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

Hartwick, Andrew1; Than, Tammy2; Rodic-Polic, Bojana3; Johnson, Spencer4; Migneco, Mary5; Shorter, Ellen6; Harthan, Jennifer7; Morettin, Christina7; Whiteside, Meredith8; Olson, Christian9; Margolis, Mathew9; Huecker, Julia10; Storch, Gregory11; Gordon, Mae12

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™ immunosassay (Quidel, San Diego CA)
• The AdenoPlus™ immunosassay 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/fear 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

• Of 56 randomized participants with positive immunoassay (AdenoPlus™), 28 (50%; 12 AT group, 16 in PVP-I group) had confirmed Ad-Cs following subsequent qPCR analysis.

• In participants with qPCR-confirmed Ad-Cs, those receiving 5% PVP-I showed significant improvement in certain signs and symptoms compared to 5% PVP-I 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.

Discussion

• The positive predictive value of the AdenoPlus immunosassay (used as study eligibility criterion) was 50%, a value that is lower than reported previously (range: 63-94%).1-4
• In participants with qPCR-confirmed Ad-Cs, those receiving 5% PVP-I showed significant improvement in certain signs and symptoms and trends towards lower viral titers at day 4 compared to those who received AT.

References

1. Atteberry M. A guide to understanding adenovirus, the disease it causes and the best ways to treat these conditions. Review of Ophthalmology. 2010.

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