INPLASY PROTOCOL

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None declared.

Efficacy and safety of corticosteroid therapy in patients with cardiac arrest: a meta-analysis of randomized controlled trials

Zhang, Y[1].

Review question / Objective: **Our goal was to assess the effect of primary treatment outcome (overall survival rate at hospital discharge, rate of sustained ROSC) and secondary outcomes (favorable neurological outcomes at hospital discharge and adverse events including hyperglycemia, insulin infusion, hypernatremia, infection, gastrointestinal bleeding, new or changing antibiotics, paresis, renal failure).**
Information sources: **Two researchers (Zhou FW and Liu C) independently searched the PubMed, Embase, The Cochrane Library, Web of Science and China National Knowledge Internet (CNKI) databases from inception to 11 October, 2022 by using medical subject headings (MeSH), Emtree, and text word with no language limitations.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 07 January 2023 and was last updated on 07 January 2023 (registration number INPLASY202310014).

INTRODUCTION

Review question / Objective: **Our goal was to assess the effect of primary treatment outcome (overall survival rate at hospital discharge, rate of sustained ROSC) and secondary outcomes (favorable neurological outcomes at hospital discharge and adverse events including hyperglycemia, insulin infusion, hypernatremia, infection, gastrointestinal bleeding, new or changing antibiotics, paresis, renal failure).**

Condition being studied: **Cardiac arrest (CA) is an important public health problem worldwide. The estimated number of in-hospital cardiac arrest (IHCA) in the USA alone stands annually around 200,0001. Despite advancement in the management of CA over the past decades, the outcome remains dismal2,3. The treatment of CA**

includes basic life support (e.g., chest compressions and ventilations), advanced life support (e.g., defibrillation and drugs), and post-cardiac arrest care4,5. However, there is limited evidence to support many of the advanced therapies currently used during CA and there is an unmet need for new pharmacological interventions to improve patient outcomes6.

Cardiopulmonary resuscitation (CPR) is an effective treatment to save patients' lives, but there is still a high incidence of multiple organ dysfunction and neurological damage after resuscitation. Its occurrence is the result of systemic ischemia-reperfusion and the secondary systemic inflammatory response syndrome (SIRS)7. The incidence of SIRS after successful cardiopulmonary resuscitation was about 68.3%, and the recovery rate was only 2%-22%8. Glucocorticoids are widely involved in the regulation of physiological functions of various organs and systems in the body, with anti-inflammatory, immunosuppressive, antitoxin, anti-shock and other effects.

In recent years, several studies9-11 have explored the use of glucocorticoids in addition to conventional CPR to observe its effect on the success of resuscitation and survival and discharge rate, but the results are still controversial. Andersen et al. found that among adult patients with an IHCA, the use of vasopressin and glucocorticoids when compared to placebo, resulted in improved return of spontaneous circulation9. Wongtanasarasin et al. also found that steroid administration during CA was associated with better outcomes of resuscitation11. But in the study of LI et al, due to the inherent limitations of the studies in this review, they have not been able to reach definitive conclusions10.

In general, at this stage, it is difficult to assess the efficacy and safety of steroid therapy for the prognosis of CA patients based on the few studies available. Therefore, given the ongoing debate, we attempted to evaluate the efficacy and safety of corticosteroid therapy in CA patients by performing a systematic review of randomized controlled trials (RCTs), including survival rate at hospital discharge, sustained return of spontaneous circulation (ROSC), and neurological outcomes at discharge.

METHODS

Participant or population: The subjects were patients with cardiac arrest caused by various reasons.

Intervention: The experimental group was treated with glucocorticoids in routine cardiopulmonary resuscitation.

Comparator: We considered information regarding the effect of corticosteroid therapy on in-hospital cardiac arrest patients with or without a comparator.

Study designs to be included: RCTs.

Eligibility criteria: (1) For repeated publications, the largest or latest publication was selected; (2) Literature with incomplete or unavailable research data, as well as abstracts, reviews, systematic reviews, experience summaries, theoretical discussions, case reports, qualitative studies, etc.

Information sources: Two researchers (Zhou FW and Liu C) independently searched the PubMed, Embase, The Cochrane Library, Web of Science and China National Knowledge Internet (CNKI) databases from inception to 11 October, 2022 by using medical subject headings (MeSH), Emtree, and text word with no language limitations.

Main outcome(s): Our goal was to assess the effect of primary treatment outcome (overall survival rate at hospital discharge, rate of sustained ROSC) and secondary outcomes (favorable neurological outcomes at hospital discharge and adverse events including hyperglycemia, insulin infusion, hypernatremia, infection, gastrointestinal bleeding, new or changing antibiotics, paresis, renal failure).

Quality assessment / Risk of bias analysis: The overall quality of evidence was evaluated by two authors (Zhou FW and Liu C) according to The Grading of

Recommendations Assessment, Development and Evaluation (GRADE) criteria, evaluating the evidence on i) study limitations, ii) inconsistency, iii) imprecision, iv) indirectness, and v) publication bias. Any disagreement between the two authors was first resolved by discussion and then by consulting with a third author (Zhang Y) or the senior author (Zhou FC).

Strategy of data synthesis: STATA 16.0 (Stata Corp LP, College Station, TX, USA) was used to perform statistical analyses. Labbe plots and meta-regression were used for intuitive judgement of heterogeneity. For the remaining circumstances, a random effect model was used to pool the effect size to calculate statistical heterogeneity. Heterogeneity was analysed by I2 and χ2 statistics. If there was significant heterogeneity, a L'Abbe plot and Galbraith plot were conducted to evaluate the consistency and quality of the results. Sensitivity analysis, subgroup analysis and meta-regression were performed to determine sources of heterogeneity. Publication bias was evaluated using Begg's and Egger's tests and funnel plots.

Subgroup analysis: Sensitivity analysis, subgroup analysis and meta-regression were performed to determine sources of heterogeneity. Publication bias was evaluated using Begg's and Egger's tests and funnel plots.

Sensitivity analysis: Sensitivity analysis, subgroup analysis and meta-regression were performed to determine sources of heterogeneity. Publication bias was evaluated using Begg's and Egger's tests and funnel plots.

Country(ies) involved: China.

Keywords: Steroid; Corticosteroid; Cardiac arrest; Survival; Systematic review; Meta-analysis.

Contributions of each author:

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