

**The Analysis Study of Effectiveness and Safety of Topical
Treatment for Vernal Keratoconjunctivitis: A Comprehensive
Systematic Review**

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ABSTRACT

Background: This systematic review aims to evaluate and synthesize evidence on the efficacy and safety of topical treatments for VKC, focusing on the effectiveness of treatments like cyclosporine A, tacrolimus, and other topical therapies in alleviating symptoms and improving clinical outcomes. **Methods:** The review followed PRISMA 2020 guidelines, including studies published in English from 2014 to 2024. **Results:** Eight studies met the inclusion criteria. The review found that both cyclosporine A and tacrolimus significantly reduced symptom and sign scores in VKC patients. Rebamipide was comparable in efficacy to cyclosporine and tacrolimus. Tacrolimus showed efficacy in corticosteroid-refractory cases, while cyclosporine A reduced steroid dependency and related side effects. **Conclusion:** Topical cyclosporine A and tacrolimus are effective in managing VKC, with improvements in symptoms and clinical signs observed across studies. Cyclosporine A is particularly effective in reducing reliance on corticosteroids, while tacrolimus is beneficial for corticosteroid-refractory VKC. Personalized treatment strategies should be considered based on individual patient responses and tolerability.

Keyword: cyclosporine A, ocular allergy, topical treatments, tacrolimus, Vernal Keratoconjunctivitis (VKC)

INTRODUCTION

Vernal keratoconjunctivitis (VKC) is a chronic, bilateral condition commonly seen in children, often starting in the first decade of life. While it predominantly affects younger individuals, cases in adults have also been reported.¹ The prevalence of VKC varies significantly by region, with the highest incidence found in African countries and decreasing with increasing distance from the equator. The condition is marked by symptoms such as itching, light sensitivity, white mucous discharge, tearing, a foreign body sensation, and pain from corneal shield ulcers.^{2,3} Key features of VKC include Trantas dots (clusters of epithelial cells and eosinophils), cobblestone giant papillae on the upper tarsal lid, and shield ulcers. Additional signs may include conjunctival hyperemia, gelatinous infiltrates at the limbus, corneal neovascularization, and pseudogerontoxon.⁴ VKC can present in three forms: tarsal, limbal, and mixed. The tarsal form is

distinguished by papillae on the upper tarsal lid, while the limbal form is characterized by gelatinous infiltrates in the limbus, Trantas dots, and potentially punctate keratitis and shield ulcers. The mixed form involves both corneal and tarsal conjunctival involvement.^{5,6}

Although VKC often resolves after puberty, inadequate treatment can lead to severe visual impairments, including progressive vision loss (reported in 5-30% of cases), shield ulcers, cataracts, and glaucoma, particularly from prolonged steroid use.⁷ Treatment options vary: mild cases are typically managed with antihistamine eye drops, mast cell stabilizers, eosinophil inhibitors (like ketotifen), and short-term topical steroids. Moderate to severe cases may require extended steroid courses and/or immunomodulatory therapy with cyclosporine or tacrolimus eye drops. In rare instances, surgical intervention may be necessary for ulcer debridement or to address advanced glaucoma and cataracts.^{8,9}

VKC falls under the category of ocular allergies, one of six subtypes that also include seasonal allergic conjunctivitis (SAC), perennial allergic conjunctivitis (PAC), atopic keratoconjunctivitis (AKC), contact blepharoconjunctivitis (CBC), and giant papillary conjunctivitis (GPC). The exact causes of VKC remain uncertain, but its development likely involves a complex interplay of genetic, endocrinological, immune-mediated, and environmental factors.⁷

The purpose of this systematic review is to evaluate and synthesize the available evidence regarding the efficacy and safety of various topical treatments for VKC. This comprehensive systematic review seeks to determine which topical therapies offer the most effective relief from VKC symptoms, including itching, photophobia, and mucous discharge, as well as improvements in clinical outcomes such as the resolution of corneal shield ulcers and Trantas dots. The review aims to assess the safety profiles of different topical treatments, identifying any adverse effects or complications associated with their use. This

includes evaluating long-term consequences, such as the risk of cataracts or glaucoma resulting from prolonged steroid use. By comparing the effectiveness and safety of various treatment options—including antihistamines, mast cell stabilizers, eosinophil inhibitors, and corticosteroids—the review intends to guide clinical decision-making and optimize treatment strategies for VKC. Furthermore, the review will highlight gaps in current knowledge, such as the long-term efficacy of newer treatments or the effectiveness of combination therapies. This identification of research gaps will help inform future studies and improve management practices for VKC.

METHODS

Protocol

The author of the study meticulously adhered to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 guidelines. This was done to ensure that all regulations were met by the study. The chosen methodology was carefully developed

to ensure the accuracy and consistency of the study findings.

Criteria for Eligibility

This article offers a thorough review of research conducted over the past decade on the efficacy and safety of topical treatments for vernal keratoconjunctivitis. It aims to enhance and clarify patient treatment practices through detailed data analysis. The primary goal of this review is to highlight key topics that are prevalent across various sources in the literature.

Particular inclusion and exclusion criteria were implemented in order to guarantee the accuracy of the data used in this investigation. To be eligible for inclusion, items must have been published in English between 2014 and 2024. Editorials, submissions without a DOI, published reviews, and duplicate journal entries are a few of the exclusion criteria.

Search Strategy

The study's keywords include "topical therapy vernal keratoconjunctivitis". For this

research, the following Boolean MeSH keywords were entered into the databases (("topical"[All Fields] OR "topically"[All Fields] OR "topicals"[All Fields]) AND ("therapeutics"[MeSH Terms] OR "therapeutics"[All Fields] OR "therapies"[All Fields] OR "therapy"[MeSH Subheading] OR "therapy"[All Fields] OR "therapys"[All Fields]) AND ("conjunctivitis, allergic"[MeSH Terms] OR ("conjunctivitis"[All Fields] AND "allergic"[All Fields]) OR "allergic conjunctivitis"[All Fields] OR ("vernal"[All Fields] AND "keratoconjunctivitis"[All Fields]) OR "vernal keratoconjunctivitis"[All Fields])) AND (y_10[Filter]).

Data retrieval

Before beginning this methodical investigation, the authors carefully read the abstract and title of each publication to assess its significance. Only those papers that satisfied the inclusion requirements and supported the article's objectives were given more weight. Ultimately, a recurring pattern discovered via

multiple queries yielded a conclusive response. Only English-language full-text entries were accepted. The strictest screening methodology was used to produce content that met all planned inclusion criteria and had a clear relationship to the subject matter of the study. Studies that did not follow these trends were usually ignored, and their findings were missed. During the assessment, a large number of items were located and examined, including titles, authors, publication dates, locations, study methodologies, and variables.

Quality Assessment and Data Synthesis

The research described in each article's title and abstract was evaluated independently by the writers to identify the papers that required more research. The next step involved going over each document that met the predetermined criteria to be included in the review. The outcomes of the evaluation process determined which articles would be included in the review. This criterion was able to facilitate a thorough analysis of prior research and the

factors that qualified them for the review by expediting the selection of articles for additional evaluation.

Tabel 1. Metode strategi pencarian artikel

Database	Strategi Pencarian	Hits
Pubmed	((("topical"[All Fields] OR "topically"[All Fields] OR "topicals"[All Fields]) AND ("therapeutics"[MeSH Terms] OR "therapeutics"[All Fields] OR "therapies"[All Fields] OR "therapy"[MeSH Subheading] OR "therapy"[All Fields] OR "therapy s"[All Fields] OR "therapys"[All Fields]) AND ("conjunctivitis, allergic"[MeSH Terms] OR ("conjunctivitis"[All Fields] AND "allergic"[All Fields]) OR "allergic conjunctivitis"[All Fields] OR ("vernal"[All Fields] AND "keratoconjunctivitis"[All Fields]) OR "vernal keratoconjunctivitis"[All Fields])) AND (y_10[Filter])).	217
Science Direct	<i>topical: "topical"[All Fields] OR "topically"[All Fields] OR "topicals"[All Fields] therapy: "therapeutics"[MeSH Terms] OR "therapeutics"[All Fields] OR "therapies"[All Fields] OR "therapy"[Subheading] OR "therapy"[All Fields] OR "therapy's"[All Fields] OR "therapys"[All Fields] vernal keratoconjunctivitis: "conjunctivitis, allergic"[MeSH Terms] OR ("conjunctivitis"[All Fields] AND "allergic"[All Fields]) OR "allergic conjunctivitis"[All Fields] OR ("vernal"[All Fields] AND "keratoconjunctivitis"[All Fields]) OR "vernal keratoconjunctivitis"[All Fields]</i>	303
Sagepub	topical therapy vernal keratoconjunctivitis	60

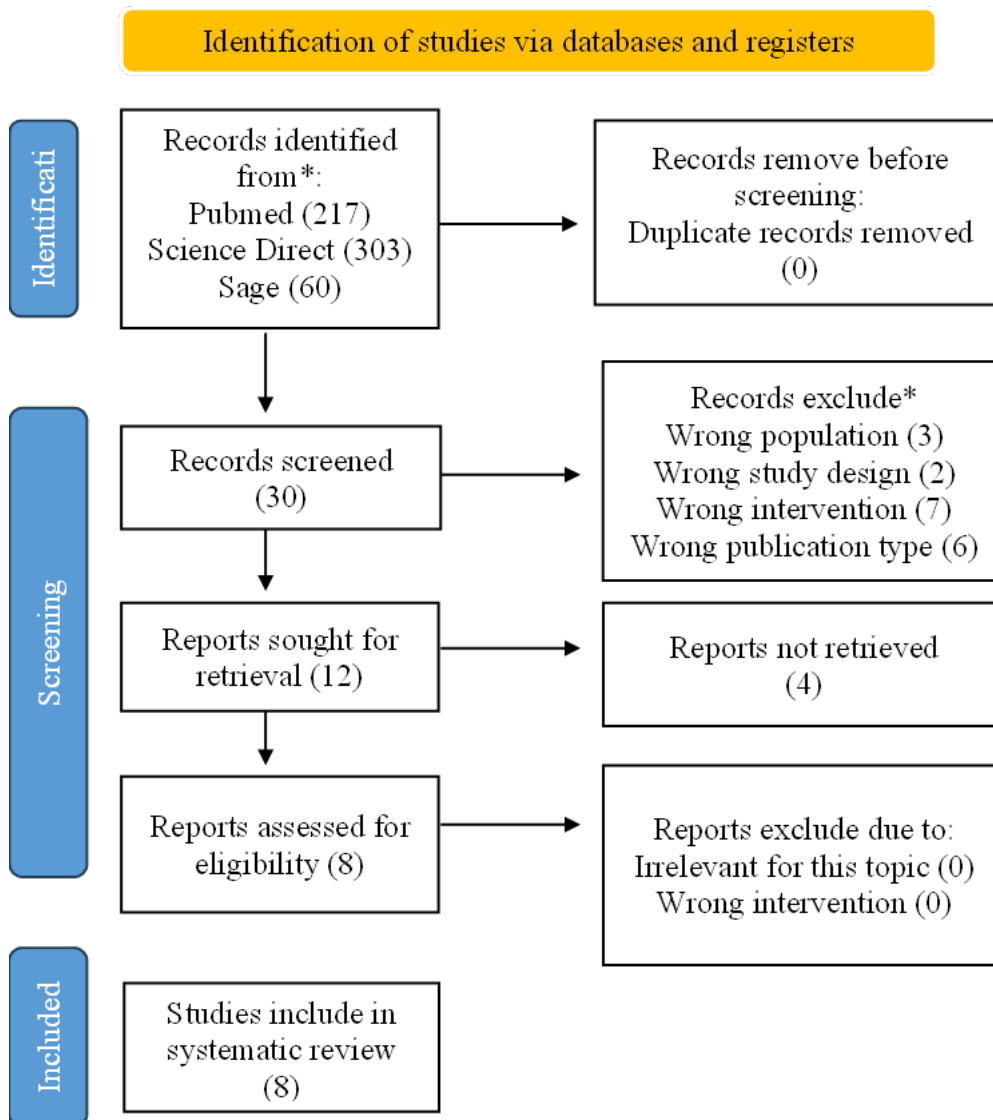


Figure 1. Article search flowchart

RESULT

Our research team first gathered publications from reputable sources such as Science Direct, PubMed, and SagePub. After a thorough three-level screening procedure, only eight papers were determined to be directly relevant to our ongoing systematic examination. Following that, these sections were picked for additional research and a close reading of the entire manuscript. The material that was evaluated for this analysis is compiled in Table 2 for ease of viewing.

Table 2. The literature include in this study

Author	Origin	Method	Sample Size	Result
Malhotra et al., 2021. ¹⁰	India	Prospective, interventional study.	38 patients with moderate to severe VKC	Total sign and symptom scores reduced significantly in all 4 subgroups (all p's <0.05) at 12 weeks. Reduction of mean sign scores between rebamipide and tacrolimus (-4.67 ± 4.63 and -2.80 ± 3.18 respectively) and between rebamipide and cyclosporine (-6.00 ± 3.74 and -5.42 ± 3.68 respectively) was comparable. Reduction in symptom scores was also comparable between subgroups.
Chatterjee et al., 2016. ¹¹	India	open-label, nonrandomized study.	Thirty patients were enrolled in the study, but only 23 patients were available for outcome analysis.	The composite scores for symptoms (10.8, 3.8, 3.4) and signs (8.7, 4.7, 4.0) in 23 patients showed a statistically significant (P, 0.05) improvement from baseline to the 4- and 12-week visits. Among the signs, upper tarsal papilla showed improvement only at 12 weeks, but the scores for giant cobblestone papillae did not reach statistically significant reduction even at 12 weeks. There was improvement in visual acuity at 12 weeks, although it was not statistically significant (P = 0.05). Treatment failure was recorded in 17% patients. The only adverse effect reported was transient stinging sensation lasting for a few days.
Chatterjee et al., 2019. ¹²	India	This study is an analytical observational research with cross-sectional design.	Total subjects in this study were 76 patients	Significant reduction in symptom score and sign score was seen in both groups. Cs A group significantly showed more reduction in symptom (P < 0.0001 in all follow-up visits) and sign (P < 0.0001 in all follow-up visits) scores compared to the placebo group. At day 7, mean steroid usage reduced from 4 to 3.44 ± 0.5 and 3.79 ± 0.4 in Cs A and placebo groups, respectively (P < 0.0001). Steroid drops completely stopped in 21 patients at day 60 in the Cs A group compared to none in the placebo group. No significant rise in IOP or any side effects were noted in either group.

Subedi et al., 2020.¹³	Indonesia	a prospective, hospital-based study	Fifty patients of moderate, severe to very severe vernal keratoconjunctivitis were selected for the study.	Vernal keratoconjunctivitis, being a chronic disease showed marked improvement with immunomodulator therapy. There was significant improvement in the symptom and sign score initially, at the first follow up itself with symptom score reduction from median of mean of 2.4 to 0.6 (p=0.00) and a similar sign score reduction from 1.75 to 0.625 (p=0.00). There was gradually more improvement as therapy continued and the beneficial effects were maintained till the end point of the study at three months where median of mean symptom score was 0.4 (p=0.00) and similar sign score of 0.375 (p= 0.000).
Kumari et al., 2018.¹⁴	India	A prospective randomised double blinded comparative study was conducted at a tertiary eye center	46 Patients of VKC	With treatment both TSSS and TOSS decreased consistently in both groups without any adverse effects but an increase in scores was noticed within two weeks after drug withdrawal.
Müller et al., 2019.¹⁵	Brazil	Non-randomized, cohort retrospective study.	The study cohort consisted of 21 patients who met the eligibility criteria.	The study cohort consisted of 21 patients who met the eligibility criteria. The mean duration of tacrolimus use was 41.3 ± 18.5 months. Fourteen patients (66.7%) continuously used tacrolimus, and three (14.3%) discontinued treatment following complete remission. Four patients (19%) did not use tacrolimus as prescribed or interrupted tacrolimus use on their own: two (9.5%) because of discomfort upon application and two (9.5%) because of the lack of improvement. Ten patients (47.6%) maintained disease control without the use of corticosteroids, whereas 11 (52.4%) required an average of 2.70 ± 1.35 corticosteroid cycles to control symptoms. The only reported side effect was discomfort upon application.
Haral et al., 2024.¹⁶	India	Prospective interventional study.	40 patients (32 male and eight female).	The study included 40 patients (32 male and eight female) with a mean age of 8.05 ± 2.33 years. Mean baseline TSSS and TOSS were 6.71 ± 0.564 and 6.59 ± 0.262 , respectively, which reduced to 2.71 ± 0.011 (P = 0.040) and 2.96 ± 0.210 (P = 0.032), respectively, at 4 weeks and further reduced to 0.42 ± 0.552 and 0.47 ± 0.434 , respectively, at 8 weeks. After 6 months of stopping the drug, mean TSSS and TOSS did increase to 2.80 ± 0.820 (P = 0.044) and 2.50 ± 0.520 (P = 0.030), respectively, but was still statistically

				significant improvement compared to the baseline. Also, no ocular or systemic side effects were observed anytime during the study period.
Liu et al., 2019.¹⁷	Thailand	A retrospective study.	10 patients diagnosed with severe VKC refractory to steroid treatment.	Clinical signs and symptoms improved substantially after tacrolimus treatment. Significant reduction in size of papillae, decrease of discharge, improvement in hyperemia, and shield ulcer healing with re-epithelization were observed in all patients. Six out of 10 (60%) patients did not receive steroid treatment. Long-term maintenance of tacrolimus was required to prevent episodic exacerbation. Patients' only treatment-related complaints were of mild burning sensations during medication application to eyelids, and this sensation disappeared a few days after treatment.
Yücel et al., 2016.¹⁸	Turkey	Experimental study	total of 30 patients with VKC that was resistant to topical corticosteroids, antihistamines and mast cell stabilisers were treated with topical CsA 0.05%	At baseline, the median values of the symptom and sign scores were 10.0 (range 5.0–18.0) and 6.0 (range 2.0–13.0), respectively. At Week 4 of treatment with topical CsA 0.05%, the median values of the symptom and sign scores were 3.0 (range 0–14.0) and 3.0 (range 0–8.0), respectively. The reductions in the symptom and sign scores were statistically significant. The reduction in the need for corticosteroid was statistically significant by Week 12 of therapy. No significant side effects were reported.

Table 3. Critical appraisal of Study

Parameters	Malhotra et al., 2021.	Chatterjee et al., 2016.	Chatterjee et al., 2019.	Subedi et al., 2020.	Kumar i et al., 2018.	Müller et al., 2019. Haral et al., 2024.	Liu Et al., 2019.	Yücel et al., 2016.
1. Bias related to temporal precedence Is it clear in the study what is the “cause” and what is the “effect” (ie, there is no confusion about which variable comes first)?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. Bias related to selection and allocation Was there a control group?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
3. Bias related to confounding factors Were participants included in any comparisons similar?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
4. Bias related to administration of intervention/exposure Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?	Unclear.	Unclear.	Unclear.	Unclear.	Unclear.	Unclear.	Unclear.	Unclear.

5. Bias related to assessment, detection, and measurement of the outcome

Were there multiple measurements of the outcome, both pre and post the intervention/exposure?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were the outcomes of participants included in any comparisons measured in the same way?	Yes.	No.	No.	No.	No.	No.	No.	No.
Were outcomes measured in a reliable way?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

6. Bias related to participant retention

Was follow-up complete and, if not, were differences between groups in terms of their follow-up adequately described and analyzed?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
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7. Statistical conclusion validity

Was appropriate statistical analysis used?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
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DISCUSSION

These literature reviewed provides valuable insights into the effectiveness and safety of various topical treatments for Vernal Keratoconjunctivitis (VKC), with a focus on immunomodulators such as cyclosporine A and tacrolimus. Chintan Malhotra et al. (2021) conducted a prospective interventional study in India, comparing 2% Rebamipide suspension with topical cyclosporine and tacrolimus in 38 patients with moderate to severe VKC. They found significant reductions in both sign and symptom scores across all treatment groups after 12 weeks. The reduction in mean sign scores was comparable between Rebamipide and the other two treatments, indicating that Rebamipide could be as effective as cyclosporine and tacrolimus in managing VKC symptoms.¹⁰

Chatterjee et al. (2016) explored tacrolimus as a treatment for corticosteroid-refractory VKC in India. Their open-label, nonrandomized study involving 23 patients showed significant

improvement in symptom and sign scores after 4 and 12 weeks, though some signs, such as giant cobblestone papillae, did not reach statistical significance. This study highlighted tacrolimus's potential in treating VKC that does not respond to corticosteroids, despite a 17% treatment failure rate and transient stinging as a reported side effect.¹¹ In a cross-sectional study in India, Chatterjee et al. (2019) assessed topical cyclosporine A in 76 pediatric VKC patients. Significant improvements were observed in both symptom and sign scores, with cyclosporine A demonstrating more substantial reductions compared to placebo. Notably, the use of cyclosporine A also led to a reduction in steroid use, highlighting its potential as an effective alternative to corticosteroids without significant side effects.¹²

Subedi et al. (2020) also found significant improvement in symptom and sign scores in a prospective study conducted in Indonesia with 50 patients. The study demonstrated that cyclosporine therapy led to substantial symptom reduction, with

improvements sustained through the study period. This reinforces the efficacy of cyclosporine A as a treatment for chronic VKC.¹³ Kumari et al. (2018) compared tacrolimus and cyclosporine in a prospective randomized double-blinded study involving 46 VKC patients in India. Both treatments resulted in decreased sign and symptom scores, although there was a noticeable increase in scores after drug withdrawal. This suggests that while both medications are effective, their benefits may diminish once treatment is stopped.¹⁴

Müller et al. (2019) conducted a non-randomized cohort study in Brazil, focusing on long-term use of tacrolimus. They observed that tacrolimus was effective for managing VKC, with a majority of patients maintaining disease control without corticosteroids. However, some patients experienced discomfort, and a subset required intermittent corticosteroid use. A similar study by Müller et al. (2019) in Indonesia reported significant reductions in symptom and sign scores after 4 and 8 weeks of tacrolimus treatment, with some

resurgence in symptoms after stopping the drug. Despite this, the improvement was statistically significant compared to baseline, and no severe side effects were reported.^{15,16}

Liu et al. (2019) in Thailand examined the use of dermatologic tacrolimus ointment in severe VKC cases. Their study showed substantial improvements in clinical signs and symptoms, with many patients avoiding steroid treatment. Mild burning sensations were the only noted side effect, which resolved shortly after treatment began.¹⁷ Lastly, Yücel and Ulus (2016) in Turkey reported that topical cyclosporine A 0.05% led to significant reductions in symptom and sign scores in patients resistant to other treatments. The therapy also reduced the need for corticosteroids, with no significant side effects observed.¹⁸

Overall, these studies collectively support the efficacy of both cyclosporine A and tacrolimus in treating VKC, with improvements in symptoms and signs observed across different settings. Cyclosporine A

shows promise in reducing steroid dependency, while tacrolimus is effective for corticosteroid-refractory cases. The choice between these treatments may depend on individual patient response and tolerance, emphasizing the need for personalized treatment approaches in managing VKC.

Behavioral rules are fundamental in managing Vernal Keratoconjunctivitis (VKC). Key recommendations include avoiding contact with aeroallergens such as flowers and plants, minimizing prolonged sun exposure, wearing sunglasses, applying cold eye compresses, using artificial tears to dilute allergens, and frequently washing the face, hands, and hair. While these measures can help, they are generally insufficient to control VKC symptoms on their own, except in milder cases.¹⁹

Effective pharmacological treatments for VKC include topical antihistamines, anti-inflammatory eye drops, steroidal eye drops, cyclosporine, tacrolimus, and recently, omalizumab. These medications are particularly effective

in mild forms of VKC but may not fully control the disease on their own. Often, a combination of antihistamines, anti-inflammatory drugs, and steroidal eye drops is required for adequate symptom management. Ketorolac and diclofenac eye drops can reduce itching and conjunctival hyperemia by interfering with prostaglandin synthesis but do not affect papillae size or corneal lesion repair.^{20,21}

Steroidal drugs are a cornerstone of VKC treatment, offering significant anti-inflammatory benefits. They work by reducing leukocyte activity, blocking IL-2 production, inhibiting fibroblast proliferation, and interfering with COX-2 activity. Despite their efficacy, steroidal eye drops can cause severe adverse effects, such as increased intraocular pressure, corneal infections, cataracts, and glaucoma. Therefore, the goal is to use the lowest effective dose.²²

Steroidal treatments can be administered as eye drops, conjunctival injections, or oral medications. Eye drops are the most common and effective method. If no

clinical improvement is seen within a few days, further evaluation for possible ocular infections is needed. Loteprednol, a newer steroidal drug, is considered safer than previous options. Typically, local steroids are used in various regimens, with a 3-5 day cycle being most effective.²³

In severe VKC cases, supratarsal corticosteroid injections can be used, with dexamethasone, triamcinolone, and hydrocortisone as options. These injections have shown rapid improvements without significant adverse reactions in some studies. Oral steroids, though effective, are rarely used due to their severe side effects and the risk of long-term complications, such as bacterial infections, herpetic keratitis, ocular hypertension, glaucoma, and cataracts.²⁵

Cyclosporine eye drops offer an alternative to corticosteroids, providing effective control without causing cataracts or glaucoma. They work by blocking lymphocyte activation, reducing IL-2 production, and inhibiting histamine release. Side effects are minimal, with burning at instillation being the most common.

Cyclosporine's effectiveness varies with concentration, and while it is generally well-tolerated, systemic absorption is minimal.²³

Tacrolimus, another immunomodulatory option, acts similarly to cyclosporine but may be more effective in some cases. It has shown good results in reducing VKC symptoms and signs, with a lower incidence of side effects compared to oral steroids. Omalizumab, an anti-IgE monoclonal antibody, has shown promise in treating severe VKC, though its use is primarily for refractory cases. It is generally well-tolerated with minimal adverse effects. Dupilumab and other monoclonal antibodies are also under investigation for their potential in treating VKC, showing varying degrees of efficacy. Recent studies have also explored the use of houttuynia and olopatadine eye drops, which have demonstrated rapid symptom relief without significant adverse effects. In summary, while behavioral modifications and artificial tears are helpful, a combination of pharmacological treatments is often necessary to

manage VKC effectively, especially in more severe cases.^{24,25}

This study faces several limitations that impact the interpretation and generalizability of its findings. Firstly, the variability in study designs among the included research introduces challenges in comparing results. The differences between prospective and retrospective studies, as well as randomized and non-randomized trials, create inconsistencies that may affect the overall conclusions. This heterogeneity can obscure clear patterns and outcomes across the studies. Additionally, many of the studies reviewed are characterized by small sample sizes. This limitation restricts the ability to generalize findings to larger populations and may reduce the statistical power of the analysis. Small sample sizes can lead to results that are less reliable and less representative of broader patient groups.

Another significant limitation is the potential for publication bias. Studies with positive or significant results are more likely to be published, while those with negative

or inconclusive findings may be underreported. This bias can skew the results of the review, leading to an overestimation of treatment effectiveness. The review also encounters issues with heterogeneity among the studies. Variations in treatment regimens, outcome measures, and follow-up durations create challenges in aggregating results. This diversity makes it difficult to draw definitive conclusions, as different studies may yield varied outcomes based on these factors. Furthermore, many studies focus primarily on short-term outcomes, with a notable lack of data on long-term efficacy and safety. This gap in long-term information limits the ability to assess the sustained effects and potential risks of the treatments over extended periods.

The quality of evidence across the studies varies, with some potentially having methodological flaws that impact the validity of their findings. This variation necessitates cautious interpretation of the results, as some studies may not be as reliable as others. The inconsistent reporting of adverse effects across studies also

presents a challenge. Without standardized and comprehensive reporting, it is difficult to fully evaluate the safety of the treatments, leaving gaps in understanding the complete range of potential side effects. The diversity of geographical locations and patient populations in the included studies affects the applicability of the results. Variations in treatment responses and outcomes across different populations can influence the generalizability of the findings.

Finally, inconsistencies in outcome measures and scoring systems used across studies complicate the comparison of results. This lack of standardization affects the ability to draw unified conclusions about treatment efficacy. Addressing these limitations will be crucial for enhancing the reliability and robustness of future research in this area, providing clearer insights into treatment effectiveness and safety.

CONCLUSION

The systematic review of topical treatments for Vernal Keratoconjunctivitis (VKC)

highlights significant insights into the efficacy and safety of various therapeutic options. VKC, a chronic allergic condition primarily affecting children, presents with symptoms such as itching, photophobia, and mucous discharge, with potential complications including visual impairments if inadequately treated. The review synthesizes findings from recent studies focusing on immunomodulators like cyclosporine A and tacrolimus, among other treatments. Notably, cyclosporine A has demonstrated substantial effectiveness in reducing symptoms and steroid dependence, while tacrolimus has shown potential, particularly in corticosteroid-refractory cases. Both treatments have been associated with improvements in sign and symptom scores, with cyclosporine A also leading to reduced steroid usage without significant side effects.

Studies reviewed indicate that Rebamipide may be as effective as cyclosporine and tacrolimus, offering an additional option for managing VKC. The evidence supports the use of these immunomodulators as viable

alternatives to corticosteroids, with a focus on personalized treatment based on patient response and tolerance. Overall, the review shows the importance of tailored treatment strategies and highlights areas for future research, including long-term efficacy and the effectiveness of combination therapies. By addressing current gaps and refining treatment approaches, clinicians can better manage VKC and improve patient outcomes.

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