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Seven Days of 100% Watermelon Juice Intake Improves Blood Pressure during Pregnancy: A Quasi-Controlled Intervention

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A B S T R A C T

This study assessed the impact of consuming watermelon juice at a concentration of 100% on blood pressure among pregnant women. For the duration of one week, thirty healthy pregnant women in good health participated in this quasi-experimental study by consuming 700 mL of 100% watermelon juice daily. Before and after each intervention, a blood sample was taken to ensure normal blood glucose. The evaluation of vascular function encompassed two assessments, including systolic and diastolic pressures. The study employed general linear models (GLM) to analyze the effects of the intervention, specifically focusing on intent-to-treat analyses. Although there was a notable treatment effect on the levels of blood pressure parameters ($p < 0.000$). The juice intervention yielded a modest yet statistically significant rise in decreasing blood pressure ($p < 0.001$), while there were no notable changes in other variables. The clinical significance of glucose balance was shown to be negligible. Prior research has provided evidence to substantiate the efficacy of watermelon extracts in enhancing vascular function among individuals. Therefore, we examined the benefit of it among pregnant women to prevent preeclampsia/eclampsia.

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INTRODUCTION

The term "hypertension" originates from the Latin terms "hyper" and "tension." The term "hyper" denotes an excessive amount, whereas "tension" refers to the application of pressure. Hypertension, alternatively referred to as high blood pressure, is a pathological condition distinguished by chronically elevated blood pressure levels; it results in detrimental health consequences and an elevated mortality risk. An individual is considered to be experiencing high blood pressure or hypertension when their systolic blood pressure exceeds 140 mmHg, and their diastolic blood pressure exceeds 90 mmHg.

Hypertensive diseases of pregnancy (HDP), including preeclampsia and eclampsia, are frequently linked to preexisting chronic hypertension. Preeclampsia or eclampsia has a prevalence ranging from 2% to 10% among pregnant women, and it is responsible for significant pregnancy-related difficulties. The previously mentioned condition is responsible for more than 70,000 maternal deaths each year, the vast majority of which took place in low and middle-income nations (LMICs) (Lugobe et al., 2023). HDP contributes to maternal mortality and has the potential to affect the course of the pregnancy; it typically manifests around the 20th week of gestation. A broad spectrum of factors contributes to an estimated 75% of maternal fatalities. These include but are not restricted to, severe hemorrhage, infection, hypertensive disorders (especially pre-eclampsia or eclampsia) during pregnancy, complications during childbirth, unsafe abortion methods, infections, malaria, and long-term medical conditions like heart disease or diabetes (Say et al., 2014).

Prior research has shown evidence to substantiate the efficacy of watermelon extracts in enhancing vascular function among individuals in the middle age bracket (Ellis et al., 2021) and pregnant women (P. C. Tan et al., 2023). For instance, a prior study utilized a randomized placebo-controlled clinical trial approach to examine the beneficial effects of watermelon as its extract intake for six weeks on a subset of postmenopausal women. The findings of this study demonstrated a significant reduction in arterial stiffness as a result of the watermelon extract supplementation. Another study found that in a clinical study including women who were hospitalized for hyperemesis gravidarum (HG), the meal items that received the highest agreeability scores and exhibited the lowest rates of nausea and vomiting were apple and watermelon (G. N. Tan, Tan, Hong, Kartik, & Omar, 2021). Despite watermelon benefits, studies which observed its positive effects on pregnancy-induced hypertension found limited. The provision of dietary advice for pregnant women is a commonly used approach in the field of management. However, it is worth noting that there is a lack of trial evidence upon which to substantiate such advice.

The potential protective benefits of watermelon on vascular function may be attributed to its considerable abundance of arginine and citrulline, two amino acids known to induce the production of nitric oxide, a molecule that dilates blood vessels (Smeets, Mensink, & Joris, 2021). The increased lycopene content of watermelon could potentially provide cardioprotective benefits. Watermelon is widely recognized as a rich dietary source of lycopene, and there

exists empirical support indicating a correlation between elevated lycopene concentrations in the circulation and improved cardiovascular health. (Naz, Butt, Sultan, Qayyum, & Niaz, 2014).

Recent clinical trials and observational studies have begun to dispute the accepted view that individuals with a documented history of vascular disease benefit more from sustaining lower blood pressure levels. For a significant duration, the correlation between hypertension and cardiovascular disease as well as mortality has been widely recognized. When vascular disease is absent, a distinct correlation is observed between blood pressure and both vascular and total mortality in individuals. This correlation endures in the absence of any obvious minimum threshold, encompassing blood pressure readings that are equal to or exceed 115/75 mm Hg. We hypothesize, in light of these findings, that watermelon may improve blood pressure. Therefore, we conducted an inquiry into the viability of utilizing pure watermelon liquid as a viable and prolonged method for providing the vascular benefits linked to watermelon intake.

The argument surrounding the health advantages and risks associated with the consumption of 100% fruit juice has been a topic of discussion in recent years. Certain specialists suggest restricting the intake of juice due to its high sugar content and absence of fiber, which might result in consuming excessive calories without feeling full. Hence, intervention studies must incorporate the potential consequences of juice consumption on glucose homeostasis and body composition. Acknowledging the potential therapeutic advantages of watermelon in preventing the circulatory system and the deficiencies in current research, the primary aim of this investigation was to assess the effects of pure watermelon juice supplementation on the HDP.

THEORETICAL REVIEW

Prior research has shown evidence to substantiate the efficacy of watermelon extracts in enhancing vascular function among individuals in the middle age bracket (Ellis et al., 2021) and pregnant women (P. C. Tan et al., 2023). For instance, a prior study utilized a randomized placebo-controlled clinical trial approach to examine the beneficial effects of watermelon as its extract intake for six weeks on a subset of postmenopausal women. The findings of this study demonstrated a significant reduction in arterial stiffness as a result of the watermelon extract supplementation. Another study found that in a clinical study including women who were hospitalized for hyperemesis gravidarum (HG), the meal items that received the highest agreeability scores and exhibited the lowest rates of nausea and vomiting were apple and watermelon (G. N. Tan, Tan, Hong, Kartik, & Omar, 2021). Despite watermelon benefits, studies which observed its positive effects on pregnancy-induced hypertension found limited. The provision of dietary advice for pregnant women is a commonly used approach in the field of management. However, it is worth noting that there is a lack of trial evidence upon which to substantiate such advice.

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METHODOLOGY

A quasi-experimental design was employed to allocate 30 participants into two distinct groups: a control group and an intervention group. The intervention group participants were provided with a daily supply of 700 mL of fresh watermelon juice in a bottle for one week. Before intervention enrolment, the Health Polytechnic Ethics Committee granted consent for the intervention (approval date: 03/03/2023; reference number 54/III/KE.PE/2023). Written informed assent was obtained from every participant. Recruitment of the initial participant commenced on March 7, 2023.

Participants

Primary Health Care Centres (PHCs) in Muara Teweh, Central Kalimantan, served to recruit participants. They were healthy pregnant women of any gestational age between the ages of 20 and 35 who resided in Muara Teweh and had diastolic blood pressure greater than 90 mmHg and systolic blood pressure greater than 120 mmHg. Individuals with diabetes mellitus who were also users of anti-hypertension medication were ineligible to participate. The gestational age was verified through the self-report of the initial and final menstrual cycle.

To calculate the sample size, we assume a 2 mmHg difference in the change of the blood pressure parameter by the outcome of the intervention, with standard deviations from both groups accounted for at 2.9. With a significance level of 80% and a significance value of 0.01, 15 individuals are needed for each group, for a total of 30. As a result, thirty expectant women were recruited from the PHCs. After approaching eligible women and providing them with an informed consent document, a trained research assistant conducted interviews with them. In this study, randomized allocation to the interventions was not implemented for the participants as the treatments were apparent and easily recognized. Their assignment was determined by the researcher.

To minimize the potential confounding variables arising from the influence of women in the control group's motivation to consume watermelon, we carefully excluded based on criteria throughout the selection process. "The effect of watermelon juice dietary guidance during pregnancy: a prospective intervention" was the title of this study specified in the Participant Information Sheet.

The participants who were assigned to the watermelon and dietary advice leaflet group were provided with 700 mL watermelon juice in a bottle. This watermelon was made freshly from in the morning and was consumed completely in an hour. The watermelons were purchased at an approximate unit cost of $2.6 from a nearby grocery store. The participants were given instructions to consume the entire juice on a daily basis, dividing it into smaller volumes over the course of the morning period. Furthermore, to assure participation, they were accompanied by a research assistant.
Throughout the trial, the participants were directed to adhere to their usual physical exercise schedules. The participants maintained their normal dietary routines, except for avoiding consuming lycopene-rich foods for the duration of the intervention period and the week preceding it. During the screening procedure, a full list of lycopene-containing foods was presented to the participants. Participants were subsequently instructed to limit their daily intake of these foods to a maximum of two servings for the duration of the study. The dietary intake of the participants was meticulously monitored through the daily submission of food frequency reports that were carried out before the intervention. The assessment of complying to the supplement and placebo schedule was performed using diary forms that comprised checkboxes for every dose that was administered.

Systolic/diastolic blood pressure assessment

Applying a calibrated and automated monitor called the OMRON (HEM-7140T), produced by OMRON in Matsusaka, blood pressure readings were taken in the workplace. All measurements were performed in conformance with established standard protocols. After a minimum of five minutes of repose, during which the non-dominant arm was raised to heart level, a minimum of two measurements were acquired, with a minimum one-minute interval between each reading. If there was a discrepancy in the readings over five mmHg, a supplementary measurement was conducted, and the two measurements were afterwards averaged.

Other relevant physical assessments

At each visit, participants' weight was collected using a calibrated scale, whereas their height was measured using a stadiometer. At each visit, the body mass index (BMI) was calculated by dividing the weight in kilograms by the square of the height in meters. Without fasting, blood glucose levels were recorded at each visit, both prior to and after each treatment group.

Statistical analysis

The data was entered into SPSS (SPSS Statistics, Version 26, IBM). Applying the Kolmogorov-Smirnov test, the conformance of continuous data to a normal distribution was evaluated. For categorical variables, the data were presented as percentages; for continuously variable means and non-normal distributions, the median [interquartile range IQR] was utilized; and for ordinal or non-normally distributed continuous variables, the mean ± standard deviation was applied. The paired t-test was utilized to compare means of

variables that adhere to a normal distribution, whereas the Mann-Whitney U test was applied to variables that were ordinal in nature. Instead of employing the chi-square test, nominal data sets were analyzed using the Fisher test. The statistical significance of both hypotheses was established through the presentation of two-sided p-values in the study. It is generally accepted to consider a significance level of $\rho < 0.05$ as indicative of statistical significance. In conducting the multivariate analysis, a linear regression approach was utilized.

RESULTS

A cohort of thirty expectant women was allocated to one of two groups: treatment or control. All thirty participants fulfilled the study with accomplishment (refer to Figure 1). The demographics and baseline characteristics of the participants who completed the intervention successfully are detailed in Table 1. Figure 2 presents the systolic and diastolic measurements obtained after consuming juice and during each intervention. In addition to the recommended beverages, the examination of dietary intake did not identify any significant variations in the consumption of carbohydrate, protein, dairy, and fast food between the two groups under investigation (data not presented). The juice intervention was generally well-tolerated.

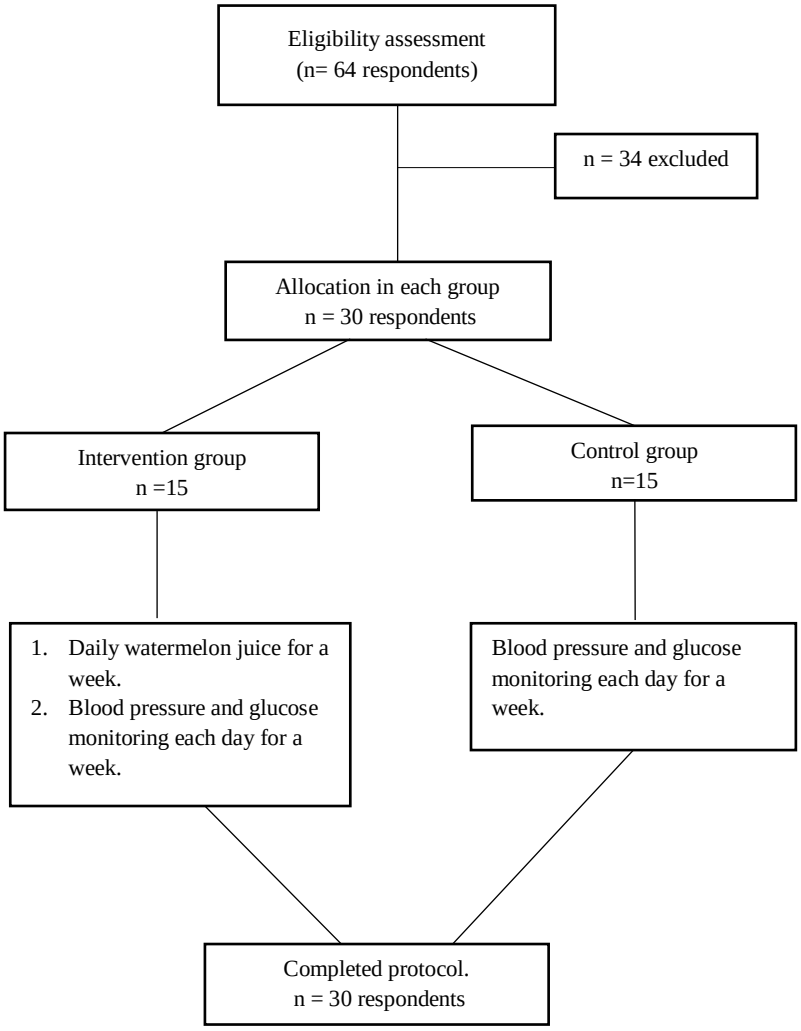

Figure 1. Intervention method flow diagram

Table 1. Baseline characteristics of participants

Variable	Frequency	Percentage (%)
Age		
20-35 years	25	83.3
>35 years	5	16.7
Parity		
Primipara	9	30.0
Multipara	20	66.7
Grande multipara	1	3.3
Sleeping duration		
6-7 h/day	7	23.3
7-8 h/day	23	76.7
Body mass index (BMI) kg/m^2		
Underweight	0	0
Normal	6	20.0
Overweight	17	56.7
Obesity	7	23.3

y = year; h/day = hour per day

Pregnant women who participated in this study comprised of mostly 20-35 y (83.3%) and ever had at least one up to 4 children (66.7%). Nearly 80% of them reported sufficient sleeping duration 7-8 h/day. None of them suffered from underweight during pregnancy. However, overweight and obesity were common (80%).

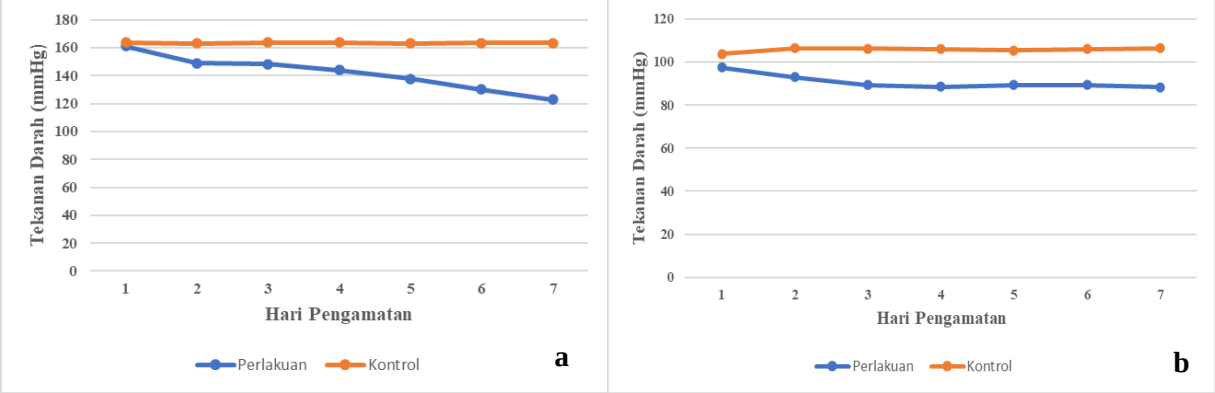

Figure 2. Systolic and diastolic changes each day during a 7-day intervention

Figure 2a depicts systolic blood pressure changes, starting from day 1 to day 7. Figure 2b shows diastolic blood pressure changes during the 7-day intervention. The blue line represents the intervention group while the orange line represents the control group

As seen in Figure 2, a decrease in the blood pressure was observed in the intervention group both in systolic (a) and diastolic (b). The decrease is seen relatively steep in systolic blood pressure which went down gradually from day 1 to day 7, whereas diastolic parameter remains stable except in the second day of the intervention. In the meantime, those who were in control group had constant systolic and diastolic blood pressures.

Participant characteristics in both groups were comparable ($\rho>0.05$) in all observed aspects. These can be seen in Table 2.

Table 2. Participant characteristics in each group (n=30)

Variable	Intervention (n=15)	Control (n=15)	Total	ρ-value
Age				
20-35 y	11 (73.3%)	14 (93.3%)	25 (83.3%)	0.330*
>35 y	4 (26.7%)	1 (6.7%)	5 (16.7%)	
Parity				
Primipara	5 (33.3%)	4 (26.7%)	9 (30%)	1.000*
Multipara	10 (66.7%)	11 (73.3%)	21 (70%)	
Sleeping duration				
6-7 h/day	4 (26.7%)	3 (20%)	7 (23.3%)	1.000*
7-8 h/day	11 (73.3%)	12 (80%)	23 (76.7%)	
BMI kg/m^2				
Normal	4 (26.7%)	2 (13.3%)	6 (20%)	0.651*
Overweight	11 (73.3%)	13 (86.7%)	24 (80%)	

**Insignificant at > 0.05 using the fisher tests; Parity classification was merged into two group in which grande multipara was incorporated with multipara due to lack of participants. Likewise, obesity was merged into overweight group.*

Unadjusted systolic and diastolic blood pressure before and after intervention

As previously reported in a paper (Ellis et al., 2021), the results of this study suggested that supplementation with watermelon juice resulted in a significant reduction in vascular pressure (ρ-value < 0.05) in comparison to the control group (Table 3). Significant changes were observed in the systolic and diastolic pressures, except the diastolic pressure change in the control group (ρ-value=0.378), as indicated in Table 3.

Table 3. Unadjusted blood pressure measures before and after each intervention (n=15)

Intervention						Control				
Blood pressure		Mean	Min	Max	ρ-value	Blood pressure	Mean	Min	Max	ρ-value
Systolic	Before	167.1	155	175	0.000**	Before	163.3	148	176	0.005**
	After	115.7	100	155		After	164.8	148	179	
Diastolic	Before	102.1	100	110	0.000**	Before	104	90	116	0.378
	After	85.0	80	90		After	105.4	100	112	

***Significant at < 0.05 using paired t-test*

Adjusted systolic and diastolic blood pressure after intervention with other confounding variables (n=30)

The findings of the research suggest that the intervention failed to result in statistically significant changes in age, BMI, systolic/diastolic before, sleeping duration, or age, as determined by the linear regression model (ρ>0.05). In contrast, the inclusion of watermelon juice in the experimental group did not result in a statistically significant improvement in systolic and diastolic parameters in comparison to the control group (Beta coefficient = 0.026 and 0.335, p = 0.891 and 0.071, respectively). The statistical significance of the relationship was observed solely in the diastolic change, as presented in Table 4.

Table 4 Adjusted systolic and diastolic blood pressure after intervention with other confounding variables (n=30)

Variable	After			
	Sistolik		Diastolik	
	β	P-Value	β	P-Value
Systolic/diastolic before	-0,315	0,235	-0,324	0,238
Groups	0,026	0,891	0,335	0,071
Age	-0,204	0,487	0,028	0,908
Parity	0,344	0,248	0,569	0,037**
BMI	0,260	0,459	-0,351	0,244
Sleeping duration	-0,235	0,504	0,058	0,842

***Significant at <0.05 using linear regression*

DISCUSSION

HDP is the leading cause of mortality among pregnant women across the globe (Engin-Ustun et al., 2019; Say et al., 2014). The main concern of HDP relates to the potential adverse consequences that may arise from the onset of pre-eclampsia or eclampsia. Despite the implementation of adequate prenatal care, which includes vigilant monitoring for indications of pre-eclampsia and timely delivery to mitigate or prevent negative outcomes, morbidity, and mortality persist. In light of the existing research supporting the positive impact of watermelon extracts on vascular health (Kurauchi et al., 2017; P. C. Tan et al., 2023) and the prevalent use of watermelon juice as a food with nutritional value, we aimed to examine the effects of administering a physiological dosage of pure watermelon juice on vascular function indicators among pregnant women.

The consumption of watermelon juice as a dietary supplement failed to have statistically significant effects on vascular function assessments. The findings that were observed contrary to our initial hypothesis, given that previous randomized controlled trials demonstrated that blood pressure improved with a six-week supplementation of watermelon extract (Massa et al., 2016). Age appeared to be a deteriorating factor in endothelial dysfunction and arterial rigidity. The decline in condition was linked to an elevation in oxidative stress and a reduction in the bioavailability of nitric oxide (Seals, Jablonski Kl Fau-Donato, & Donato). Citrulline, a non-essential amino acid that can be effectively converted to arginine in the renal system, is notably present in watermelon (Hashemi, Arab, Seifi, & Muhammadnejad, 2021). Prior to entering the bloodstream, arginine undergoes substantial hepatic and intestinal processing, whereas citrulline evades initial extraction by the splanchnic system. Consequently, it has been demonstrated that supplementation with citulline reduces blood pressure (D., M., M., D., & D., 2019).

In this current study, although watermelon juice contained a recommended intake of citrulline daily, our intervention did not show decrease blood pressure after adjusted other factors. This result shows the opposite effects of watermelon juice which was similar to a result from a study by Ellis et al. (2021). Ellis reported that serum arginine was not observed after consuming 720 mL/day of 100% watermelon juice in which this resulting in zero alteration of blood pressure.

The aforementioned observation is of significant interest, particularly in light of numerous other investigations that have demonstrated elevated levels of arginine in the bloodstream subsequent to the administration of 100% watermelon juice as a dietary supplement. Inconsistencies in findings could perhaps be attributed to variations in days of trial, as several prior investigations have employed more than a week of watermelon juice intake (Ellis et al., 2021; Figueroa, Wong, Jaime, & Gonzales, 2017; Shanely et al., 2020). Further investigations into the pharmacokinetics of watermelon's bioactive components are warranted to evaluate their bioavailability among persons with varying gestational age and body compositions as well as detection of serum parameters related to watermelon consumption. Through the later, we can enable the visibility of, for instance lycopene serum. The administration of watermelon juice at a 100% concentration for a duration of four weeks resulted in a substantial and statistically significant rise in the levels of fasting serum lycopene. In contrast to arginine and citrulline, lycopene is not capable of being produced internally (Mozos et al., 2018), requires obtaining it through dietary means (Fulgoni & Fulgoni, 2022). Additionally, the application of thermal processing, such as pasteurization, enhances the availability of lycopene by promoting isomerization. Lycopene exhibits robust antioxidant action due to the presence of many conjugated double bonds within its chemical structure (Chen, Huang, & Chen, 2019). Given the premise that endothelial dysfunction is rooted in oxidative stress, it was hypothesized that augmenting levels of the antioxidant lycopene would lead to enhanced vascular function (Mozos et al., 2018). Nevertheless, despite the observed elevation in serum lycopene levels, no significant alterations were detected in any of the vascular parameters examined.

CONCLUSIONS AND RECOMMENDATIONS

This study aimed to examine the impact of a four-week intervention involving the consumption of 100% watermelon juice on the vascular function of pregnant women. The results of the study indicated that supplementation was shown to be efficacious in enhancing the levels of blood pressure in the unadjusted model. However, the observed alterations in vascular measurements did not align with the findings from earlier studies conducted on individuals who had pre-existing risk factors for vascular diseases.

FURTHER STUDY

The observed variations in other vascular parameters among individuals with pre-existing risk factors reported in prior research were not conducted. We

also limited our intervention duration to a week; therefore, any observed changes after 7 days were not recorded.

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