An Indirect Comparison of Polihexanide 0.08% Versus Currently Used Treatments for Acanthamoeba Keratitis

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Aim

The objective of this study was to compare the efficacy of polihexanide 0.08% versus currently used off-label anti-amoebic therapies in patients with acanthamoeba keratitis (AK).

Background

- 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]
- Akantior (polihexanide 0.08%) has recently become the first EMA-approved medicinal product for treating AK. There are no other approved treatments in any country.[6]
- There are also currently no clinical guidelines for the management of AK.[6]

Methods

Data Sources and Comparator Treatments

- A propensity score analysis (PSA) was conducted using individual patient data (IPD) from:
  - **Polihexanide 0.08%:** A phase 3 trial 043/SI (NCT03274895)
  - **Current therapies:** The largest retrospective study in people with AK (Papa 2020[7])
- For the Papa 2020 data, three populations were analysed:
  - Whole study population, referred to as **'any initial pharmacological treatment'**
  - Patients treated with **polihexanide 0.02% plus a diamidine 0.1%**
  - Patients treated with **chlorhexidine with or without propamidine 0.1%**

Endpoint of Interest

- **Difference in clinical resolution rate (CRR)**
- Defined as cure without no surgery within 12 months of treatment
- Discontinuations from baseline therapy were considered as 'failure'

PSA Approach

- A PSA with overlap weights normalised to account for the study sample size
- IPD were reweighted to balance study populations for key prognostic factors and/or treatment effect modifiers: age; gender; AK disease stage; prior use of corticosteroids; prior use of antivirals; delay in starting treatment from diagnosis.
- The calculated estimate was based on the average treatment effect
- CRR was assessed using logistic regression methods to estimate the absolute difference between treatments and the corresponding 95% confidence interval (CI)

Results

- The CRR before and after weighting are shown in Table 1.
- The baseline characteristics and effective sample sizes in the weighted populations suggested that the indirect treatment comparison had successfully aligned the analysis populations.
- The absolute differences in CRR between polihexanide 0.08% and comparator treatments are shown in Figure 1.
- In all comparisons, the CRR was significantly higher with polihexanide 0.08% than the comparator treatment, with differences ranging from 24% to 45% higher.

Figure 1: PSA Results

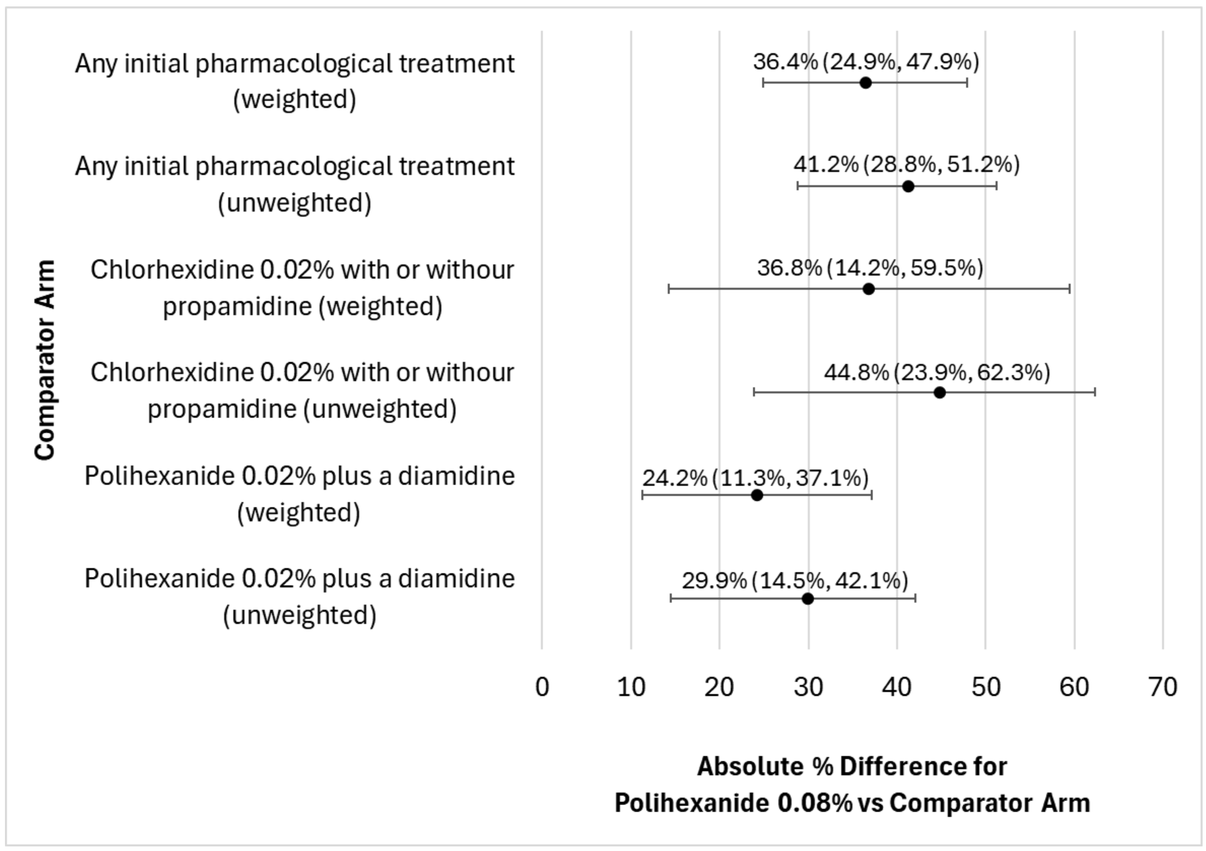

Table 1: Summary of Cure Rates

Study	Papa 2020		NCT03274895	
Weighting	**Unadjusted**	**Adjusted**	**Unadjusted**	**Adjusted**
Arm	**Any initial pharmacological treatment**		**Polihexanide 0.08%**	
N[a]	227	174.0	66	64.8
% (95% CI) cured without surgery	43.6 (37.1, 50.3)	48.3 (41.8, 54.8)	84.8 (73.9, 92.5)	84.7 (76.1, 93.4)
Arm	**Chlorhexidine with or without propamidine**		**Polihexanide 0.08%**	
N[a]	35	25.7	66	41.9
% (95% CI) cured without surgery	40.0 (23.9, 57.9)	46.4 (29.9, 63.0)	84.8 (73.9, 92.5)	83.3 (74.3, 92.3)
Arm	**Polihexanide 0.02% plus a diamidine**		**Polihexanide 0.08%**	
N[a]	111	97.5	66	62.5
% (95% CI) cured without surgery	55.0 (45.2, 64.4)	60.9 (51.9, 70.0)	84.8 (73.9, 92.5)	85.1 (76.6, 93.7)

[A] N in the 'Adjusted' column is the Effective Sample Size estimated from the weighted data.

Conclusion

These analyses suggest an improved efficacy with polihexanide 0.08% compared with currently used anti-amoebic therapies in achieving clinical resolution with no surgery in AK.

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