Topical calcineurin inhibitors for atopic dermatitis

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Clinical question

What are the risks and benefits of using topical calcineurin inhibitors for atopic dermatitis?

Bottom line

For improvement of atopic dermatitis, 0.1% tacrolimus ointment is at least equivalent to moderate-potency topical corticosteroids. Use of 1% pimecrolimus cream is better than placebo but is likely inferior to 0.1% tacrolimus ointment and moderate-potency corticosteroids. Burning skin sensation is common with early use (30% to 50% of users) but tapers off for most (<10% at 6 months).

Evidence

Results are statistically significant unless indicated. Four systematic reviews with meta-analyses published between 2014 and 2023 were identified.[1-4]

- Topical calcineurin inhibitor versus vehicle or low-potency topical corticosteroids
  - -Use of 0.1% tacrolimus ointment (2 randomized controlled trials [RCTs], 464 patients) improved atopic dermatitis in 48% to 67% of patients versus 16% to 38% with vehicle or 1% hydrocortisone acetate ointment (number needed to treat [NNT]=3 to 4 at 3 weeks).[5,6] Another RCT produced similar results.[7]
  - -Use of 1% pimecrolimus cream (meta-analysis: 8 RCTs, 2298 patients) improved atopic dermatitis in 44% versus 22% with vehicle at 6 weeks (NNT=5).[1]
- Topical calcineurin inhibitor versus moderate- or high-potency topical corticosteroids
  - -With 0.1% tacrolimus ointment, 2 RCTs (1540 patients) reported improved atopic dermatitis for 73% to 93% versus 52% to 88% with corticosteroids at 3 to 12 weeks.[8,9] One other small RCT reported similar findings.[10] Four RCTs (523 patients) found no difference at 2 weeks to 11 months.[11-14]
  - -With 1% pimecrolimus cream, 1 RCT (2418 patients) found no difference at 3 weeks.[15] Two RCTs (745 patients) found atopic dermatitis improved for 37% to 53% of patients with 1% pimecrolimus cream versus 68% to 88% with corticosteroids at 3 weeks, with corticosteroids superior (NNT=3 to 4).[16,17]
- Comparison of calcineurin inhibitors
  - -In a meta-analysis (3 RCTs, 543 patients), 35% of patients had good responses with 0.1% tacrolimus ointment versus 19% with 1% pimecrolimus cream at 2 to 6 weeks (NNT=7).[2]
  - -A network meta-analysis found no difference.[18]
- Adverse effects with calcineurin inhibitors versus topical corticosteroids (3 to 52 weeks)[4]
  - -Skin burning was reported by 30% versus 9%, respectively (number needed to harm=4).
  - -Skin atrophy was noted in 0% versus 0.8%, respectively, which was not a statistically significant difference.
- Limitations: Most RCTs were industry funded.[2]

Context

- Compared with 0.03% formulations, 0.1% tacrolimus ointment is superior, with similar side effects.[2]
- Regarding age, 1% pimecrolimus cream is approved for those 3 months and older,[19] while 0.1% tacrolimus ointment is approved for those older than 15 years.[20]
- Application site reactions (skin burning, pruritus) are usually transient. For example, with 0.1% tacrolimus ointment, reports of skin burning decreased over time, from 51% (week 1), to 17% (week 2), to 7% (month 6).[8]
- Reports of an association between calcineurin inhibitors and lymphoma have been inconsistent.[21-23] Health Canada removed its related warning from tacrolimus ointments in 2021.[24]
- Cost[25]: 30 g of 0.1% tacrolimus costs approximately $103; 30 g of 0.1% betamethasone valerate, $13.

Implementation

Atopic dermatitis is a chronic, relapsing-remitting disease characterized by scaly pruritic lesions. Treatment starts with patients taking short daily baths with soap-free cleansers and applying fragrance-free emollient twice daily.[26] Topical corticosteroids are used for flare-ups twice daily until rash and itch have resolved, which may take days to weeks.[26] Low-potency corticosteroids (eg, 1% hydrocortisone cream) can be used on the face and moderate- to high-potency corticosteroids (eg, 0.1% betamethasone valerate) on the body.[26] Topical calcineurin inhibitors may be used for flare-ups (especially if steroids are to be avoided, or for facial or flexural lesions) or maintenance (steroid sparing); pimecrolimus is recommended for mild to moderate disease, tacrolimus for moderate to severe disease.[26]

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Competing interests
None declared

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