

November 15, 2018

Ya-Juan Ma
Science Editor, Editorial Office
Baishideng Publishing Group, Inc.
World Journal of Clinical Oncology

Dear World Journal of Clinical Oncology Editorial Board,

Thank you for your ongoing consideration of our manuscript "Long-term outcomes of interventions for radiation-induced xerostomia: a review."

We found the reviewers' comments very helpful and appreciate the feedback. We have addressed each comment as outlined point-by-point with our responses below. The manuscript has been updated to reflect reviewer comments. We have changed the manuscript type to a more appropriate "Mini-Review," rather than a "Systematic Review," as this is more fitting with the content and the intent of our manuscript.

We believe the updated paper is stronger and has significantly benefited from the review. We hope you find our responses satisfactory.

Sincerely,

Anurag K. Singh, MD
Professor of Medicine
University at Buffalo School of Medicine
Professor of Oncology
Director of Radiation Research
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Reviewer #1: The authors undertook a review concerning long-term outcomes of interventions for radiation induced xerostomia. The manuscript is well-written with in with adequate Reference to the current Medical literature in the field. The content of the text is satisfactory enough. The review can be published for educational purposes especially for clinicians in the Field.

Reply: Thank you to all reviewers for taking the time to read the manuscript and for providing feedback.

Reviewer #2: Dr. Ma and the other authors made a review of various methods for radiation-induced xerostomia in head and neck cancer patients and evaluated the long-term efficacy. The review is short but informative for readers interested in the topic. One shortcoming is that it did not include evaluation of more traditional or alternative medicine. If this part can be added, it would be a comprehensive review.

Reply: The results section includes all studies that met inclusion criteria which includes one study on acupuncture. The discussion section now includes an elaboration of other more traditional modalities including acupuncture and herbal remedies in the treatment of xerostomia in order to increase the comprehensiveness of the review.

The following paragraph has been added to the discussion:

Traditional therapies have been explored as avenues for managing treatment side effects like xerostomia. In the only included study involving traditional acupuncture, Blom et al. were unable to demonstrate differences in xerostomia outcomes or salivary flow rate between two groups that received either acupuncture or superficial sham acupuncture [54]. A later study from the same investigators, demonstrated contradictory findings by showing increased unstimulated and stimulated salivary flow at 6-month follow-up after 24 treatments of acupuncture [59]. However, this study suffers severe limitations as no control group was used and all patients were treated with 24 sessions of acupuncture. Herbal-based interventions have also been examined and a randomized, open-label study comparing herbal therapy in the form of *Alcea digitata* and *Malva sylvestris* to artificial saliva for the treatment of radiation-induced xerostomia found significantly improved patient-reported QoL and dry mouth scores in the herbal intervention group [60]. Of course, the open-label nature of this study calls into question whether the benefits of treatment perceived by patients were a result of bias.

Reviewer #3: The authors submit a systematic review manuscript focusing on long-term outcomes of interventions for radiation-induced xerostomia. After reading the entire

manuscript, the content would have potential interest and benefit to the related medical care providers. Can the authors also provide representative of clinical picture of xerostomia in the first paragraph of the introduction? This would enhance of the impact of the manuscript, to my opinion.

Reply: We agree that a clinical picture of xerostomia would benefit the introduction. A clinical description of xerostomia and its etiologies has been added to the introduction.

The following lines have been added:

Xerostomia or dry mouth is the subjective sense of dryness due to changes in salivary composition or reduction in salivary flow. The etiology of xerostomia most commonly involves certain medications, diseases of the salivary gland such as Sjögren syndrome, dehydration, or irradiation [2] Xerostomia is associated with numerous complications including trouble eating, speaking, and swallowing, which can lead to depression and limited social activities[3, 4]. In fact, xerostomia can become so severe that a large number of patients report that dry mouth affects every aspect of life[4].