INPLASY

Protective role of curcumin in the dynamic progression of acute lung injury and idiopathic pulmonary fibrosis: A meta-analysis

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ADMINISTRATIVE INFORMATION

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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 08 September 2023 and was last updated on 08 September 2023.

INTRODUCTION

Review question / Objective Acute lung injury (ALI) and idiopathic pulmonary fibrosis (IPF) are devastating lung diseases with high mortality rates and a lack of effective treatments.ALI and its most severe form, acute respiratory distress syndrome (ARDS), are characterized by dyspnea, refractory hypoxemia, and noncardiogenic pulmonary edema, with direct lung injury accounting for 57% of all cases; indirect lung injury accounts for the remaining 43%, with more than 200,000 people in the United States and more than 3 million worldwide suffering from ARDS each year, and the average mortality rate for patients with ARDS is 30-40%, resulting in a severe economic health burden.The progression of ARDS to advanced stages results in a fibro-proliferative response leading to pulmonary fibrosis (PF), and the deterioration of lung compliance and oxygenation indices due to PF is closely associated with poor prognosis and high mortality in ARDS. And with the continued prevalence of new crowns this problem becomes more and more urgent.IPF is the most prevalent and fatal PF, with more than 50,000 patients with IPF worldwide, and the number of cases is further increasing globally.Acute exacerbation of IPF is the most common and fatal complication, which is often seen as a rapid worsening of respiratory symptoms, an acute worsening of hypoxemia, and a 90-day mortality rate of 42.9%-48.0%, accounting for about half of IPF-related deaths.

Condition being studied Curcumin (CUR) is considered to be the main active ingredient of turmeric and has been used for centuries in traditional Chinese medicine and Ayurveda.In recent years, CUR, a natural polyphenolic compound, has been used in the treatment of a variety of respiratory disorders, such as COPD, asthma, PF, and ALI, and CUR can modulate a variety of cellular signaling pathways to play an active role.CUR possesses anti-inflammatory, anti-oxidation, anti-fibrosis, immunomodulation, membrane protection and anti-tumor, etc. CUR exerts its biological effects by regulating the

expression of transcription factors, inflammatory cytokines, protein kinases and key enzymes mediating various signaling pathways.

METHODS

Search strategy To identify relevant animal studies without language restrictions, publications from four electronic databases, PubMed, Embase, Web of Science and the Cochrane Library, were systematically searched from the build deadline to 19 April 2023.

Participant or population Animal studies.

Intervention Treatment group received any dose, time, frequency and any mode of administration of curcumin as a single treatment.

Comparator This includes moulding only, or receiving the same amount of non-functional fluid or no treatment.

Study designs to be included Only animal studies that assessed the protective effects of Curcumin in animal models of ALI/IPF were included regardless of publication statuso language.

Eligibility criteria We included controlled studies assessing the administration of Curcumin for in animal models of ALI/IPF stablished by different methods, regardless of animal species, age, weight and gender.

Information sources Electronic searches were conducted in four databases with no language restrictions from the build deadline to 19 April 2023: PubMed, Embase, Web of Science and the Cochrane Library.

Main outcome(s) Tumor Necrosis Factor (TNF)-α Concentration as the Primary Outcome Indicator.

Additional outcome(s) Inflammation-related indices (including Myeloperoxidase (MPO) activity, the concentration of Interleukin (IL)-6, IL-1β, IL-10, MPO), lung fluid clearance-related indices (including Wet/dry weight of animal lung (WD), bronchoalveolar lavage fluid (BALF) protein content, Evans blue dye (EBD), lung index), oxidative stress-related indices (including Malondialdehyde (MDA), Superoxide dismutase (SOD), and other indices). dismutase (SOD), nitric oxide (NO)), fibrosis-related indices (including Hydroxyproline (HYP) content, the concentration of transforming growth factor (TGF)-β), and arterial blood gas (including Oxygenation index (PaO2/FiO2), Partial Pressure of Oxygen (PaO2), Partial pressure of carbon dioxide (PaCO2)) were the secondary outcome indicators.

Quality assessment / Risk of bias analysis The Systematic Review Center for Laboratory Animal Experiments (SYRCLE) risk of bias was used.

Strategy of data synthesis Stata 16 and R 4.3.1 were used to integrate data from all included studies, and given that all outcome indicators were continuous variables, effect sizes were expressed through standardized mean deviations (SMDs) with 95% confidence intervals (CIs). Heterogeneity between studies and subgroups was assessed by I2 and Q-tests; when heterogeneity of included studies was small (I2 ≤ 50%), it was analyzed using a fixed-effects model; when I2 > 50%, it was analyzed using a random-effects model. If the heterogeneity of the included studies was large, sensitivity analyses were performed to assess the stability of the overall results; for outcome metrics that included more than 10 studies, meta-regression and subgroup analyses were used to assess the sources of heterogeneity, and publication bias was assessed by funnel plots, Egger's test, and Begg's test.Garphpad Pism 9.5 and Origin 2021 were used to report the results, respectively. Stratified meta-analysis and analysis of dose-time-effect relationship. $p \leq 0.05$ was considered statistically significant.

Subgroup analysis Eight subgroups were prespecified to assess their influence on the effect size: (1) animal species, (2) animal sex, (3) dose of CUR administration, (4) route of CUR administration, (5) choice of time of intervention, (6) duration of therapy, (7) choice of animal model of direct or indirect lung injury and (8) source of specimens of inflammatory factors. In addition, subgroup analyses can be used to track sources of heterogeneity.

Sensitivity analysis If the heterogeneity of the included studies was high, sensitivity analyses were performed to assess the stability of the overall results.

Country(ies) involved China.

Keywords Curcumin; ALI; ARDS; IPF; PF; Animal Models.

Contributions of each author
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