Clinical Evidence on Acanthamoeba Keratitis Treatments: Systematic Literature Review

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Background

- Acanthamoeba keratitis (AK) is a rare, potentially devastating, microbial keratitis.[1]
- Approximately 90% of AK cases occur in contact lens wearers.[2-5]
- AK is associated with pain, photophobia, blurred vision, and tearing.[1]
- There are currently no approved medicinal products for treating AK in any country.[6]
- There are also currently no clinical guidelines for the management of AK.[6]

Aim

To describe the clinical outcomes for patients with AK treated with agents with anti-amoebic activity by conducting a systematic literature review (SLR)

Methods

- The SLR was prospectively registered on PROSPERO (CRD42022345288).[7]

Searches and screening

- To address the search question (Figure 1), the following sources were searched in July 2022:
  - Electronic databases (1992-2022)
  - Proceedings of six relevant conferences (2017-2022)
  - Manufacturer websites
  - Eligible publications from a targeted literature review used to develop protocol
- Forward and backward citation searching was conducted.
- Screening and data extraction were conducted by two independent reviewers, with a third reviewer holding the casting vote for conflicts.

Risk of bias assessment

- Assessed at study level by two independent reviewers.
- Used National Heart, Lung, and Blood Institute's Study Quality Assessment Tools.
- One reviewer also rated the overall body of evidence for each outcome using GRADE.

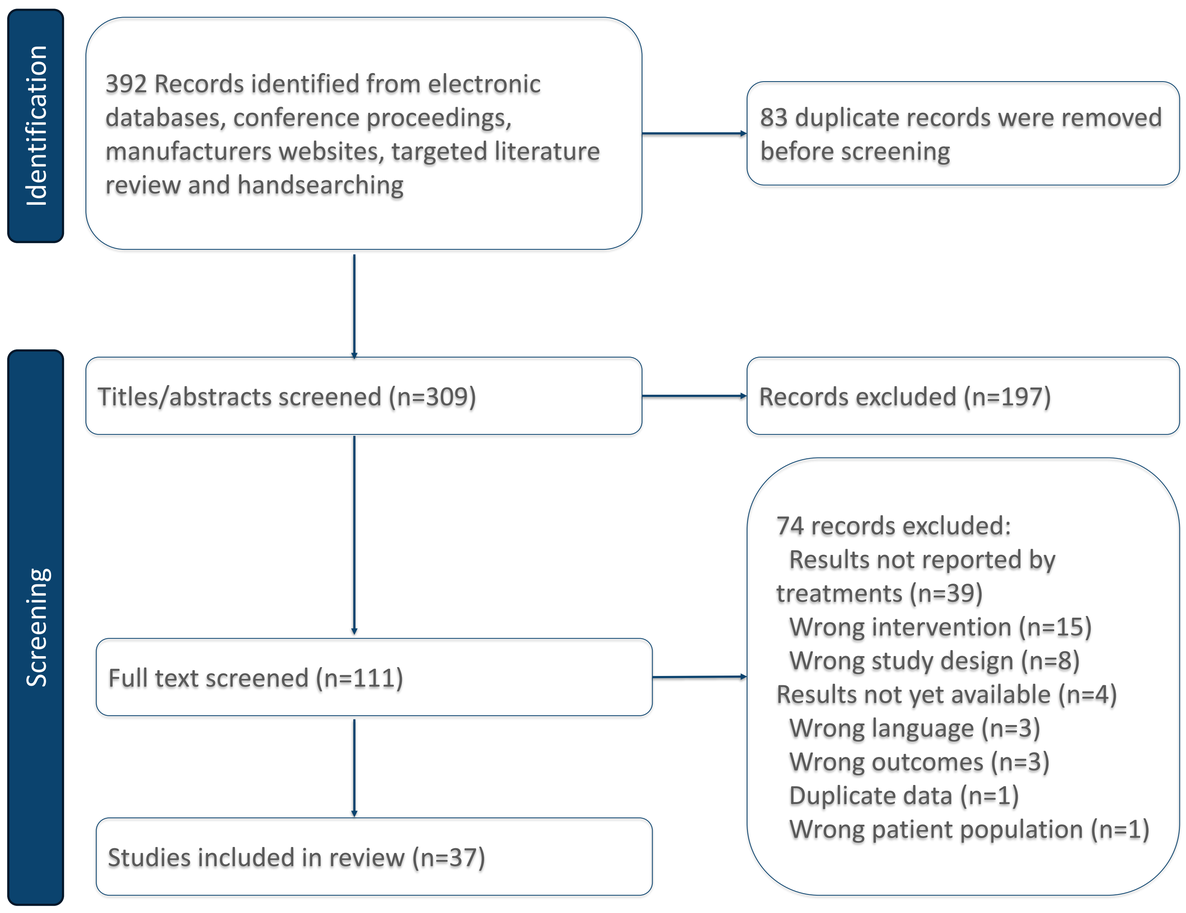
Analysis

- Range (weighted mean) was calculated at eye-level across treatment arms with ≥5 treated eyes.
- Weighted mean was also calculated by overall study quality (good vs fair/poor).

Figure 1: Research question

Population	Patients (of any age) with a confirmed diagnosis of AK
Intervention	Any agent with anti-amoebic activity administered as eye-drops or orally in any concentration or combination
Comparator	Any or no control
Main outcomes	Clinical resolution and best-corrected vision acuity (BCVA)
Study type	Any clinical trial or observational study with at least five participants published from January 1992 onwards

Figure 2: Flow of studies through the SLR



Results

Description of the studies

- 37 articles were eligible (Figure 2), 35 of which were observational studies.
- Average follow-up length was 85 to 4782 days.
- Most studies were conducted in Europe (n=18) or Asia (n=12).
- The studies included 2043 patients (mean age: 21.1-53.0 years; % males: 0%-82%).
- Treatment regimens were greatly heterogeneous, with at least 31 different regimens used.
- 56.8% studies were rated as good quality, 27.0% as fair quality, and 16.2% as poor quality.

Description of main outcomes of interest in 37 eligible studies

Finding	Clinical resolution	LogMAR BCVA (continuous)	BCVA (categorical)	
GRADE score	Moderate	Moderate		
Comparability across study outcome measurements				
Total N studies	20	8	24	
Timing	Final follow-up (n=9) Unreported timepoint (n=4) After completion of medical therapy (n=3) 12 months (n=2) 4 months (n=1) 3 months (n=1)	Final follow-up (n=4) After treatment (n=2) Multiple timepoints (n=1) Unreported timepoint (n=1)	Final follow-up (n=15) Unreported timepoint (n=4) End of treatment (n=2) Multiple timepoints (n=1) 4 months (n=1) 2 weeks (n=1)	
Definition	Definitions differed between studies. 3 studies did not provide a clear definition. Most definitions included or implied a healed cornea without inflammation and after discontinuation of an agent with anti-amoebic activity, regardless of vision level.	Change from baseline (n=1) or absolute value (n=7)	There were different definitions. The most commonly available were improvement from baseline and BCVA of 6/12 or better on a Snellen scale.	
Reported outcome	**% cured (based on study definition)**	**Mean absolute follow-up BCVA**	**% improved BCVA**	**% with BCVA of 6/12 or better**
N studies/treatment arms	20 / 34	7 / 19	10 / 22	13 / 28
N patients / eyes	634 / 643	157 / 164	181 / 183	397 / 409
Weighted mean (range) across treatment arms with ≥5 treated eyes				
All studies	60.1% (4% to 100%)	0.5 (0.03 to 0.89)	72.9% (38.5% to 100.0%)	78.7% (29.0% to 100.0%)
Good quality studies	57.6%	0.5	65.1%	76.8%
Fair/poor quality studies	66.0%	N/A (no studies)	87.6%	80.0%

Conclusions

A considerable body of evidence is available and no published evidence syntheses were identified, suggesting that evidence syntheses are needed to establish efficacy estimates for key treatments and outcomes.

Study quality and comparability challenges should be considered when estimating the impact of AK, with substantial between-study heterogeneity limiting options for robust evidence synthesis.

This review highlights the importance of standard outcome definitions to better assess comparability of treatments for AK.

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