

SHORT REPORT

Efficacy of sodium hypochlorite (bleach) baths to reduce *Staphylococcus aureus* colonization in childhood onset moderate-to-severe eczema: A randomized, placebo-controlled cross-over trial

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Abstract

Background: *Staphylococcus aureus* (*S. aureus*) colonization/infection is an important factor in the pathophysiology of atopic dermatitis (AD). Clinical trials have demonstrated conflicting efficacy of diluted bleach baths in treating moderate-to-severe AD. We conducted a double-blinded, placebo-controlled (water), cross-over trial among patients with AD to investigate the efficacy of bleach baths in reducing *S. aureus* colonization and AD severity. **Method:** In this cross-over trial, 40 patients with moderate-to-severe AD were randomized to receive twice-weekly bleach and water baths, each for four consecutive weeks with a four-week wash-out period in between. Condition of *S. aureus* growth and SCORing Atopic Dermatitis index (SCORAD) were recorded at baseline and four-weekly intervals. Patients' blood was collected in first and second visits to investigate blood eosinophil count, serum levels of total IgE and specific IgEs against *Staphylococcal* enterotoxins A and B. In every visit, Children Dermatology Life Quality Index (CDLQI), skin hydration (SH), transepidermal water loss (TEWL) and usage frequency of prohibited medications (topical antibiotic, steroid and oral antihistamine) were recorded. **Results:** All 40 patients completed the trial, but 14 were non-adherent. By intention-to-treat (ITT) approach, comparing with water baths, bleach baths conferred no significant efficacy in CDLQI, SH, TEWL, blood eosinophil count, total IgE and the two specific IgEs over four weeks. Water baths caused a greater reduction in affected area of SCORAD than bleach baths (-5.7 ± 15.4 for water vs. 0.6 ± 12.4 for bleach; $p = 0.03$) by ITT, and in objective SCORAD and affected area ($p < 0.05$) from per-protocol approach. Bleach baths reduced topical corticosteroid use (mean difference = 1.1 ± 2.6 days/week; $p = 0.014$) and topical antibiotic use (mean difference = 1.0 ± 2.8 days/week; $p = 0.044$) in within-group analysis. **Conclusions:** This study demonstrated that a four-week, twice-weekly regime of diluted bleach baths is not more useful than water baths in reducing *S. aureus* colonization/infection and improving AD. A longer treatment period is needed to evaluate if the short treatment duration was the main cause for the discrepancy in outcome from other bleach-bath trials. The usage of a portable bath tub obviates the problems associated with unavailability of bathing facilities in some families.

Keywords

Atopic eczema, bleach bath, quality of life, randomized cross-over trial, *S. aureus*, SCORAD, *Staphylococcal* enterotoxin

History

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Introduction

Atopic dermatitis (AD) is a common chronic relapsing disease in children associated with allergy and atopy (1). Children with AD often have significant impaired quality of life as a result of pruritus, scratching and sleep disturbance (2–7). The pathophysiology is complex and involves genetic, immune and infectious components (1,8,9). Many children with moderate-to-severe disease are colonized and/or infected with *Staphylococcus aureus* (*S. aureus*), especially during episodes of disease

exacerbation (1,10–12). The enterotoxins, such as *Staphylococcal* enterotoxins A (SEA) and B (SEB), produced by the pathogen act as superantigens, engender and inhibit the activity of T regulatory cells that normally control inflammation, and generate a state of steroid resistance that confounds treatment of AD (13–17). Antibiotic therapy against *S. aureus* is an important component of treatment for AD. However, continuing use of antibiotic therapy, whether systemic or topical, can increase the risk of bacterial resistance. Bleach (sodium hypochlorite NaOCl) has been used in medicine as a disinfectant and antiseptic since the eighteenth century (18). Dilute NaOCl has antimicrobial activity against *S. aureus*, including MRSA. Bleach baths have broad spectrum of action, and do not lead to development of antimicrobial resistance (19,20). In a randomized trial, Huang et al. demonstrated that bleach baths and intranasal mupirocin

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treatment improve eczema severity without evolution of resistant strains of *S. aureus* (21). Nevertheless, the study was weakened by the usage of oral antibiotics, not documenting the exact amount of topical steroid usage, and not using intention-to-treat (ITT) approach. This study evaluated the effects of bleach bathing on *S. aureus* colonization/infection, eczema severity, skin biophysiology, blood markers and patient acceptability in childhood-onset eczema.

Patients and methods

Subject recruitment

Index cases were children suffering from AD, aged 4–18 years old, who were managed in outpatient clinics of our university-affiliated teaching hospital. The diagnosis of AD was made according to criteria proposed by Hanifin and Rajka (22). The disease activity of AD is divided into three groups according to the objective criteria (extent and intensity of the lesions) of SCORing Atopic Dermatitis index (SCORAD). In brief, “mild” is the group with objective SCORAD <15 points; “moderate” is defined as 15–40 points; “severe” is defined as >40 points (23,24). Only patients with moderate-to-severe disease and previous documentation of *S. aureus* colonization (positive skin swab cultures of *S. aureus* observed in the most recent visit from the hospital database) were recruited. Exclusion criteria included current or recent use (within the past four weeks) of oral antibiotics, intercurrent illness for two weeks prior to study, and coexisting skin diseases other than eczema. Ethical approval and informed written consent was obtained from the patients’ parents prior to study.

Treatment protocol

A three-month single-centre, randomized cross-over, double-blinded and placebo-controlled clinical trial was conducted.

Patients were assigned randomly through computerized randomization (sealed envelope using numbers) generated by a research staff (not involved in the clinical management and patient assessment), to the treatment or placebo study arm (Figure 1). Patients were instructed to add either 83 ml of 6% bleach from a prepared bottle (final concentration: 0.005%; treatment arm) or water (placebo arm) to 100 L of water; the amount of administered bleach solution or water was adjusted by the family on the basis of the bathtub size and estimated height of bathtub water. Patients were instructed to bathe in the dilute bleach baths or placebo baths for 10 min 2–3 times weekly. Patients bathing fewer than two times per week were considered non-adherent. Each patient was maintained a stable regimen of emollient therapy throughout the three-month study period. New medications were prohibited. Parents and patients were requested not to use any prior medications such as topical corticosteroid and oral antihistamine if possible, but the amounts of usage would be recorded if used. Each patient underwent a four-week treatment with bleach baths or placebo and wash-out period of four weeks followed by four weeks of cross-over treatment. Bleach and water with patient identification numbers were dispensed in identical opaque bottles with the same brand-name labels (Figure 2). Investigators were blinded to the contents of the bottles. Dispensing of these items sequentially, according to patient identification numbers will be performed by a research assistant in a separate room from the principal investigator who assesses the patients. Neither patients nor clinicians knew the patients’ assigned study arm. These bottles were brown plastic bottles and the selected dilution was pretested by the pharmacist so that the colour and odour was similar. However, patients and/or family members might differentiate the pure bleach container from the water container on the basis of odour and were instructed at the beginning not to disclose their suspicions to the investigators. Bathing in the dilute bleach baths was not associated with any odour of bleach, and investigators were not able to distinguish study arms during examinations.

Figure 1. Flow chart: randomized control cross-over trial.

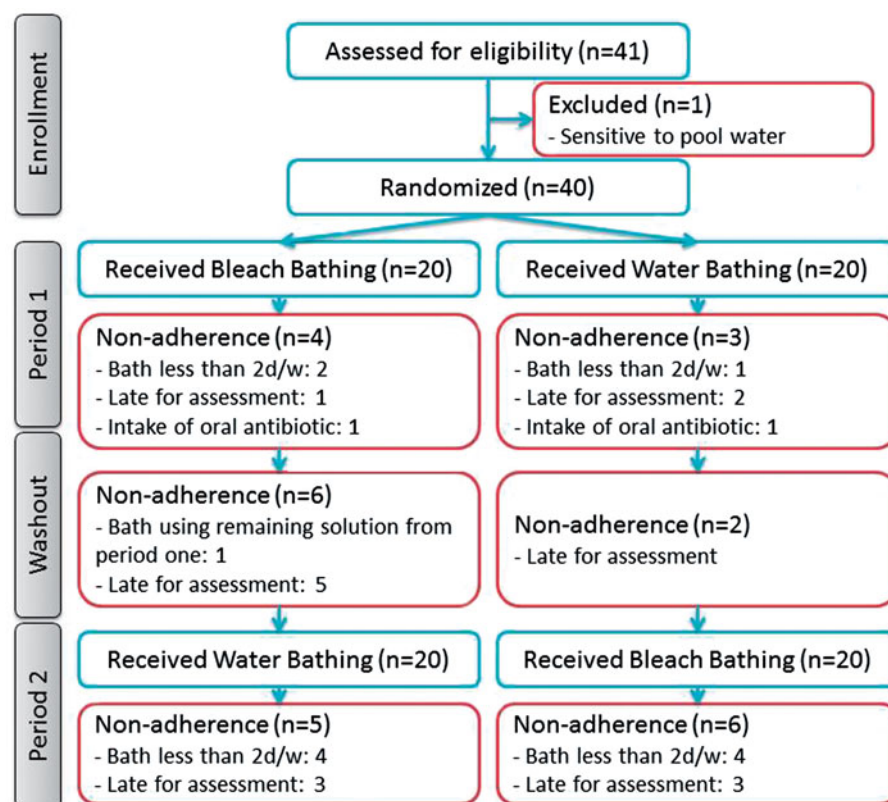


Figure 2. Bleach, placebo and bath basin.

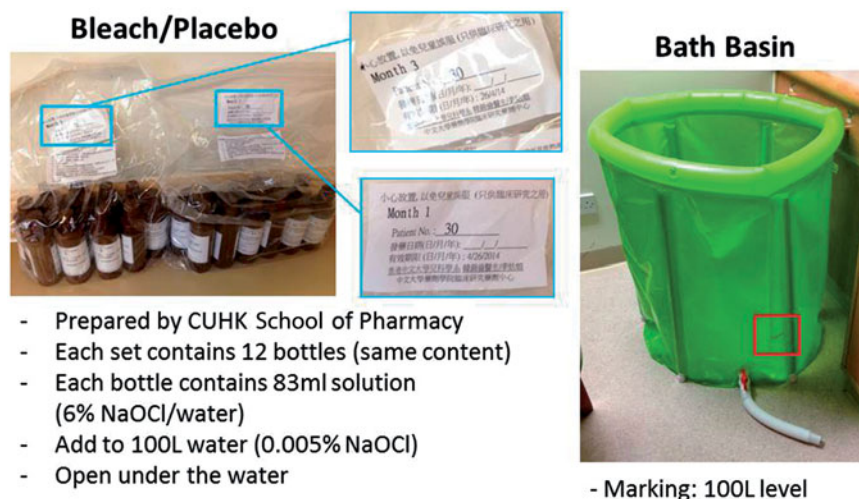


Table 1. Baseline characteristics of 40 patients in the randomized control cross-over trial.

Demographic parameters	Both arms (n = 40)	Arm 1 (n = 20) Bleach → Water	Arm 2 (n = 20) Water → Bleach	p Value Arm 1 vs. Arm 2
Age at visit 1 (y)	12.1 ± 4.2	11.9 ± 4.2	12.4 ± 4.3	0.685
Male (n (%))	23 (57.5)	9 (45.0)	14 (70.0)	0.110
AD onset ≤1 year old (n (%))	27 (67.5)	16 (80.0)	11 (55.0)	0.091
Personal asthma (n (%))	19 (47.5)	9 (45.0)	10 (50.0)	0.752
Personal allergic rhinitis (n (%))	28 (70.0)	14 (70.0)	14 (70.0)	>0.999
Paternal atopy (n (%))	25 (62.5)	14 (70.0)	11 (55.0)	0.327
Maternal atopy (n (%))	10 (25.0)	6 (30.0)	4 (20.0)	0.465
Sibling atopy (n (%))	22 (75.9) (n = 29)	12 (85.7) (n = 14)	10 (66.7) (n = 15)	0.390*
Dust mite sensitization (n (%))	37 (94.9) (n = 39)	19 (95.0) (n = 20)	18 (94.7) (n = 19)	>0.999*
Food allergen sensitization (n (%))	31 (79.5) (n = 39)	17 (85.0) (n = 20)	14 (73.7) (n = 19)	0.451*
Medication use				
Topical emollient ≥3 times/day (n (%))	26 (65.0)	15 (75.0)	11 (55.0)	0.185
Topical antibiotic (days/week) (IQR)	0.5 (6.8)	1.5 (7.0)	0 (3.8)	0.231**
Topical corticosteroid (days/week) (IQR)	5.0 (5.0)	6.0 (4.0)	4.5 (6.0)	0.478**
Topical immunomodulant, days/week (IQR)	0.5 (3.0)	0.5 (3.0)	0.5 (3.0)	0.989**
Oral antihistamine, days/week (IQR)	3.5 (7.0)	4.0 (7.0)	2.5 (7.0)	0.738**
Disease parameters				
Condition of <i>S. aureus</i> growth (n (%))#				
No	4 (10.0)	2 (10.0)	2 (10.0)	0.338*
Scanty	18 (45.0)	7 (35.0)	11 (55.0)	
Moderate	15 (37.5)	8 (40.0)	7 (35.0)	
Heavy	3 (7.5)	3 (15.0)	0 (0.0)	
SCORAD				
Objective SCORAD	44.0 ± 11.0	44.1 ± 13.1	43.9 ± 8.8	0.971
Affected area, %	54.7 ± 14.8	55.0 ± 16.8	54.4 ± 12.8	0.891
Intensity	9.5 ± 2.5	9.5 ± 2.9	9.5 ± 2.0	>0.999
Pruritus	6.7 ± 1.9	6.9 ± 1.9	6.6 ± 1.9	0.560
Sleep loss	5.9 ± 2.8	5.9 ± 2.9	6.0 ± 2.8	0.911
CDLQI (IQR)	10.0 (8.0)	9.0 (8.0)	11.5 (9.0)	0.127**
SH	32.8 ± 13.5	30.2 ± 13.1	35.4 ± 13.7	0.227
TEWL	12.1 ± 1.7	12.8 ± 1.8	11.4 ± 1.2	0.006
Blood markers				
White blood cell count, 10 ⁹ /l	8.3 ± 1.6	8.8 ± 1.9	7.7 ± 0.9	0.036
log (eosinophil count, %)	1.0 ± 0.2	1.0 ± 0.2	1.0 ± 0.2	0.938
log (total IgE count, kU/l)	3.8 ± 0.5	3.9 ± 0.4	3.7 ± 0.6	0.116
Anti-SEA IgE (kU/l) (IQR)	0.9 (2.7) (n = 37)	0.6 (2.0) (n = 18)	1.5 (3.4) (n = 19)	0.298**
Anti-SEB IgE (kU/l) (IQR)	0.9 (3.1) (n = 37)	1.1 (2.8) (n = 18)	0.8 (2.1) (n = 19)	0.518**

The values highlighted in bold were statistically significant ($p < 0.05$).

*Fisher's Exact test.

**Mann-Whitney *U*-test.

#Condition of *S. aureus* growth at any one of two sites with the highest *S. aureus* colonization.

Primary and secondary study outcomes

The primary outcome in this study was to compare the presence of *S. aureus* at right antecubital fossae and most severely infected or eczematous lesions before and following each treatment period.

Swab for bacteriology culture will be obtained from the two sites to document if *S. aureus* colonization/infection is present and to evaluate if resistant organisms may emerge (see previous publication for procedure) (10). These results were not analysed until the research project was completed.

Table 2. Changes from baseline (ITT).

Global acceptability of treatment (GAT)	Bleach (n = 39)	Water (n = 39)	Between-treatment difference	p Value
Number of patients scoring 3 or 4 on GAT scale (n (%))#	29 (74.4)	26 (66.7)	/	0.508
Medication use	Bleach (n = 40)	Water (n = 40)	Between-treatment difference	p Value
Apply topical emollient ≥ 3 times/day (n (%))	26 (65.0)	30 (75.0)	/	0.289
Mean changes of topical antibiotic (days/week)	-0.96 ± 2.77	0.00 ± 2.68	$-0.96 [-2.45 \text{ to } 0.53]$	0.366
Mean changes of topical corticosteroid (days/week)	-1.06 ± 2.55	-0.49 ± 3.07	$-0.58 [-1.97 \text{ to } 0.82]$	0.687
Mean changes of topical immunomodulant (days/week)	-0.59 ± 2.43	0.03 ± 1.95	$-0.61 [-1.71 \text{ to } 0.49]$	0.275
Mean changes of oral antihistamine (days/week)	-0.84 ± 2.59	0.04 ± 2.77	$-0.88 [-2.28 \text{ to } 0.53]$	0.180
Disease parameters				
Condition of <i>S. aureus</i> growth after bathing (n (%))+				
No	13 (32.5)	9 (22.5)	/	0.090
Scanty	12 (30.0)	19 (47.5)		
Moderate	13 (32.5)	7 (17.5)		
Heavy	2 (5.0)	5 (12.5)		
Change in <i>S. aureus</i> growth (n (%))+				
Better	10 (25.0)	11 (27.5)	/	0.958
Same	21 (52.5)	20 (50.0)		
Worse	9 (22.5)	9 (22.5)		
Mean changes of SCORAD				
Objective SCORAD	-0.50 ± 10.63	-3.95 ± 10.54	$3.45 [-1.66 \text{ to } 8.55]$	0.060
Affected area, %	0.56 ± 12.39	-5.74 ± 15.43	$6.30 [-0.36 \text{ to } 12.96]$	0.032
Intensity	-0.18 ± 2.50	-0.80 ± 2.39	$0.63 [-0.54 \text{ to } 1.79]$	0.158
Pruritus	-0.20 ± 2.29	-0.03 ± 1.54	$-0.18 [-1.13 \text{ to } 0.78]$	0.539
Sleep loss	-0.23 ± 2.44	-0.25 ± 2.38	$0.03 [-1.04 \text{ to } 1.09]$	0.813
Mean changes of CDLQI	-0.53 ± 3.87	-1.43 ± 4.18	$0.90 [-1.32 \text{ to } 3.12]$	0.546
Mean changes of SH	-0.74 ± 13.66	-3.13 ± 13.22	$2.39 [-3.48 \text{ to } 8.26]$	0.436
Mean changes of TEWL	-0.98 ± 2.17	-0.19 ± 2.50	$-0.79 [-1.93 \text{ to } 0.35]$	0.285
Blood markers	Bleach (n = 19)	Water (n = 19)	Between-treatment difference	p Value
White blood cell count ($10^9/l$)	-0.45 ± 1.50	0.26 ± 2.08	$-0.71 [-1.90 \text{ to } 0.48]$	0.525
Eosinophil count (%)	-0.53 ± 4.70	-2.05 ± 5.34	$1.53 [-1.78 \text{ to } 4.83]$	0.795
Total IgE count (kU/l)	-1447 ± 4722	-549 ± 1376	$-897 [-3243 \text{ to } 1449]$	0.751
Anti-SEA IgE (kU/l)	-0.12 ± 0.33 (n = 18)	-0.16 ± 1.01	$0.04 [-0.47 \text{ to } 0.55]$	0.730
Anti-SEB IgE (kU/l)	0.11 ± 0.89 (n = 18)	0.19 ± 0.79	$-0.08 [-0.64 \text{ to } 0.49]$	0.271

The values highlighted in bold were statistically significant ($p < 0.05$).

*Mann–Whitney *U*-test.

#The proportions of patients with GAT of “3 = good” or “4 = very good” were compared.

+*S. aureus* growth at any one of two sites with the highest *S. aureus* colonization was selected for presentation and comparison.

Secondary outcomes will include disease severity (SCORAD and Objective SCORAD), *S. aureus* antimicrobial resistance patterns, dermatologic parameters (skin hydration (SH) and transepidermal water loss (TEWL)), blood markers (white blood cell, eosinophil, total IgE and specific IgEs against SEA and SEB), topical steroid usage, quality of life (Children Dermatology Life Quality Index, CDLQI) and patient acceptability of treatment according to our established protocol (3,10,25–27). Adverse effects such as allergic reactions (acute contact dermatitis, urticaria and anaphylaxis) and compliance to treatment were recorded.

Sample size

We adopted a cross-over approach and recruited 40 patients with moderate-to-severe eczema and signs of active bacterial skin infection (weeping, crusting and/or pustules). Exclusion criteria included current or recent use (within the past four weeks) of oral antibiotic preparations. The target sample size (40 patients) was determined by specifying 80% power to detect an estimated 31% reduction in the number of patients carrying *S. aureus* in the treatment (bleach) group vs. no reduction in the placebo (water) group with a significance level of 0.05. We determined the desired reduction in *S. aureus* carriage percentage by using the results of a previous antibiotic/corticosteroid cream study conducted in the same paediatric outpatient clinic that used *S. aureus* growth as one of the outcome measures for moderate-to-severe AD (28).

Statistical analysis

Numerical data will be expressed in either mean and SD or median and IQR as specified. Independent samples *t*-test and

Pearson’s chi-squared test were used to compare, respectively, the baseline numerical variables and the before-treatment categorical values between patients switching from bleach to water baths and those switching from water to bleach baths unless otherwise stated; while Wilcoxon signed-rank test and McNemar’s test were used to compare, respectively, the changes in numerical variables and the after-treatment categorical values between the bleach and water bathing groups. All comparisons will be made two-tailed, and *p* values less than 0.05 considered statistically significant.

Results

Forty patients took part in the cross-over trial between December 2012 and November 2014 (Figure 1). All 40 patients completed the trial, but non-adherence was noted in 14 patients. Non-adherence was defined as using baths less than two times per week or delayed return for assessment for more than 10 days (i.e. come to visit after 40 days since the last visit for the bathing period), or intake of oral antibiotic during the bathing period. There was no difference in their baseline characteristics (Table 1). By ITT approach, *S. aureus* (at either the right antecubital fossae or the most severe site) was isolated in 80% and 85% of patients before bleach and water baths; 25% and 28% of patients had reduced *S. aureus* growth after bathing, respectively ($p = 0.958$). There was no significant reduction in the colony counts after bathing for both two bathing groups in within-group analysis. No significant difference was observed in the antibiotic resistance pattern between *S. aureus* isolated before and after bathing for both two groups. Comparing with water baths, bleach baths conferred no significant efficacy in CDLQI, SH,

Table 3. Changes from baseline as per protocol approach ($n = 26$).

Global Acceptability of Treatment (GAT)	Bleach ($n = 26$)	Water ($n = 26$)	Between-treatment difference	p Value
Number of patients scoring 3 or 4 on GAT scale (n (%))#	19 (73.1)	17 (65.4)	/	0.727
Medication use				
Apply topical emollient ≥ 3 times/day (n (%))	16 (61.5)	18 (69.2)	/	0.687
Mean changes of topical antibiotic (days/week)	-1.40 ± 2.78	0.27 ± 2.51	$-1.67 [-3.39 \text{ to } 0.04]$	0.093
Mean changes of topical corticosteroid (days/week)	-1.73 ± 2.43	-0.40 ± 3.50	$-1.33 [-3.39 \text{ to } 0.74]$	0.255
Mean changes of topical immunomodulant (days/week)	-0.92 ± 2.40	0.00 ± 2.23	$-0.92 [-2.44 \text{ to } 0.60]$	0.247
Mean changes of oral antihistamine (days/week)	-1.00 ± 2.81	0.69 ± 2.87	$-1.69 [-3.51 \text{ to } 0.13]$	0.079
Disease parameters				
Condition of <i>S. aureus</i> growth after bathing (n (%))+				
No	9 (34.6)	8 (30.8)	/	0.186
Scanty	5 (19.2)	11 (42.3)		
Moderate	11 (42.3)	5 (19.2)		
Heavy	1 (3.8)	2 (7.7)		
Change in <i>S. aureus</i> growth (n (%))+				
Better	5 (19.2)	10 (38.5)	/	0.572
Same	13 (50.0)	10 (38.5)		
Worse	8 (30.8)	6 (23.1)		
Mean changes of SCORAD				
Objective SCORAD	0.98 ± 11.08	-4.66 ± 11.75	$5.64 [-1.24 \text{ to } 12.52]$	0.041
Affected area, %	2.19 ± 12.04	-5.81 ± 15.01	$8.00 [0.15 \text{ to } 15.85]$	0.045
Intensity	0.15 ± 2.59	-1.00 ± 2.68	$1.15 [-0.42 \text{ to } 2.73]$	0.064
Pruritus	0.15 ± 1.67	-0.19 ± 1.02	$0.35 [-0.32 \text{ to } 1.01]$	0.211
Sleep loss	-0.15 ± 1.69	-0.65 ± 2.15	$0.50 [-0.53 \text{ to } 1.53]$	0.245
Mean changes of CDLQI	-0.42 ± 4.26	-1.92 ± 4.66	$1.50 [-1.70 \text{ to } 4.70]$	0.403
Mean changes of SH	-0.33 ± 13.64	-2.12 ± 13.60	$1.80 [-5.19 \text{ to } 8.78]$	0.603
Mean changes of TEWL	-0.94 ± 2.27	-0.44 ± 2.63	$-0.50 [-2.02 \text{ to } 1.02]$	0.703
Blood markers	Bleach ($n = 16$)	Water ($n = 16$)	Between-treatment difference	p Value*
White blood cell count ($10^9/l$)	-0.33 ± 1.56	0.43 ± 2.17	$-0.76 [-2.13 \text{ to } 0.60]$	0.590
Eosinophil count (%)	-1.00 ± 4.10	-1.50 ± 4.82	$0.50 [-2.73 \text{ to } 3.73]$	0.985
Total IgE count (kU/l)	-1493 ± 5109	-533 ± 1494	$-961 [-3762 \text{ to } 1840]$	0.809
Anti-SEA IgE (kU/l)	-0.13 ± 0.34	-0.18 ± 1.11	$0.05 [-0.55 \text{ to } 0.64]$	0.838
Anti-SEB IgE (kU/l)	0.13 ± 0.95	0.15 ± 0.82	$-0.02 [-0.66 \text{ to } 0.62]$	0.381

The values highlighted in bold were statistically significant ($p < 0.05$).

*Mann-Whitney U -test.

#The proportions of patients with GAT of “3 = good” or “4 = very good” were compared.

+*S. aureus* growth at any one of two sites with the highest *S. aureus* colonization was selected for presentation and comparison.

TEWL, WBC, eosinophil, serum levels of total IgE and specific IgEs against SEA and SEB over four weeks. Water baths caused a greater reduction in “affected area” of the SCORAD component score than bleach baths (-5.7 ± 15.4 for water vs. 0.6 ± 12.4 for bleach; $p = 0.032$) by ITT, and in objective SCORAD ($p = 0.041$) and affected area ($p = 0.045$) from per-protocol approach (Tables 2 and 3). By within-group analysis, water baths improved objective SCORAD ($p = 0.003$), affected area ($p = 0.027$) and intensity ($p = 0.021$) of SCORAD, and CDLQI ($p = 0.040$). Bleach and water arms had no difference in frequency of topical emollient, antibiotic, corticosteroid or oral antihistamine use by inter- or intra-group analysis. However, bleach baths reduced topical corticosteroid use (mean difference = 1.1 ± 2.6 days/week; $p = 0.014$) and topical antibiotic use (mean difference = 1.0 ± 2.8 days/week; $p = 0.044$) in within-group analysis. Regression analysis for different variables controlling for age, gender and age of onset demonstrated no difference in outcome measures between the two arms.

Adverse effects were generally mild and included stinging and itch (Table 4), but one patient who had *S. aureus* colonization before and during trial was hospitalized with eczema exacerbation during the placebo phase. Hence, the AE was considered an exacerbation of *S. aureus* infection.

There were in total 14 patients violating the study protocol, half of which were in the arm of receiving placebo after bleach (bleach to placebo arm). In both arms, there was one patient having oral antibiotic intake during his first period bathing. In bleach to placebo arm, two patients had violated the protocol by

Table 4. Adverse effects.

	Bleach ($n = 40$)	Water ($n = 40$)	p Value
Subjects with hospitalization (n (%))	0 (0)	1 (2.5)	/
Subjects with at least one AE (n (%))	8 (20.0)	13 (32.5)	0.227
AEs (n (%))			
Stinging	2 (5.0)	4 (10.0)	0.625
Itch	4 (10.0)	5 (12.5)	>0.999
Dry skin	2 (5.0)	1 (2.5)	>0.999
Erythema	1 (2.5)	1 (2.5)	>0.999
Urticaria	1 (2.5)	1 (2.5)	>0.999
Oozing	1 (2.5)	0 (0)	/
Dizzy	0 (0)	1 (2.5)	/

AE, Adverse event.

One patient was hospitalized during the placebo phase, who had *S. aureus* colonization before and during trial. Hence, the AE was considered an exacerbation of *S. aureus* infection.

both being late for assessment and bathing not accordingly. For the remaining, one had assessment violation (late for assessment), and three had bathing violation, one of which bathed using the remaining bottles of solution obtained from the first bathing period during the wash-out period. In placebo to bleach arm, the patient who had oral antibiotic intake had both assessment and bathing violation as well. For the remaining, three had assessment violation and three had bathing violation.

Patients were asked if they thought the bath was bleach or water, or if they did not know which. Blinding and carryover effects were assessed and considered insignificant.

Discussion

This study demonstrated that a four-week, twice-weekly regime of diluted bleach baths may not be useful in reducing *S. aureus* colonization/infection and improving AD. Conversely, regular water baths improved symptomatology and quality of life, and would be a more efficacious alternative for AD. Our findings are different from two other randomized trials on bleach baths and AD. In the trial by Huang et al., all patients received orally administered cephalexin for 14 days as well as regular nasal mupirocin which could have confounded the seemingly efficacious effects of bleach bathing (21). Our findings are opposite to the findings of a Malaysian study (29). The Malaysian trial had similar sample size but involved more adult patients and took a parallel non-cross-over approach. Possible reasons of the different outcomes may be that adults are often more adherent to treatment and that Malaysia had a warm and humid climate with little seasonality. Non-adherence, namely bathing for less than twice per week or being late for assessment (come to visit after 40 days since the last visit in bathing period), or intake of oral antibiotic, was prevalent among our patients.

The common reasons for bathing violation were the difficulty in bath setup, or other private reasons such as travelling. There was one patient in the bleach to placebo arm bathing not accordingly in the second bathing period because of improvement at that time. There were only two patients violating bathing protocol due to adverse effects observed, one of which experienced itch effect during bleach bathing period, and another one experienced dryness effect and was even hospitalized during water bathing period. The finding that there was no significant difference in the adverse events experienced between the two bathing periods also implied that the irritation potential of the diluted bleach used in our study was low (Table 4).

An updated Cochrane review on interventions to reduce *S. aureus* in the management of atopic eczema failed to find any evidence that commonly used antistaphylococcal interventions are clinically helpful in people with eczema that is not clinically infected (30). The review opined that the significant findings of bleach baths when compared with bathwater alone could have been explained by regression to the mean (30,31).

Blinding and cross-over effects were shown to be insignificant in our study. One merit of our trial is that we took a number of steps to ensure blinding is effective. We used diluted bleach in opaque plastic bottles and asked the parents not to attempt to smell the content in the bottle but to open the bottle underneath water in the bath. In every visit, we recorded the patients' thought about the content in the bottles, namely bleach, placebo or do not know.

Most Hong Kong citizens live in small apartments which do not have bath tubs. We overcame such problem by giving away plastic disposable bath tubs to fit into their bathing areas. The usage of the portable bath tub obviates the problems associated with unavailability of bathing facilities in some families.

S. aureus is an important factor in the pathogenesis of AD, but factors other than this (e.g. SH and inflammatory reactions) may also contribute to the pathogenesis. In our study, although we have not restricted patients' use of their current medications (unethical), their weekly frequency of medication usage such as topical emollient and corticosteroid was clearly recorded and analysed to investigate if the medication usage was significantly different during the two different bathing periods. Also, patients were told to avoid using newly prescribed medications during the whole trial, so as to avoid the confounding effects of other factors.

Since nasal nares are another part of body that *S. aureus* commonly colonizes, the higher chance of *S. aureus* recolonization to skin from the nasal cavity may lead to the reduced treatment effects of bleach baths in our study when compared with the trial by Huang et al. that had used intranasal mupirocin along with bleach baths (21). However, in the Malaysian study, the bleach arm could still achieve better clinical improvements than the placebo arm without the application of intranasal antibiotics (29). Although this finding implies that the recolonization of *S. aureus* from the nasal cavity may only account for a small part of the different results in our study, whether colonization of *S. aureus* in nasal cavity affects the efficacy of bleach baths is still worth to investigate through collecting data of *S. aureus* isolated from there in the future. In a previous study, we documented that moderate-to-heavy growth of *S. aureus* was only present in 22% of nasal swabs (10). Other limitations of this trial are the relative small sample size and short duration of treatment of only four-weeks in each phase.

This study demonstrated that a four-week, twice-weekly regime of diluted bleach baths may not be useful in reducing *S. aureus* colonization/infection and improving AD. Instead, regular water baths would be a more efficacious alternative for AD. A longer treatment period is needed to evaluate if the short treatment duration was the main cause for the discrepancy in outcome from other trials. AD is a complex allergic disease and bleach baths alone as a mean to suppress *S. aureus* colonization is unlikely to be successful.

Declaration of interest

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