Thus, vitamin D deficiency could contribute to the hallmark signs of AD: altered barrier function, immune dysregulation, and inadequate bacterial defence," wrote the authors, who reported no conflicts of interest.

The study was supported by a grant from the Massachusetts General Hospital Center for D-receptor Activation Research in Boston.

► **Rosiglitazone maleate.** Used as an add-on therapy at doses of 2-4 mg twice daily, rosiglitazone (Avandia) was associated with increased control of severe atopic dermatitis in 6 patients nonresponsive to first- and second-line therapies, according to a retrospective review (Arch. Dermatol. 2008;144:84-8).

The six patients, aged 16-75 years, showed decreased extent of the disease, of inflammation, and of number of flares. In addition, rosiglitazone, which is indicated for the treatment of type II diabetes, allowed for gradual reduction or elimination of systemic steroids in the three patients who used them.

Major clinical improvement appeared between weeks 4 and 12, which suggests that some patients may require at least 3 months for a clinical response, according to lead author Ramona Behshad, principal investigator Dr. Kevin Cooper, and senior author Dr. Neil Korman, all of whom are with Case University, Cleveland.

No serious adverse events were seen in the study patients. The investigators suggested rosiglitazone may serve as a "good alternative to current systemic immunosuppressants used for severe AD," but urged caution in interpreting the promising results because of study design limitations and two previous randomized trials of rosiglitazone in psoriasis that failed to demonstrate any notable efficacy, compared with placebo.

The study was supported in part by the National Institute of Arthritis and Case Medical Center.

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Probiotics' Role to Prevent/Treat Atopy Remains Controversial

BY PATRICE WENDLING
Chicago Bureau

CHICAGO — The value of probiotics in atopic disease remains controversial, but clues are beginning to emerge in the literature about probiotics' role in treatment and prevention.

Dr. Sharon S. Raimer highlighted the conflicting trail of evidence surrounding probiotic supplementation for the prevention and treatment of pediatric atopic dermatitis (AD) at a meeting sponsored by the American Academy of Pediatrics.

"It looks like at the present time that probiotics are really not very good for treatment, but they might help in prevention; but you have to give the probiotic prenatally for it to really work," said Dr. Raimer, chair of dermatology, University of Texas at Galveston.

These considerations are largely based on a recent meta-analysis of six prevention and four treatment double-blind randomized controlled trials of probiotics and pediatric AD (J. Allergy Clin. Immunol. 2008;121: 116-21).

The analysis identified a significant risk reduction—by as much as 61%—associated with the use of prenatal and/or postnatal probiotics for primary pediatric AD prevention among 1,581 participants, but only a marginal effect of treatment among 299 participants.

Such meta-analyses are complicated by the variety of bacteria strains and strengths studied, Dr. Raimer said.

Probiotic trials also typically have small sample sizes and heterogeneity of protocols, and might not assess for use of potential confounders such as concomitant antibiotics, topical corticosteroids, and antigen-eliminating diets.

An early trial supporting the role of probiotics in allergy prevention randomized mothers with a family history of atopic eczema, allergic rhinitis, or asthma to two capsules containing placebo or 1×10^{10} colony-forming units of *Lactobacillus rhamnosus* GG daily for 2-4 weeks before date of delivery.

After delivery, breastfeeding mothers were given the capsules, while infants who were not breastfed were given the capsule contents mixed with water, for 6 months.

Atopic eczema was diagnosed in 46 of 132 (35%) children at 2 years of age, with the frequency of eczema in the probiotic group half that of the placebo group (23% vs. 46%) (Lancet 2001;357:1076-9).

A follow-up study of these at-risk children revealed that 14 of 53 (26%) receiving *Lactobacillus* had developed atopic eczema at 4 years, compared with 25 of 54 (46%) receiving placebo (Lancet 2003;361:1869-71), suggesting that the preventive effect of *Lactobacillus* extends beyond infancy. Skin-prick test reactivity was found to be the same in both groups.

'It looks like ... probiotics are really not very good for treatment, but they might help in prevention; but you have to give the probiotic prenatally.'

Early probiotic supplementation alone appears not to be beneficial in reducing the risk of AD and might actually increase the risk of allergen sensitization in high-risk children, said Dr. Raimer, also a professor of dermatology and pediatrics.

She cited an Australian study that found no difference in AD rates at 6 and 12 months between 177 infants who received *Lactobacillus acidophilus* or placebo for the first 6 months of life, and a significantly higher rate of sensitization to common allergens in the probiotic group at 12 months (Allergy Clin. Immunol. 2007;119:184-91).

Finally, a prospective randomized trial of supplementation during pregnancy and early infancy adds even more intrigue to the probiotic controversy.

Supplementation with 5×10^9 colony-forming units of *Lactobacillus* GG twice daily for 4-6 weeks before delivery and 6 months postnatally neither reduced the incidence of atopic eczema nor altered disease severity in AD affected children, but was associated with an increased rate of recurrent episodes of wheezing bronchitis in the study children (Pediatrics 2008;121:e850-6).

The German researchers concluded that *Lactobacillus* GG cannot be generally recommended for primary prevention of atopic eczema. ■