MEDISAINS
Jurnal Ilmiah Ilmu - Ilmu Kesehatan

Original Article

Red ginger (*Zingiber officinale* var. rubrum) nanoparticle extracts on reducing the blood pressure for postpartum hypertension

Ummu Luthfiyah [1]✉, Runjati [1], M. Choiroel Anwar [1]

[1] *Postgraduate Program in Applied Health, Poltekkes Kemenkes Semarang, Central Java, Indonesia*

ARTICLE INFORMATION

Received: September 27, 2022
Revised: January 18, 2023
Accepted: January 21, 2023

KEYWORDS

Nanoparticles; Ginger; Antihypertensive Agents; Postpartum Period

CORRESPONDENCE

Phone: +6282386846218

E-mail: luthfiyahummu@gmail.com

A B S T R A C T

Background: Red ginger contains flavonoids, which can cause vasodilation and decreased cardiac output and pressure. Previous research on red ginger on blood pressure has been carried out and showed significant results. However, it has yet to be studied in nanoparticle extracts, where nanoparticles are the best drug carrier system, so it is necessary to research.

Purpose: Making and testing red ginger nanoparticle administration (*Zingiber officinale* var. rubrum) to reduce blood pressure in hypertensive postpartum mothers.

Methods: This is an experimental study with a pre-post control group design. The sample consisted of 40 postpartum hypertensive mothers divided into two groups, namely 20 interventions and 20 controls. The intervention group was given red ginger nanoparticles made using the bottom-up method with a dose of 300 mg and the antihypertensive drug nifedipine, while the control group was given the antihypertensive drug nifedipine alone; both were given for two weeks. Data analysis used the Independent t-test and reapeted ANOVA tests.

Results: The systolic blood pressure in the intervention group decreased by 12.95 mmHg on the 7th and 28.4 mmHg on the 14th day ($p<0.001$) while the control group was 7.05 mmHg on the 7th day and 14.8 mmHg on the 14th day ($p<0.001$). Diastolic blood pressure in the intervention group decreased by 3.55 mmHg on the 7th day and 11.90 mmHg on the 14th day ($p<0.001$), while the control group was 2.88 mmHg on the seventh day ($p<0.007$) and fifth day 35 mmHg on day 14 ($p<0.002$).

Conclusion: Giving red ginger nanoparticles can reduce blood pressure in postpartum hypertension.

INTRODUCTION

Hypertension during the puerperium complicates 10-15% of pregnancies and has a considerable role in morbidity and mortality in mothers and babies.[1] Hypertension that continues into the postpartum period can threaten the well-being and even death.[2] Based on the Ministry of Health in 2020, the most common causes of maternal death in Indonesia were bleeding in 1,330 cases (28.59%), hypertension in pregnancy 1,110 cases (23.86%), and infection in 216 cases (4.64%).[3] Mothers with postpartum hypertension can experience various complications, including brain hemorrhage, stroke, retinal injury, eye disorders, heart problems, pulmonary edema, and liver necrosis. Other researchers also reported that maternal complications of postpartum hypertension include kidney disorders, kidney failure, and damage to blood vessels.[4] Efforts to reduce morbidity and mortality in postpartum women with hypertension require treatment by providing therapy according to the program set by the government and also with complementary use. Handling hypertension in postpartum mothers aims to prevent complications that can be done through pharmacological and non-pharmacological treatment. Antihypertensive drugs, including ACE inhibitors, Ca blockers, Beta blockers, and diuretics, are given as pharmacological treatment.[5]

Currently, non-pharmacological treatments are widely used by the public because of their low cost and low side effects. One of the non-pharmacological treatments for high blood pressure is red ginger. Red ginger contains

https://doi.org/10.30595/medisains.v21i1.15165

many essential oils and has oleoresin compounds, including 25% gingerol, 29.7% zingerone, and 18% shogaol. Gingerol can inhibit blood clotting so that it can lower high blood pressure.[6] Red ginger also contains flovanoid compounds, non-flovanoid saponins, and phenols. Flavonoids inhibit the activity of an Angiotensin-Converting Enzyme (ACE), so the formation of angiotensin II results in vasodilation, decreased cardiac output, and blood pressure. Ginger type of red ginger is suitable as an essential ingredient for medicines and herbal medicine.[7–9]

Various studies regarding other non-pharmacological interventions on blood pressure such as research by giving chayote extract 500 mg once a day for 11 days, giving tomato juice 250 ml once a day for 14 days, giving rosella tea 10 grams brewed with 200 ml water once a day for four days and chocolate 60 mg for 15 days.[9–12] These studies have not yielded the expected results, indicating that the research's strength is its weakness. So researchers want to examine whether red ginger nanoparticles reduce blood pressure in postpartum hypertensive mothers.

Much research has been done on red ginger, but only a few have examined its relationship to blood pressure, and no one has researched it in the form of nanoparticles. In addition, some research on red ginger herbal is still limited to processing by extraction, and the weaknesses of herbal medicines, such as low solubility, bioavailability, absorption, and toxicity, are difficult to predict; nanoparticle innovation can be an excellent solution to overcome this problem.[13] Nanoparticles are the best drug delivery systems because they can manipulate particle size and modify their basic properties such as solubility, diffusivity, and absorption; the particle size is tiny. The use of nanotechnology in the pharmaceutical field has various benefits and advantages, including increasing the solubility of compounds, reducing medication doses, and increasing absorption.[14] This study aims to make and test red ginger nanoparticle extract to reduce blood pressure in hypertensive postpartum women.

METHOD

Study Desain

This is an experimental study with a pre-post control group design.[15]

Setting and Respondent

This research was conducted at Bhakti Wira Tamtama Hospital and Bhayangkara Hospital in Semarang City from March to May 2022. The population in this study were postpartum mothers with hypertension. The number of samples in the study was 40, which were divided into two groups randomly, namely 20 samples from the intervention group and 20 samples from the control group.[15] The criteria inclusion is a postpartum mother with reproductive age 20-35 years, parity ≤4, systolic blood pres-sure 140-159 mmHg or diastolic 90-109 mmHg, full awareness, taking antihypertensive drugs and postpartum mothers who are willing to be research respondents by signing informed consent. The criteria exclusion is postpartum mothers with diabetes mellitus, heart disease, kidney disease, hyperlipidemia, and postpartum mothers who are not willing to be respondents.

Making Red Ginger Nanoparticles

In this study, the process of extracting red ginger powder was carried out by maceration method using 96% ethanol solvent. They mixed 4 grams of chitosan with 25 mL of concentrated acetic acid in 500 mL water by preparing red ginger nanoparticles with ionic gelation. After forming a clear chitosan solution, 250 mL of 96% ethanol and 250 mL of red ginger liquid extract were added. In order to form cross-link bonds, 25 mL of 0.1% Sodium tripolyphosphate was added. Mixing is done using a magnetic stirrer. Crystallization is carried out so that the nanoparticle liquid can become powder by evaporation at the evaporation temperature assisted by flowing air to speed up the process. After the sample thickens, it is transferred to a food dehydrator to make it harder to crush it with a blender. Red ginger that has nanoparticles is then tested for particles and flavonoid content. Red ginger leaf nanoparticles were put into a capsule of 300 mg and then into a closed bottle.[16]

Experimental Procedure

The intervention group was given red ginger nanoparticles at a dose of 300 mg and an antihypertensive drug (Nifedipine) once a day for 14 days, while the control group was only given an antihypertensive drug once a day for 14 days.

Variables, Instruments, and Measurements

The variables measured in this study were systolic and diastolic blood pressure. The mother's blood pressure variable was measured using a digital sphygmomanometer, carried out at the pretest, 7th day, and posttest (14th day).

Data Analysis

The independent t-test and repeated measures ANOVA was used to see the difference in blood pressure between the intervention and control groups.

Ethical Consideration

This research has passed the ethical test conducted by the Semarang Ministry of Health Poltekkes Ethics Commission with number No. 0100/EA/KEPK/2022.

RESULTS

Figure 1 shows red ginger nanoparticles in capsule dosage forms containing 40.5 mg QE/g of flavonoids. Based on table 1 shows that all respondents aged 20-35 years

with parity are mostly multipara; most of the respondents have a history of gestational hypertension and do not have a family history of hypertension.

Based on Figure 2 AB, the results of the repeated measured ANOVA statistical test showed a p<0.05 on the pretest, seventh day, and post-test measurements in both the intervention and control groups. While testing the mean difference between the intervention and control groups using the independent t-test at the post-test obtained p<0.001, there is a difference in systolic and diastolic blood pressure between the intervention group and the control group.

Figure 1. Red Ginger Nanoparticle Capsules

Table 1. Characteristics of Respondents (n=40)

Characteristics	Results
Age, yrs	
Mean±SD	28.72±4.26
Min-Max	20-35
Parity	
Primipara	7 (17.5%)
Multipara	33 (82.5%)
History of Gestational Hypertension	
Yes	37 (92.5%)
No	3 (7.5%)
Family History of Hypertension	
Yes	13 (32.5%)
No	27 (67.5%)

DISCUSSION

The results of this study indicate that red ginger nanoparticle extract can reduce systolic and diastolic blood pressure in postpartum hypertensive women. Blood pressure will be much more elevated postpartum than before birth and during labor. This occurs due to a combination of factors of loss of pregnancy vasodilatation during postpartum, extracellular fluid mobilization during postpartum, and postpartum consuming non-steroidal anti-inflammatory drugs. Oxidative stress also has an essential role in the pathophysiology of hypertension, metabolic syndrome, and atherosclerosis because oxidative stress can induce endothelial dysfunction and hypertension through stimulation of Nitric Oxide Synthase (NOS), one of which is mediated by Radical Oxygen Species (ROS). In this case, antioxidants are needed to inhibit oxidative stress, which consists of compounds that inhibit oxidation. One of the electrolyte content that has high antioxidants is flavonoids.[17]

The decrease in systolic and diastolic blood pressure in postpartum hypertensive women occurred because red ginger nanoparticles given to postpartum hypertensive women at a dose of 300 mg for 14 days contained 40.5 mg QE/g of flavonoids. The flavonoid content in red ginger nanoparticles used in this research inhibits the activity of the angiotensin-converting enzyme (ACE), so the formation of angiotensin II causes the dilation of blood vessels, which has an impact on reducing blood pressure.[7] In addition, saponins play a role in inhibiting the renin-angiotensin-aldosterone system (RAA), thereby reducing the formation of angiotensin II which then decreases blood pressure.[18] Ginger helps reduce high blood pressure through the blockade of voltage-dependent calcium channels. Ginger blocks calcium channels that usually cause contractions of the smooth muscle tissue found in organs and artery walls. Reducing smooth muscle contraction results in more relaxed artery walls allowing blood to flow freely at lower pressures.[19] Red ginger contains some nutrients such as vitamins, minerals, protein, carbohydrates, and fat.[20]

The results of this study support previous research, which showed differences in the average systolic blood pressure and blood pressure before and after being given red ginger extract. Based on data analysis shows that red ginger extract has the potential to reduce blood pressure in women with gestational hypertension.[21] The oleoresin compound in red ginger can help speed up and improve blood vessel circulation and ease the work of the heart by increasing blood circulation.[22] Red ginger oleoresin contains gingerol, shogaol, zingerone, resin, and essential oils.[20] The non-volatile content, namely gingerol, can cause a spicy taste in ginger. 20 Research on ginger extract has also been carried out in previous studies with a dose of 500 mg/kg BW of 70% ethanol extract of red ginger rhizome, bangle, Fingerroot, and *Curcuma zedoaria* in mice induced by adrenaline. The results showed that the most significant systolic decrease occurred in the red ginger rhizomes, with a decrease of 27.35%.[23] Researchers have suggested that consuming ginger can protect against heart disease. Ginger has been found to help with many conditions related to the circulatory system, such as blood pressure, heart attack prevention, stomach ulcer relief, blood clot prevention, and lowering cholesterol levels.[24]

The results of other studies state that red ginger can treat various diseases such as rheumatism, stroke, asthma, toothache, diabetes, muscle pain, cramps, and sore throat, overcome colds, reduce nausea, fever, and -

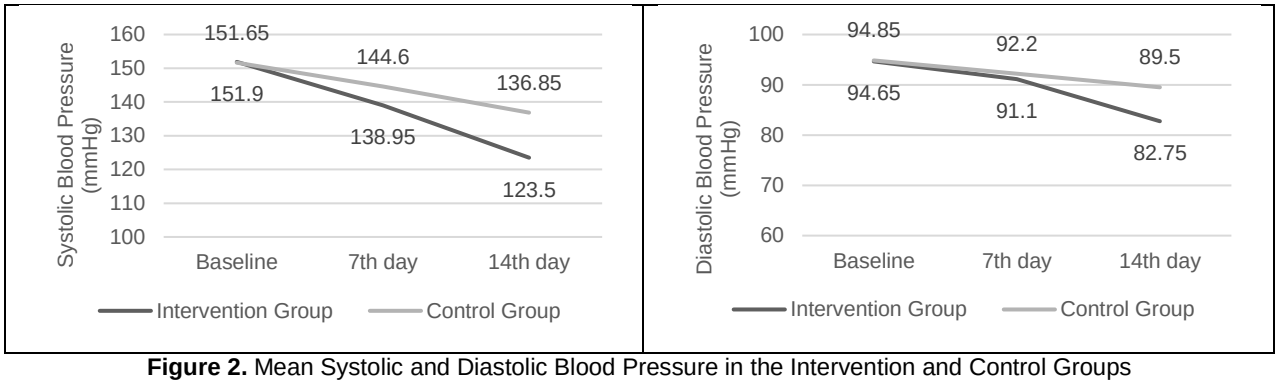

Figure 2. Mean Systolic and Diastolic Blood Pressure in the Intervention and Control Groups

infection, and can reduce high blood pressure.[25] In this study,the mean difference in systolic and diastolic blood pressure in the intervention group showed a more significant decrease than in the control group. It can be concluded that the administration of red ginger nanoparticles and antihypertensive drugs significantly reduced systolic and diastolic blood pressure in postpartum hypertensive mothers compared to pharmacological therapy alone. Therefore, red ginger nanoparticle extract can be used as an innovation to help reduce blood pressure in postpartum hypertensive women.

CONCLUSIONS AND RECOMMENDATION

Giving red ginger nanoparticles and antihypertensive drugs has a higher effect in reducing systolic and diastolic blood pressure in postpartum hypertensive women compared to those who are only given pharmacological therapy. Health workers are expected to conduct outreach to the community, especially mothers with postpartum hypertension, to consume red ginger nanoparticles to accelerate blood pressure reduction.

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