INPLASY PROTOCOL

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Review Stage at time of this submission: **The review has not yet started.**

Conflicts of interest: **No.**

Effect of grelin on TRX expression in chronic heart failure tissue: a protocol of systematic review and meta-analysis

Chen, Z[1]; Feng, Y[2]; Zhang, RB[3]; Li, X[4]; Xu, JB[5].

Review question / Objective: **Is grelin effective on TRX expression (TRXE) in chronic heart failure tissue (CHFT)?**
Condition being studied: **Chronic heart failure; grelin.**
Information sources: **The following databases will be utilized to retrieve relevant studies from inception to the March 1, 2020 in MEDLINE, EMBASE, Cochrane Library, Cumulative Index to Nursing and Allied Health Literature, PEDro, the Allied and Complementary Medicine Database, Chinese Biomedical Literature Database, and China National Knowledge Infrastructure. We will not place any restrictions to the language and publication status. We will build a search strategy sample of MEDLINE. The equivalent search strategies will be modified for other electronic databases. We will also search secondary literature sources, such as Google Scholar, website of clinical trial registries, reference lists of relevant reviews.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 14 April 2020 and was last updated on 14 April 2020 (registration number INPLASY202040078).

INTRODUCTION

Review question / Objective: **Is grelin effective on TRX expression (TRXE) in chronic heart failure tissue (CHFT)?**

Condition being studied: **Chronic heart failure; grelin.**

METHODS

Participant or population: In this study, we will select CHFT as our research target.

Intervention: Any types of grelin will be used for the treatment in the interventional group.

Comparator: Any managements (such as no treatment, inhibitor) will be utilized as a comparator in the control group. We will exclude studies used any forms of grelin as their controls.

Study designs to be included: This study will include randomized controlled trials (RCTs) of grelin on TRXE in CHFT, regardless language and publication status limitations.

Eligibility criteria: This study will include RCTs of grelin compared with other intervention on TRXE in CHFT.

Information sources: The following databases will be utilized to retrieve relevant studies from inception to the March 1, 2020 in MEDLINE, EMBASE, Cochrane Library, Cumulative Index to Nursing and Allied Health Literature, PEDro, the Allied and Complementary Medicine Database, Chinese Biomedical Literature Database, and China National Knowledge Infrastructure. We will not place any restrictions to the language and publication status. We will build a search strategy sample of MEDLINE. The equivalent search strategies will be modified for other electronic databases. We will also search secondary literature sources, such as Google Scholar, website of clinical trial registries, reference lists of relevant reviews.

Main outcome(s): Primary outcome are protein and gene expressions of TRXE. Protein expression of TRXE is measured by any related test, such as immunohistochemistry. Gene expression of TRXE is detected by reverse transcription polymerase chain reaction test or other related tests.

Additional outcome(s): Secondary outcomes include left ventricular end-diastolic diameter, left ventricular end-systolic diameter, end-diastolic left ventricular posterior wall thickness, left ventricular ejection fraction, left ventricular systolic blood pressure, left ventricular end diastolic pressure, maximum left ventricular pressure increase rate, and maximum left ventricular pressure decrease rate.

Data management: Two researchers will separately perform data collection using pre-constructed data extraction sheet. It includes publication information (title, first author, year of publication, et al), targeted subject, sample size, study methods (randomization, blind, et al), details of interventions and controls (types of managements, dosage, et al), outcomes, results, conclusions, conflict of interest, and other related information. Any disagreements will be settled by a third researcher via discussion. If we identify any unclear or missing information, we will contact primary authors to request it.

Quality assessment / Risk of bias analysis: Two researchers will separately assess study quality of all included studies using Cochrane risk of bias tool. It covers seven items, and each item is rated as low, unclear, or high risk of bias. A third researcher will be invited to tackle any differences through discussion.

Strategy of data synthesis: The statistical analysis will be undertaken by RevMan 5.3 software. The treatment effect will be estimated as weighted mean difference or standardized mean difference and 95% confidence intervals (CIs) for continuous data, and risk ratio and 95% CIs for dichotomous data. Statistical heterogeneity will be examined by I^2 test. The values of I^2 ≤50% show fair homogeneity and a fixed-effects model will be applied. On the other hand, the values of I^2 >50% mean obvious heterogeneity, and a random-effects model will be practiced. If homogeneity is identified, we will perform a meta-analysis when sufficient data are extracted. If significant heterogeneity is examined, we

will carry out a subgroup analysis to find out sources of heterogeneity.

Subgroup analysis: Subgroup analysis will be suggested to explore possible reasons for the substantial heterogeneity in accordance with different types of treatments, controls, and outcome measurements.

Sensibility analysis: Sensitivity analysis will be performed to test the robustness of study results by eliminating low quality studies.

Country(ies) involved: China.

Keywords: Chronic heart failure; grelin; TRX expression; effect.