INPLASY

Intranasal corticosteroid for COVID-19 infection related olfactory dysfunction - A Systematic Review and Meta-analysis of Randomized Controlled Trials

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 25 September 2023 and was last updated on 25 September 2023.

INTRODUCTION

Review question / Objective To investigate the treatment effect of nasal corticosteroid on post COVID-19 infection induced olfactory dysfunction.

Rationale Intranasal corticosteroid plays a role in downregulating the recruitment and influx of inflammatory cells and inhibiting the secretion of pro-inflammatory mediators during the late phase of the inflammatory response. This process is evidenced by reduced levels of histamine, leukotrienes, and mast cells recovered in the nasal fluid and mucosa of patients treated. Local administration of steroids is recommended for olfactory dysfunction arising from chronic sinusitis. However, the role of intranasal corticosteroid for treating post COVID-19 infection olfactory dysfunction remained controversial based on current understanding. The aim of this study was to review all available randomized control trials (RCTs) with corresponding data in a trial registry to provide an updated meta-analysis on the effect of intranasal corticosteroid for post- COVID olfactory loss.

Condition being studied The PICO (population, intervention, comparison, outcome) setting of the current meta-analysis included: (1) P: Post COVID-19 infection people with olfactory loss; (2) I: intranasal corticosteroid spray; (3) C: placebo or no treatment; and (4) O: changes in the scores of olfaction.

METHODS

Search strategy Two authors (YC Chang and YC Lee) made independent electronic searches in the PubMed, EMBASE, and Cochrane Database of Systematic Reviews and Clinical Trials with keyword of ("covid" OR "covid 19" OR "COVID-19"

OR “COVID 2019” OR "coronavirus" OR “coronavirus 2019” OR "long covid" OR "SARS-CoV-2 ") AND (' "nasal spray" OR "mometasone" OR “triamcinolone acetonide” OR “intranasal corticosteroid” OR “nasal corticosteroid” OR “corticosteroid therapy”) AND ("olfaction" OR "smell disorder” OR "anosmia" OR "hyposmia” OR “olfactory dysfunction” OR “smell loss“) through the earliest record to March 20th, 2023.

Participant or population Post COVID-19 infection people with olfactory loss.

Intervention Intranasal corticosteroid spray.

Comparator Placebo or no treatment.

Study designs to be included Randomized controlled trials.

Eligibility criteria To generate a recruited study list, the following inclusion criteria will be used: (1) Adult patients over 18 years of age with confirmed history of COVID-19 infection. (2) Studies treating olfactory dysfunction with intranasal corticosteroid. (3) Clearly defined experimental and control groups. (4) Outcomes measurements included either subjective olfactory measurement or objective olfactory measurement.

Information sources Two authors (YC Chang and YC Lee) made independent electronic searches in the PubMed, EMBASE, and Cochrane Database of Systematic Reviews and Clinical Trials with keyword of ("covid" OR "covid 19" OR "COVID-19" OR “COVID 2019” OR "coronavirus" OR “coronavirus 2019” OR "long covid" OR "SARS-CoV-2 ") AND (' "nasal spray" OR "mometasone" OR “triamcinolone acetonide” OR “intranasal corticosteroid” OR “nasal corticosteroid” OR “corticosteroid therapy”) AND ("olfaction" OR "smell disorder” OR "anosmia" OR "hyposmia” OR “olfactory dysfunction” OR “smell loss“) through the earliest record to March 20th, 2023.

Main outcome(s) Intranasal corticosteroids had a positive effect on olfaction function caused by COVID-19 infection, and both nasal irrigation and nasal spray can improve olfaction function. Additionally, using betamethasone as a steroid regimen may yield better results than other types ofregimens.

Additional outcome(s) None.

Data management Demographic data, study design, details of intranasal corticosteroid and control treatment, and values of the outcomes. The evaluators paid special attention to the effect direction of the scale used in each trial to avoid mis-interpretation.

Quality assessment / Risk of bias analysis To investigate the methodological quality of recruited studies, we used the Cochrane risk-of-bias tool for randomized trials, version 2 (RoB 2), which consisted of 6 main items: randomization process, intervention adherence, missing outcome data, outcome measurement, selective reporting, and overall risk of bias. In the intervention adherence section of RoB 2, there are two options for literature assessment: intention-to-treat (intervention assignment) or per-protocol (intervention adherence). In this meta-analysis, we chose the per-protocol evaluation, since it fits the design of our included studies.

Strategy of data synthesis Because of the heterogeneity of the target populations in the enrolled studies, the current meta-analysis was conducted with a random-effects model, using Comprehensive Meta-Analysis software, version 4 (Biostat, Englewood, NJ). A two-tailed p value less than 0.05 was considered statistically significant. We chose Hedges' g and 95% confidence intervals (CIs) to quantify the primary outcomes. A Hedges' g of 0.2, 0.5, and 0.8 is considered a small, moderate, and large effect size, respectively. The I2 and Cochran’s Q statistics were used to evaluate the degree of heterogeneity among studies. An I2 value of 25%, 50%, and 75% was considered low, moderate, and high heterogeneity, respectively.

Subgroup analysis Subgroup analyses based on the type of treatment and steroid regimen were performed. Meta-regressions of the treatment effects on were conducted to see if the efficacy of intranasal corticosteroid correlated with the aforementioned parameters.

Sensitivity analysis To confirm the robustness of the meta-analysis, the sensitivity analyses were performed using one-study removal method to see if there was a significant change in the summary effect size after removing a particular trial from the analysis.

Language restriction No language limit.

Country(ies) involved Taiwan.

Other relevant information None.

Keywords intranasal corticosteroid, olfactory dysfunction, clinical trials, meta-analysis, systematic review.

Dissemination plans None.

Contributions of each author

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