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Protocol for systematic review and meta-analysis on the effect of natural products use on blood pressure in Iran

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ABSTRACT

Background: Today, hypertension is a significant public health problem globally, widely recognized as a major risk factor for death. Blood pressure-lowering herbal medicines and natural products have been used for centuries. The protocol aims to determine the effect of natural product use on blood pressure in Iran using data from previously published randomized controlled trials. The current protocol for a systematic review and meta-analysis is designed to determine the effect of natural product use on blood pressure in Iran.

Methods: The protocol is developed using PICO (participants, interventions, comparisons, and outcomes) items to assess the effect of natural products on blood pressure reduction in randomized clinical trials (RCTs) in Iran. Specific MESH terms will be used to search Google Scholar, PubMed, and the Cochrane Central Register for randomized controlled clinical trials, as well as national databases such as Barekat Gostar, SID, Magiran, and IranDoc. The I^2 index and the Q-test will be used to examine heterogeneity in the effect sizes of individual studies.

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) of RCTs will be reported per Cochrane guidelines, and all forms will be based on validated Cochrane templates.

Discussion: This protocol will detail the effects of natural products (interventions) in comparison to a placebo or other control group (comparators).

Registration: The current protocol was also registered on PROSPERO (ID: CRD42021231837, https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=231837, Date: February 18, 2021).

Study Protocol

Implication for health policy/practice/research/medical education:
Hypertension is a significant public health problem globally, widely recognized as a major risk factor for death. Blood pressure-lowering herbal medicines and natural products have been used for centuries. This protocol aims to determine the effect of natural product used on blood pressure in Iran using data from previously published RCTs.

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Introduction

Hypertension is the leading cause of death worldwide (1) and is one of the most common and chronic diseases in developed and developing countries (2,3). Hypertension is the most prevalent chronic disease in developed societies, claiming approximately 7.1 million lives each year (4). Different definitions have been proposed for hypertension. However, according to the national committee for the prevention, diagnosis, evaluation, and treatment of hypertension in adults' model, if a person's diastolic blood pressure is 85 mm Hg or greater for two consecutive days with a medium interval, or if their systolic blood pressure

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is 130 mm Hg or greater, the person is said to be suffering from hypertension (5).

Therefore, hypertension is frequently referred to as a "silent killer" (6-9). Risk factors for hypertension include race, gender, genetic factors, smoking, obesity, inaction, and high salt intake (9-12).

Hypertension is a significant risk factor for cardiovascular disease (13) and the leading cause of stroke and kidney failure in adults, particularly the elderly (14). Thus, high blood pressure affects three vital organs, including the brain, heart, and kidneys (15), and as people age, hypertension and its complications, including cerebral hemorrhages, stroke, and renal failure, become more prevalent (16).

Medicinal plants are one of the earliest drugs used by humans and were instrumental in the development and evolution of conventional medicine, with many of them still being used and consumed in their natural state (17). Due to the adverse effects associated with the use of numerous chemicals and the high cost of some drugs, the use of medicinal plants has increased in recent decades. Today, more than 20% of drugs used in the United States are derived from plants (18,19). This study aims to investigate the effect of natural product use on blood pressure by analyzing data from previously published randomized controlled trials (RCTs).

Materials and Methods

Study design

The following protocol adheres to the PRISMA-P (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) guidelines (20). The protocol for a systematic review and meta-analysis on the effect of natural product use on blood pressure in Iran was developed according to the Cochrane library's guidelines.

Eligibility criteria

We will conduct a systematic review and meta-analysis (participants, interventions, comparisons, and outcomes [PICO]) of phase II and phase III RCTs involving subjects with hypertension who had received one of the natural products.

Inclusion criteria

The initial studies in this protocol will consist of RCTs with or without blinding or a quasi-experimental design. The intervention group consists of natural product consumers (i.e., plant leaves, plant oil, fruit, fruit juice, and plant various forms, including tablets and extracts of natural products). On the other hand, the comparison group will consist of those receiving the placebo or no intervention. Eligible trials must include an assessment of either systolic or diastolic blood pressure.

Exclusion criteria

The following studies will be excluded from the protocol; case reports, studies deemed to be of low-quality using the Cochrane organization's clinical trial quality assessment checklist, as well as studies that lack the required information report, studies that express the effect of natural products on blood pressure qualitatively, studies that examine the effects of both natural products and a chemical medicine concurrently, and studies lacking full-text availability.

Types of participants, interventions, comparisons, and outcomes

Patient population: All individuals who used various natural products to reduce their blood pressure. Intervention: Different forms and types of natural products. Comparison; A group of individuals who did not receive a natural product or received a placebo. Outcomes; Systolic and diastolic blood pressure readings.

Search strategy

This review and meta-analysis of the literature will be conducted using systematic searches of multiple databases, including PubMed, Scopus, Web of Science, Embase, and Cochrane, and national databases such as Barekat Gostar, SID, Magiran, and IranDoc. Additional Google Scholar searches will be performed. The following keywords are to be used in the search process: "Natural products," "Medicinal plants," "Herbal medicines," "Traditional treatment," "High blood pressure," "Hypertension," "Meta-analysis," and "Systematic review" based on their Persian MeSH (Medical Subject Headings) equivalents. The reference lists of key full-text articles included in the review will be screened to identify potentially eligible studies. Additionally, their combinations will be searched using the AND & OR operators in English language databases. The searches will be unrestricted by historical timelines. A meta-analysis requires a minimum of two studies (21).

Assessment of methodological quality (risk of bias)

After identifying the initial studies, two authors will independently evaluate them using the Cochrane quality evaluation checklist. This checklist contains seven different items, each assessing a different dimension or type of significant bias in clinical trials. Additionally, each item on this checklist is rated according to one of three bias categories: high risk, low risk, or unclear. Two evaluators will initially assess the bias risk in each study, then evaluate any disagreements between the options in each study, and finally, mutually agree upon a single option.

Study selection

Additional clarification from the study authors will be

sought as necessary to determine eligibility. The authors will document the reasons for each study's exclusion and summarize the screening results using the PRISMA flow diagram (20).

Data collection process

Two researchers will independently extract data from studies to minimize report bias and data collection errors. These researchers will enter the extracted data into a checklist that includes the researcher's name, the year the study was published, the title of the study, the sample size, the mean and standard deviation of systolic and diastolic blood pressure levels before and after the intervention, as well as the amount and duration of natural product use. A second researcher will investigate the extracted data for inconsistencies. If necessary data is not included in one of the initial articles or studies, an email is to be sent to the corresponding author requesting that they be included. If the email does not generate a response, it will be resent up to three times during different times (at least once every five days).

Outcome measures

Primary endpoint: Our study's primary outcome measure will be systolic and diastolic blood pressure. A sphygmomanometer is the standard instrument for measuring a person's blood pressure.

Secondary endpoint: The secondary outcomes include lipid and glucose profiles.

Discussion

This study will employ a systematic review and meta-analysis to determine the efficacy of natural products and herbs in lowering blood pressure levels in individuals. This study will examine all of the natural products consumed in Iran. To enable a comparison of the types of natural products, their doses, and their duration of use, among other factors, will be used to determine which product is the most effective at lowering blood pressure levels and which product has the least effect. Moreover, as a secondary outcome, the effect of consuming each of the natural products on blood sugar and lipid levels in Iranian patients will be assessed.

Given the nature of the current study, which is a meta-analysis, we will discuss studies that have been published and for which the full text is available. As a result, studies in the submission stage and those whose full text is not available are not covered, and no information about them will be provided.

Authors' contribution

All authors contributed to the completion of this work. MF conceptualized the study, collected data, assessed documents, and wrote the first draft. MA oversaw the research project, contributed to original data, and critically edited and reviewed the manuscript. AF's second supervisor on the research project contributed to the study's design and analysis of data and the manuscript's critical editing and review. MM improved the research design, edited, and reviewed the manuscript. SSY assisted in document assessment, data extraction, editing, and manuscript review. All authors read and signed the final paper.

Availability of data and materials

The review's studies will be made available upon request.

Protocol amendments

If the current protocol is significantly amended following its inception and has an effect on the study's conduct (including eligibility criteria, study objectives, study design, study procedures, and analysis), the amendment will be agreed upon by all collaborators prior to implementation and documented in a note to a subsequent publication or report (section "Differences between protocol and review").

Conflicts of interest

The authors declare that they have no competing interests.

Ethical considerations

This protocol of systematic review and meta-analysis was conducted in accord with the World Medical Association Declaration of Helsinki. The institutional ethical committee of Mazandaran University of Medical Sciences approved all study protocols (IR.MAZUMS. REC.1399.8528). The current protocol was also registered on PROSPERO (ID: CRD42021231837, https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=231837, Date: February 18, 2021). Besides, ethical issues (including plagiarism, data fabrication, double publication) were completely observed by the authors.

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