INPLASY

INPLASY202410034

doi: 10.37766/inplasy2024.1.0034

Received: 09 January 2024

Published: 09 January 2024

The Effect and Safety of Levosimendan Treatment in Adults Patients with Heart Failure Complicating Kidney dysfunction：A Meta-analysis of Randomized Controlled Trials

Hu, ZH[1].

Corresponding author:
Zhonghua Hu

1915383174@qq.com

Author Affiliation:
China, liaoning Province, Shengjing Hospital affiliated to China Medical University.

ADMINISTRATIVE INFORMATION

Support - None.

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

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202410034

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 09 January 2024 and was last updated on 25 March 2024.

INTRODUCTION

Review question / Objective In the 1980s, during the treatment of congestive heart failure (CHF), a new class of patients with acutely decompensated chronic heart failure was discovered: levosimendan.Levosimendan was first approved for clinical use in October 2000,when authorization was granted by Swedish regulatory authorities .Afterward,Qilu Pharmaceutical Company Limited is the first listed in China(1,2), as a representative drug of calcium sensitizer.More than 20 years of clinical research data reveal that It is mainly used in acute or chronic heart failure owing to multiple etiologies in adults, and other possible indications for levosimendan have been described in some observational studies,such as perioperative use, cardioprotection, cardiogenic shock, sepsis, right ventricular dysfunction, and ARDS, [3]etc.Clinical studies have shown little interaction with other cardiovascular drugs, It do not affect the use of other drugs, and has good safety,and to achieve a good clinical curative effect in combination with three types of drugs commonly used to treat heart failure in clinical application.[4-7]Although the indications of this drug have not been mentioned in newborns and children, levosimendan also plays a positive role in the treatment of heart failure in children. Furthermore,several literature reports have confirmed the safety and effectiveness of levosimendan in pediatric heart failure in many domestic and foreign literature reports[8,9]。 However, some scholars prove that It has not achieved good clinical results in clinical application.Therefore, it remains to be determined whether levosimendan can improve the long-term prognosis of patients after short-term or intermittent reuse, and whether the patients can further expand the use population and the scope

of use, and achieve good clinical results. Dobutamine is commonly used in clinical practice for the treatment of heart failure. Therefore, the comparative efficacy of dobutamine and levosimendan in treating patients with heart failure complicated by renal insufficiency has been explored, with numerous clinical trial reports currently available.

Condition being studied Clinical options for treating heart failure with concomitant renal insufficiency are limited, with conventional clinical use of drugs such as dobutamine often yielding suboptimal results. Currently, opinions on the efficacy of levosimendan in treating such patients are mixed. The purpose of this study is to analyze and compare the safety and effectiveness of intravenous levosimendan versus dobutamine in adult patients with heart failure and renal insufficiency.

METHODS

Search strategy In Pubmed as an example,the retrieval strategy ia as follows:1 #"Simendan"[Mesh]simendan OR “levosimendan” [Title/Abstract]; 2# heart failure"[Title/Abstract] OR "cardiac failure" OR "heart decompensation"[Title/Abstract] OR "right sided heart failure"[Title/Abstract] OR "myocardial failure"[Title/Abstract] OR "congestive heart failure"[Title/Abstract] OR "left sided heart failure"[Title/Abstract]; dobutamine; 3 # "renal insufficiency"[MeSH Terms] OR ("renal"[All Fields] AND "insufficiency"[All Fields]) OR "renal insufficiency"[All Fields] OR (("renal"[All Fields] OR "renals"[All Fields]) AND "insufficiencie*"[All Fields]) OR ("renal insufficiency"[MeSH Terms] OR ("renal"[All Fields] AND "insufficiency"[All Fields]) OR "renal insufficiency"[All Fields] OR ("kidney"[All Fields] AND "insufficiency"[All Fields]) OR "kidney insufficiency"[All Fields]) OR (("kidney"[MeSH Terms] OR "kidney"[All Fields] OR "kidneys"[All Fields] OR "kidney s"[All Fields]) AND "failure*"[All Fields]) OR (("renal"[All Fields] OR "renals"[All Fields]) AND "failure*"[All Fields] 4 # 1 # and 2 # and 3 # .

Participant or population Patients with clinically determined heart failure with renal insufficiency or cardiorenal syndrome, according to the New York Heart Association (NYHA) heart failure classification criteria, at the same time, with different stages of renal impairment; gender is not limited, age > 18 years.

Intervention the experimental group received levosimendan on the basis of placebo or conventional treatment.

Comparator The control group received conventional treatment or placebo combined with intravenous dobutamine.

Study designs to be included RCTs; controlled trials.

Eligibility criteria Randomized Controlled Trials (RCTs) published domestically and internationally, regardless of the use of blinding, in Chinese and English languages. Exclusion criteria include: 1. Non-rct; 2. Documents with incomplete data or the full text cannot be obtained, and the data cannot be extracted or converted; 3. The diagnosis and treatment of diseases are not uniform and standardized; 4. Animal experiments, reviews, meta-analyses, conference abstracts; 5. Repeated publication of literature; 6. On the basis of HF, other underlying diseases are combined, such as malignant tumors, liver failure, hypotension and other organic diseases.

Information sources PubMed、EMbase、Cochrane、web of science 、CMB、CNKI、Wanfang Data.

Main outcome(s) Main outcome measures: left ejection fraction (LVEF), glomerular filtration rate (eGFR), total response rate, B-type natriuretic peptide level, mortality.

Additional outcome(s) 6 MWP、LVESD、N-PROBNP.

Quality assessment / Risk of bias analysis The risk of bias in the included studies was assessed using the Cochrane Risk of Bias tool.

Strategy of data synthesis Counting data were expressed by relative risk ratio (RR). Continuous variables were expressed by weighted mean difference (WMD) if they were based on the same unit of measure, and standardized mean difference (SMD) if the units of measure were different or the mean differed greatly. Both were expressed with 95% interval confidence (CI). The statistical heterogeneity of the included studies was analyzed by the ◕ 2 test (the test level was α = 0.1), and the size of the heterogeneity was quantitatively judged by combining I2. When I2 ≤ 50% or P > 0.1, the homogeneity among the studies was considered to be good, and the fixed-effect model was used. When I2 > 50% or P ≤ 0.1, the heterogeneity

among the studies was considered to be large, and the source of the heterogeneity was further analyzed and the random-effect model was used. Significant heterogeneity was treated by subgroup analysis or sensitivity analysis, or only descriptive analysis was performed.

Subgroup analysis If substantial heterogeneity exists, and there is a sufficient number of included studies (> 10), we will complete subgroup analysis according to the following prespecified characteristics.

Sensitivity analysis Sensitivity analyses will be conducted, excluding studies at high risk or unclear risk of bias on the allocation concealment and blinding domains of Cochrane's'Risk of bias' assessment tool. Additional sensitivity analyses include: 1.fixed-effect analyses for the pairwise and network meta-analyses will be run; 2.trials where missing data were imputed will be removed; 3.trials that use a non-operationalised diagnostic criteria will be removed.

Language restriction English、Chinese.

Country(ies) involved China (Zhonghua Hu/ Fushun Mineral Bureau General Hospital；Hong Li/ Shengjing Hospital affiliated to China Medical University).

Keywords Levosimendan; Dobutamine; Heart failure; Renal insufficiency; Cardiorenal syndrome; Retrospective study; Meta-analysis.

Contributions of each author

Author 1 - zhonghua Hu.
Email: 1915383174@qq.com