INPLASY PROTOCOL

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Conflicts of interest:
None.

Effects of Tonifying Kidney and Strengthen Bone Therapy on Non-dialysis Patients With Chronic Kidney Disease-Mineral and Bone Disorder: a protocol for the systematic review and meta-analysis of randomized controlled trials

Wu, Z[1]; Li, L[2]; Wu, G[3]; Xie, Y[4]; Li, J[5]; Peng, R[6].

Review question / Objective: **To systematically review literature about the efficacy and safety of Tonifying Kidney and Strengthen Bone (TKSB) therapy combined with western medicine (WM) for non-dialysis patients with Chronic Kidney Disease - Mineral and Bone Disorder (CKD-MBD).**
Condition being studied: **Chronic kidney disease (CKD) is a major disease threatening human health in the world. Chronic Kidney Disease-Mineral and Bone Disorder(CKD-MBD) is one of the most common complications of CKD, the exist therapy just focus on how to correct the disorder of calcium and phosphorus metabolism in the body while ignores the protection of renal function. Traditional Chinese medicine (TCM) is widely used in protecting and improving renal function, the classic therapy of TCM for CKD-MBD is Tonifying Kidney and Strengthen Bone(TKSB). Based on this, we intend to conduct a meta-analysis to provide a better therapy.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 16 December 2020 and was last updated on 16 December 2020 (registration number INPLASY2020120086).

INTRODUCTION

Review question / Objective: **To systematically review literature about the efficacy and safety of Tonifying Kidney and Strengthen Bone (TKSB) therapy combined with western medicine (WM) for non-dialysis patients with Chronic Kidney**

Disease - Mineral and Bone Disorder (CKD-MBD).

Condition being studied: Chronic kidney disease (CKD) is a major disease threatening human health in the world. Chronic Kidney Disease-Mineral and Bone Disorder(CKD-MBD) is one of the most common complications of CKD, the exist therapy just focus on how to correct the disorder of calcium and phosphorus metabolism in the body while ignores the protection of renal function. Traditional Chinese medicine (TCM) is widely used in protecting and improving renal function, the classic therapy of TCM for CKD-MBD is Tonifying Kidney and Strengthen Bone (TKSB). Based on this, we intend to conduct a meta-analysis to provide a better therapy.

METHODS

Participant or population: Patients with CKD-MBD who do not receive renal dialysis treatment will be included. Patients who did not meet the diagnostic criteria or received dialysis treatment in the treatment group or control group will be excluded.

Intervention: The treatment must include one type of TKSB therapy(e.g. bushen, yishen, tonifyingkidney, bugu, jiangu, zhuanggu, strengthen bone) combined with one type of WM(e.g. calcium carbonate tablets, calcitriol).

Comparator: The control group should received WM treatment alone. If the control group contains other TCM therapy or dialysis treatment, it will be excluded.

Study designs to be included: Randomized controlled trial and quasi-RCT including combination therapy of TKSB will be included.

Eligibility criteria: 1.Types of study: Randomized controlled trial and quasi-RCT including combination therapy of TKSB will be included. 2.Participants: Patients with CKD-MBD who do not receive renal dialysis treatment will be included. Patients who did not meet the diagnostic criteria or received dialysis treatment in the treatment group or control group will be excluded. 3.Intervention:The treatment must include one type of TKSB therapy(e.g. bushen, yishen, tonifyingkidney, bugu, jiangu, zhuanggu, strengthen bone) combined with one type of WM(e.g. calcium carbonate tablets, calcitriol). 4.Comparator: The control group should received WM treatment alone. If the control group contains other TCM therapy or dialysis treatment, it will be excluded.

Information sources: We will comprehensively search the following 7 databases: PubMed, EMBASE, Cochrane Library, Wanfang database,Chinese National Knowledge Infrastructure (CNKI), China Biological Medicine (CBM) and VIP Journals Database. Ambiguous literature will be manually searched to avoid missing eligible trials. Ongoing registered clinical trials will be searched on the websites of the chinese clinical trial registry (http://www.chictr.org.cn/) and international clinical trial registry (http://clinicaltrials.gov/). We will contact the original investigators for more complete details of the study to solve questions about eligibility if necessary.

Main outcome(s): Included studies should contain at least four of the following evaluated outcomes: (a) clinical effective rate; (b) serum Ca level; (c) serum P level; (d) parathyroid hormone (PTH); (e) blood urea nitrogen (BUN) level; (f) serum creatinine (SCr) level; (g) adverse events from TKSB therapy or WM.

Quality assessment / Risk of bias analysis: For eligible studies, the following data were independently extracted by two authors: first author, publication year, region, sample size, detail of intervention, treatment courses, and outcome parameters. The quality analysis was conducted by the other two authors, according to the Cochrane risk of bias assessment tool. The assessed items included six domains: (1) random sequence generation; (2) allocation concealment; (3) blinding method; (4) integrity of data; (5) selective reporting; (6) other bias. For any

disagreement between the two authors, it would be settled through discussion with a third author.

Strategy of data synthesis: Review Manager 5.3, compiled by the Cochrane Collaboration, will be employed to pool and analyze data. Dichotomous variables will summarize as risk ratios (RR) with 95% confidence intervals (CI), while continuous variables will summarize as mean difference (MD) with 95% CI. Heterogeneity will be examined by the I2 test. The result of I2 test above 50% will be considered to indicate significant heterogeneity, and the meta-regression model will be applied to find out the sources of the heterogeneity. Additionally, if necessary, a sensitivity analysis will be carried out to evaluate the stability and reliability of the results by removing individual studies at a time.

Subgroup analysis: Subgroup analysis will be handled according to the difference in the type of intervention, the difference stages of CKD-MBD, patient basic conditions, or treatment duration.

Sensibility analysis: Sensitivity analysis will be performed by removing the inclusion of studied one by one, for evaluating whether the results of the meta-analysis is reliable and finding the potential sources of heterogeneity. The funnel plot analyses would be performed to determine potential publication bias if every comparison group included more than 10 studies.

Country(ies) involved: China.

Keywords: Chronic Kidney Disease-Mineral and Bone Disorder, Tonifying Kidney and Strengthen Bone therapy, meta-analysis, randomized controlled trials (RCT), Traditional Chinese Medicine.

Contributions of each author:

Author 1 - Zijian Wu - The author drafted the manuscript.
Author 2 - Liang Li - The author provided statistical expertise.
Author 3 - Guiling Wu - The author contributed to the risk of bias assessment strategy.
Author 4 - Youqiong Xie - The author read, provided feedback and approved the final manuscript.
Author 5 - Jia Li - The author contributed to the development of the selection criteria.
Author 6 - Rui Peng - The author designed the study protocol.