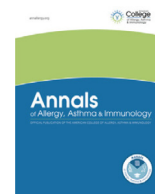




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Editorial

Bleach baths for atopic dermatitis Evidence of efficacy but more data are needed



During the past few decades, dilute bleach baths have become a common and inexpensive adjunctive therapy for maintaining control in patients with moderate-to-severe atopic dermatitis (AD) and are recommended in the 2014 American Academy of Dermatology guidelines for use of topical therapies.¹ The 0.005% concentration of sodium hypochlorite (NaOCl), used twice weekly to daily for baths (half cup of the standard 5%–8% bleach per full 40-gallon tub), has been adapted for use in tubs for infants and hand/foot soaks (80% of a teaspoon per gallon or 1 cc/L), and in a commercially available 0.006% concentration for administration in the shower.² Undiluted bleach can cause burns, emphasizing the need for proper proportions and mixing before exposure. However, little toxicity has been reported with the low concentrations used in bleach baths. Some patients note skin dryness, pruritus, and if used when the skin is highly excoriated or infected, stinging/burning. Because of the latter, bleach baths are often held until a few days after antibiotic initiation during infections.

Despite the widespread use and experience with bleach baths, few studies have formally evaluated their value and potential risks. Bleach baths are primarily for long-term maintenance, but only 2 studies have tested the impact of the approximately 10-minute baths beyond 4 to 6 weeks. Even these two 3-month trials were heterogeneous in methodology and results. One compared bleach-only vs water-only baths and monthly intranasal mupirocin ointment vs petrolatum after a 10-day initial course of oral antibiotics, with a significantly greater reduction in Eczema Area and Severity Index scores (physician-reported) in the bleach bath plus intranasal mupirocin group.³ The other, which excluded patients with infection at the onset found a reduction in AD severity (on the basis of both physician and patient-reported SCORing Atopic Dermatitis assessment) to be similar between topical corticosteroids (TCS) alone vs TCS plus bleach baths (61.8% and 65.8% reduction, respectively).⁴

The primary reasons for the few and underpowered studies include: (1) little to no funding to test an inexpensive product without industry investment; and (2) the inability to be double-blinded, given the distinctive bleach odor, even when diluted, which could influence patient- or proxy-reported outcomes. Bakaa et al⁵ have pooled the results of 9 trials to assess the efficacy and safety of dilute bleach baths. These studies have few patients and vary in their methodology and outcomes. However, using sophisticated statistical analyses to allow comparison, the authors found dilute bleach baths to improve AD severity by 22% and cause little toxicity.

Many questions remain. Bakaa et al⁵ suggested a required sample size of 200 to study further bleach bath efficacy. We would further qualify that, in addition to needing a much larger sample size, this

study should have the following characteristics: (1) be randomized (single-blinded, for reasons noted above); (2) include both children and adults with moderate-to-severe AD despite a stable AD treatment regimen; (3) control for key confounders; (4) include both physician- and patient-reported outcome measures despite the single-blind nature; and (5) have a minimum duration of 12 to 16 weeks given the ease of use for maintenance. Ideally, such a study should also evaluate the mechanism of action of bleach baths.

Staphylococcus aureus skin colonization is typically, if not universally, observed in patients with AD. Increases in *S. aureus* and reduction in microbial diversity are both associated with disease flares. The biologic effects of type 2 cytokines (eg, reductions in antimicrobial peptide expression) and skin barrier dysfunction have been blamed for bacterial overgrowth.⁶ Sodium hypochlorite has been used as a topically-applied antimicrobial agent for decades (ie, Dakin's solution [0.025%]). Whether the 0.005% to 0.006% concentration can reduce *S. aureus* load is controversial. In vitro studies suggest a requirement of at least 0.01% concentration,⁷ given that a 0.005% concentration has no effect on virulence factor function.⁸ Sodium hypochlorite 0.005% had no antibacterial effect on *S. aureus*–colonized pig skin⁸ or human AD skin in an ex vivo model.⁷ Nevertheless, these laboratory-based observations may not reflect the impact on AD skin in vivo, and some studies have suggested an antimicrobial impact. Reduction in lesional crusting, which suggests bacterial overgrowth, has been noted anecdotally. Bleach baths and compresses (0.005% to 0.01% concentrations) are routinely used to reduce the bacteria-induced odor in patients with skin thickening, such as congenital ichthyoses, suggesting that these concentrations may impact the production of odor-causing volatile substances. In the 3-month study comparing patients with AD treated with TCS vs TCS plus bleach baths (without initial antibiotic), swabs for microbiome assessment were obtained from 3 lesional and 1 nonlesional site and compared with these sites in healthy children.⁴ Both groups experienced a reduction in the relative abundance of *S. aureus* and greater microbial diversity, but the relative abundance of *S. aureus* in patients treated with the bleach baths was lower than with TCS alone. This observation suggests that bleach baths, even at this low concentration, impact the relative composition of the skin microbial community. Nevertheless, it would be important to pair these observations with measurements of absolute *S. aureus* abundance (by quantitative polymerase chain reaction for *S. aureus*–specific genes and quantitative culture techniques [colony forming unit/mL]).

It is possible that shifts in microbial communities are not the direct action of NaOCl, but rather an indirect effect of NaOCl on the epithelial compartment (keratinocytes, Langerhans cells, nerve endings, etc) or the production of bacterial products (from both *S. aureus* and commensal skin bacteria). The NaOCl 0.005% concentration inhibits keratinocyte expression of nuclear factor- κ B–dependent genes and nuclear factor- κ B

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activation.⁹ Topically-applied soaks of 0.005% NaOCl reduce radiation dermatitis and enhance keratinocyte proliferation associated with aging in mouse models through I κ B kinase modulation,⁹ further suggesting a direct anti-inflammatory effect on the skin.

The improvement of AD from the use of dupilumab, the first biologic approved by the Food and Drug Administration for AD treatment, has diminished the need to recommend bleach baths. Other injectable biologics and oral Janus kinase inhibitors are also coming on the market. Nevertheless, the high cost, potential risks (especially with Janus kinase inhibitors), and pain of injection (biologics) provide an opportunity for a painless, inexpensive, and safe AD add-on treatment, such as bleach baths. We applaud Bakaa et al⁵ for acknowledging the need for and providing an outline of a more definitive bleach bath trial that will evaluate efficacy and safety. Such a study will inform us on whether bleach baths should be part of future AD guidelines, including regarding selection of patients and regimen. Should such a study confirm the usefulness of bleach baths, determining the mechanism(s) of action is critical. Given the minimal invasiveness of skin swabs (for the microbiome, metagenome, and *S. aureus* absolute abundance) combined with skin tape strips (for transcriptomic, lipidomic, and proteomic assessments), a better understanding of the mechanism of action of a cheap and easy-to-implement treatment, such as bleach baths, is a “low hanging fruit.”

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