The Reducing Adenoviral Patient-Infected Days (RAPID) Study: A Randomized Trial Assessing Efficacy of One-Time, In-Office Application of 5% Povidone-Iodine for Treatment of Adenoviral Conjunctivitis

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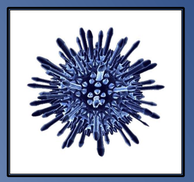

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Introduction

Adenoviral conjunctivitis (Ad-Cs) is a highly contagious, prevalent condition that has significant morbidity and economic impact.

There is no FDA-approved treatment for Ad-Cs. The 'off-label' use of ophthalmic 5% povidone-iodine (PVP-I) has gained adherents among eye care practitioners.[1-3] However, the efficacy of PVP-I against Ad-Cs has yet to be tested in a well-controlled, randomized trial.

We report on the efficacy of a one-time, in-office application of 5% PVP-I for the treatment of Ad-Cs in the Reducing Adenoviral Patient Infected Days (RAPID) study, a double-masked and randomized pilot clinical trial.

Methods

- 212 participants with presumed Ad-Cs were screened at 9 study centers
- Inclusion criteria included age ≥ 18 years, red eye symptoms ≤ 4 days and a positive AdenoPlus™ immunoassay (Quidel, San Diego CA)
- The AdenoPlus™ immunoassay was performed by swabbing conjunctiva with applicator per manufacturer's instructions
- One eye of 56 eligible participants was randomized to single administration of ophthalmic 5% PVP-I or preservative-free artificial tears (AT)
- Five follow-up visits were at days 1 to 2, 4, 7, 14 and 21
- At each visit, a masked clinician graded clinical signs, administered a 10-symptom survey and obtained a conjunctival/tear swab sample
- Swab samples were placed in Universal Viral Transport medium (BD, Franklin Lakes NJ) and stored frozen at -80°C
- qPCR assays of swab samples were later performed using adenovirus-specific primer set and an Integrated Cycler (DiaSorin Molecular, Cypress CA)

Results

Figure 1. Participant Progress Flowchart for RAPID Study
Of 56 randomized participants with positive immunoassay (AdenoPlus™), 28 (50%; 12 in AT group, 16 in PVP-I group) had confirmed Ad-Cs following subsequent qPCR analysis.

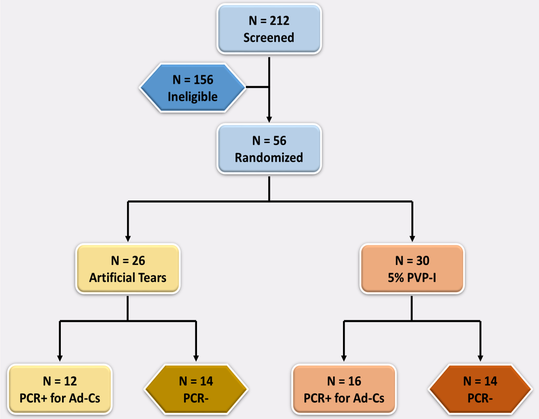


Figure 2. Effect of 5% PVP-I on qPCR-Derived Viral Titers
Mean (± SD) adenovirus titers (log units) in samples collected at each visit from participants treated with either artificial tears or 5% PVP-I (# of subjects listed on each bar). p>0.05 for treatment group comparisons at each visit day, with p=0.07 for Day 4.

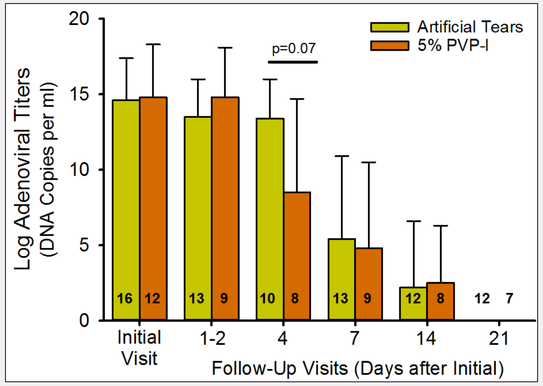


Figure 3. Participant-Reported Symptoms at Day 4
Grading (0 = not bothersome, 10 = very bothersome) of 10 symptoms provided by (top) those with qPCR-confirmed Ad-Cs (n=8 AT, n=8 PVP) and (bottom) those determined to have non-Ad etiology (n=11 AT, n=9 PVP). * p<0.05

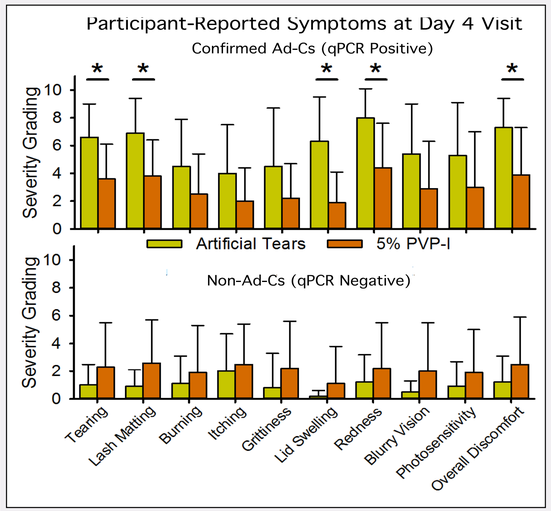
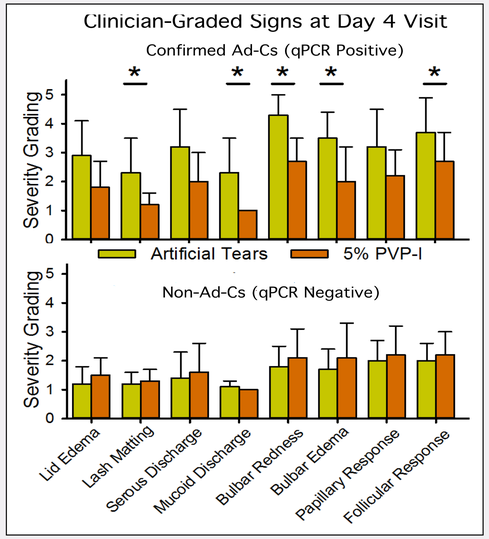


Figure 4. Masked Clinician-Graded Signs at Day 4
Grading (1 = absent, 5 = severe) of 8 signs by masked examiners of (top) eyes with qPCR-confirmed Ad-Cs and (bottom) those with non-Ad etiology (n as in Fig 3). * p<0.05 ** p<0.01



Discussion

- The positive predictive value of the AdenoPlus immunoassay (used as study eligibility criterion) was 50%, a value that is lower than reported previously (range: 63-94%).[4-6]
- In participants with qPCR-confirmed Ad-Cs, those receiving 5% PVP-I showed significant improvement in certain signs and symptoms and trended towards lower viral titers at day 4 compared to those who received AT.
- There were no significant differences between the groups in viral titers, symptoms or signs at the 1-2, 7, 14 or 21 day F/U visits in participants with confirmed Ad-Cs.
- In randomized participants who tested negative for Ad-Cs by qPCR, the 5% PVP-I did not significantly improve signs and symptoms at any visit with the exception of clinician-graded eyelid matting on the day 1-2 F/U visit.
- Whether multiple applications of PVP-I across different visits can expand the time-frame of the therapeutic effect beyond 4 days remains a question for future research.

Conclusion: These results indicate that a single, in-office application of ophthalmic 5% PVP-I can improve clinical signs and symptoms in individuals with Ad-Cs four days after treatment.

References

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Clinical Trial Registration: https://clinicaltrials.gov/ct2/show/NCT02472223