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Review

Efficacy of hydrotherapy, spa therapy, and balneotherapy for psoriasis and atopic dermatitis: a systematic review

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Abstract

Background Atopic dermatitis (AD) and psoriasis are chronic inflammatory diseases that have significant skin complications.

Objective The purpose of this systematic study was to evaluate the evidence obtained from human studies on the effects of hydrotherapy, spa therapy, and balneotherapy in psoriasis and atopic dermatitis.

Methods The present systematic review was conducted according to the guidelines of the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) statements. Also, for this study databases such as Embase, PubMed, Scopus ProQuest, and sciences direct database were searched from the beginning to April 2021.

Results All human studies that examined the effect of balneotherapy, spa therapy, and hydrotherapy on psoriasis and atopic dermatitis were published in the form of a full article in English. In the end, only 22 of the 424 articles met the criteria for analysis. Most studies have shown that balneotherapy, spa therapy, and hydrotherapy may reduce the effects of the disease by reducing inflammation and improving living conditions. In addition, the results of the Downs and Black score show that seven studies received very good scores, three studies received good scores, nine studies received fair scores, and three studies received poor scores.

Conclusions The results of studies also showed that hydrotherapy leads to an improvement in the PASI score index. Nevertheless, more clinical trials are needed to determine the mechanism of action of hydrotherapy on these diseases.

Introduction

Atopic dermatitis (AD) and psoriasis are chronic inflammatory diseases that have significant skin complications.[1,2] Psoriasis is estimated to affect about 2–3% of the world's population (approximately 125 million people), mostly in the adult age range of 18–39 years.[3–5] Atopic dermatitis also affects 1–10% of adults and 15–20% of children worldwide.[6] Although both psoriasis and AD are considered skin diseases, numerous studies have shown that these diseases are associated with other complications.[7] AD is associated with mental health symptoms and disorders including sleep dysregulation, attention-deficit (hyperactivity) disorder, anxiety, and depression, as well as other atopic disorders (such as asthma), obesity, cardiovascular disease, and stroke.[8,9] Psoriasis is associated with metabolic, cardiovascular, hepatic, and psychiatric disease.[10,11] Psoriasis and AD are caused by complex disorders, host genetics, immune system disorders, skin barriers, and environmental factors.[12–15] In both diseases, chronic systemic inflammation leads to an increase in the number of leukocytes, lymphocytes, cytokines, and chemokines (T helper: Th1 and Th17 pathways are involved in psoriasis, and Th2 pathways are involved in AD).[16–20] Treatments for AD and psoriasis, including oral systemic medications and in a wide range of diseases, were limited to topical immunosuppressive drugs.[21] Also, biological agents have been recommended as attractive therapeutic options for cases with moderate-to-severe psoriasis or AD who have not had an appropriate response to other medications; however, these drugs are costly and have several complications.[22,23] Some biological drugs such as etanercept, ustekinumab, and adalimumab have been approved by the European Medicines Agency (EMA) and Food and Drug Administration (FDA) for psoriasis, while dupilumab was approved for adult atopic dermatitis.[22,23]

Studies have shown that these drugs have a strong anti-inflammatory effect that reduces inflammation in psoriasis and AD through several mechanisms.[24] Biologic drugs diminish inflammation by reducing the expression of nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB,) proteins, which play an important role in immunity, inflammatory, cytokines, (including TNF-α, IL-1, iNOS, and COX-2), and cell

cycle regulation.[25,26] Moreover, biologic drugs can decrease the expression of inducible cyclooxygenase-2 (COX-2), nitric oxide synthase (iNOS), the activation of activator protein-1 (AP-1), and p38 mitogen-activated protein kinases (P38-MAPK).[27,28]

Biologics can inhibit NF-κB gene expression by suppressing IκB kinase-α (IKK-α) phosphorylation, subunits.[24,29,30]

AD and psoriasis are strongly associated with poor health-related quality of life (QOL), high direct and indirect costs of care, side effects of drugs, and lack of definitive treatment response, etc. This indicates the need for optimal disease control.[31,32] Different types of complementary therapies as hydrotherapy (HT) can be helpful in chronic diseases without serious side effects. Balneotherapy (BT) or the use of mineral water or clay can be one of the safe and natural treatments for skin diseases.[33,34] Spa therapy is a universal, old, and well-known medicine.[35] These ways are used in the treatment of various skin diseases such as psoriasis, skin dryness, atopic dermatitis, chronic inflammatory diseases, and rheumatologic diseases.[35,36] The effects of hydrotherapy, spa therapy, and balneotherapy treatment on the skin are mechanical, thermal, and chemical through reducing the thickness of the stratum corneum and lucidum layer of the epidermis, increasing the number of lymphocytes and eosinophil granulocytes, as well as increasing skin permeability and reducing inflammation also improves microcirculation and safety.[37,38] The World Health Organization (WHO) proposes a method for treating water and psoriasis that has evidence-based effects on different parts of the body.[38] Balneotherapy has been used for many years in different parts of the world, such as Europe and Asia, for patients with arthritis, AD, and psoriasis.[39,40] The anti-inflammatory, antifungal, antibiotic, keratolytic, and mineral water effects have been proven completely.[38] Although many studies have reported the effects of balneotherapy, hydrotherapy, and spa therapy, there is no systematic review in psoriasis and AD. This systematic study was performed to investigate the possible effect of various balneotherapy, hydrotherapy, and spa treatments on some chronic skin diseases such as psoriasis and AD.

Methods

Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Checklist method has been used to write this systematic review.[41]

Search strategy

Two separate authors (AM and RND) conducted online searches in several databases on articles published through April 2021. We searched EMBASE, Scopus, PubMed/Medline, and Cochrane databases. The keywords used in our online search were as follows: "hydrotherapy" [Mesh] or "spa therapy" [Mesh] or “balneotherapy" [Mesh] or “mineral water" [tiab] or “therapeutic spa" [tiab] or “sulfurous water" [tiab] or “aqua therapy" [tiab] AND "psoriasis” [Mesh] or “Atopic dermatitis" [Mesh] or "eczema" [tiab].

Inclusion criteria

Population, Intervention, Comparison, and Outcome approach (PICO) was used for the inclusion criteria of this systematic review. PICO questions included the following criteria: (1) All clinical trials using various forms of hydrotherapy, including hydrotherapy, spa therapy, balneotherapy, mineral water, (2) patients with psoriasis and AD, (3) articles published in English.

Exclusion criteria

Articles that were excluded from the study due to lack of inclusion criteria include: (1) the effect of hydrotherapy on other diseases; (2) animal studies; (3) case studies – evidence and case reports.

Data extraction

Two authors (A.M. and R.N.D.) independently reviewed the full text of chosen articles and screened them for information extraction. Each study’s extracted data consisted of the first names of authors, the subject of the study, and the main conclusion. A third author (M.H.A.) of our study evaluated the quality and accuracy of the extracted information.

Quality assessment

To assess the quality of the randomized and nonrandomized studies included in this review, we selected the Downs and Black scale, which has shown good reliability and internal consistency of most of its five subscales. The final question was modified in that the score of 5 points was changed to 0 or 1 point, where 1 indicates that power or sample size was calculated and 0 means that this was not done and it was not determined whether the number of subjects was appropriate for the objectives established.[42] This modified version of the Downs and Black scale has been validated by other authors. The total score is 28. Scores for methodological quality are expressed in percentages as follows: under 50% indicates weak; 50–69% fair; 70–79% good; and 80–100% very good.

Risk of bias assessment

Two independent researchers (A.M. and R.N.D.) evaluated the degree of bias for all chosen studies. The overall degree of bias in the randomized controlled trials was evaluated based on the Cochrane risk of bias (ROB) assessment tool.[43] These tools contained seven domains, including random sequence generation, allocation concealment, reporting bias, performance bias, detection bias, attrition bias, and other bias sources. Each domain was given a “high risk” score if the study comprised methodological defects that may have affected its findings, a “low risk” score if there was no defect for that domain, and an “unclear risk” score if the information was not sufficient to determine the impact. If the trial had “low risk” for all domains, it

was considered a high-quality study with a totally low risk of bias.

Results

Selected articles

A total of 424 articles were identified in the primary review of the electronic databases, including 104 from Embase, 124 from Scopus, 122 from Science Direct, 25 from Cochrane, and 49 from PubMed. After review, 315 duplicate articles were removed, and the rest of the articles were analyzed in terms of title and summary. After initial screening, 87 articles, including seven book chapters, 33 reviews, five notes, 10 conference abstracts, and 31 unrelated articles, were removed. Finally, 22 articles after critical analysis of the title, abstract, and full text were included in the analysis (Fig. 1). The gender of the participants was not specified in some studies. In one of the 22 studies, the age of the participants was not specified, and in nine of the 22 studies, only the age range and mean age of the participants were specified. Among the studies reviewed, the age range of participants varied from 1 to 76 years. The characteristics of the study participants are presented in Table 1. In this systematic study, 16 studies on psoriasis, four studies on atopic dermatitis, and two studies on psoriasis and atopic dermatitis were performed simultaneously. Information on study design, type of intervention, treatment duration, water or pool temperature, and conclusion can be found in Table 1. The type of valued studies in this study included nine clinical trials, four randomized controlled clinical trials, one prospective, randomized open clinical trial, one prospective, non-randomized open clinical trial, one quasi-experimental method, one open, randomized, clinical trial, one blind, multicenter, pragmatic randomized controlled trial, one randomized, controlled, comparative study, one-blind, right/left comparative study, one pilot, one randomized placebo-controlled pilot study, and one randomized, observer-blinded, paired control trial. The interventions tested were in 16 studies BT, in five studies spa, and in two studies HT. The duration of studies in BT was between 2 weeks to 36 months, in spa therapy between 2 weeks to 1 year and in the HT study the study period was 6 weeks to 3 months. The number of participants in this study who used the BT method was between 10 and 367, in spa therapy 18 and 143, and hydrotherapy was between 5 and 836. The water temperature used in these studies was between 25 and 40°C, and in five studies, the water temperature was not specified.

Balneotherapy (BT)

BT includes treatments with natural mineral waters and mud, including gases, and exercises performed in water.[36] Recently, many advances have been made through the effect of BT on the treatment of psoriasis and dermatitis.[35,58] In this systematic review, we examine the effects of hydrotherapy, spa therapy, and balneotherapy on AD and psoriasis disease. In another study, Peroni, et al.[48] found that BT treatment at 36–37°C for 2 months significantly reduced PASI, SAPASI, and Skindex-29 scores in the first and second weeks compared to before treatment. They also concluded that BT combined with light therapy had better results in reducing these indices than BT alone. Farina, et al.,[52] conducted a study on patients with AD. Patients used AD containing thermal water with calcium and magnesium 36–37°C at pH 7.5–7.6 once or twice a day for 2 months. The results of their study showed that the number and duration of relapses were significantly lower in patients treated with BT compared with those treated with topical corticosteroids. BT therapy also improved IGA, PSGA, DLQI, and FDIQ indices for 4 months in patients with AD. Pagliarello et al.[55] evaluated that BT therapy and BT (oligomineral and rich in bicarbonate, calcium and magnesium, 27.7°C, pH 7.26) for 20 minutes, 6 days a week for 2 weeks, led to a decrease in SAPASI and Skindex −17. In addition, the decrease in SAPASI was greater in the BPT group than in the BT, but there was no difference between the two groups in the Skindex-17 variable. The study by Wang, et al.[36] with psoriasis patients used combined and non-combined BT with Chinese herbal medicine once a week for 8 weeks. The results of their study showed that there was no significant difference in PASI between the two groups at the end of treatment. In another study conducted by Kimata et al.[62] on AD patients, they observed that daily consumption of 500 ml of deep sea water for 1 year led to increased levels of Mg/K and Ca/Mg ratios, and Al, Hg, and Pb were elevated in these patients. It also significantly reduces the production of IgE and IgE-inducing cytokines such as IL-4, IL-13, and IL-18.

Spa therapy

Spa therapy includes a wide range of treatments including balneotherapy, hydrotherapy, physiotherapy, and exercise. This treatment method is successfully used in many European and Asian countries in traditional medicine as a treatment method for various diseases such as burns, rheumatoid arthritis, psoriasis, and edema.[63,64] Peter et al.[34] conducted a study on patients with psoriasis. Patients used a complex spa treatment for 3 weeks, 5 days per week for 30 minutes each time. The results of their study showed that CRP and PASI decreased significantly in the treatment group.

Golušin et al.[45] also concluded that topical calcipotriol combined with thermal mineral water at 38–42°C and peloids causes a significant reduction in PASI and desquamation scores compared to the calcipotriol alone.

Hydrotherapy (HT)

Hydrotherapy is mainly used in different countries to treat various disorders such as low back pain, chronic rhinosinusitis, or osteoarthritis. Hydrotherapy may be one of the most effective treatment methods for the management of skin diseases such as psoriasis; there were only two hydrotherapy studies on psoriasis and AD.

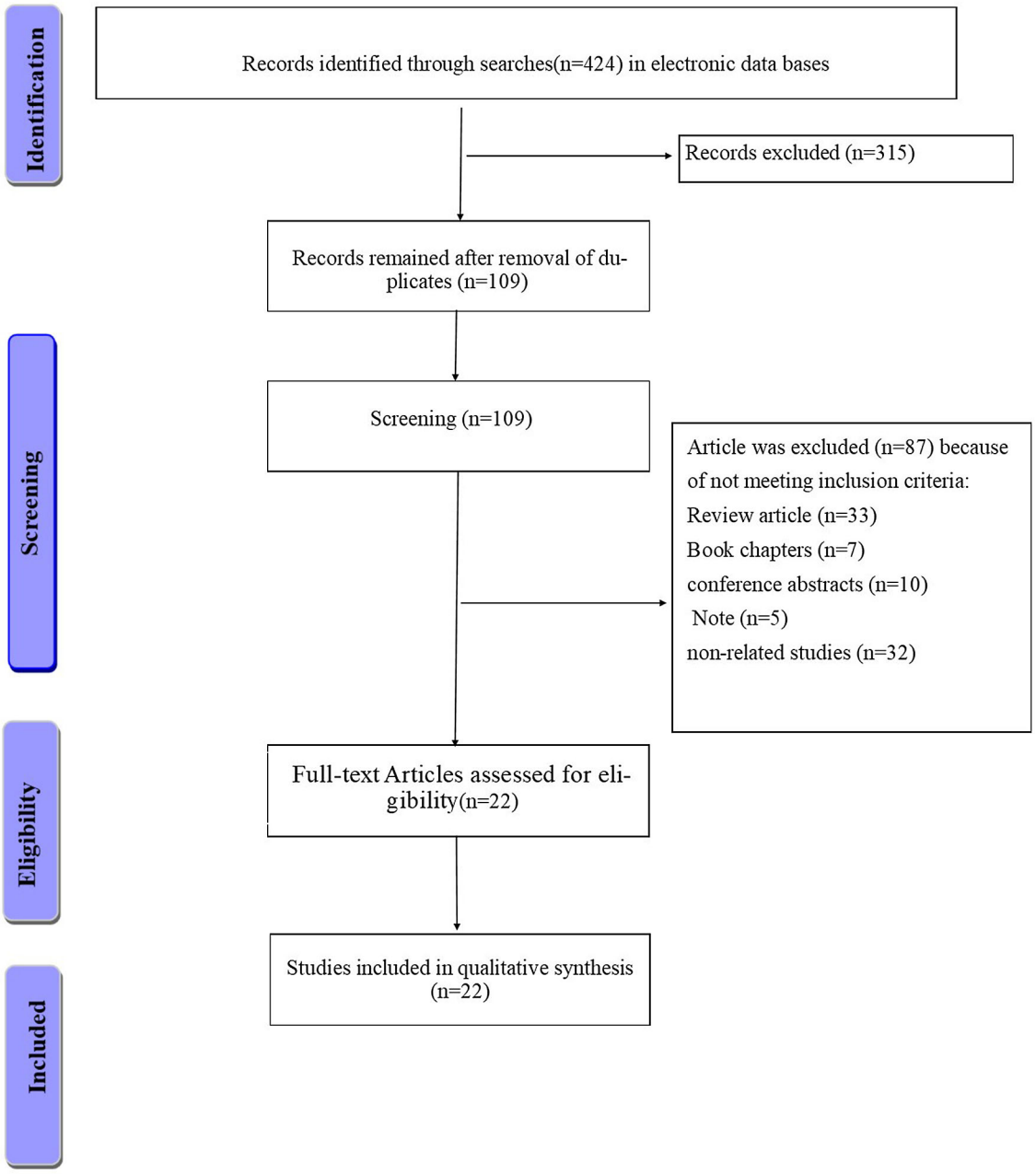


Figure 1 Flowchart of the process for selecting studies for the systematic review

Casas et al.[50] assessed that HT daily for 3 weeks significantly reduced PASI SCORAD, IL-8, and enterotoxin D. In another study conducted by Taieb et al.[51] on patients with psoriasis and AD, they found that SPA treatment for 20 minutes for 3 months improved the quality of life of adult and pediatric patients with psoriasis and atopic dermatitis/eczema. In two studies which Brockow et al.[53] and Léauté-Labreze et al.[54] performed on patients with psoriasis, the results of the studies showed that SPA therapy improved the PASI score in the treatment group compared to the control group. In another study conducted by Taieb et al.[51] on patients with psoriasis and AD, they found that HT for 3 weeks improved the quality of life of adult and pediatric patients with psoriasis.

Downs and Black score

The Downs and Black Scale categorized seven randomized trials from 22 very good studies, including an observational retrospective study, a randomized study, a prospective study

Table 1 Characteristics of studies

First author, date, reference	Study design	*N*	Population type	Control group/comparison	Age	Patient assessment/ follow-up	Water type	>Intervention	Results
Wang et al. (2020)[36]	Randomized controlled trial	190	Psoriasis vulgaris patients (M + F)	UTG: combined CHM balneotherapy and NB-UVB/daily when PASI score dropped to 1.8–2.2 points but then the treatment stopped N:93	5–72 years old	Once a week for 36 months	Balneotherapy, water 37–39°C	CTG: combined CHM balneotherapy and NB-UVB/daily when PASI score dropped to 1.8–2.2 points/two times a week for 4 weeks and then once a week for 8 weeks N:97	No marked difference in PASI score, adverse reactions between two groups, Significantly increased remission time in CTG compared to UTG ($P = 0.001$) and Significant increased risk of recurrence of psoriasis in UTG compared to CTG ($P < .001$) at the end of treatment
Tabolli et al. (2009)[44]	Observational prospective study	111	Moderate–severe chronic plaque psoriasis (M + F)	BT: daily bath treatments alone/2 weeks N:45	<18 years old	2 months	Balneotherapy, hypotonic, 27.7°C/PH 7.2	BPT: 12–14 total immersion baths/20 min/daily and then Ultraviolet-B (UVB) 15 min/2 weeks N:66	Significantly decreased SAPASI in two groups but decrease in BPT greater than BT group. Statistically significant decreased GHQ-12 in BPT group. No adverse side effects in two groups
Peter et al. (2017)[34]	Clinical trial	80	Psoriatic vulgaris patients (M + F)	No control group	Mean 63.7 years old	3 weeks	Spa therapy, sulfuric water	Spa therapy-based rehabilitation/30 min/5 days a week/for 3 weeks	Significant decrease in PASI ($P < 0.001$) and decreased CRP ($P = 0.026$) after treatment
Golušin, et al. (2015)[45]	Randomized controlled clinical trial	60	Plaque-type psoriasis	Topical calcipotriol N:30	>16 years old	1 month	Spa therapy, oligomineral, hypothermal, alkaline, mineral waters, 38–42°C	Mineral baths/20-min/twice a day+hot peloid packs daily+calcipotriol ointment/twice a day/ 21 days N:30	Significantly decreased PASI score (59.45%) ($P < 0.05$), decreased desquamation ($P < 0.001$) and increased therapeutic efficacy at the end of treatment and on day 30 in treatment group compared to calcipotriol group
Ninković, et al. (2014)[46]	Randomized controlled clinical trial	60	Psoriasis patients (M + F)	G1: standard therapeutic modalities N:26	Adult	3 months	Balneotherapy, thermal mineral water, 30.6°C/highly alkaline/with low mineralization	G2: baths or hot tubs and swimming in the pool/ 30 min/ twice a day/3 weeks N:19 G3: standard therapeutic modalities combined with balneotherapy N:15	Statistically marked difference in the duration of remission in G3 compared to G1 ($P = 0.019$) and G2 ($P = 0.032$)
Tsoureli-Nikita et al. (2002)[35]	Clinical trial	10	Symmetrical, bilateral psoriasis	Left arm immersed in double-distilled water 27°C/ 30 min + exposed to the sun/60 min; N:10	23–58 years old	2 months	Balneo heliotherapy, mineral waters, hypotonic water rich in sulphate, 27.2°C	Right arm immersed in Leopoldine water/30 min/ twice a day+exposed to the sun/60 min/ 4 weeks N:10	Improvement in PASI for the Leopoldine (85.9%), Significantly decreased number of epidermal $CD4^+$, decreased $CD8^+$ T cell, decreased CD1a + Langerhans cells, decreased epidermal keratinocyte expression of intercellular adhesion molecule-1 and IL-8 and decreased dermal expression of $CD4^+$ and decreased $CD8^+$ T cell in the Leopoldine spa water treatment. All treatments were well tolerated

Table 1 Continued

First author, date, reference	Study design	*N*	Population type	Control group/comparison	Age	Patient assessment/ follow-up	Water type	>Intervention	Results
Benevento-Italy (2015)[47]	Randomized, double blind, placebo-controlled pilot study	58	Plaque-type psoriasis (M + F)	Pharmacological topical therapy+sulfurous mud-balneotherapy N:25	14–78 years old	2 weeks	Balneotherapy, sulfurous mineral water (36–37°C)	Sulfurous mineral waters+mud-/10–12 min/ 2 weeks N:33	Significantly decreased PASI, DLQI, ROM ($P < 0.05$) in two groups in comparison with before treatment. No adverse reaction and good tolerated
Peroni et al. (2008)[48]	Clinical trial	300	Chronic plaque psoriasis (M + F)	One -twice daily baths/ 15 min + daily irradiation with narrowband UVB/ 2 weeks N:131	18–85 years old	4 months	Balneotherapy, Comano water (36–37°C)	Once-twice daily baths/total immersion in bath tub/ 20 min/2 weeks N:169	Significant decrease in PASI, SAPASI, and Skindex-29 in two groups especially in the second week in the photobalneotherapy group ($P < 0.001$) compared to before treatment. All treatments were well tolerated
Sitepu (2012)[49]	Clinical trial	40	Patients with atopic dermatitis	No intervention N:20	–	2 weeks	Balneotherapy, hot water	Balneotherapy with green tea in hot tub water/10–20 min and then bath/30 min/2 weeks N:20	Marked decreased itching ($P < 0.05$) in balneotherapy group comprised to without balneotherapy group after treatment
Casas et al. (2011)[50]	Clinical trial	57	Patients with psoriasis or atopic dermatitis	Healthy volunteers N:57	1–7 and >18 years old	–	Hydrotherapy, running water at 32°C	Showers and spray baths/ 20 min + compresses+drinking water+under water massages/daily/3 weeks N:57	Significantly decreased SCORAD, IL-8, *S. aureus* colonization and Enterotoxin D in patients with atopic dermatitis and decreased PASI, IL-8, and enterotoxin N in psoriasis at the end of treatment compared to the beginning
Taieb et al. (2011)[51]	Clinical trial	836	Atopic and psoriatic patients (M + F)	Standard treatments	26.9–52.2 years old	6 months	Thermal spring water at 32°C	Bath/20- min + hydromassages+shower+vaporization of water/6 days per week/3 weeks	Significantly decreased DLQI and decreased SF-12 in $Week_3$ and $Month_3$ and $Month_6$ with psoriasis and atopic dermatitis/eczema in adults and children in comparison with day 0
Farina et al. (2011)[52]	Randomized, clinical trial	104	Children with mild to moderate AD (M + F)	TCS: Topical corticosteroids N:50	1–14 years old	4 months	Balneotherapy, Comano water oligometallic thermal/36–37°C/pH: 7.5–7.6	Immersion in bathtub/20 min/once or twice daily/ 2 weeks N:54	Significantly decreased number and decreased duration of relapses in balneotherapy group compared to TCS ($P < 0.0001$) at month 4 Improvement in IGA, PSGA, CDLQI, and FDIQ were similar in two groups at week 2 All treatments were well tolerated and no major adverse reaction
Brockow et al. (2007)[53]	Randomized controlled trial	143	Moderate to severe psoriasis (M + F)	UVB N:64	49.9 years old	3- and 6-month	Spa therapy, low concentrated saline (NACL 4.5% and 12%)/37°C	Bath by low concentrated saline water+ultraviolet B (LC-SSW-UVB)/thrice a week/ 6 weeks N:79	Statistically increased marked PASI-50 in balneotherapy group compared to UVB group. No serious adverse events

Table 1 Continued

First author, date, reference	Study design	*N*	Population type	Control group/comparison	Age	Patient assessment/ follow-up	Water type	>Intervention	Results
Léauté- et al, 2001[54]	Randomized controlled trial	71	Psoriasis vulgaris patients (M + F)	GB:UVB N:21 GC:UVB + Spa water N:24	19–76 years old	1 year	Thermal mineral saline water,/35–37°C	GA: jet shower with spa water/3 min+bath/20 min 5 days a week/21 days N:22	Decreased PSAI 29% in GA and minor therapeutic effect compared with GB and GC ($P < 0.001$). Electrolytes blood no marked changes in end of treatment in three groups More adverse reaction in GA & GC but not significant
Pagliarello et al. (2012)[55]	Clinical trial	230	Psoriasis patients (M + F)	BPT: baths+narrowband UVB phototherapy N:82	>18 years old	2 weeks	Balneotherapy, spring water/oligomineral and rich in bicarbonate, calcium, and magnesium/ 27.7°C/pH: 7.26	BT: total immersion in bathtub with spring water/ 20 min/6 days per week/2 weeks N:139	Significant decrease in SAPASI and Skindex-17 at the end of the treatment in two groups. decreased SAPASI in BPT was superior to BT in ($P < 0.0001$) No statistical decreased marked Skindex-17 psychosocial scale in BT group compared to BPT group
Hataguchi et al. (2005)[56]	Clinical trial	33	Mild to moderate atopic eczema/dermatitis syndrome (M + F)	–	1–50 years old	6 months	Amami no Mizu a bottled water is rich in Mg	Drinking of deep-sea water 500 ml/day/6 months N:33	Significantly decreased potassium (K), ($P = 0.0004$), increased selenium (Se) ($P = 0.0001$) and increased ratio of Na/K ($P = 0.0065$), Significantly decreased K/Fe, Ca/Mg, Zn/Se and decreased mercury and lead. Improvement of skin symptoms in 81% patients
Galve et al. (2012)[57]	Randomized controlled trial	46	Mild to moderate psoriasis vulgaris (M + F)	Distilled water/twice a day/ 15 days N:18	18–65 years old	–	Balneotherapy, sulfurous mineral waters/18–25°C	SMW spray on skin at home/twice a day/15 days N:19	Improved PASI in two groups after intervention but no significant differences between two groups. Significant improvement of DLQI in control groups at the end of treatment. No adverse reactions
Dawe et al. (2005)[58]	Randomized controlled trial	60	Patients with chronic plaque psoriasis (M + F)	NB-UVB phototherapy N:30	19–79 years old	1 year	Balneotherapy, salt solution/37°C	Dead Sea (DS) salt solution /15 min + NB-UVB/ 8 weeks N:30	Slightly lower mean area of plaque psoriasis and slightly greater improvement in SEI score with balneophototherapy than NB-UVB alone Minor side effects in balneophototherapy
Gambichler et al. (2001)[59]	Randomized controlled trial	10	Psoriasis with chronic plaques (M + F)	Other elbow in tap water 30°C/20 min + UVB N:10	>18 years old		Balneotherapy, highly concentrated salt water/30°C	One elbow in 24% NaCl solution/30°C/20 min/4 times per week+UVB/30 sessions N:10	No significant reduction in clinical baseline score was observed after 30 treatments.
Klein et al. (2011)[60]	Randomized clinical trial	367	Moderate–severe psoriasis	PT: UVB N:184	<18 years old	6 months	Balneotherapy, Dead Sea salt	sBPT: Synchronous balneophototherapy UVB PT+bathing in 10% Dead Sea salt solution 30 min/3–5 per week/35 sessions N:183	Statistically significant decreased PASI and difference in clinically relevant between sBPT and PT group from baseline to after treatment (49.5%). Both treatments were safe and well tolerated

Table 1 Continued

First author, date, reference	Study design	N	Population type	Control group/comparison	Age	Patient assessment/ follow-up	Water type	>Intervention	Results
Melandri et al. (2020)[61]	Randomized controlled trial	91	Psoriatic patients without pustular (M + F)	G2: Clay peloid+bath with tap water+heliotherapy N:35	<18 years	3–6 months	Balneotheraphy, water containing sodium chloride, bromide, and iodide ("Acqua Madre)/38°C	G1: liman applications (40°C)/40 min + bath with Acqua Madre/20 min + heliotherapy/10 min–3 h/18 days N:56	Decreased NS in PASI in G1 at the end of treatment and after 3 and 6 months compared with G2. Significant decrease in delta-PASI, delta-PASI3 and psoriasis recurrences 3,6 and topical use of both cortisone and nonsteroid drugs in G1 as compared with G2
Kimata et al. (2002)[62]	Clinical trial	18	Patients with atopic eczema/dermatitis syndrome	Drinking of distilled water (without minerals)/ 500 ml/daily N:10	21–52 years old	1 year	Amami no Mizu (Deep sea water obtained at 344 m depth rich in Mg)	Drinking of deep sea water/500 ml/daily /1 year N:8	No side effects in two groups Marked alteration in skin symptoms, returned Mg/K and ca/Mg ratios, Al, Hg, and Pb levels to normal, Significantly decreased levels of anti-Dermatophagoides pteronyssinus and anti-Japanese cedar pollen IgE, and IgE-inducing cytokines IL-4, IL-13, and IL-18 in DSW group

↑, increase; ↓, decrease; AD, atopic dermatitis; BT, balneotherapy; CDLQI, children's dermatology life quality index; CHM, Chinese herbal medicine; CRP, C-reactive protein; CTG, consolidated therapy group; dAEs, dermatologic adverse events; DLQI, dermatology life quality index; DM, diabetes mellitus; DS, Dead Sea; FDIQ, family dermatitis impact questionnaire; FLQA-d, Freiburg Life Quality Assessment; GHQ-12, General Health Questionnaire; IGA, investigator global assessment; NS, not significant; PASI, Psoriasis Area Severity Index; PDI, Psoriasis Disability Index; PGWBI, psychological well-being; PGWBI, general psychological well-being; PSGA, patients' self global assessment; QoL, quality of life; ROMs, reactive oxygen metabolites; SAPASI, self-administered PASI; SAPASI, self-administered psoriasis area and severity index; sBPT, Synchronous balneophototherapy; SCORAD, SCORing Atopic Dermatitis; SEI score, Scaling, Erythema and Induration; SIP, Sickness Impact Profile; Skindex-17, disease-specific QoL questionnaire; SMW, Sulfurous Mineral Waters; TEWL, transepidermal water loss; UTG, unconsolidated therapy group.

evaluating pre-test intervention, and a controlled experiment, which was a pragmatism, pre- and post-treatment, a pilot study, and a follow-up controlled pilot study. Three studies out of 22 studies were classified as good, nine as fair, and three as weak, and seven studies as very good. The mean score of all studies was 11–21 and the maximum score was 27 (Table 2).

Findings from the quality assessments

In human studies, the sequence generation method was reported in 13 studies. Nine studies adequately described the nature of the method to allocation concealment. Only five human studies applied the blinding of participants and researchers, and was unclear in most studies. The blinding of outcome assessment was low risk in 13 studies, unclear in eight studies, and high risk in two studies. Incomplete outcome data were sufficiently reported in most investigations, resulting in a low risk of attrition bias for these articles. According to the reporting bias, low risk was identified for 13 articles, eight articles were scored as unclear risk of bias, and two articles were scored as high risk for this question (Table 3).

Discussion

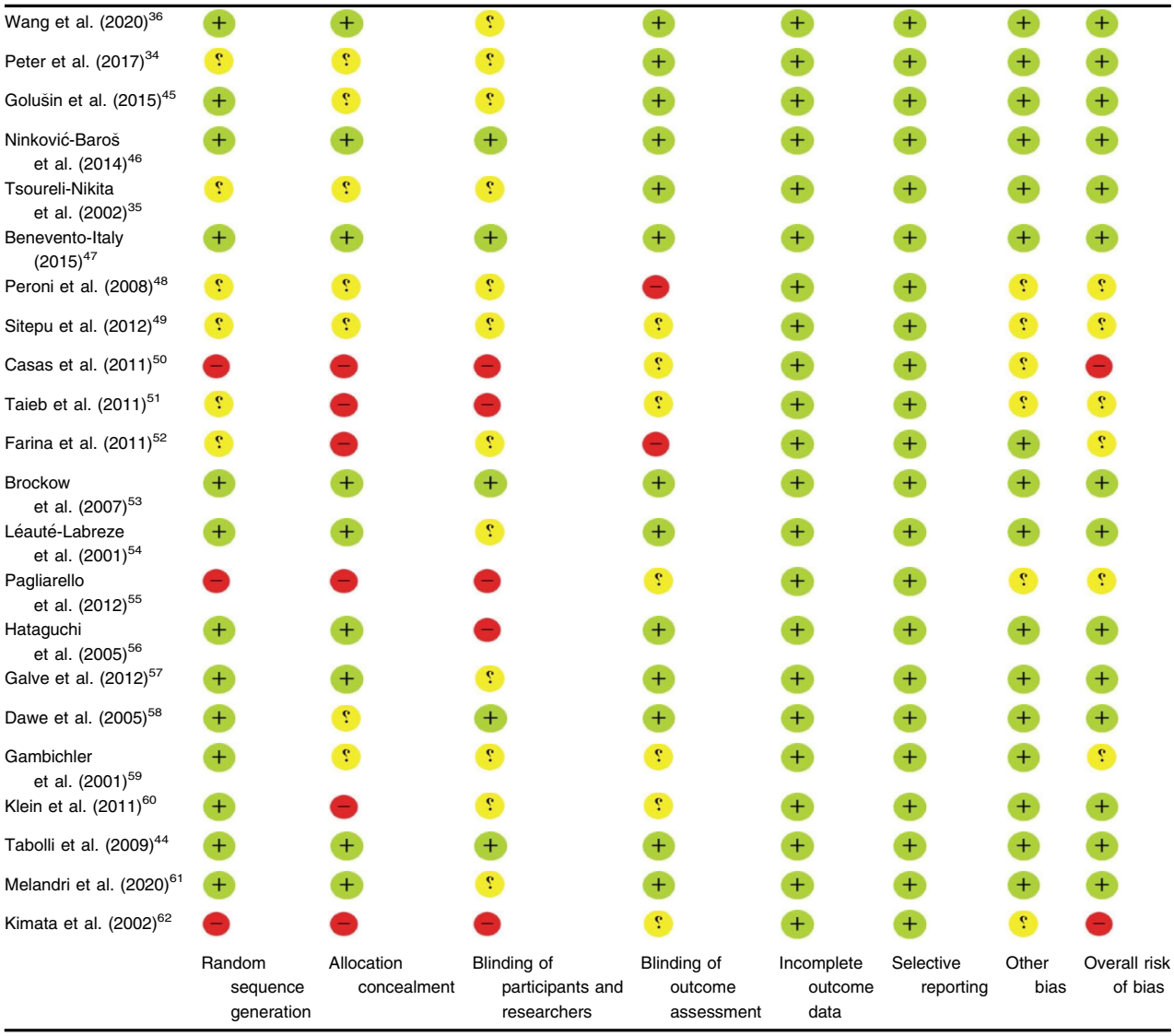
Traditional medicine recommends mineral water (including salty and sulfur water) for the treatment of various skin diseases such as psoriasis due to strengthening, keratolytic, and regenerative effects. In modern medicine, many studies have been performed to prove the absorption, chemical, thermal, mineral, and radiological properties of the skin in mineral waters on skin diseases such as psoriasis and AD. In addition, mineral waters with properties such as antibacterial properties increase blood flow to the surface layers of the skin, and antiproliferative properties can be effective in the treatment of skin diseases, especially atopic dermatitis and psoriasis. Because mineral water can reduce the thickness of the skin, as well as increase the proliferation of skin cells, it can improve the condition of atopic dermatitis and psoriasis.

Mineral waters contain substances such as sulfur and salt that may be very effective in treating skin diseases.[46] Sulfate sources can be used in many chronic inflammatory diseases due to the properties of keratolytic, antifungal, antioxidant, and anti-inflammatory and antiproliferative effects.[38,65,66] Hydrogen sulfide is a small permeable gas that can enter the skin's intracellular molecules and have many effects. Hydrogen sulfide can inhibit the proliferation of T lymphocytes and interleukin-8, as well as decrease cellular adhesion.[33,46,66] Lee et al.[67] showed that balneotherapy by immunomodulatory leads to a decrease in the production of Th1 and Th2-dependent cytokines such as intercellular adhesion molecule 1 expression, and E-selectin can be in human endothelial cells and thus reduce the complications of this disease. Also, some studies have shown that in in vitro conditions, balneotherapy is able to modulate the immune system due to the high amount of sulfur in its composition. In addition, sulfur waters can prevent the increase of T lymphocytes, and the release and production of interferon-gamma, il-2, il-6, and tumor necrosis factor-alpha (TNFα), which are inflammatory mediators associated with psoriasis.[34,68,69]

Table 2 Downs and Black score

Author (year), reference	Reporting (0–11)	External validity (0–3)	Bias (0–7)	Confounding (0–6)	Power (0–1)	Total (0–28)	Percentage (%)	Classification
Wang et al. (2020)[36]	8	2	4	3	1	18	64	Fair
Tabolli et al. (2009)[44]	7	2	4	1	1	15	53	Fair
Peter et al. (2017)[34]	9	2	5	4	1	21	78	Good
Golušin et al. (2015)[45]	9	3	6	5	1	24	85	Very good
Ninković, et al. 2014[46]	7	2	4	3	1	17	61	Fair
Tsoureli-Nikita et al. (2002)[35]	10	3	6	4	1	24	85	Very good
Benevento-Italy (2015)[47]	6	1	4	3	0	13	51	Fair
Peron,i et al. (2008)[48]	8	2	4	3	1	18	64	Fair
Sitepu etal. (2012)[49]	5	1	3	2	1	12	44	Weak
Casas et al. (2011)[50]	7	2	4	2	1	16	58	Fair
Taieb et al. (2011)[51]	6	2	3	3	1	15	53	Fair
Farina et al. (2011)[52]	10	3	6	5	1	26	92	Very good
Brockow et al. (2007)[53]	9	3	5	5	1	23	82	Very good
Léauté-Labreze et al. (2001)[54]	6	2	3	3	1	15	53	Fair
Pagliarello et al. (2012)[55]	5	1	3	2	1	12	44	Weak
Hataguchi et al. (2005)[56]	8	2	5	4	1	20	71	Good
Galve et al. (2012)[57]	10	3	6	6	1	27	97	Very good
Dawe et al. (2005)[58]	7	2	4	4	1	18	64	Fair
Gambichler et al. (2001)[59]	9	3	6	5	1	24	85	Very good
Klein et al. (2011)[60]	11	3	6	5	1	26	91	Very good
Melandri et al. (2020)[61]	8	2	5	5	1	21	75	Good
Kimata et al. (2002)[62]	5	1	3	2	0	11	38	Weak

Table 3 Results of risk of bias assessment for human studies



Each domain was scored as: − if it contained methodological flaws that may have affected the results, + if the flaw was deemed inconsequential, and ? if information was insufficient to determine. If a study got + for all domains, it considered as a high quality study with totally low risk of bias.

One of the substances in mineral water is magnesium, which plays an important role in regulating the rate of activation of epidermal adenylate cyclase and thus the production of cyclic adenosine monophosphate (cAMP), which is involved in psoriasis.[33,70] Magnesium may also improve the disease by reducing the production of some polyamines that are involved in the spread of psoriasis.[33,70] Sulfur is closely related to cysteine and its metabolites, as well as less so in the vessels of psoriasis patients as in healthy individuals, which may be compensated by absorption through the skin.[33,34,57]

Similarly, sulfur-containing mineral waters, which are used for drinking, also have antioxidant properties. Studies have shown that hydrogen sulfide reduces keratinocyte cell adhesion, cell proliferation, and human proliferation in psoriasis.[69] Thermal water reduces the degranulation of basophils in atopic patients. Balneotherapy with sulfur reduces the accumulation of leukocytes and the production of cytokines in the skin, as well as increases β-endorphins in the skin, and also significantly reduces the PASI score in psoriasis patients.[57] Studies have shown that saline water reduces the thickness of the skin and also reduces inflammation caused by the disease by regulating immune system processes.[45,71] In addition, water containing saline solutions has a direct effect on blood flow by regulating the production of elastase enzymes in different

layers of the skin and by dilating capillaries and reducing the concentration of fibrinogen, and can reduce the complication of psoriasis.[53,58,72] Saline water treatments as a treatment for psoriasis increase the patient's quality of life and improve the expression of PASI score in patients.[73] The heat in hot water causes an increase in norepinephrine, the plasma prolactin, adrenocorticotropic hormone, cortisol, and growth hormone, and plasma β-endorphins.[74] B-Endorphins also play an important role in the functioning of the immune system through the production of interleukin-10.[33,74] Furthermore, thermal water reduces the degranulation of basophils in atopic patients.

Limitation

Among the main limitations of this systematic review are the lack of control groups in some studies, the uncertainty of water temperature and pH in some studies, and the small number of participants in some experiments. Moreover, the age of the participants was not mentioned in some studies. Also, double-blind studies existed only in some studies.

Conclusion

Mineral waters around the world due to the presence of substances such as sulfur and salt can be one of the auxiliary methods of therapy in the treatment of various diseases such as psoriasis and AD. Evidence from studies shows that hydrotherapy, spa therapy, and balneotherapy can reduce the symptoms of psoriasis and dermatitis by improving the inflammatory status and PASI score. However, a large number of clinical studies are needed to reach a definitive conclusion in this regard.

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Author contributions

The authors' responsibilities were as follows: R.N.D and A.M wrote the original paper; M.H.A and A.N contributed to data collection, provided advice and consultation, and contributed to the final revision of the manuscript. All authors read and approved the final version of the manuscript.

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