

ORIGINAL ARTICLE

Efficacy and safety of sodium hypochlorite (bleach) baths in patients with moderate to severe atopic dermatitis in Malaysia

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ABSTRACT

Staphylococcus aureus is frequently found in patients with atopic dermatitis (AD) and contributes to disease exacerbation. The objective of this study was to evaluate the efficacy and safety of bleach baths as an adjunctive treatment in AD patients. Patients between 2 and 30 years old with moderate to severe AD were enrolled in a prospective, randomized, placebo-controlled study. Patients soaked in diluted bleach or distilled water baths for 10 min, twice a week for 2 months. Efficacy assessments included the Eczema Area and Severity Index (EASI) scores and *S. aureus* density was determined using quantitative bacterial cultures. Patients in the treatment group showed significant reductions in EASI scores. A 41.9% reduction in *S. aureus* density from baseline was seen at 1 month further reducing to 53.3% at 2 months. Equal numbers of patients in both groups experienced mild side-effects. This study demonstrates that diluted bleach baths clinically improved AD in as little as 1 month. No patient withdrew from the treatment arm because of intolerance to the baths.

Key words: atopic dermatitis, bleach baths, sodium hypochlorite, *Staphylococcus aureus*.

INTRODUCTION

Patients with atopic dermatitis (AD) have an increased susceptibility to colonization with *Staphylococcus aureus*, contributing to increased severity of AD and disease exacerbation.^{1,2} *S. aureus* is the most frequent microbe found in these patients and more than 90% of patients with AD are colonized with *S. aureus* compared with 5% in normal individuals.^{3,4} Therefore, reduction of bacterial colonization is an important part of the management of these patients. In clinical practice, our treatment of AD is often reactive, treating flares when they occur. However, management should include early and effective measures to control skin inflammation and *S. aureus* colonization, thus reducing the number of flares.

Many studies have been conducted using various interventions to reduce *S. aureus*, including bath additives, soaps, topical antibiotics/corticosteroid combinations, topical calcineurin inhibitors, antiseptic preparations and certain textiles.⁵ However, there is still a continuing need for a simple, effective, cheap and safe preparation.

Sodium hypochlorite has both *in vitro* and *in vivo* antimicrobial activity against *S. aureus*, including methicillin-resistant *S. aureus* (MRSA).^{6,7} Fisher *et al.*⁸ in 2008 reported that in a series of *in vitro* experiments, sodium hypochlorite 6% (bleach) at a concentration of 2.5 µL/mL was effective in killing invasive

and colonizing clinical community-acquired MRSA (CA-MRSA). Sodium hypochlorite at concentrations as low as 0.005% have also been shown to be effective against *S. aureus* in wounds and skin ulcers.⁹ A study by Huang *et al.*¹⁰ in 2009 showed that diluted bleach baths with intermittent intranasal mupirocin ointment decreased the clinical severity of AD. However, qualitative bacterial cultures continued to yield *S. aureus* from both skin and nares even at 3 months.

In Malaysia, sodium hypochlorite is cheap and widely available. However, the use of bleach baths as an adjunctive treatment in patients with AD is not widely practiced here. Malaysia is hot and humid all year round, and most people shower rather than take baths. There have also been concerns of skin irritation with the use of bleach baths in patients with AD and evidence of its efficacy and safety in our Asian population is lacking. We therefore sought to determine if the addition of sodium hypochlorite (bleach) baths as an adjunctive treatment could result in improvement of the clinical severity of AD and a reduction of *S. aureus* density in patients with moderate to severe AD in our Malaysian population.

OBJECTIVE

To evaluate efficacy and safety of bleach baths as an adjunctive treatment in patients with moderate to severe AD.

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METHODS

Study population

Patients were recruited from the dermatology clinic, Hospital Kuala Lumpur, a tertiary care center in Malaysia, and were randomly assigned to the treatment or placebo study arms. Inclusion criteria included patients aged between 2 and 30 years old with a diagnosis of AD using Hanifin and Rajka Criteria 1980,¹¹ which is rated moderate to severe using Rajka and Langeland Criteria 1989.¹² Exclusion criteria included patients with known sensitivity to sodium hypochlorite (bleach), had eczema herpeticum or other cutaneous infections, patients who were on systemic antibiotics or systemic corticosteroids at the time of recruitment or during the study period, those on other antiseptic baths and patients who were pregnant or lactating.

Study design

This was a 2-month prospective, randomized, double-blinded, placebo-controlled study. Bleach and distilled water were dispensed in identical bottles by the pharmacy. Patients were instructed to add 100 mL of sodium hypochlorite 5% (bleach, treatment arm) or 100 mL of distilled water (placebo arm) in 100 L of water (equivalent to approximately half a bathtub full), diluting the sodium hypochlorite to a concentration of 0.005%. For children less than 12 years old, 50 mL was added to a quarter tub of water (50 L). Patients were given clear oral and written instructions on how to dilute the solution and were instructed to soak neck down in the diluted baths for 10 min, twice a week for 2 months. After each bath, patients rinsed off with normal tap water. Patients were given a diary to record the bathing schedule and any adverse events noted. Scheduled visits were conducted at baseline/day 1, week 2, week 4 and week 8/end of treatment.

Each patient was maintained on a stable regimen of topical anti-inflammatory and emollient therapy throughout the 2-month period. No new topical or systemic treatment was introduced before and during the study period. They were issued aqueous cream as soap to standardize their bathing regime.

Study approval

This study was approved by the National Medical Research Register, Malaysia. Informed consent was obtained from the patients and/or guardian before initiation of the study.

Efficacy assessments

Efficacy assessments included the Eczema Area and Severity Index (EASI) score, a validated composite score of body surface area (BSA) from four regions (head and neck, upper limbs, trunk and lower limbs) and a physician's assessment of erythema, edema/induration/papulation, excoriation and lichenification on a 4-point scale ("absent" to "severe").¹³ The total score ranged from 0 (clear) to 72 (very severe). Patients' assessment of overall response (ranging from "much worse" to "much better") and intensity of itch using a Visual Analog Scale from 1 to 10 were also assessed.

Bacteriological assessments

Quantitative bacterial cultures were done by taking swabs from the worst affected sites at baseline/day 1, week 4 and week 8/end of treatment using a sterile cotton swab. The swabs were sampled over a standard area of 1 cm × 1 cm and directly plated onto 8.5-cm diameter contact plates. The plates contain cysteine, lactose, electrolyte-deficient agar which gives good colony differentiation of *S. aureus* and prevents swarming of *Proteus* spp. After aerobic overnight incubation at 37°C, the growth of *S. aureus* was identified. *S. aureus* density was determined by counting the number of colonies of *S. aureus* per contact plate. The density of *S. aureus* was expressed as colony-forming units/cm².

Safety assessments

Safety assessments were based on clinical adverse events reported by patients or observed by the physician.

Statistical analysis

Statistical analyses were done using the Statistical Package for Social Science version 16.0 (SPSS, Chicago, IL, USA). All statistical tests were two-sided, with a significance level of $P < 0.05$. Demographic information was summarized using descriptive statistics. For efficacy end-points, a paired Student's *t*-test was used to evaluate effects before and after treatment. The independent Student's *t*-test was used to compare between categorical and continuous data and the χ^2 -test to compare between two groups of categorical data.

RESULTS

Forty-two patients were recruited, of which 36 patients completed the 2-month study (Fig. 1). Baseline demographic data showed no significant difference between the two study arms (Table 1). All the patients were on emollients and the most potent topical corticosteroid used in this cohort was betamethasone valerate ointment 0.05% (Fig. 2).

Efficacy assessments

EASI score. At 2 months, there was a significant difference between the treatment and placebo groups ($P = 0.02$). Patients in the treatment group showed a significant reduction in the EASI scores at both 1 and 2 months ($P < 0.001$; Fig. 3). Scores for erythema, papulation, lichenification and excoriation showed a significant improvement in the treatment arm compared to placebo over the upper limbs, trunk and lower limbs at 2 months. Despite showing improvement over time, head and neck scores were not statistically significantly when compared with placebo. Figure 4 shows an example of clinical improvement in a study patient. When divided into different age groups (Table 2), the baseline EASI scores for all groups were not significantly different, except for those aged 12–17 years where the mean baseline EASI score was lower at 16.0 ± 1.4 . However, at 2 months, the EASI scores showed significant reduction from baseline across all age groups in the treatment arm.

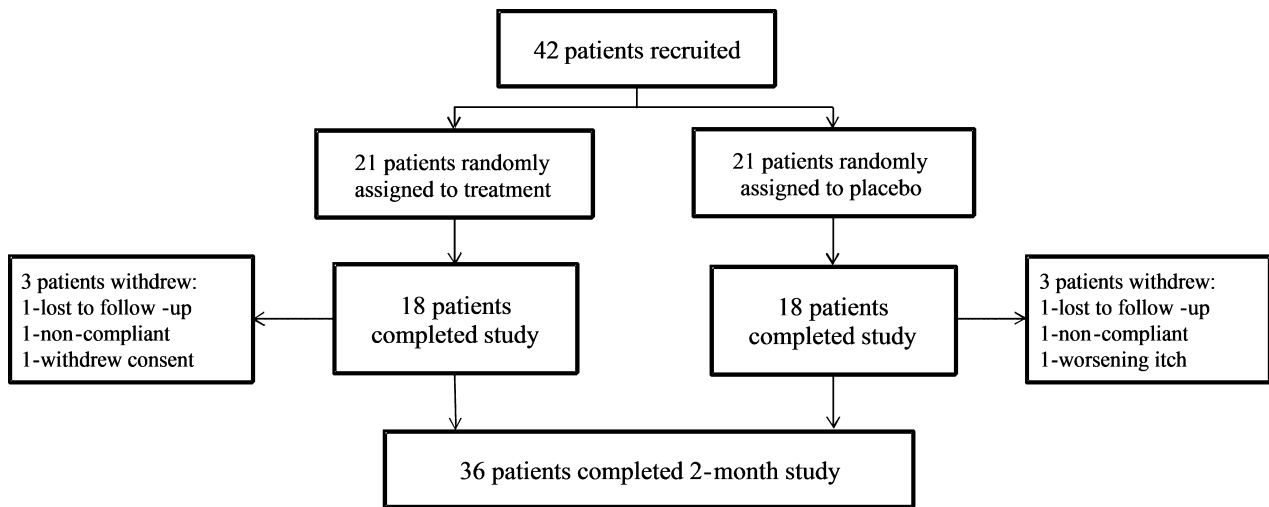


Figure 1. Patient enrolment.

Table 1. Baseline demographic data

Sample size, <i>n</i> (total <i>n</i> = 36)	Treatment (<i>n</i> = 18)	Placebo (<i>n</i> = 18)	<i>P</i> -value
Age, years			
Mean ± SD	11.1 ± 5.8	12.5 ± 8.0	0.54
Range	4.0–24.0	3.0–30.0	
Sex (%)			
Male	4 (22)	7 (38.9)	0.47
Female	14 (77.8)	11 (61.1)	
Ethnicity (%)			
Malay	11 (61.1)	13 (72.2)	0.68
Chinese	4 (22.2)	4 (22.2)	
Indian	2 (11.1)	1 (5.6)	
Others	1 (5.6)	0 (0)	
EASI score			
Mean ± SD	50 ± 18.1	53.1 ± 19.9	0.63
Range	25.0–82.0	20.0–83.0	
Body surface area (%)			
Mean ± SD	50 ± 18.1	53.1 ± 19.9	0.63
Range	25.0–82.0	20.0–83.0	
Itch score			
Mean ± SD	6.3 ± 1.9	6.1 ± 1.0	0.67
Range	3.0–10.0	3.0–10.0	

EASI, Eczema Area and Severity Index; SD, standard deviation.

BSA affected

Patients in the treatment arm showed greater reduction of mean BSA affected from baseline at both 1 and 2 months ($P < 0.001$). There was significant difference between the treatment and placebo arms at 2 months ($P = 0.002$; Fig. 5).

Bacteriological assessment

At baseline, 94.4% of patients cultured *S. aureus* from lesional skin. Of these, 61.1% cultured *S. aureus* only and 33.3% had mixed growth of *S. aureus* and other organisms such as *Strep-*

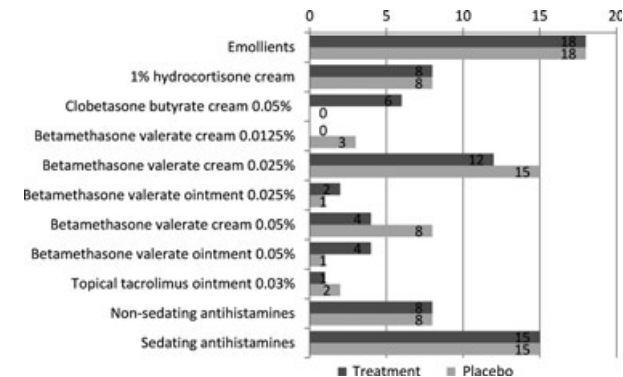


Figure 2. Topical treatment at baseline.

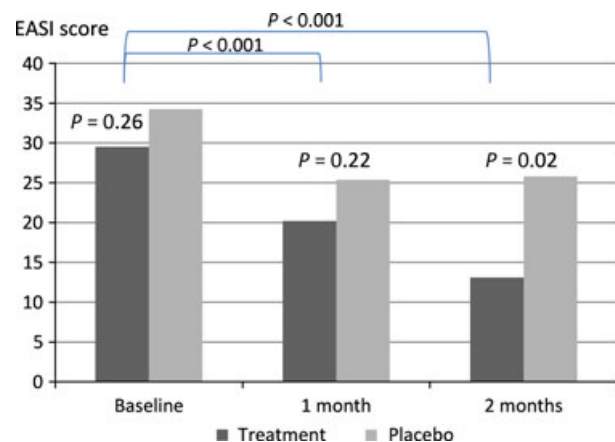


Figure 3. Eczema Area and Severity Index (EASI) scores.

tococcus, Gram-negative rods (pseudomonas) and Gram-positive rods of bacillus species and yeasts. Two patients did not yield any organisms at baseline.



Figure 4. (a) Improvement of eczema over the trunk and upper limbs. (b) Improvement of eczema over the back.

Table 2. EASI scores before and after bleach baths according to age groups

<i>n</i> = 18 Age groups (years)	EASI score (mean $\pm$ SD)		
	At baseline	At 1 month	At 2 months
0–5	34.7 $\pm$ 11.7	26.0 $\pm$ 9.5	15.4 $\pm$ 7.1
6–11	31.5 $\pm$ 7.5	21.1 $\pm$ 14.5	15.1 $\pm$ 9.3
12–17	16.0 $\pm$ 1.4	12.2 $\pm$ 8.1	6.4 $\pm$ 2.3
18–23	35.3 $\pm$ 9.9	20.6 $\pm$ 10.4	16.4 $\pm$ 7.6
24–30	40.7	27.1	10.4

EASI, Eczema Area and Severity Index; SD, standard deviation.

In the treatment group, there was a 41.9% reduction in *S. aureus* density at 1 month, and a continued reduction to 53.3% 2 months after baseline (Fig. 6). Although there was a reduction in *S. aureus* density with time, this was not statistically significant when compared to placebo.

Itch scores. Both treatment and placebo groups showed a reduction in itch scores over time (Fig. 7). There was no significant difference between treatment and placebo groups at either 1 or 2 months. However, in the treatment group, there was significant reduction in the itch scores at 2 months from baseline ($P = 0.02$).

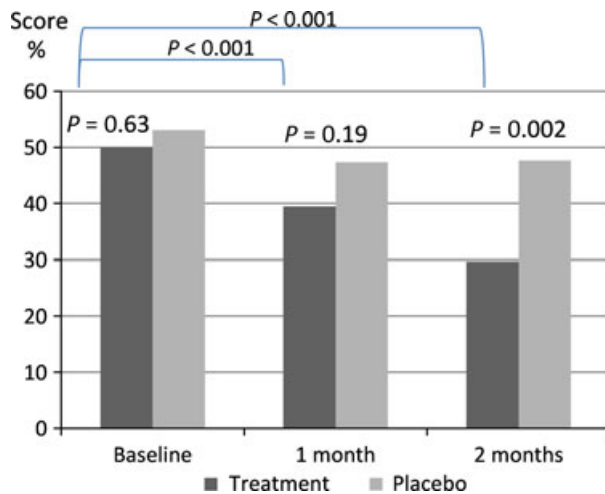


Figure 5. Body surface area affected.

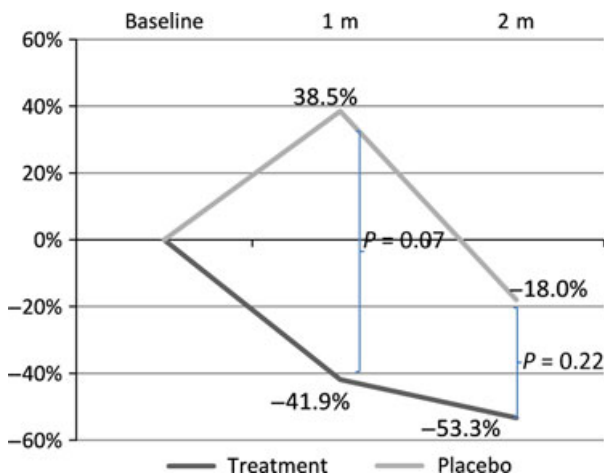


Figure 6. Percentage change in mean bacterial density.

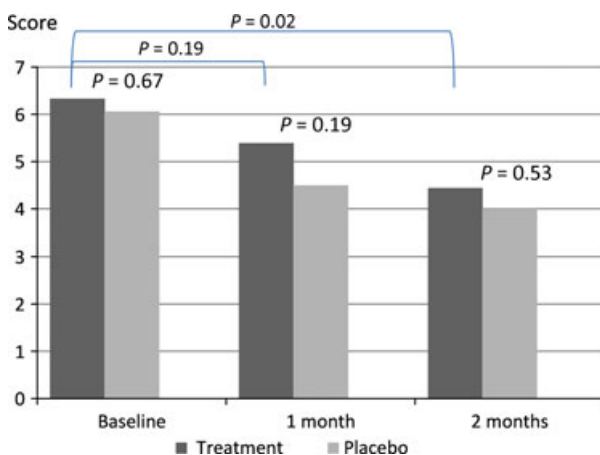


Figure 7. Itch scores.

Patients' overall assessment of response

After 1 month, six patients in the treatment group reported that their AD was "slightly better" compared to four patients in the placebo group; while after 2 months, 11 patients in the treatment group reported their skin being "much better" and "better" compared to nine patients in the placebo group. Three patients in the placebo group reported that their AD was "slightly worse" (two patients after 1 month, and one after 2 months), while no patients in the treatment group reported worsening of their skin condition (Fig. 8). There were no statistically significant differences between treatment and placebo groups at either 1 or 2 months.

Safety assessments

Five out of 18 (27.8%) patients in the treatment group experienced side-effects of burning/stinging (two patients) and dry skin (three patients) which were mild in intensity. Similarly, in the placebo group, five patients also experienced side-effects of mild burning/stinging and dry skin.

DISCUSSION

The results of this study demonstrate the efficacy and safety of bleach baths in patients with moderate to severe AD. Efficacy was demonstrated clinically using the EASI scores. The results showed a significant reduction in EASI scores in the treatment arm apparent at 1 month and a significant difference between treatment and placebo arms at 2 months. The data suggests that diluted sodium hypochlorite baths clinically improve AD after 1 month, with continued improvement of the EASI scores after 2 months of treatment. Other factors such as topical or oral treatments which could influence eczema severity were kept as similar as possible. All the patients were trained how

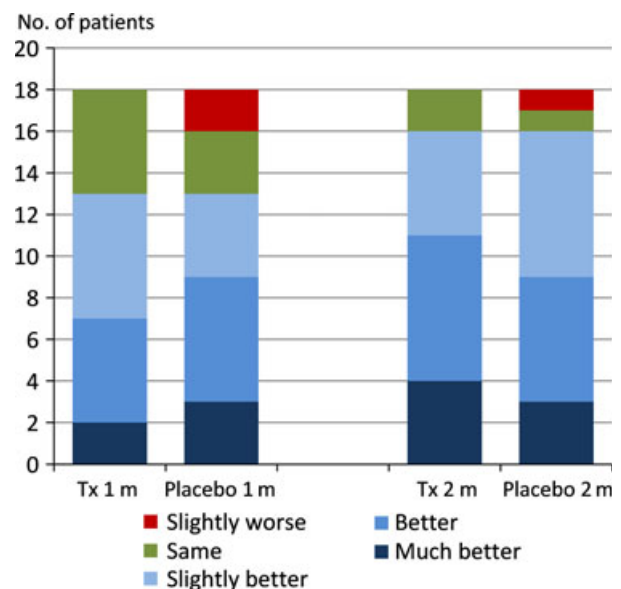


Figure 8. Patients' overall assessment of response.

to prepare and use the baths and were told to continue application of their usual topical treatment. There was no addition of any new topical or oral medication to their current regimen and all patients were using aqueous cream as soap. The most potent topical corticosteroid used in this cohort of patients was betamethasone valerate ointment 0.05% (half strength), which was part of the usual treatment in five patients.

The areas of the body which were submerged in the baths, such as the upper limbs, trunk and lower limbs, showed a reduction in the EASI scores with significant difference between treatment and placebo groups in the various clinical parameters at 2 months. The mean EASI scores for erythema, papulation, excoriation, ooze and lichenification over the head and neck showed improvement over time in the treatment group, but this was not statistically significant when compared to placebo. A likely explanation for this is because patients were instructed to soak in the baths from the neck down, therefore, these areas were only partially submerged. Areas such as the upper limbs, trunk and lower limbs which were fully submerged in the baths showed a greater and statistically significant improvement. In the treatment group, there was also a significant reduction in the percentage BSA affected over time with significant differences between treatment and placebo groups at 2 months. The results showed similar improvement in all four individual body areas analyzed. This trend is consistent with the improvement in the EASI scores seen clinically. Bleach baths seemed to be beneficial across all age groups, in children as well as adults, as seen in the significant reduction in EASI scores in the treatment arm.

At baseline, 94% of patients yielded *S. aureus* from lesional skin, which is consistent with other studies, where more than 90% of patients with AD are colonized with *S. aureus* compared with 5% in normal individuals.^{3,4} The study by Huang *et al.*¹⁰ had a *S. aureus* colonization rate of 87% over lesional skin. Although most cultures in the treatment group at 1 month and 2 months continued to yield *S. aureus*, there was a reduction in the density of the organism over time, although this was not statistically significant. There was also no statistical difference in colony counts between treatment and placebo groups at either 1 or 2 months. However, there was a significant clinical improvement in the patients, which is consistent with a similar study by Huang *et al.*¹⁰

In vitro studies have showed that sodium hypochlorite at various concentrations was an effective antimicrobial agent and was able to eradicate *S. aureus* and other bacterial strains.⁷ However, in patients in real clinical situations, the sodium hypochlorite baths were not able to eradicate the bacteria entirely although there was a reduction in the density. One possible explanation for this is our study did not address the nasal carriage of *S. aureus* and this may have been a potential source of re-colonization of the skin. Another study using chlorhexidine whole-body wash to reduce MRSA colonization also showed that although chlorhexidine wash was effective in eradicating MRSA in the nose and mouth, these patients still had repeated colonization of the skin.¹⁴ In addition, potential re-colonization of the skin in our cohort of patients might have been caused by environmental sources or

other unrecognized carriers. Perhaps a longer duration of treatment and follow up, with a greater number of patients may give a clearer picture of the trend of bacterial density over time.

Itch scores also showed a significant reduction in mean scores from baseline at 2 months in the treatment group. Patients in the placebo group also showed some improvement in itch scores and the results were not significantly different between the treatment and placebo groups. This lack of clear efficacy may be due to patient variability. It is well known that itch is a very subjective sensation and even with clinical improvement, a small area of eczema may itch badly depending on the individual patient's perception of severity of itch. Again, greater patient numbers and longer study duration may yield clearer results.

With regards to the patient's overall assessment of response, in general, patients in the treatment group reported their skin to be better compared to patients in the placebo group. Surprisingly, in the placebo group, more patients reported that their AD was "better" and "much better" after 1 month and "slightly better" after 2 months than at baseline. This may be partly due to the Hawthorne effect, where patients perceive their skin to be better because they might have been more diligent in applying their topical treatment throughout the study period. Interestingly, although the patients in the placebo group reported that their skin was better, the clinical assessment of EASI scores did not reflect this. In addition, three patients in the placebo group reported their skin to be "slightly worse", while none in the treatment group noted worsening of their eczema.

In general, diluted bleach baths were well tolerated with the only adverse events experienced being mild burning/stinging and dry skin. The same number of patients experienced adverse events in both treatment and placebo groups. No patient withdrew from the treatment arm because of intolerance to the baths. In a similar study by Huang *et al.*,¹⁰ they reported only one patient in the treatment arm who had itching and skin irritation.

A limitation of this study includes the relatively short duration of treatment and follow up (2 months). In addition, patients administered the baths at home and not in a controlled environment under supervision. Despite extensive education on dilution and bathing regime, there might have been possible issues of compliance, proper dilution of baths and timing between baths which could have influenced the results. In addition, our study did not look into the nasal carriage of *S. aureus* which may be a potential source of re-colonization for some patients with AD. However, a larger study with greater patient numbers evaluating the suppression of *S. aureus* in parallel would add considerably to determining the true treatment effect of sodium hypochlorite baths.

Diluted sodium hypochlorite baths twice a week as an adjunctive treatment in patients with moderate to severe AD decreases the clinical severity by reducing the EASI scores, BSA affected and itch scores. In addition, sodium hypochlorite baths may reduce *S. aureus* colony counts in these patients. The baths were also well tolerated, with a similar incidence of

mild adverse events in both treatment and placebo groups which improved over time. Similar studies involving a larger number of patients conducted over longer treatment periods may provide clearer information on the efficacy and safety of sodium hypochlorite baths.

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CONFLICT OF INTEREST: None.

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