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Topical Calcineurin Inhibitors in the Management of Chronic Pruritus in Older Adults: A Research Letter

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ABSTRACT

In this study, we aimed to analyze the literature to date on the utilization of topical calcineurin inhibitors in the management of pruritus among older adults, ages 65 and older. The 16 studies included in final analysis demonstrated that topical calcineurin inhibitors are well-tolerated across ages and are effective in treating a wide variety of chronic pruritic conditions. Collectively, these findings support that topical calcineurin inhibitors should be considered a safe, plausible option for managing age-associated itch.

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INTRODUCTION

Chronic itch is common among older adults, however, without overt serologic or histologic abnormalities, many geriatric patients have no discernible cause of their pruritus. In these cases, it is postulated that itching may be due to age-related immunologic and neuropathic pathophysiologic changes.[1] However, in the absence of a cohesive diagnosis, there is significant variability in the therapeutic strategies for managing itch in this population. This often results in undertreatment, exclusionary payer practices, and limited research efforts.

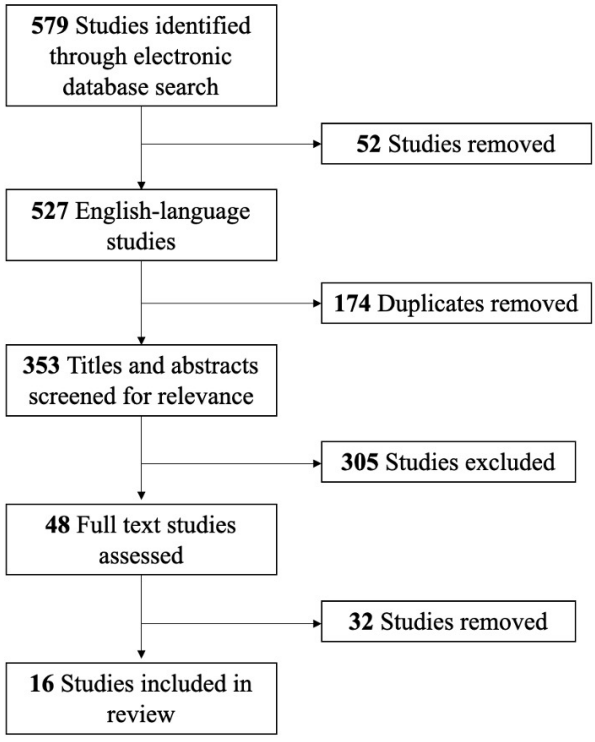
Topical calcineurin inhibitors (TCIs) are approved by the United States Food and Drug Administration for atopic dermatitis and have been reported to provide safe, rapid pruritus relief in these patients.[2] In addition to their anti-inflammatory effects, TCIs may also reduce itch by depleting pruritic neuropeptides in cutaneous nerve fibers,[3] and therefore, may serve as a therapeutic option for both inflammatory and neuropathic itch.[1]

Given the prevalence of itch among older adults and the anti-pruritic effects of TCIs, this study aims to evaluate the literature to date on the utilization of TCIs for pruritus management in older adults with the hopes of exploring another treatment option for age-associated itch.

MATERIALS AND METHODS

In May 2022, a scoping review of PubMed was conducted, limited to the English language, with search terms: 'calcineurin inhibitors', 'tacrolimus', 'pruritus', 'itch', 'elderly', 'older adult', and 'geriatric'. Studies were limited to those that included participants over the age of 65. The database search yielded a total of 579 articles, including 527 English-language studies.

FIGURE 1. Study selection methods.



Study selection flow diagram for the review of published studies on the use of topical calcineurin inhibitors in geriatric patients.

After removing 174 duplicate records and screening the remaining titles and abstracts for relevance, 48 full-text articles were reviewed (Figure 1).

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TABLE 1.

Studies Evaluating the Efficacy of Topical Calcineurin Inhibitors in the Management of Pruritic Conditions

Author	Diagnosis	Topical Therapy	Sample Size	Ages (years)	Itch Reduction	Medication-Related Adverse Effects
Ständer et al 2006[4]	Chronic pruritus, prurigo nodularis, anogenital pruritus	0.1% tacrolimus and 1.0% pimecrolimus	20	26-76	Mean reduction in itch of 67%	Burning (30%)
Ochi et al 2016[5]	Notalgia paresthetica	0.1% tacrolimus	7	Mean: 64.6	Reduction in itch intensity or frequency in 86% of patients	Burning (14%)
Patsatsi et al 2013[6]	Genital lichen sclerosis	Tacrolimus	46	Mean: 58.8	A significant decrease in itch (P=0.016)	None reported
Kelekci et al 2008[7]	Vulvar lichen simplex chronicus	1.0% pimecrolimus	12	44-65	A substantial decrease in pruritus at 1 (P<0.01) and 3 months (P<0.001)	Burning (33.3%)
Ucak et al 2013[8]	Pruritus ani	0.03% tacrolimus	32	18-66	Significant reduction in itching score at 4 (P=0.001), 6 (P=0.001), and 10 weeks (P=0.002)	Burning (12.5%)
Duque et al 2005[9]	Hemodialysis-related pruritus	0.1% tacrolimus	20	Mean: 59.6	No major difference in itch reduction between the tacrolimus and vehicle groups (P= 0.5).	Warmth/burning (67%)
Schulz et al 2007[10]	Asteatotic eczema	1.0% pimecrolimus	40	20-81	Pruritus severity was reduced by 65% (P=0.042)	None reported
Kim et al 2007[11]	Seborrheic dermatitis	1.0% pimecrolimus	20	22-79	Significant reduction in mean pruritus scores (P<0.001)	Burning/tingling (45%)
Acar et al 2010[12]	External auditory pruritus	1.0% pimecrolimus	43	24-69	Significant reduction in itch severity at 1 and 3 months (P<0.001)	Contact allergy (2.3%)
Kuypers et al 2004[13]	Uremic pruritus	0.1% tacrolimus	21	Mean: 61.6	Modified pruritis assessment score significantly reduced by 81.8% after 6 weeks of treatment	Tingling (19%), Stinging (4.8%), Rash (4.8%)
Weisshaar 2008[14]	Genital pruritus	1.0% pimecrolimus and 0.03% tacrolimus	2	67-73	Case 1: (1.0% pimecrolimus): Complete resolution of pruritus within 1 week through 3-month follow up Case 2: (0.03% tacrolimus): Complete resolution of pruritus within 2 weeks through 1-year follow up	None reported
Aguilar-Bernier et al 2005[15]	Primary biliary cirrhosis	0.1% tacrolimus	1	67	Complete resolution of pruritus and excoriations after 1 month of treatment without relapse at 6-month follow-up	None reported
Hanifin et al 2001[16]	Atopic dermatitis	0.03% and 0.1% tacrolimus	632	15-79	Significant reduction in pruritus score for both treatment groups (P<0.001)	No specific adverse events reported
Luger et al 2001[17]	Atopic dermatitis	0.6% and 1.0% pimecrolimus	130	18-71	Pimecrolimus 0.6% and 1.0% groups had a significant reduction in pruritus scores (P=0.001 and P=0.007)	Warmth/burning (43-49%)
Kaufmann et al 2006[18]	Atopic dermatitis	1.0% pimecrolimus	137	18-81	Significant improvement in pruritus (P=0.001)	Burning (3%)
Tan et al 2015[19]	Scrotal lichen simplex chronicus	0.1% tacrolimus	40	22-82	Significant reduction in mean itch score and itch frequency (P<0.0005)	Warmth or burning (30%)

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RESULTS

Among the 16 studies included in final analysis (Table 1), TCIs were used to treat various pruritic conditions, including chronic generalized pruritus. Only one study included exclusively patients over the age of 65 (n=2). Most studies (15/16) found that TCIs significantly improved pruritus. The most common adverse effect reported was transient application site burning, reported in 10/16 studies. There was a single report of a mild erythematous rash and one report of a contact allergy to TCIs, but there were no reports of serious infection or malignancy.

DISCUSSION

TCIs are generally well-tolerated and adverse effects are typically mild without increased concern of known side effects for older adults as compared younger populations. While a limited number of cases of lymphoma or skin cancer have been reported in patients receiving TCI therapy,[2] there is sparse evidence associating TCI use with malignancy.[20] When comparing this information to current treatment options for pruritus, TCIs avoid systemic immunosuppression, do not result in sedation, a potentially debilitating side effect for older adults, and are not associated with skin thinning.[21]

Still, data evaluating the efficacy of TCIs for pruritus in geriatric patients remains limited. This is unsurprising given the general underrepresentation of older adults in clinical trials.[22,23] Despite the paucity of primary literature, multiple articles highlight the use of TCIs as a plausible therapeutic option for pruritus in geriatric patients.[1,3,24] To our knowledge, this is the largest evaluation to date of its use in this neglected and underrepresented population. In conclusion, the summation of these studies helps providers and payers identify TCIs as a safe therapeutic option for age-associated itch.

DISCLOSURES

The authors have no conflict of interest to declare.

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