Author’s response to reviews

Title: The effect of diluting povidone-iodine on bacterial growth associated with speech

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Author’s response to reviews:

Hiroyuki Nakashizuka, Ph.D., M.D. (Reviewer 2): 1. As authors commented as follows, these experiments methods are unrealistic and brought unrealistic results. At least, the following sentence should be added in the discussion section.

1. The time duration was chosen to maximize the potential bacterial dispersal onto the blood agar plates and by extension assess the effectiveness of the various PI concentrations under a heavy bacterial load. While this may be unrealistic, our aim was to assess the effectiveness of PI concentrations under a heavy bacterial load.

The manuscript (discussion section, page 11, Line 251-254) already includes the following sentence: The time duration was chosen to maximise the potential bacterial dispersal onto the blood agar plates and by extension assess the effectiveness of PI under a heavy bacterial load.

2. Furthermore, author used blood agar plate. This may cause povidone iodine ineffective at once. Because blood agar plate will contain blood and protein which can accelerate inactivation of PI. From this point of view too, this study is unrealistic. This may be the reason why 1% PI was ineffective for bacterial growth in this study.

Povidone Iodine may undergo a degree of inactivation through exposure to organic compounds including blood, protein, lipids and mucin. Any reduction in activity through exposure to the blood agar plate will be uniform throughout our study. The methodology for our study stems from similar previous studies and is mentioned in our manuscript. (Discussion section, Page 11, Line 257-258)

3. Lower concentrations of PI have been shown to have greater concentrations of free iodine. Authors comment about diluted PI has not satisfied us. In fact, recent report also showed that
application of diluted PI solution is an effective alternative 5% PI for endophthalmitis. In this report, the incidence of endophthalmitis has been reported to be 0.04% for 5% PI, 0.02% for dilute PI, and 0.31% for no PI prophylaxis.

Authors should add detail comment about diluted PI referring these studies.

Peden MC, Hammer ME, Suñer IJ

DILUTE POVIDONE-IODINE PROPHYLAXIS MAINTAINS SAFETY WHILE IMPROVING PATIENT COMFORT AFTER INTRAVITREAL INJECTIONS.


A number of In vivo and In vitro studies have looked into the antiseptic activity of PI (Discussion section, Page 10, Line 228-42). Lower concentrations of PI have been shown to have greater concentrations of free iodine which is cytotoxic to cells and leads to cell death.[1,2] In vitro, Berkelman RL et al showed greater bactericidal efficacy at concentrations of PI ranging from 0.1 to 1%.[3] This was reproduced by Roberts et al in a study on the ocular surface of dogs and Grimes SR et al showed in a small study of 22 patients 0.02% PI irrigation was comparable to 5% PI drops.[4, 5]. In the reviewer referenced article, Peden et al demonstrated in their retrospective chart review a lower incidence of infective endophthalmites with dilute PI compared to 5% PI.[6] This adds to the body of evidence supporting the use of lower PI concentrations for antisepsis, especially when patient factors are also considered.

However, evidence to the contrary also exists – Ferguson et al found 5% PI had higher bactericidal activity than 1% PI, similarly Li et al showed 10% PI was better than 5% PI and 1% PI at reducing conjunctival bacterial load pre-operatively.[7,8] Hosseini et al exposed endophthalmitis bacterial isolates to different concentrations of PI for different durations and found higher concentrations (5% and 10% PI) to be better at preventing bacterial growth.[9]

While we accept the reviewer’s assertion that there is evidence to support lower PI concentrations as an effective alternative – we are also mindful that this is not yet accepted practice and evidence to the contrary also exists. We believe our study adds to this debate.

We have added a sentence regarding the recent findings by Peden et al (discussion section, Page 10, Line 235-237)


4. Authors commented in the discussion section as follows. However, there is now sufficient evidence to support the notion that the use of topical antibiotics is not associated with a reduced incidence of endophthalmitis in the context of IVI injections and could contribute to drug resistance. The statement below seems to be out of date.

Even under this heavy bacterial load, 5% PI did not generate any growth on 8 of the 21 (38%) plates; supporting the claim that effective pre-injection antisepsis is essential for reducing the risk of endophthalmitis.

Bhatt SS, Stepie KE, Joshi K. Prophylactic antibiotic use after intravitreal injection: effect on endophthalmitis rate. Retina 2011;31:2032-2036


The authors agree that there is sufficient evidence to support the notion that use of topical antibiotics is not associated with a reduced incidence of endophthalmitis in the context of the IVI injection and that this practice could contribute to drug resistance. In the sentence highlighted by the reviewer (Discussion section, Page 11, line 254-256) the pre-injection antisepsis referred to is the use of Povidone Iodine, not additional topical antibiotics.