Predictive Value of FDA-Approved Immunoassay for Adenoviral Conjunctivitis

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Background

Adenoviral conjunctivitis (Ad-Cs) is a prevalent and highly contagious eye infection for which there is no FDA-approved treatment. The RAPID (Reducing Adenoviral Patient-Infected Days) study is a 2-year planning study to investigate key parameters for a definitive randomized trial to assess the safety and efficacy of 5% povidone-iodine in treating Ad-Cs. Timely and accurate diagnosis of Ad-Cs at presentation is crucial to the success of such a trial. Here, we report the predictive value of a commercial immunoassay for Ad-Cs, using a quantitative PCR assay as the comparator. We also report on the time-course for Ad-Cs resolution, as measured in terms of qPCR-derived viral titer levels.

Methods

A total of 168 participants, aged ≥ 18 years and presenting with "pink eye" of ≤ 4 days since symptom onset were screened for eligibility in 9 clinics through February, 2018. The AdenoPlus™ (Quidel Corporation, San Diego, CA) immunoassay was performed after swabbing the participants' conjunctiva with the applicator and the manufacturer's instructions were followed. An additional conjunctival/tear sample was obtained with a flocked sterile swab, placed in Universal Viral Transport medium (BD, Franklin Lakes NJ) and then stored frozen at -80°C. The qPCR assays of these samples were later performed using adenovirus-specific primer set and an Integrated Cycler (DiaSorin Molecular, Cypress CA). Participants with a positive AdenoPlus were enrolled in the study and seen at five (1-2, 4-5, 7, 14, 21 day) follow-up visits in which additional conjunctival swabs were obtained.

Results

At screening, 52 of the 168 participants had a positive AdenoPlus result and were enrolled in the study for further follow-up. Subsequent qPCR analysis confirmed the presence of adenovirus in 26 of the 52 baseline samples collected from these participants, resulting in a positive predictive value of 50%. For the 116 samples collected from AdenoPlus-negative participants, 114 were qPCR-negative (negative

predictive value = 98%). Assessments of conjunctival/tear samples during follow-up visits to 21 days from the 26 RPS+ and qPCR+ participants confirmed that qPCR was a responsive indicator of outcome. The normalized viral titers (peak titers set at 100%) in all study participants decreased to 8.0% (±9.5 SD) at Day 4-5 to 0.006% (±0.002) on day 14 visits and were undetectable on day 21.

Conclusions

In a sample of 168 patients presenting with "pink eye", the AdenoPlus immunoassay exhibited a sensitivity of 93% and a specificity of 81%. Although the negative predictive value (98%) for this assay was higher than previously reported (71% to 95%), its positive predictive value (50%) was lower than that reported previously (63% to 94%), presenting a challenge in its use as an eligibility criterion for clinical Ad-Cs trials. The qPCR assay can serve as an objective outcome measure of decreasing viral load over time, which decreased by >99.99%, on average, by the 14-day follow-up visit.