Reducing Adenoviral Patient Infected Days (RAPID) Study: Design and Baseline Characteristics

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Introduction

Adenoviral conjunctivitis (Ad-Cs), also known as “pink eye”, is a prevalent condition that is highly contagious. The morbidity associated with this infection has considerable economic impact on society. An estimated $670 million is spent annually on the management of acute conjunctivitis, and afflicted patients miss on average five days of work or school. As one recent high profile example, the prolonged work absence of Bob Costas during the 2014 Sochi Olympics illustrated the potential impact of this condition.

There are currently no FDA-approved treatments for Ad-Cs. Povidone iodine (Betadine) is inexpensive, has broad-spectrum antimicrobial effectiveness and has an excellent safety profile. Off-label use of Betadine to treat Ad-Cs has been promoted by influential medical societies while evidence-based guidelines recommend against its use in Ad-Cs. Our previous survey data indicates that a significant proportion of clinicians have treated Ad-Cs with Betadine. A randomized clinical trial of a new diagnostic and grading test for adenoviral conjunctivitis is warranted.

RAPID Study Design

Patients that are ≥ 18 years old and presenting with a red eye with symptom onset ≤ 4 days are screened for eligibility. Screened patients are clinically examined and administered symptom table (Figure 1).

To be eligible for treatment randomization, patients must test positive on the AdenoPlus adenoviral immunossay test. Patients with mild conjunctivitis (Rapid Pathogen Screening, Inc., Sarasota, FL) must be pregnant, and must not have a thyroid condition or allergy.

Eligible patients are randomized to an in-office lavage of artificial tears of 5% Betadine solution. Both groups are given single-use preservative-free artificial tears for home use.

Results

Over the first 15 weeks, 17 patients that were 2-18 years old (42.9-14.4 years: 70.6% females), and presenting with a red eye of 5.4 days onset, were screened for the study.

Of the 17 patients, 10 tested positive using the AdenoPlus immunossay test. The patient-reported symptom survey scores (Figure 2) and the examiner-grader clinical signs (Figure 3) for the AdenoPlus-negative (n = 7) and AdenoPlus-positive (n = 10) patient groups were tabulated and compared.

The mean scores for patient-reported symptoms and examiner-grader signs trended higher in the AdenoPlus-positive patients, but only the clinical grading of follicular and papillary responses was statistically higher, as compared to the AdenoPlus-negative subjects, in this initial sample or early enrollees.

Conclusions

This work describes the RAPID study design and baseline characteristics (gender, age, and symptoms) of the red eye patients that were screened early in the study. The initial data indicates Ad-Cs is a condition associated with significant clinical signs as well as highly bothersome patient-reported symptoms.

Of patients presenting with a red eye that were screened for the study, 58% tested positive using the AdenoPlus immunossay test.

A high retention rate (100%) during the 21 days of follow-up was observed in this cohort of early patient enrollees, supporting the feasibility of a larger scale clinical trial.

References


Support

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

Table 1. Summary of procedures at baseline and follow-up visits. Procedures in unshaded boxes are performed on all screened subjects; those in shaded boxes are performed on eligible subjects with an AdenoPlus-positive test that are randomized to treatment. Subjects and examiners for follow-up visits are masked to treatment.

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Screening Exam</th>
<th>Follow-up Exam</th>
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</thead>
<tbody>
<tr>
<td>Pupil Dilatation</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Schirmer's Test</td>
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<td>Goldmann Applanation Tonometry</td>
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<td>Corneal Topography</td>
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<td>AdenoPlus Testing</td>
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<td>Randomization to active or placebo</td>
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Figure 1. A) Survey of 649 optometrists and ophthalmologists that attended 7 clinical conferences in 2013 revealed that over a quarter had used Betadine in the past to treat Ad-Cs. B) Of those that responded yes, the % of Ad-Cs patients that they reported using Betadine to treat the condition.

Figure 2. Dot density plots showing the severity of symptoms, reported on a scale from 0 (not at all bothersome) to 10 (very bothersome), in subjects that tested negative (n = 7) and positive (n = 10) using the RPS AdenoPlus test. Both groups were statistically different (p > 0.05, Mann-Whitney test) between the two subject groups.

Figure 3. Dot density plots showing the frequency of graded signs, reported on a scale from 0 (absent) to 4 (severe), observed during slit lamp examination by examiner on AdenoPlus-negative (n = 7; blue circles) and positive (n = 10; red circles) subjects. Horizontal lines represent mean values for clinical signs in AdenoPlus-negative (blue) and positive (red) subjects. No scores were statistically different (p < 0.05, Mann-Whitney test) between the two subject groups.

Figure 4. Percentage of AdenoPlus-negative (n = 7; blue bars) and AdenoPlus-positive (n = 10; red bars) subjects that had palpable lymph nodes (submandibular, retroauricular, preauricular). 60% of the AdenoPlus-positive patients had at least one palpable lymph node (submandibular, retroauricular or preauricular), as compared to 14% of the AdenoPlus-negative subjects (Figure 4).