INPLASY PROTOCOL

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None declared.

Comparative efficacy and safety of different mouthwashes on preventing oral mucositis for cancer patients receiving radiotherapy and chemotherapy: a systematic review and network meta-analysis

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Review question / Objective: **What are the efficacy and safety of different mouthwashes on preventing oral mucositis for cancer patients receiving radiotherapy and chemotherapy?**
Condition being studied: **Cancer patients receiving radiotherapy and chemotherapy.**
Eligibility criteria: **Studies were considered if they met the following criteria: (1) randomized controlled trials (RCTs); (2) sample size > 10 participants in each group and patients older than 18 years of age with any type of invasive cancer who underwent RT, CT or CRT; (3) the mouthwash includes one of the following: honey, sucralfate, chlorhexidine, povidone iodine, sodium bicarbonate, Kangfuxin solution, bendamine, normal saline, granulocyte- macrophage clony-stimulating factor (GM-CSF), compound borax solution, studies that compare a mouthwash with a placebo, blank control or another mouthwash were included; (4) OM outcomes by authors reported such as incidence of OM, adverse reactions, weight loss, onset of OM, duration of OM, etc.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 29 September 2021 and was last updated on 29 September 2021 (registration number INPLASY202190106).

INTRODUCTION

Review question / Objective: **What are the efficacy and safety of different mouthwashes on preventing oral mucositis for cancer patients receiving radiotherapy and chemotherapy?**

Condition being studied: **Cancer patients receiving radiotherapy and chemotherapy.**

METHODS

Search strategy: **Electronic databases of PubMed, Embase, the Cochrane Library**

and Web of Science, were performed using medical subject headings (MeSH) and keywords. Additionally, Chinese databases such as Chinese National Knowledge Infrastructure (CNKI), WanFang, and SinoMed databases were searched to select Chinese literature. We also retrieved from searches in major clinical trial registries including, but not limited to, ClinicalTrials.gov, WHO International Clinical Trials Registry Platform, the International Standard Randomized Controlled Trial Number (ISRCTN) Registry, and the Australian New Zealand Clinical Trial Registry (ANZCTR), as well as the reference lists of included RCTs and relevant SRs or meta-analysis were also manually reviewed to identify more potential trials. The following search terms were used: "oral mucositis", "stomatitis", "mouthwash*", "oral rinse*", "clinical trial*", "randomized controlled trial", full details of the search strategy are displayed in online Appendix 1.

Participant or population: Adults cancer patients receiving radiotherapy and chemotherapy.

Intervention: The mouthwash includes one of the following: honey, sucralfate, chlorhexidine, povidone iodine, sodium bicarbonate, Kangfuxin solution, bendamine, normal saline, granulocyte-macrophage clony-stimulating factor (GM-CSF), compound borax solution.

Comparator: Placebo, blank control or another mouthwash.

Study designs to be included: Only randomized controlled trial will be included.

Eligibility criteria: Studies were considered if they met the following criteria: (1) randomized controlled trials (RCTs); (2) sample size > 10 participants in each group and patients older than 18 years of age with any type of invasive cancer who underwent RT, CT or CRT; (3) the mouthwash includes one of the following: honey, sucralfate, chlorhexidine, povidone iodine, sodium bicarbonate, Kangfuxin solution, bendamine, normal saline, granulocyte- macrophage clony-stimulating factor (GM-CSF), compound borax solution, studies that compare a mouthwash with a placebo, blank control or another mouthwash were included; (4) OM outcomes by authors reported such as incidence of OM, adverse reactions, weight loss, onset of OM, duration of OM, etc.

Information sources: The literature search will be conducted in the Cochrane Library, PubMed, Embase, Web Of Science, Chinese databases and major clinical trial registries from inception until May 31, 2021.

Main outcome(s): The primary outcome was incidence of OM and adverse reactions, for incidence of OM, we mainly took the incidence of severe OM (grade 3 or higher) into consideration.

Quality assessment / Risk of bias analysis: Two well-trained reviewers (YML and NMM) independently assessed the quality of the included RCTs using RoB 2.0 tool, which is the latest revised tool for assessing risk of bias in RCTs recommended by Cochrane. The tool comprises of 22 items divided into seven domains: bias arising from the randomization process (items 1.1-1.3), bias due to deviations from intended interventions (items 2.1-2.7), bias due to missing outcome data (items 3.1-3.4), bias in measurement of the outcome (items 4.1-4.5), and bias in selection of the reported result (items 5.1-5.3). The evaluation of each item selects "Yes", "Probably yes", "Probably no", "No", "Not applicable" and "No information" according to the degree of compliance. The bias risk determination flow chart of each domain is shown in Appendix 4. The bias assessment in each domain can be divided into three levels: "Low", "Some concerns" and "High", and the corresponding bias degrees are "Low", "Medium" and "High" respectively. The total bias risk is judged according to the evaluation results of each domain. If the score of each domain is "Low", the total bias risk assessment is "Low", which is a low bias risk; if at least one domain result is "Some concerns" and there is no "High risk" score in each domain, then the total bias risk judgment is

"Some concerns", which is the medium bias risk. If the evaluation result of at least one area is "High", then the total bias risk judgment "High", then RCT has a high bias risk.

Strategy of data synthesis: Statistical analyses were performed using Stata 15.0 and R 4.1, 0 (R Foundation for Statistical Computing, Vienna, Austria) software. The NMA was conducted in a Bayesian framework. Data analysis was performed using R software. The result of direct comparisons would be acquired through the traditional meta-analysis. If the available data are not suitable for synthesis, we will perform a narrative review and summarize the evidences.

Subgroup analysis: Not applicable.

Sensitivity analysis: Sensitivity analysis was used to determine the stability of the results of NMA. This study mainly excluded low-quality studies to judge the degree of change in the results. If there is no significant change, it showed that the results were more reliable. The publication bias was evaluated by drawing funnel diagrams using the netfunnel command of Stata 16.0 software.

Country(ies) involved: China.

Keywords: mouthwashes, oral mucositis, chemo/radiotherapy, network meta-analysis.

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