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From the Cochrane Library: Interventions for hand eczema

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From the Cochrane Library: Interventions for hand eczema

To the Editor: Hand eczema is a heterogeneous dermatologic condition that can create a diagnostic and therapeutic challenge.[1] Despite the availability of various treatment options for hand eczema, their efficacy remains largely unknown. Herein, we highlight findings from a recently published Cochrane review, "Interventions for hand eczema."[2] Findings of oral and topical interventions are summarized in Tables I and II, respectively.

Nine randomized controlled trials (RCTs) assessed the efficacy of topical corticosteroids, with 7 of these comparing different potencies and classes of corticosteroids to one another. In a double-blinded RCT ($n = 125$) that compared clobetasol propionate foam to placebo vehicle foam, participants rated clobetasol as a superior therapy (risk ratio [RR] 2.32, CI 1.38 to 3.91) (Table II). However, based on the investigator's rating scale, there was no significant difference between clobetasol use and vehicle following a 2-week application (RR 1.43, 95% CI 0.86 to 2.40). It is important to highlight that vehicles contain emollients, which may have influenced the results of this study. In addition, more adverse effects were reported in the treatment group when compared to the vehicle (RR 2.24, 95% CI 0.82 to 6.06). The final RCT ($n = 44$) in this subgroup compared betamethasone cream 0.1% to urea 5%; no significant difference was noted between the 2 groups (RR 0.75, 95% CI 0.55 to 1.03).

Three RCTs explored the utility of topical calcineurin inhibitors for hand eczema treatment. In a double-blinded, placebo-controlled RCT ($n = 28$), the use of tacrolimus resulted in an improvement in investigator-rated control of symptoms (RR 29.00, CI 1.90 to 443.25). In contrast, another double-blinded RCT ($n = 294$) demonstrated that pimecrolimus failed to achieve a significant improvement in investigator-rated control of symptoms following 3 weeks' application (RR 1.53, 95% CI 0.99 to 2.36). Even after 6 weeks' application, another double-blinded RCT ($n = 652$) did not identify significant results (RR 1.28, 95% CI 0.99 to 1.66).

Compared to placebo, application of local ultraviolet B did not yield significant results (RR 2.00, 95% CI 0.26 to 15.62). In another RCT ($n = 60$), there was no significant difference between local ultraviolet B and psoralen and ultraviolet A among patients unresponsive to topical clobetasol (RR 0.50, CI 0.22 to 1.16).

Of all treatments included in this review, there is high-certainty evidence supporting the use of alitretinoin, a retinoid derivative, for the treatment of hand eczema (Table I). Pooled analysis of 2 large trials ($n = 781$) demonstrated that even a low dose of oral alitretinoin (10 mg) resulted in improvement of both participant-rated (RR 1.73, 95% CI 1.25 to 2.40) and investigator-rated control of symptoms (RR 1.73, 95% CI 1.25 to 2.40) (Table I). Investigators were required to rule out diagnoses of psoriasis or infectious dermatoses before including participants in these trials. Oral alitretinoin has been approved for the treatment of hand eczema in Canada and Europe. To date, no published RCTs have evaluated the efficacy of topical alitretinoin on hand eczema.

This Cochrane review highlights the heterogeneity in outcome measures, making it difficult to assess the best treatment option for hand eczema. Despite the limited evidence, and based on the findings derived from the Cochrane review, topical corticosteroids remain the first-line treatment. For severe hand eczema refractory to topical corticosteroids, and if accessible, practitioners may consider prescribing oral alitretinoin.

We would like to thank the original Cochrane authors (Christoffers et al) for giving us permission to write the above summary derived from the Cochrane systematic review article. Authors who contributed to this manuscript are distinct from the original authors who designed and wrote an extensive and comprehensive systematic review paper on this topic. We do not take credit for the original work written by the Cochrane authors.

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Table I. Oral interventions for hand eczema

Comparison	Investigator-rated good/excellent control	Percentage of participants with self-rated good/excellent control	Adverse events
Oral azathioprine and topical clobetasol vs topical clobetasol	Clobetasol 0.05 + 50 mg Azathioprine vs Clobetasol 0.05 only: At 8 weeks: RR: 1.98 95% CI (1.31-3.01) At 24 weeks: RR: 2.33 95% CI (1.61-3.38)	Not measured	AEs not reported
Oral Cyclosporin vs Topical Betamethasone	Cyclosporin vs betamethasone: 60% vs 31%: RR: 1.88, 95% CI (0.88-3.99)	Good/very good efficacy: Cyclosporin vs Betamethasone: (60% vs 48%): RR: 1.25, 95% CI (0.69-2.27)	In Cyclosporin vs betamethasone: Dizziness, vomiting, and facial edema; no significant AEs between the 2 groups: $P = 1.00$; RR: 2.90 95% CI (0.12-68.15)
Oral cyclosporin vs alitretinoin	At 24 weeks: 3/7 (42.9%) in Cyclosporin group vs 2/7 (28.5%) in Alitretinoin group reached clearance: RR: 1.50 95% CI (0.35-6.40)	Cyclosporin group: 4/7 (57.1%) vs 2/7 (28.6%) in Alitretinoin group experienced complete or near-complete clearance: RR: 2.00 95% CI (0.53-7.60)	At least 1 AE (fatigue, myalgia) reported in both groups: RR: 1.50, 95% CI (0.35-6.40)
Alitretinoin vs placebo	Alitretinoin 40 mg: RR: 1.97, 95% CI (1.30-3.00) Alitretinoin 30 mg: RR: 2.75 95% CI (2.20-3.43) Alitretinoin 20 mg: RR: 1.49 95% CI (0.94-2.34) Alitretinoin 10 mg: RR: 1.58 95% CI (1.20-2.07)	Alitretinoin 40 mg, 30 mg, 20 mg, and 10 mg, respectively: RR: 3.51 95% CI (1.80-6.82) RR: 2.75 95% CI (2.18-3.48) RR: 2.74 95% CI (1.37-5.46) RR: 1.73 95% CI (1.25-2.40)	Headache: RR: 3.43 95% CI (2.45-4.81)
Oral triethylenetetramine vs placebo	Control vs placebo: (improvement in 6/20 vs 10/20)	Not measured	AEs not reported
TETDS vs placebo	Clearance was described as "healed": RR: 2.95 95% CI (0.71-12.34); $P = .182$	Not measured	In treated group: Hepatic toxicity: RR: 5.00 95% CI (0.26-96.13), $P = .48$; headache RR: 3.00 95% CI (0.13-68.26), $P = 1.0$
LND and disulphiram vs normal diet and placebo	Clearance of hand eczema was achieved in 10/11 participants in LND group vs 1/10 in control group: RR: 9.09, 95% CI (1.40-58.91) $P = .0003$	Not measured	In the treated group: metallic taste: RR 6.42: 95% CI (0.37-110.71); mild drowsiness RR: 4.58 95% CI (0.25-85.33), $P = .4762$
DSCG vs LND	Not measured	Pruritus improvement: DSCG vs LND (5/8 vs 1/8) achieved clearance: RR: 5.00: 95% CI (0.74-33.78) $P = .1189$	AEs not reported
Ranitidine vs placebo	Clear or markedly improved RR: 2.22 95% CI (1.20-4.10)	Not measured	AEs not reported
Oral evening primrose oil vs placebo	Evening primrose oil epogam vs placebo (mean and SD) 18 ± 12.37 vs 30.4 ± 23.36	Not measured	AEs not reported

AE, Adverse effect; *DSCG*, disodium cromoglycate diet; *LND*, low-nickel diet; *RR*, risk ratio; *TETDS*, tetraethylthiuram disulfide.
Christoffers et al[2] (Cochrane authors) defined 3 primary outcome measures (included in each column of this table). "Not measured" refers to individual RCTs that include results of their intervention but do not include primary outcomes.

Table II. Topical interventions for hand eczema

Comparison	Investigator-rated good/excellent control	Self-rated good/ excellent control	Adverse events
Emollient E-DO vs Vehicle	Investigator rated as good/ excellent *n* = 37 (58.73%) in the E-DO group vs 36 (57.14%) in the vehicle group	E-DO group vs Vehicle 34.92% vs 36.51%	In the E-DO hands group: *n* = 6 vs *n* = 2 in vehicle hands group reporting pruritus
Fluprednidene Acetate Cream vs Betamethasone-Valerate	After 3 weeks of treatment: RR: 0.59 95% CI (0.28-1.23)	Not measured	AEs (redness, swelling, irritation, dryness) were reported in both groups: RR: 0.90 95% CI (0.36-2.23)
Betamethasone-Dipropionate Film-Forming Lotion vs Betamethasone-Dipropionate Thick Lotion	In the betamethasone-dipropionate film-forming lotion: *n* = 5/28 achieved good-excellent symptom control vs 0 in the control group (*P* = .051)	Not measured	Stinging reported in both groups RR: 1.33 95% CI (0.33-5.44)
Clobetasol Propionate Cream vs Intermittent Fluprednidene Acetate Cream	In Clobetasol group: *n* = 32/46 (70%) vs *n* = 14/46 (30%) in the fluprednidene group	Not measured	Burning sensation: (Clobetasol and Fluprednidene, *n* = 2); reversible atrophy and brittle skin (Clobetasol *n* = 1)
Clobetasol Propionate Foam 0.05% vs Vehicle Foam	38.7% (24/62 participants) had an ISGA score of 0 or 1 vs. 27% (17/63 participants) in the vehicle group: RR: 1.43, 95% CI (0.86-2.40)	RR: 2.32 95% CI (1.38-3.91), favors Clobetasol	AEs (burning, pruritus): RR: 2.24 95% CI (0.82-6.06)
Desonide Cream 0.1% vs Desonide Cream 0.05%	Not measured	Not measured	Stinging reported in both groups
Mometasone vs Vehicle (at different frequency)	Mometasone furoate 3 times/ week vs emollients only: RR 3.13: 95% CI (1.75-5.59) Mometasone 2 times/week vs emollients only: RR: 2.55 95% CI (1.40-4.67)	Not Measured	Reversible atrophy (in Mometasone group): RR: 1.76 95% CI (0.45-6.83)
Clobetasol (0.05%) and 2.5% Zinc Sulfate Cream vs 0.05% Clobetasol Cream	(clobetasol vs zinc + clobetasol): Improvement in scaling (*n* = 3 vs *n* = 25); Redness (*n* = 1 vs *n* = 41) Lichenification (*n* = 7 vs *n* = 24)	Not measured	AEs not reported
Betamethasone-Valerate 0.1% Cream Twice Daily vs Betamethasone-Valerate 0.1% Cream and Urea 5% Cream	Clearance was defined as a score ≤3 on the HEES: RR: 0.75 95% CI (0.55-1.03)	Not measured	AEs not reported
Topical Tacrolimus vs Vehicle	RR: 29.0 95% CI (1.9-443.25)	Not measured	Burning/itching at application site. RR: 0.9 95% CI (0.53-152.93)
Topical Pimecrolimus vs Vehicle	At 3 weeks: RR 1.53 95% CI (0.99-1.66) at 6 weeks: RR 1.28 (0.99-1.66). For IHE: RR: 1.7 95% CI (0.93-3.10). For AHE: RR: 1.33 95% CI (0.30-5.96). For EHE: RR: 1.32 95% (0.75-2.33)	Not measured	Erythema or irritation RR: 0.56 95% CI (0.3-1.06) Itching RR: 0.89 95% CI (0.52-1.53) Warmth, stinging, burning RR: 0.82 95% CI (0.52-1.29) HSV infection: RR: 0.6 95% CI (0.15-2.51)

Continued

Table II. Cont'd

Comparison	Investigator-rated good/excellent control	Self-rated good/ excellent control	Adverse events
Topical Antibacterial Agents: Betamethasone-Valerate/ Clioquinol Cream vs Betamethasone-Valerate/ Fusidic Acid	Investigator rated as clear or almost clear: RR: 1.03 95% CI (0.74-1.43)	Not measured	At least 1 AE reported in both groups: RR: 1.14 95% CI (0.51-2.56)
Topical Retinoid: Bexarotene 1% gel vs Bexarotene with Corticosteroids	Bexarotene only vs Bexarotene + Mometasone RR: 0.85 95% CI (0.4-1.8) Bexarotene only vs		Bexarotene + Hydrocortisone RR: 1.83 95% CI (0.61-5.53) Bexarotene + Mometasone vs Bexarotene + Hydrocortisone RR: 2.15 95% CI (0.67-6.89)
Not measured	Irritation/rash: RR: 0.93 95% CI (0.34-2.53) stinging/burning: RR: 0.23 95% CI (0.05-1.11) exacerbation of dermatitis: RR: 5.31 95% CI (0.32-89.44). For Bexarotene 1% gel vs		Bexarotene + Hydrocortisone: AEs include: Stinging/burning RR: 0.5 95% CI (0.08-3.19) Irritation/rash: RR: 1 95% CI (0.36-2.76) Exacerbation of dermatitis: RR 0.63 [0.2-1.97]
Furpalmate 0.3% Cream vs Hydrocortisone Acetate 0.5% cream	RR: 0.9 95% CI (0.76-1.07)	Not measured	AEs not reported
Fumaric Acid 5% Cream vs Triamcinolone 0.1% Cream	Not measured	Not Measured	Burning RR: 0.93 95% CI (0.14-6.18)
Fumaria Parviflora vs Vehicle Cream	Not measured	Not measured	Erythema and papules in treated group: RR: 3.00 95% CI: (0.13-69.87)
Local UVB Alone vs Placebo	RR: 2.00 95% CI (0.26-15.62)	Not measured	AEs not reported
Whole-Body UVB + Local UVB Hands vs Placebo	RR: 3.67 95% CI (0.90-14.97)	Not measured	AEs not reported
Whole-Body UVB + Local UVB Hands vs Local UVB Hands Alone	RR: 2.20 95% CI (0.83-5.84)	Not measured	AEs not reported
Local Narrow Band UVB vs Local PUVA	RR: 0.50 95% CI (0.22-1.16)	Not measured	Erythema reported in local narrow UV band RR: 19.00 95% CI (1.16-312.4), $P = .0019$

AE, Adverse event; *HEES*, Hand Eczema Extent score; *ISGA*, Investigator's Static Global Assessment; *PUVA*, psoralen and ultraviolet A radiation; *RR*, risk ratio; *UVB*, ultraviolet B.
Christoffers et al[2] (Cochrane authors) defined 3 primary outcome measures (included in each column of this table). "Not measured" refers to individual RCTs that include results of their intervention but do not include primary outcomes.

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Conflicts of interest

Dr Dellavalle is a Joint Coordinating Editor for Cochrane Skin, a dermatology section editor for UpToDate, a Social Media Editor for the *Journal of the American Academy of Dermatology* (*JAAD*), a Podcast Editor for the *Journal of Investigative Dermatology* (*JID*), and editor for the *Journal of Medical Internet Research* (*JMIR*) *Dermatology*. He is a coordinating editor representative and cochair on Cochrane Council. Dr Maghfour is a subinvestigator for Incyte, Immune Tolerance Network, and Avita Recell. He is an editorial board member of the *Journal of Dermatology Nurses' Association* (*JDNA*) and *JMIR Dermatology*. Author Strock has no conflicts of interest to declare.

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