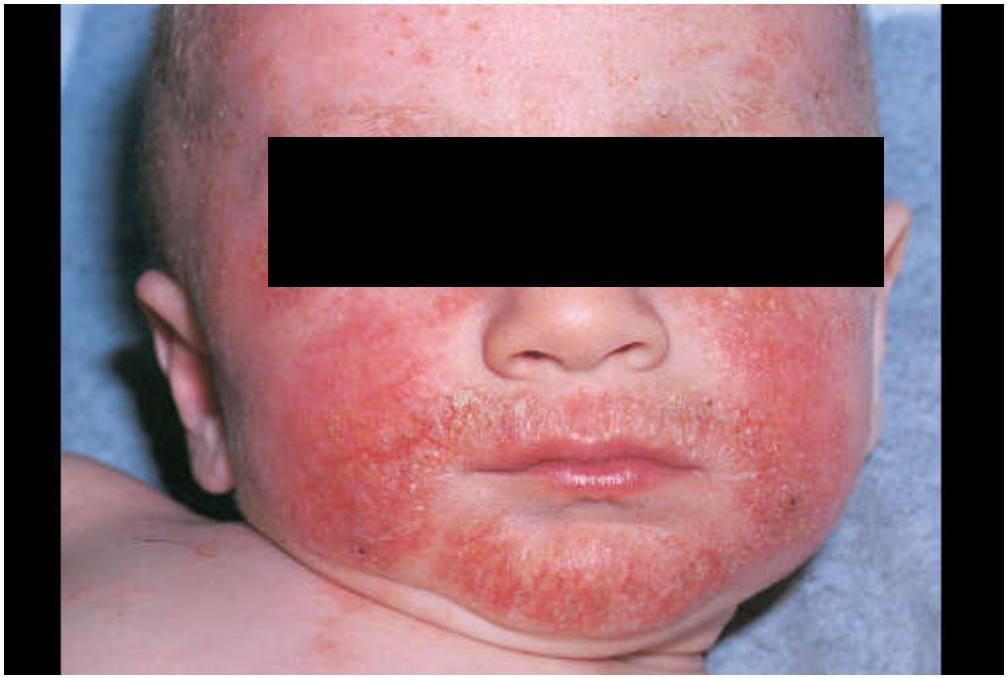
Topical tacrolimus for atopic dermatitis

Atopic dermatitis (AD) (or atopic eczema) is a chronic inflammatory skin condition



Drugs

- **Topical glucocorticosteroids (corticosteroids)** *first-line therapy*
- Antihistamines
- Systemic glucocorticosteroids
- Cyclosporine
- Azathioprine
- Methotrexate
- Topical calcineurin inhibitors (TCIs) : **Tacrolimus** & pimecrolimus : *alternative treatment.*

- Tacrolimus (0.03% and 0.1%)
- isolated in Japan in 1980
- first approved for the treatment of AD in Japan in 1999
- in USA in 2000
- in The European Union in 2002

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Topical tacrolimus for atopic dermatitis (Review)

Cury Martins J, Martins C, Aoki V, Gois AFT, Ishii HA, da Silva EMK

Cury Martins J, Martins C, Aoki V, Gois AFT, Ishii HA, da Silva EMK.
Topical tacrolimus for atopic dermatitis.
Cochrane Database of Systematic Reviews 2015, Issue 7. Art. No.: CD009864.
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Study characteristics

- 20 studies, with 5885 participants, until 6/2015.
- **Selection criteria**
  - All randomised controlled trials (RCTs) of participants with **moderate to severe** atopic dermatitis (both children and adults) using topical tacrolimus at any dose, course duration, and follow-up time compared with other active treatments.
- Outcomes :
  - the physicians' assessment of improvement,
  - the participants' self-assessment, and
  - any adverse effects.
  - Others : SCORAD (SCORing Atopic Dermatitis, a tool for measuring atopic dermatitis severity) and the affected body surface area.

1. Tacrolimus 0.1% compared with corticosteroids

Physician's assessment of global response of improvement : Three studies

- **For 3 weeks**
  - better than low-potency corticosteroid(1) *(RR 3.09, 95% CI 2.14 to 4.45, 1 study, 371 participants)*
  - No significant differences : tacrolimus 0.1% and a mid-potency corticosteroid(2) (*RR 0.95, 95% CI 0.78 to 1.16, 1 study, 377 participants)*

(1) hydrocortisone acetate 1% ointment

(2) hydrocortisone butyrate 0.1% ointment

1. Tacrolimus 0.1% compared with corticosteroids

- **For 6 months :** better than a mid-potency corticosteroid used **on the trunk and extremities** and a low-potency corti- costeroid used **on the face and neck** *(RR 1.32, 95% CI 1.17 to 1.49, 1 study, 972 participants)*
- **For 12 months** : no difference *(RR 1.35, 95% CI 0.86 to 2.12, 1 study, 80 participants)*

1. Tacrolimus 0.1% compared with corticosteroids

Participant's self-assessment of global response of improvement : one study, comparing tacrolimus 0.1% and hydrocortisone butyrate 0.1% (mid-potency corticosteroid), significantly **higher number of participants** in the tacrolimus group reporting improvement *(RR 1.21, 95% CI 1.13 to 1.29, 1 study, 972 participants).*

1. Tacrolimus 0.1% compared with corticosteroids

Adverse

- Burning : more frequent in the tacrolimus 0.1% group (4 studies).
- When assessing “pruritus” and “skin infection” : no significant differences.

2. Tacrolimus 0.03% versus corticosteroids :

- **Physician's assessment of global response of improvement** Five studies
- tacrolimus 0.03% better than low-potency corticosteroid :
  - tacrolimus 0.03% once a day vs a low-potency corticosteroid twice a day *(RR 2.05, 95% CI 1.36 to 3.08, 1 study, 411 participants) in children;*
  - tacrolimus 0.03% twice a day vs the same low-potency corticosteroid *(RR 2.58, 95% CI 1.96 to 3.38, 2 studies, 790 participants).*
- no significant : with mid-potency corticosteroids *(RR 0.45, 95% CI 0.13 to 1.57, 2 studies, 409 participants).*

2. Tacrolimus 0.03% versus corticosteroids :

Participant's self-assessment of global response of improvement :Two studies

- Tacrolimus 0.03% in both once or twice daily groups, reported better or much better improvement than hydrocortisone acetate 1% *(RR 1.33, 95% CI 1.13 to 1.57, 1 study, 411 participants; RR 1.64, 95% CI 1.41 to 1.90, 1 study, 416 participants, respectively).*
- The comparison of tacrolimus 0.03% and fluticasone 0.005% found no differences between the groups *(RR 0.98, 95% CI 0.92 to 1.05, 1 study, 473 participants; Analysis 3.2).*

2. Tacrolimus 0.03% versus corticosteroids

Occurence and severity of adverse effects : Five studies

- higher incidence of burning and pruritus in the tacrolimus (RR 2.48, 95% CI 1.96 to 3.14, 5 studies, 1883 participants)
- Skin infection : no significant difference (RR 1.07, 95% CI 0.69 to 1.66, 4 studies, 1643 participants)

3. Tacrolimus 0.03% versus tacrolimus 0.1%

Physician's assessment of global response of improvement 6 studies

•a statistically significant difference in the physician's assessment of global response (clear or excellent) favouring tacrolimus 0.1% *(RR 0.82, 95% CI 0.72 to 0.92, 6 studies, 1640 participants)*

3. Tacrolimus 0.03% versus tacrolimus 0.1%

Participant's self-assessment of global response of improvement : one study

- no difference: 76% (32 out of 42) versus 91% (38 out of 42) (P = 0.08, Chi^2 test).

3. Tacrolimus 0.03% versus tacrolimus 0.1%

Occurence and severity of adverse effects

•Four 3-week studies, no significant difference in the incidence of adverse events (RR 0.95, 95% CI 0.86 to 1.06, 4 studies, 986 participants; Analysis 4.2).

•A 12-week study, also failed to find any significant difference between the groups, adjusted incidence of 42.7% versus 33.7% for **burning** and 41.2% versus 32.2% for **pruritus.**

Summary of main results

- The variability of drug doses, outcomes, and follow-up periods made it difficult to carry out meta-analyses.
- Tacrolimus was better than low-potency corticosteroids.
- Adverse :
  - burning and itching were more frequent than TCS
  - no difference in skin infection
  - **no risk of skin thinning, even for longer periods.**
  - not find any evidence associating a risk of malignancies

Thank you