Reducing Adenoviral Patient Infected Days (RAPID): Success in Masking Subjects and Clinicians From Identifying Treatment with Ophthalmic Povidone-Iodine 5% (PVP-I)

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Introduction

The Reducing Adenoviral Patient Infected Days (RAPID) is a double-masked randomized pilot trial investigating the efficacy of a one-time administration of 5% ophthalmic Povidone-Iodine (PVP-I 5%; betadine) for the treatment of qPCR confirmed adenoviral conjunctivitis.

One objectives of the RAPID study was to determine the ability to successfully double-mask to minimize bias from knowledge of treatment assignment by participants and clinicians[1,2].

- CONSORT recommends reporting masking methods and evaluation of masking success[3,4].
- Despite this recommendation, most clinical trials do not assess the success of masking. In a review of 2467 RCTs, only 66 reported on blinding[6].

In the RAPID pilot study, we calculate the Bang Blinding Index (BI) to quantitate success of masking in each randomization group.

Methods

- Participants randomized to receive one-time in office treatment of either PVP-I or artificial tears (ATs).
- After 1 drop of ophthalmic proparacaine 0.5%, 4-5 drops of PVP-I or ATs were placed in the eye by an unmasked clinician. Two minutes after instillation, the eye was lavaged with preservative-free sterile saline.
- Participants were asked to guess whether they received: “PVP-I, ATs, or were unsure” at time of treatment and day 4. Masked clinicians were asked the same question on day 14.

Results

	Participants At Treatment	Participants Day 4	Masked Clinicians Day 14
Correct Guess: Povidone Iodine	65.5% (19/29); BI[†]: 0.59, P<0.01	68.4% (13/19); BI[†]: 0.53, P<0.01	61.1% (11/18); BI[†]: 0.56, P<0.01
Correct Guess: Artificial Tears	29.6% (8/27); BI[†]: 0.15, P=0.12	47.6% (10/21); BI[†]: 0.29, P=0.04	64.7% (11/17); BI[†]: 0.41, P=0.02
Correct Guess: Overall	48.2% (27/56)	57.5% (23/40)	62.8% (22/35)

[†]The Bang Blinding Index (BI) has a range from -1 to 1 for each randomization group where: if all guesses are incorrect, BI= −1; if 50% of guesses are correct and 50% are incorrect then BI=0; if all guesses are correct, BI=1[5].

References

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Discussion

One objective of the RAPID study was to determine success of masking participants and clinicians, despite known ocular discoloration and irritation with PVP-I. In order to overcome these issues:

- at treatment, an unmasked clinician administered proparacaine before administering PVP-I, and cleaned any ocular colorants afterwards.
- after treatment, all subsequent evaluations were done by a masked clinician.

Masking of participants receiving ATs was fairly successful at Day 4 (BI: 0.29, P=0.04). Masking was less in clinicians at Day 14 (BI: 0.41, P=0.02). Masking of the PVP-I group was partial for participants on Day 4 (BI: 0.53, P<0.01) and clinicians (BI: 0.56, P<0.01) on Day 14.

In the future, masking might be improved by altering ATs to simulate sting, smell or discoloration from betadine. It is possible treatment efficacy biased clinicians assumption of treatment group; future surveys of clinicians may reveal this information.

While imperfect masking might bias the signs and symptoms reported by clinicians and patients, it will not affect the primary outcome of qPCR.

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