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Measurement on the medication adherence in the clinical trials on herbal medicine: a scoping review protocol

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ADMINISTRATIVE INFORMATION

Support - None.

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

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 05 June 2024 and was last updated on 05 June 2024.

INTRODUCTION

Review question / Objective The research purpose of this scoping review is to assess current status of how methods for measuring medication adherence are utilized and what types of methods are employed in clinical trials dealing with herbal medicine.

Background For this reason, the SPIRIT 2013 reporting guideline for developing clinical trial protocols addresses strategies for improving adherence and methods for monitoring adherence under item 11c [1]. Direct methods to assess adherence in drug clinical trials include counting pills or medication packages, checking patient medication diaries or recall, using electronic monitoring systems that record the number of times the container is opened, and indirect methods like periodically analyzing blood or urine for active drug substances or metabolite levels or markers [2]. SPIRIT 2013 recommends documenting specific methods to evaluate adherence in study protocols, and many drug studies set and assess medication adherence as a key research outcome [3].

With the rising interest in herbal medicine used in traditional medicine worldwide, including traditional Chinese medicine, many clinical studies having been conducted to evaluate clinical evidence on its efficacy and safety. Unlike synthetic drugs, herbal medicines do not have well-established profiles on active ingredients and metabolites, making it difficult to measure drug-related substances or metabolites in blood or urine. However, adherence is a significant factor influencing outcomes in drug clinical studies, necessitating the development of appropriate monitoring techniques suited to the characteristics of herbal medicine. In this context, this scoping

review aims to examine the methods used to monitor medication adherence in clinical studies of herbal medicine since the publication of SPIRIT 2013, and how drug adherence was utilized in outcome analysis. Through this, we intend to propose suitable methods for evaluating medication adherence in future clinical studies of herbal medicine.

Rationale Medication adherence is a critical factor directly linked to the effectiveness of pharmacotherapy. Especially in clinical trials, medications must be administered according to the study protocol to ensure a fair evaluation of efficacy and safety. Non-adherents are reported to have poorer clinical outcomes compared to adherents [4]. Existing studies indicate that lower adherence affects the reliability of research results [5,6]. Consequently, adherence issues in clinical trials must be appropriately controlled and considered when interpreting results, as they can lead to significant bias in study findings.

METHODS

Strategy of data synthesis For this study, clinical trials using herbal medicine as the test intervention are searched in the PubMed, Embase, and Cochrane CENTRAL databases from January 2013 to May 2024. The search strategy combines subject terms and natural language, with the PubMed search strategy as follows:
("plant extracts"[MeSH Terms] OR "herbal medicine"[MeSH Terms] OR "phytotherapy"[MeSH Terms] OR "plants, medicinal"[MeSH Terms] OR "plant preparations"[MeSH Terms] OR "plant"[Title/Abstract] OR "plants"[Title/Abstract] OR "flower*"[Title/Abstract] OR "seeds"[Title/Abstract] OR "seed"[Title/Abstract] OR "tree"[Title/Abstract] OR "trees"[Title/Abstract] OR "phytotherap*"[Title/Abstract] OR "phyto therap*"[Title/Abstract] OR "extract*"[Title/Abstract] OR "phytopharmaceutical"[Title/Abstract] OR "decoction"[Title/Abstract]) AND ((randomizedcontrolledtrial[Filter]) AND (2013:2024[pdat])).

Eligibility criteria The PICO for this study is as follows:
Population: The study includes all types of diseases and symptoms (or sign), without restrictions on the target disease or conditions.
Intervention: The intervention explored in this review is herbal medicine. Herbal medicine refers to all forms of drugs derived from botanical sources, including powders, extracts, boiled decoctions, pills, and all other formulations used in traditional medicine or phytomedicine. This includes both single-herb preparations and combinations of multiple herbs. Studies utilizing herbal medicines from various traditional medical systems such as Traditional Chinese Medicine, East Asian Traditional Medicine, Ayurveda, and African Traditional Medicine are included. Dietary supplements using medicinal herbs are also included. If natural products contain some mineral or animal-derived ingredients, they are still considered within the scope of herbal medicine for this study. However, studies using products with synthetically produced components of natural substances are excluded. Herbal medicines mixed with synthetic drugs are also excluded.
Comparator: There are no specific limitations on the interventions for the control group in this study. Any control intervention, such as placebo, standard treatment, or waiting list, is allowed.
Outcome: The study does not consider which outcome variables are used. Therefore, studies are included regardless of the variables employed.
Design: This review includes only randomized controlled trials (RCTs). However, quasi-RCTs with non-transparent randomization methods are also included.

Source of evidence screening and selection The selection of the studies to be included will be conducted independently by THK and JWK. In cases of disagreement, resolution will be achieved through consensus. Initially, duplicates will be removed from the search results of the electronic database, followed by a first screening based on the titles and abstracts. Subsequently, the hard copies of the included studies will be reviewed for a second to determine whether to be included or not finally.

Data management The list of included studies and the extracted information will be stored using bibliographic software such as Excel or EndNote.

Reporting results / Analysis of the evidence In this review, we will assess whether drug adherence monitoring methods were used in clinical trials of herbal medicine, and if so, which methods were used. Additionally, if multiple methods were used simultaneously to assess drug adherence, we will examine whether there were differences in the drug adherence results among these various assessments. Furthermore, we will evaluate whether drug adherence was applied in the statistical analysis or interpretation of the study results. Lastly, we will compare whether there is a difference in the direction of the effect for the primary outcomes among the studies that applied drug adherence in their results and those that did not.

Presentation of the results The characteristics of the included studies, such as country (corresponding authors), type of intervention (traditional medicinal herbal drug, herbal tea, herbal supplements, etc.), type of funding body (government or public agency funding, company funding, or self-funding by researchers), study phase, etc., will be presented using bar graphs or pie charts. The proportions of studies that used monitoring methods, or did not use them (, or did not describe any methods) will be suggested with pie charts. If multiple methods were used simultaneously for assessment, the differences in drug adherence results among these various assessments and whether drug adherence was applied in the statistical analysis or interpretation of the study results will be presented in a table.

Language restriction There is no language restriction in this study.

Country(ies) involved Republic of Korea.

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Keywords Herbal medicine, phytomedicine, clinical trial, drug adherence monitoring.

Contributions of each author

Author 1 - Tae-Hun Kim - Author 1 drafted the protocol and will do searching/ data-extraction/ analysis of data/ writing draft of the research results.

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