



## Letter

**Topical application of honey along with usual care in the management of radiotherapy induced oral mucositis: Comment on Yang et al. 2019**


Dear Editor,

We would like to take the opportunity to comment on the review by [Yang et al. \(2019\)](#), which concluded that pure natural local honey could be invoked as a first-line adjuvant therapy agent for patients with cancer undergoing chemo/radiotherapy-induced oral mucositis. Here, we would like to discuss something which might be not conducted suitably by the authors.

Firstly, the authors did not include studies strictly according to the preset purpose and criteria. Both in the priori established protocol and inclusion criteria described in this article, it was stated that only randomized controlled trials were eligible in this systematic review. However, the authors included two clinical controlled trials into this review. In addition, the study by [Fogh et al. \(2017\)](#) focused on chemoradiation therapy induced esophagitis instead of oral mucositis, which was also unsuitably included in the analysis. Systematic review outcomes and analysis plans should be specified prior to seeing the results of included studies to minimize post-hoc decisions that may be based on the observed results ([Page et al., 2014](#)). Modifications that occur once the review has commenced, along with their justification, should be clearly reported ([Page et al., 2014](#)). In this review, the difference between protocol and review was not reported and discussed, which might decrease the credibility of its conclusion.

Secondly, interventions of some studies were not correctly extracted and classified. For one thing, in seven studies comparing honey with usual care, honey was topically applied along with usual care in the treatment group instead of honey alone, which was ignored by the authors. To speak strictly, the honey group should be divided into “honey” group and “honey plus usual care” group. For another thing, we did not see the strong necessity to distinguish local honey, kanuka honey, manuka honey and natural honey. Could the “local honey” be artificial? It was even described as “Local commercial Saudi honey” in the study by [Al Jaouni et al. \(2017\)](#), while the authors classified it into pure natural honey group. Therefore, we recommend to synthesize them as a whole, honey group. As for Manuka honey, due to its antibacterial effect after hydrogen peroxide removal, it could be classified as a subgroup of honey group. However, no more evidence supported kanuka honey should be divided apart from pure natural honey from the clinical view. Overall, according to the existing evidence, we recommend the application of honey along with usual oral care. Cumulative studies have shown the adjuvant effect of honey with usual care. Further studies are needed to confirm the efficacy of honey alone and the diversity among different kinds of honey.

Thirdly, the clinical heterogeneity was extremely large among included studies. The method topical application of honey differed very much. The application duration ranged from 1 min to 1 h. The timing of application might be before or after the radiotherapy, or even after the incidence of oral mucositis. The control measures also varied among studies. Usual care might be water mouthwash, normal saline mouthwash, salt–soda and benzydamine gargle, Lidocaine, Mycostatin, Daktarin mouth gel and others. As the outcome assessment, we found that follow-up duration varied from one week to six months. In addition, we did not consider that it is flexible to combine radiation-induced oral mucositis in head and neck cancer patients with mucositis due to other reasons. The clinical heterogeneity was reflected on the statistical heterogeneity ( $I^2 = 77.5\%$ ). And when the clinical heterogeneity is too large, it may be better to avoid quantitative data synthesis ([Higgins and Green, 2011](#)). Therefore, we would like to have a more conservative view on the results of meta-analysis and network meta-analysis.

To summarize, we appreciate that the authors systematically reviewed the literature about the topical application of honey in the management of chemo/radiotherapy induced oral mucositis. And we consent to the authors that honey might be a promising adjuvant therapy agent. However, according to the present evidence, we recommend the topical application of honey along with usual oral health care as the first-line adjuvant therapy. And we expect more studies to further confirm the efficacy of honey and make the standard of honey application.

#### Conflict of interest

None declared.

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