Response to "Topical agent therapy for prevention and treatment of radiodermatitis: a meta-analysis"

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To the Editor;

It was with interest that I read the recent article by Zhang et al. published in Supportive Care in Cancer [1]. This paper highlighted the importance of radiodermatitis (RD) being an unresolved and distressing clinical issue in patients with cancer undergoing radiation therapy. However, I am concerned with a number of clinical and methodological issues within this paper: (i) the clinical and operational definition of prophylaxis and treatment of RD; (ii) the accuracy of the identification of trials; and (iii) the appropriateness of the conduct of the meta-analyses.

First of all, it is important to establish the definitions of prophylaxis and treatment of RD. It has been repeatedly reported that there have not been any globally accepted definitions of prophylaxis and treatment in this area [2]. In some cases, the aim of prophylaxis may be to reduce “the time to a certain grade of RD”. For others, it could be the prevention of any reaction altogether. Indeed, a small group of patients may never develop any reaction from their radical treatment even when they receive a considerable dosage of radiation. Given meta-analysis was the primary objective of this paper, it was very important that these definitions were made clear as they could have tremendous implications on the pooling of data. For these reasons, I suggest that, for future studies and reviews, true “prophylaxis” should be reserved for use if the intent is to prevent a reaction from occurring (yes or no) [2]. And “treatment” should be used to refer to any other management strategies and outcomes after the onset of any graded RD [2].

Secondly, Zhang's paper was designed to only include randomised controlled trials (RCT). However, Masferrer et al (2010) was not a RCT, but a prospective observational study [3]. Although Zhang et al's paper is titled as a "meta-analysis", and not a systematic review, the quality standards for the identification of trials should be upheld. Duplicate study identification, where possible, can be performed for the conduct of all systematic reviews or meta-analyses. The omission of eligible studies or wrong inclusion of studies could have a direct impact on the validity and direction of results [4].

Thirdly, I would like to comment on the appropriateness of the conduct of meta-analyses. One single most common criticism of meta-analyses is that they combine "apples" with "oranges" [5]. Such argument should not mean that meta-analyses cannot be conducted at all. Rather, it should be conducted with sufficient clinical justification and methodological testings (i.e. identifying, measuring and addressing heterogeneity). Although sub-group analysis by each individual intervention comparison might not be feasible, it does not necessarily mean that the conduct of a meta-analysis including a diverse range of topical interventions is justified. These topical interventions could range from corticosteroid to antioxidant solution. Last but not least, it is very crucial that the results of the meta-analyses are interpreted with caution. Zhang et al concluded that topical agents could not prevent or treat RD [1], based on two meta-analyses comprising a number of trials [6-10] that compared one topical intervention with another topical treatment. The differences of effects in these trials should be used to conclude the effects *between* treatments, rather than the effects *of* "topical treatments".

A number of reviews have now been conducted in this space [2]. There has never been a greater need to undertake a high quality systematic review (with meta-analysis where appropriate) that can guide future research and practice for preventing and managing RD. Future research efforts/investment should be directed to the few most promising interventions that may have been reported as effective by at least one trial.

Conflict of interest: None

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