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SPECIAL REPORT

The Role of Wet Wrap Therapy in Skin Disorders – A Literature Review

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Wet wrap therapy, based on skin application of a double layer of tubular bandages or gauze with a moist first inner layer and a dry second outer layer, is utilized to treat various pruritic conditions, in particular severe and refractory atopic dermatitis. This review, by literature search, evaluates current knowledge about wet wrap therapy. Wet wrap therapy superimposed topical corticosteroids appears more efficient than emollients only, at least for short-time treatments. Despite higher efficacy, there is a tendency towards more frequent infections when topical corticosteroids are covered with wet wrap bandages compared to emollients only. While temporary suppression of hypothalamic-pituitary-adrenocortical-axis was seen due to systemic bioactivity of corticosteroids, no long-term observation studies on putative adverse effects were identified. One hypothesis suggests that wet wrap therapy may trigger increased lamellar body secretion resulting in recovery of the damaged intercellular lipid laminar structure. Otherwise, little investigation on mechanisms exists. ***Key words: atopic dermatitis; pruritic conditions; therapy; bandages; corticosteroids; water.***

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Wet wrap therapy (WWT), defined as a treatment modality using a double layer of tubular bandages or gauze, with a moist first inner layer and a dry second outer layer (1), is commonly utilized in patients with severe or refractory atopic dermatitis (AD). A 'moist environment' obtained by oil and honey wound dressings was used to heal skin lesions in Ancient Babylonia and Egypt. The Mayo Clinic in USA has utilized wet dressings at least since the 1930's for pruritic dermatoses (2, 3). Various techniques and smaller case reports were published in the 1970's and 80's (4, 5), whereas the first detailed case series with 30 pediatric AD patients was published by Goodyear in 1991 coining the term 'wet wrap' – claiming that WWT was as 'an extremely effective treatment' for acute erythrodermic eczema (6).

Several treatment protocols exist (1, 7, 8). While these vary greatly in their methodology, the overall principal typically emollients only or topical corticosteroids (TCS), diluted or non-diluted, applied on lesional skin or the entire body surface, followed by application of bandages, often made from elasticated tubular cotton (Fig. 1). The first layer of moist luke-warm bandages (usually from water, but some soak the inner layer in luke-warm cream) is followed by a second dry layer. The inner layer is often rewetted, usually by water, several times during treatment and sometimes the patient sleeps with bandages. Treatment is conducted once or twice daily, or as maintenance therapy several times weekly. Intervention period varies from a few days or may go on for several weeks. Treatment is typically time consuming and demands special nurses/parents training.

This review article evaluates current knowledge on WWT based on published literature. In particular, we aim to answer the following questions:

- What are the indications for wet wrap treatment?
- What is the evidence base for efficacy comparing (*i*) WWT to conventional 'open application' of TCS without wet wrap bandages and (*ii*) in WWT, using TCS vs. emollients only?
- What are potential adverse effects?
- What is known about the mechanisms behind the clinical effect of WWT?

METHODS

We searched PubMed and EMBASE databases from start till September 1st 2014 for published English literature on WWT using key search terms: 'wet wrap', 'wet dressings', 'wet wrap therapy', 'wet wrap dressings' and 'occlusive dressings'. Reference lists from relevant articles were manually scanned for additional publications. A synthesis of available data, current evidence and conclusions was generated.

Quality of comparative human studies were assessed using the Delphi List (9). This list is made according to consensus of experts on 10 items of methodological criteria providing a score between 0 and 8 or 10 (as blinding of patient and care provider is not applicable when comparing a treatment with or without wet wrap therapy). Studies were considered of good quality when they meet ≥ 60 % of assessed items.

RESULTS

Forty-nine articles were found regarding various aspects of WWT; 28 were original clinical trials of which

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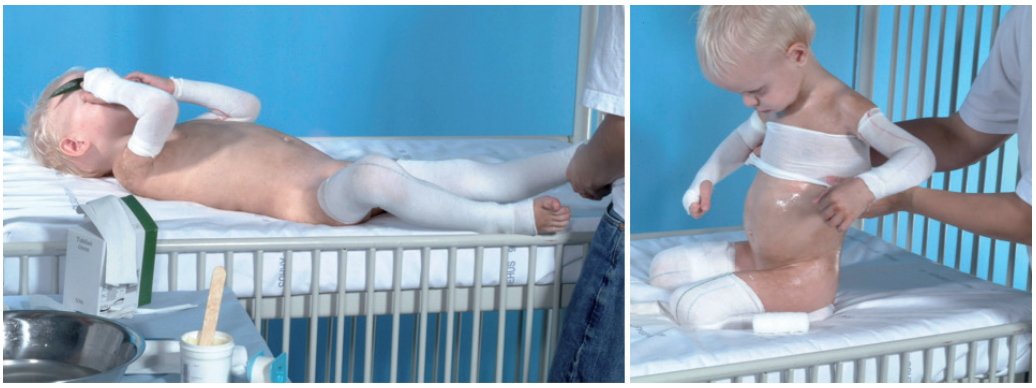

Fig. 1. Child receiving wet wrap therapy with emollients. The authors would like to acknowledge Dr. Mette Deleuran from Aarhus, Denmark for providing the clinical picture.

19 were uncontrolled case series (18 human studies (2, 3, 6, 10–24) and 1 animal study (25)) and the remaining 9 comparative studies (8 human studies (26–33) and 1 animal study (34)). Twenty-one articles provided expert opinions or were reviews (1, 4, 5, 7, 8, 35–50).

Methodological quality

Table I provides an overview of the quality assessment of the 8 human comparative studies. The scores ranged between 30–88%. Four studies obtained a score > 60%.

What are the indications for wet wrap treatment?

A questionnaire sent to 233 British pediatric dermatologists, with a response rate of 40%, showed that WWT was used in a wide range of conditions other than AD, in particular intolerable itchy conditions (37). This finding along with anecdotal reports (40, 41) was supported by a recent comprehensive retrospective study (3) of 331 patients with 54 different diagnoses treated with WWT in 391 admissions. The most frequent diagnoses were nonspecific dermatitis, AD, erythroderma, psoriasis, pruritus, cutaneous T-cell lymphoma, Sézary syndrome, dermatomyositis, prurigo nodularis, pityriasis rubra pilaris, but also a wide range of autoimmune bullous diseases and ulcerative conditions. The authors claimed improvement of pruritus (mild/moderate/marked/non-specified improvement) in 94% after one day, but only had data available from 156 of the 391 admissions (40%). According to the records, 98% experienced (data available of 357 admissions) improvement in pruritus at discharge. Unfortunately, there was no report on additional topical/systemic treatment of the patients nor reports on objective improvement.

Another retrospective study from 2005 (18) used a 'soak-smear' technique with a nightly 20 min soaking in plain water of the affected body part, followed by TCS application on the wet skin and a dry pajamas in 28 patients with various refractory chronic pruritic conditions like atopic, nummular, chronic hand and xerotic eczema along with palmar plantar psoriasis for up to 2 weeks. Without referring to an objective tool for measuring treatment outcome, > 90% of patients were reported to have 90–100% clearance. In 2007, a case-series with 11 cutaneous mastocytosis patients receiving WWT once daily with diluted flucasone propionate for 6 weeks was published (15). At the 24 weeks evaluation, a partial, but clear cosmetic improvement was found in 9/11 patients, with a mean decrease in the mastocytosis severity score, the SCORMA-index, from 38 to 26. Skin biopsies from all patients showed decrease in mast cell number, suggesting disease modification. However, N-methylhistamine, a urine-marker for disease intensity, remained unchanged.

A treatment modality for milder atopic dermatitis?

WWT has been advocated in patients with severe and/or refractory AD as crisis intervention or as an alter-

Table I. *Methodological quality assessment using the Dephi List (9)*

Trial	Item 1[a]	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Total score
Fölster-Holst et al., 2006 (27)	Yes	No	?	Yes	?	N/A	N/A	Yes	?	Yes	4 =50%
Hindley et al., 2006 (28)	Yes	Yes	Yes	Yes	Yes	N/A	N/A	Yes	No	Yes	7=88%
Beattie & Lewis-Jones, 2004 (29)	Yes	Yes	Yes	Yes	?	N/A	N/A	No	Yes	Yes	6=75%
Pei et al., 2001 (32)	Yes	Yes	?	Yes	Yes	N/A	N/A	No	?	Yes	5=63%
Janmohamed et al., 2014 (26)	Yes	No	Yes	Yes	Yes	?	Yes	Yes	Yes	Yes	8=80%
Schnopp et al., 2002 (30)	Yes	?	Yes	Yes	Yes	?	Yes	No	?	?	5=50%
Devillers et al., 2002 (31)	Yes	?	Yes	Yes	?	?	?	Yes	?	?	4=40%
Wolkerstorfer et al., 2000 (33)	Yes	No	?	?	?	?	?	Yes	?	Yes	3=30%

[a]Items assessed: 1: Was a method of randomization performed? 2: Was the treatment allocation performed? 3: Were the groups similar at baseline? 4: Were the eligibility criteria specified? 5: Was the outcome assessor blinded? 6: Was the care provided blinded? 7: Was the patient blinded? 8: Were point estimates and measures of variability presented for the primary outcome measures? 9: Did the analyses include an intention-to-treat analysis? 10: Is the withdrawal/dropout rate described?

native to systemic treatments such as corticosteroids, ciclosporin, azathioprine or photo(chemo)therapy (1, 7). While efficacy has been demonstrated in a range of case-series of AD patients with severe/refractory disease (6, 10–14, 16,17, 20, 22–24), it has been discussed whether the treatment also is effective in patients with mild disease. Beattie & Lewis-Jones (29) studied the efficacy of WWT in less severe, but wide-spread AD. They enrolled children with AD covering more than 30% of the body area surface, but only requiring mild TCS, e.g. 1% hydrocortisone. Treatment without WWT was as effective as treatment with WWT when comparing efficacy outcome by the Six Area Six Sign Atopic Dermatitis severity score (SASSAD) (51). These findings were supported by a 2009 study (34); Oranje and colleagues used mice with a transgenic overexpression of human apolipoprotein C1 as an AD mouse model. According to the adapted 'Three Item Severity Score' utilized (52), the mice had AD corresponding to mild to moderate severity. In this adapted mice model, WWT with flucasone propionate or tacrolimus had little or no added value compared to treatment with flucasone propionate or tacrolimus alone. WWT in this model was only applied 8 h daily with only one rewetting of the inner layer of bandages, compared to up to 24 h utilization with several rewettings in humans.

Reviewing the above studies provides insight to the fact that WWT is utilized with efficacy in a variety of mainly pruritic conditions other than AD. Regarding milder AD, there is insufficient data to conclude whether WWT has a place in treatment.

What is the evidence base for efficacy comparing i*) WWT to conventional 'open application' of TCS without wet wrap bandages and* ii*) in WWT, using TCS vs. emollients only?*

Eight human studies comparing different aspects were identified (Tables SI[1] and SII[1]) demonstrating large variations in methodology regarding all parameters: Study design, patient number, AD definition (if any), AD outcome score, therapy (whole body/extremities/lesions only, number of treatments per day/week, occlusion duration, various strength and dilution of TCS, eventual re-wetting of inner bandage layer), study duration, registration of adverse-effects and follow-up. All studies only investigated WWT in AD patients.

Comparing WWT to conventional 'open application' of TCS. Four studies compared TCS in combination with WWT to conventional open application of TCS (Table SI[1]). Pei et al. (32) investigated two TCS (1:10 diluted 0.05% flucasone propionate and 1:10 0.1% mometasone furoate) with and without adjunctive WWT in a 4 week study in 40 AD children. First, all patients received 2 weeks treatment with either flucasone propionate or mometasone furoate once daily without dressings. The last two weeks patients continued the same TCS once daily, but half the patients were randomized to also receive WWT 8 h overnight. At the end of week 4, no differences between the two studied corticosteroids were observed, but a significant reduction in disease severity (personal disease severity score) and extent (personal extent of disease score) was observed in the WWT treated groups. Only 27 patients completed the study, as they only 'qualified' for the last two weeks of the study, if they had $< 50\%$ improvement during the first two weeks. Thus, only patients 'failing' open treatment with TCS qualified for the WWT treatment protocol.

A British study (29) with 19 AD children covering $> 30\%$ of the body surface, but not requiring TCS stronger than 1% hydrocortisone were randomized to receive hydrocortisone once daily and WWT (week 1: twice daily, week 2: once daily) or hydrocortisone twice daily without any dressings for 2 weeks. The authors reported open treatment being as least as effective as WWT, measured by the SASSAD severity score (51). A more recent British study (28) investigating 50 AD children, of which 45 completed, also found no differences, measured by 'scoring atopic dermatitis' severity score (SCORAD) (53, 54), between groups treated with 1% hydrocortisone (or other mild TCS) and either WWT or 'open treatment' after 4 weeks of treatment. Like the aforementioned study (29), the WWT group was treated with hydrocortisone only once daily, compared to twice daily in the 'open treatment' group, but it was reported that the total amount of used hydrocortisone was similar in the groups. Finally, a German group (27) performed a short-term 'left-right study' in 24 patients, 20 adults and 4 children. They treated the patient's legs or arms with the medium strength TCS, prednicarbat, and randomly covered an arm or leg with wet wraps. After 2–3 days they reported improvements in both groups. Decrease of local SCORAD in WWT group was significantly higher.

In summary, we have presented limited data that suggest a superior effect of WWT when compared to conventional 'open therapy' with TCS alone. Three of the 4 studies obtained a quality score of more than 60%, however, we found major variation in methodology between studies, making it difficult to compare the results of the studies.

WWT with TCS or emollients only. It is commonly believed that using TCS, often diluted, beneath the wet wrap is more efficient than emollients alone. Four clinical studies compared WWT with emollient only to use of different dilutions of TCS (Table SII[1]).

In 5 children (33), a left-right study with 1:10, 1:4 and 1:2 dilutions of flucasone propionate 0.05% under WWT once daily was performed. There was no informa-

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tion of daily WWT duration. After one week treatment there was no significant difference in the objective SCORAD estimates between the dilutions. Another 8 children received either emollient only (2 patients) or dilutions (1:20, 1:10 and 1:4) of 0.05% flucasone propionate (6 patients) combined with WWT once daily. After one-week therapy, there was only minor improvement in the 2 children with emollients only, whereas there was great improvement regardless of flucasone propionate dilution (no report on significance), with a tendency to a dose-response relationship.

Devillers et al. (31) also studied side difference (left–right study) of dilutions of 0.05% flucasone propionate once daily WWT in 14 children and 12 adults the first week in their otherwise relative long study (mean duration 17 weeks). After day 4/5, they found side differences in objective SCORAD in only 5 of the 26 patients in favor of the most concentrated formulation. There were no reports on daily duration of WWT nor the level of significance of the reported side differences.

A third study (30) performed a 5-day left–right study in 20 children treated with WWT twice daily with either mometasone furoate 0.1% (not diluted) or emollient. They found improvements of the local SCORAD in both groups, though significantly better result in the mometasone furoate group than the emollients only group. They also measured transepidermal water loss (TEWL) showing improvement in both study arms without reaching statistical significant difference.

When assessing the quality of the 3 mentioned studies (30, 31, 33) according to the Delphi List (9) they all obtained rather poor ratings (Table I). Recently, 39 children were randomized to receive either WWT with a 1:3 dilution of mometasone furoate 0.1% or emollients only for 4 weeks in a well-conducted study (26) who obtained 80% in quality rating according to the Delphi List (9). In the first week, patients were treated once daily on the whole body, while the patients solely were treated 4 times per week, lesion only, during the last 3 weeks. 35 children completed the study with 4 dropouts in the emollient group, two of these because of treatment failure after one week. There was no information on the daily duration of WWT. Results showed a significantly stronger decrease in objective SCORAD in the TCS treated group. Interestingly, when examining the curve comparing the SCORAD of the two groups over time, a faster impressive decline was noticed in the TCS group compared to the emollient only group, but the groups' SCORAD approached one another toward the end (week 4). This could suggest that WWT combined with TCS is very efficient in the early phase of treatment, whereas efficacy equalizes during time when comparing the treatment modalities.

Taken together, TCS seem more efficient than emollients only underneath wet wraps, as least for short-term treatment, however, the quality of the existing studies is rather poor (Table I), so more evidence is needed to be able to draw conclusions. Also, when comparing the effect of different potencies of TCS in WWT in the same patient by 'left–right' study designs, there is currently no evidence to suggest a superior effect of stronger TCS, but a systemic impact of TCS then applying different dilutions of TCS in the same patient can be suspected.

What are potential adverse effects?

Reviewing the literature on side effects in WWT leads to a division into 3 categories (Table II): expected discomforts regarding the use of moist bandages (8, 10, 23, 36), skin infections and probably the most serious adverse effect: possible systemic bioactivity of the TCS.

Infections. While there has been conflicting data regarding WWT disposing to infections due to occlusion, the most common infections reported include folliculitis (11, 23, 31, 33), followed rarely by furunculosis (33), impetigo (31), pseudomonas (31) and herpes infections (33). Dabade et al. (13) claims no serious adverse effects including no infections in a comprehensive retrospective case-report with as many as 217 pediatric AD patients. This study must be considered short-term, as the mean duration of hospitalization (and WWT) was only 3.6 days. Another shorter-term study (Table SI[1], WWT duration 2–3 days) equally reported no side-effects during the study and 2 weeks after (27).

A longer-term retrospective study (31) (Table SII[1]), with a mean treatment duration of 17 weeks, reported that 38% of the 26 patients experienced infections, most commonly folliculitis, followed by impetigo. Another longer-term controlled study (28) (Table SI[1]) that compared TCS with and without WWT in a 4 week trial reported that 5 of 23 (22%) children needed to be treated with antibiotics (no report on types of infections) in the TCS+WWT group, whereas none were treated in the conventional group, suggesting a higher level of infections when the TCS are occluded by wet wrap for a longer period. Beattie & Lewis-Jones (29) also reported two cases (of 10 patients) with folliculitis in the group treated with TCS and WWT compared to none in the group only treated with TCS during 2 weeks study, supporting more infections may develop when occluding TCS in WWT compared to open treatment.

Besides the mentioned skin infections, Wolkerstorfer et al. (33) reported examples of balanitis, urinary upper tract infections and diarrhea among WWT-treated patients.

Systemic bioactivity of corticosteroids. In the first 'modern' case-series on WWT in 30 patients treated between 2 and 5 days, Goodyear (6) reported transient systemic uptake of TCS resulting in temporary hypothalamic-pituitary-adrenocortical (HPA)-axis suppression measured by decreased levels in morning serum-cortisol (9.00h am). Serum-cortisol levels were low immediately after treatment, but the levels normali-

Table II. *Reported adverse effects in wet wrap therapy (WWT)*

Adverse effect
Discomfort/shivering/itching due to wet bandages/gauze/pajamas (8, 10, 23, 33, 36)
Infections
Folliculitis (11, 23, 31, 33)
Impetigo, localized Pseudomonas and cellulitis infection (31)
Furunculosis, herpes infection, balanitis, urinary upper tract infection (33)
Side effects related to topical corticosteroids
Striae distensae (31)
Temporary hypothalamic-pituirary-adrenocortical-axis suppression (6, 22, 23, 31, 33)
Other side effects
Diarrhea, abdominal pain (33)

zed 2 weeks later. He also reported 'prolonged pituitary axis suppression' in long-term treated patients without revealing data on how intensive the patients had been treated, nor the extent of the suppression and eventual follow-up on the normalization of the cortisol-levels. Subsequently, other groups have reported temporary HPA-axis suppression (22, 23, 31, 33). Only Devillers and colleagues (31) reported a case of developed prolonged HPA-axis suppression in a patient also treated with inhalant corticosteroids during WWT. This patient also developed abdominal striae distensia.

Wolkerstorfer et al. (33) argued that measuring serum cortisol at 6.00h gave more precise results than 9.00h, that seems to be the routine in previous studies[2]. They measured 6.00h serum cortisol and urinary cortisol/creatinine ratios in 8 patients showing that nearly all patients had a decrease in morning cortisol levels and that 3 patients had temporary HPA-axis suppression. Suppression was related to the absolute amount of TCS applied, suggesting that using greater dilutions of TCS might result in less risk of systemic effects of corticosteroids.

McGowan et al. (19) investigated whether short-term growth (lower leg length velocity by knemometry) and bone/collagen turnover (by 24-h urinary deoxypyridinoline crosslink excretion) were affected in an uncontrolled study with 8 children receiving WWT with diluted TCS over a 12-week period (2 weeks with 24 h/day treatment, followed by less intensive treatment). They did not find significant differences before and during WWT, indicating that WWT in children is not affecting growth by systemic uptake of TCS even when using WWT for a longer period.

What is known about the mechanisms behind the clinical effect of WWT?

While WWT is believed to improve barrier functions through various mechanisms, most hypotheses have not yet been confirmed (Table III). We here review putative reasons for the clinical effect of WWT treatments.

Physical moist bandages create a mechanical barrier inhibiting scratching and thereby likely preventing the itch-cycle often seen in AD patients (4, 24, 30, 36). Moreover, bandage removal may facilitate removal of scales, crusts and exudates (4, 13). Itch is also considered to decrease through vasoconstriction secondary to cooling of skin due to gradient moisture evaporation (4, 6, 23, 32, 36). Wet wrap's effect in cooling skin was demonstrated in a 1967 study (2), showing a continued significant cooling for 14 h or more in a 24-h study of wet bandages without rewetting. Opposite, dry bandages heated skin.

The inner layer likely serves as a reservoir for constant skin moistening (23) and by trapping moisture in the stratum corneum, it has been considered, that this leads to enhanced uptake of topical medication like TCS often utilized in WWT (18).

Lee and colleagues' study (17), unique by being the only one investigating the mechanisms of WWT on the epidermal barrier, included 10 AD patients who underwent 7–14 days of WWT (8 h/day without TCS) in an uncontrolled study. Patients were studied immediately and 7 days post treatment by non-invasive methods. Skin biopsies and immunohistochemical staining were also performed to investigate keratinocyte differentiation and structure of intercellular lipids along with electron microscope examining the lamellar structure of intercellular lipids. They found increased epidermal water content, decreased TEWL, increased lamellar body release of lipids, and restoration of the laminar structure of the intercellular lipids. Surprisingly, they did not find differences in expression of filaggrin and loricrin expected to be, respectively, increased and decreased following treatment. The authors considered this due to either limited influences of WWT on keratinocyte differentiation or remaining asymptomatic inflammation, even after marked clinical improvement. Instead they advocated that the possible mechanism could be hydration by WWT causing increased lamellar body secretion causing recovery of the damaged intercellular lipid laminar structure ultimately leading to clinical improvement.

A 5-patients study with plaque-psoriasis (55) treated 7 days with water-impermeable occlusions over lesions

Table III. *Possible mechanisms of wet wrap therapy (WWT)*

Physical barrier
- Prevents scratching and improves sleeping
- Reducing itch by cooling trough vasoconstriction
Greater absorption of corticosteroids
Recovery of epidermal barrier
- Increased water content of the epidermis by trapping moisture
- Decreased transepidermal water loss
- Increasing release of lamellar bodies, restoring of lamellar structure
Reduced inflammation
- Decrease of inflammatory chemokines

[2]It has been discussed whether morning serum cortisol is a reliable marker of an eventual HPA-axis depression, as there have been reported large intra- and inter-individual variability by this measurement (33)

(thereby by us, considered an adapted WWT-model) supports the findings by Lee et al. by demonstrating normalization of barrier function by recovery of intercellular lamellar structures. Recovery of the epidermal barrier by decreased TEWL in WWT was investigated and supported in one other study by Schnopp et al. (30) who found a (non-significant) trend, towards decrease in TEWL (Table SII[1]).

Besides itch reduction, the previous mentioned vasoconstriction due to cooling of the skin probably also have an anti-inflammatory effect (11, 31). This possible effect of WWT has only been minimally investigated. A study with 6 AD patients (14), demonstrated a decrease in 4 serum chemokines playing a role in the pathogenesis of AD as inflammatory agents, whereas another small uncontrolled study (20) measuring serum soluble adhesion molecules, as possible markers of intensity of inflammation, in 18 children with AD treated with WWT found significant lower levels of serum E-selectin. Unfortunately, currently, no comparative studies regarding WWT's anti-inflammatory effect vs. other treatment modalities exist.

DISCUSSION

The literature suggests that WWT is a useful treatment modality in several dermatological conditions beyond severe/refractory AD, including all types of eczemas, pruritic diseases like prurigo nodularis, psoriasis and cutaneous lymphomas. Its place as an efficient treatment in milder AD compared to conventional therapy with TCS is, as we demonstrated, questionable, as few data exist. One should consider that WWT is time consuming and demands special training of staff and patients/parents, making it likely less attractive to treat mild disease where other efficient treatment alternatives exist.

As several types and routines of WWT exist (1), it is not surprising that we found a large diversity of methodology and quality (Table I) in the 8 comparative studies investigating WWT. This, along with generally small study populations generates little evidence, making it challenging to make final conclusions. We found little evidence supporting that WWT using TCS might be more efficient compared to emollients only. Data are conflicting concerning if diluted TCS is as efficient as concentrated TCS. Larger randomized controlled trials are needed to investigate this important question, as it is important to evaluate the lowest possible efficient concentration of corticosteroids to avoid potential side effects. Even though the sparse data suggests no systemic adverse effects of corticosteroids, likely prolonged HPA suppression or growth retardation in children, when occluded as in WWT, no studies investigated this on a longer basis.

Data regarding other adverse-effects reported in the comparing studies (Tables SI[1] and SII[1]) generated conflicting results; we surprisingly noted that some studies did not even report side-effects. Sparse evidence supports that fewer side effects as infections are seen in conventional 'open treatment' with TCS compared to WWT+TCS, but also the duration of the treatment is of importance.

WWT seems to be a fast acting treatment modality, especially with TCS beneath the bandages, which might be justifying its place in treatment of severe AD.

Unfortunately, few studies investigated remission time by follow-up past treatment or eventually during treatment with WWT as maintenance therapy. Nicol et al. (11) recently published a case-series study on 72 patients treated with WWT+TCS for a mean of 7.5 days. They performed follow-up one month after treatment, where patients were able to maintain their clinical improvements of the earlier WWT measured by a parent administrated scoring tool, the Atopic Dermatitis Quickscore (56). There was no information on eventual treatment with e.g. TCS after end WWT treatment.

The previously mentioned Devillers et al. study (31) (Table SI[1]) is currently the longest lasting study, with a mean duration of 17 weeks, using WWT with TCS as a maintenance treatment 12 h daily up to 5 times/week, finding exacerbation of AD in only 5 of 24 patients. Beattie & Lewis-Jones (29) (Table SII[1]) noticed an increase in severity just one week after end WWT (with and without TCS) of treatment. Patients were, on the other hand, only treated with emollients, not receiving any other treatment, as would be expected in patients suffering from severe AD.

Mechanisms of WWT are an interesting area not yet well studied. It would be interesting in future studies to investigate whether wet-wrap mechanism is simply by enhanced corticosteroid absorption, and thereby caused by a greater efficacy of these, or if the moist/water in WWT or simply skin occlusion's known effect on skin healing (57) that make the difference. Further studies investigating WWT's role, also without simultaneous TCS treatment, in the epidermal barrier recovery are stressed.

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