RESEARCH ARTICLE

Protocol for intervention study in reducing elevated blood pressure through intermittent fasting

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Abstract

Objective: To chart out a protocol for conducting an intervention-based study to compare the efficacy of intermittent fasting intervention and usual diet in reducing elevated blood pressure among working adults.

Method: The quasi-experimental study with single-blinded parallel groups will comprise subjects from two civil departments. The intervention group will be required to conduct 2 days of fasting and 5 days of ad libitum diet in a week, while the control group will follow the usual healthy lifestyle. The largest sample size will be taken to achieve a power of 80% and an alpha value of 5%. Based on the 30% attrition rate, the total sample size needed in the study will be 140 participants, with 70 in each of the two arms. This study will use SPSS 24 for statistical analysis.

Discussion: The study describes a unique protocol of intermittent fasting mimicking the Muslim Sunnah of fasting among people with elevated blood pressure. The findings will contribute to decrease blood pressure among those with elevated blood pressure. If proven to be effective, the intermittent fasting method would be useful for developing an effective programme to prevent elevated blood pressure among adults. The protocol will contribute to efforts to find whether or not intermittent fasting can improve elevated blood pressure as well as body weight, body mass index, waist circumference and nutrition status among adults.

Clinical Trial Number: The study was registered with clinicaltrials.gov (NCT04953650).

Keywords: Fasting, Blood pressure, Body mass index, Nutritional status, Indonesia. (JPMA 73: 2171; 2023)

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Introduction

Hypertension leads to early mortality, especially in Asia. The prevalence of hypertension was expected to increase by an estimated 60% from 2000 to 2025, with the Asia region constituting the biggest contributor.[1] According to the World Health Organisation (WHO),[2] death mostly occurred in developing countries between those aged 30-70 years, of which 30 million cases were due to high blood pressure, overweight, obesity and other risk factors. In 2008, approximately 80% of deaths were recorded in Indonesia and India due to non-communicable diseases.[3] In 2018, Indonesia had a significant increase in the prevalence of hypertension, obesity and overweight.[4,5]

The 2017 European Society of Cardiology (ESC) guidelines introduced a new classification of normal blood pressure in three separate groups, namely optimal <120/80mmHg, normal 120-129/80-84 mmHg, and high-normal 130-139/85-89mmHg. The last category indicates early symptoms for elevated blood pressure (EBP). Since EBP is often ignored, it usually progresses to stage 1.[6] Identifying EBP and proper interventions are valuable in stopping people from experiencing hypertension.

Many aspects contribute to high blood pressure, like obesity, sodium intake, alcohol consumption, sedentary lifestyle, non-healthy eating, smoking and others.[7-9] Modifying the amount of energy intake may result in weight loss and further lowering of EBP. Recently, intermittent fasting (IF) is an accepted lifestyle intervention practiced mainly to reduce weight, especially among obese and diabetic patients, mostly comprising a 2:5 method, meaning 2 days of fasting and 5 ad libitum days[10] without any restriction to zero-calorie water. By conducting IF among EBP cases, the participants are expected to reduce energy intake per day when fasting,[9] reduce body weight and further improve blood pressure. Some significant outcomes from IF are weight reduction, control of blood glucose, and blood pressure level.[7,8,10]

In Indonesia, it is assumed that the prevalence of EBP is similar to pre-hypertension due to the similarity in dietary behaviour, including high salt consumption.[11] Although there are various health promotion programmes in Indonesia, the prevalence of EBP is still increasing.[4,5] Several non-pharmacological interventions related to hypertension and EBP have been carried out either in

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hospital or community settings, but these were mostly on salt control, healthy diet and physical activity.[11,12]

Aceh is a province located on the edge of Indonesia with a very high prevalence of hypertension and obesity.[4,5] The majority (98%) of the province comprises Muslims,[13] where the adults commonly observe voluntary fasting, also known as Sunnah fasting, 2 days a week. This fasting begins from dawn to dusk without drinking and eating during the period for about 14 hours. Therefore, it is believed that it is much easier to introduce IF as a lifestyle intervention to control blood pressure. The best population to conduct an IF study on EBP is among the working-age group and at the workplace. This is to ensure time efficiency, keeping the participants motivated and compliant.

The current study was planned to chart out a protocol for conducting an intervention-based study to compare the efficacy of IF intervention and usual diet in reducing EBP among working adults.

Patients and Methods

The quasi-experimental study with single-blinded parallel groups will comprise subjects from two civil departments. In this study, blinding will only be applicable to the assessor who examines the outcome. Allocation concealment is not applicable because there is a need to identify the group assigned to participants, either intervention or control. This study will be carried out to compare IF intervention against a usual healthy lifestyle in Aceh province. One department in a district will serve as the intervention group and the other in a different district will serve as the control group, with a distance of approximately 60km between the districts, with travel time between the two departments being approximately 90 minutes, to avoid contamination.

During the intervention phase, the intervention group will have 2 days of fasting (Monday and Thursday) and the rest of the days within the week will be ad libitum, while the other group will have the usual diet. Both groups will receive health education messages weekly through WhatsApp application to ensure the outcomes will be affected by IF only when both groups have equal exposure to the health education. Hence, in the maintenance phase, both groups will have their own behaviour, but the researcher will encourage the intervention group to follow the same behaviour. This study will follow the guideline of standards protocol items: recommendation for interventional trials (SPIRIT).[14] Data related to enrolment and interventions will be summarised (Table).

The study population will consist of two civil departments in Aceh. The Aceh regional secretariat (Governor Office) will be the intervention group and Aceh Besar regency secretariat office in Aceh Besar will be the control group. These offices have the largest number of employees.[15]

The inclusion criteria will entail adults aged 18-60 years with EBP of 130-139/85-89mmHg, overweight and obese with body mass index (BMI) ≥25kg/m^2, without any gastric diseases or problems with fasting, ability to read and write, and willing to sign the informed consent. The exclusion criteria will entail disabled people on medication for either hypertension or other diseases, pregnant women, employees who will retire in the intervention duration, and employees who will undertake the Hajj pilgrimage.

In estimating the sample size, the changing outcome parameters will be used as an effect size consideration based on previous studies in estimating the sample size and period of intervention.[7-9,16] The outcome parameter of systolic blood pressure (SBP) and diastolic blood pressure (DBP) are 10mmHg and 5mmHg, respectively.[8,16] The body

Table: Summary of enrolment, intervention and assessment procedures based on the SPIRIT guideline.

	Study Period							
	Enrolment (July-September 2021)	Intervention Period (September-December 2021)			Maintenance Period (December 2021-March 2022)			Trial End
Time point	**T0**	**T1**	**T2**	**T3**	**T4**	**T5**	**T6**	**T7**
Enrolment								
Eligibility screen	X							
Informed consent	X							
Intervention								
Assessment								
SBP	X	X	X	X	X	X	X	
DBP	X	X	X	X	X	X	X	
BW	X	X	X	X	X	X	X	
Height	X							
WC	X	X	X	X	X	X	X	
Dietary assessment	X	X	X	X	X	X	X	
Socio assessment	X							
Demographic assessment	X							
Smoking behaviour	X							
Alcohol consumption	X							
Physical activity	X							
Maintenance								
Evaluation								X

SPIRIT: Standards protocol items: recommendation for interventional trials, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, BW: Bodyweight, WC: Waist circumference.

weight parameter is 1.5kg and 0.5kg/m^2 of BMI.[7] The waist circumference (WC) outcome parameter is 1cm based on the same study.[7] The last parameter will be the reduction of 500kcal of energy intake.[9] The calculation will be conducted by comparing different effect sizes for all specific objectives. Subsequently, the outcomes with the largest sample size will be chosen. Assuming the attrition rate to be 30%, the minimum sample size is likely to be 140 participants, consisting of 70 in each arm, to preserve 80% power and α=0.05. The estimation will be carried out using STATA 14.2.

Prior to intervention, firstly, permission from the head of both departments will be obtained, and all employees will be informed about the screening and the aim of the study through WhatsApp application. Furthermore, 4 enumerators for each department will assess the health condition of the individuals. After receiving the result of the health assessments, all the employees who meet the criteria will be invited to join the health education session. Hence, those willing to join the study will receive the intervention information by explaining the study's procedure.

About 3-4 employees will join the health education session to avoid the crowd and prevent any viral infection. During the education session, all participants will be informed regarding the low risk in the intervention. The actual equal studies that have been conducted globally will also be presented to convince them about no chance of adverse effects. After the session, they will receive written information about the study and will sign the informed consent form. They further will be interviewed based on sociodemographic data, such as age, marital status, health insurance, etc., using the WHO's STEP wise approach to surveillance (STEPS) questionnaire adapted by the Indonesian Ministry of Health (MoH), namely the 2016 Non-Communicable Research Questionnaire, released by the National Institute of Health Research and Development, Indonesia.[17,18] Furthermore, the physical activity will be assessed using the validated Indonesia global physical activity questionnaire (GPAQ).[19]

After completing the questions, the participants will receive the 3-day food record form to be filled in (2 working days and over the weekends), and an additional fasting logbook for the intervention group. The food record form will be used to evaluate the average dietary intake and to calculate any reduction of energy, which was made between 3 and 7 days to mimic the regular intake.[20] Meanwhile, this study will adopt the 3-day validated diet history from other literature to estimate the energy reduction of respondents. In counting the food intake, the assessors will use the household standard released by the MoH[21] and adapt to the relevant food record dietary instructions.[20]

They will also receive health brochures, including "Isi Piringku" which is recommended by the MoH as a guideline for daily meal composition.[22] A picture will also accompany each food type for a daily meal to ensure that the participants follow the principle of a balanced diet. The main meal for the diet will comprise rice, lean meat, poultry, fish, 2 cups of salad/vegetables, and 10g of oil, providing a total of 700 calories for one intake. During the health information session, each participant will receive the poster and other 5 flyers on blood pressure and nutrition; 10 guidelines of a balanced diet, recognising non-communicable diseases, preventing hypertension or EBP through a particular diet, healthy lifestyle through health education, and healthy family indicators, which the MoH has also issued.[21] Moreover, they will be informed of the actual date to start the intervention after the overall screening is conducted. The recruitment procedure and the logic model conclusion (Figures 1-2) will be noted.

The intervention is developed based on data from literature reviews[7,8,16] and the results have shown that the IF intervention is beneficial in decreasing blood pressure. Several studies on IF showed improvements in blood pressure among different health conditions and duration variability. The justification in deciding the duration of the intervention is based on a period of 5-16 weeks. It is assumed that a 24-week period would be appropriate

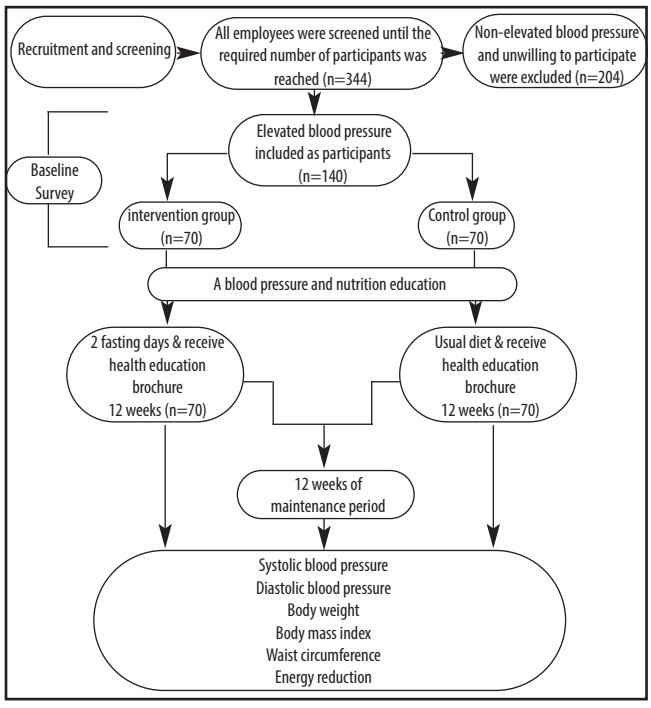

Figure-1: Intervention framework.

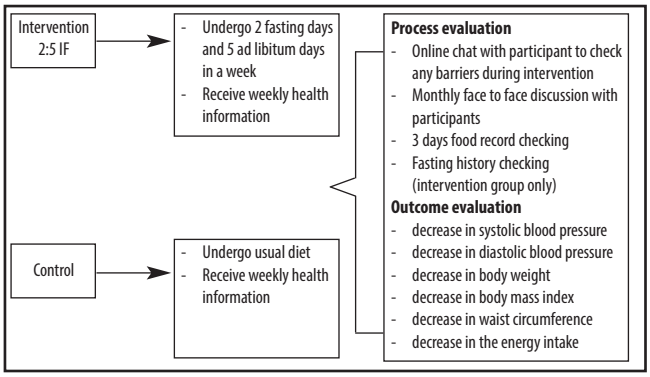

Figure-2: Logic model of the intervention.

among EBP participants. Since Muslims form the majority in Aceh, the study proposes a 2:5 type of IF, which mimics the Sunnah Muslim fasting. This indicates that the intervention group will have fasting on Mondays and Thursdays as the usual IF for 14 hours.

During fasting, the participants will be allowed to consume food and calorie water without restrictions between dusk and dawn. However, they will be allowed to have zero-calorie water during fasting period. The participants will be permitted to change the fasting day when required, but it needs to be observed in the same week except for weekends with a fix duration of 14 hours. Each participant will be required to fill out the fasting logbook form when they stop and start eating. In the 5 days with ad libitum diet, they will be allowed to have a variety of foods and drinks. Moreover, the non-consecutive and ad libitum diet days will be conducted alternately to avoid starving. The control group will consume usual daily food and will be given balanced healthy food guidelines. Since there will be no intervention applied to this group, it will be considered the control group.

The data will be collected at baseline and every month during the 12 weeks of intervention and 12 weeks of maintenance. All the employees will be screened in both offices for SBP, DBP, body weight, BMI, WC and energy intake.

The blood pressure measurement will be taken in the office centre using a sphygmomanometer (Omron HEM 7130 LP, Kyoto, Japan). The WC will be measured from navel to navel using a measuring tape. A weighing scale (Family Dr. Oserio FEP-103, Taichung, Taiwan) will be used to measure body weight in line with height measurement using Stadiometer (AU-AL 01 SAGA, Indonesia) to measure BMI. All tools will be checked and calibrated. The Nutri survey diet analysis will be used to analyse the diet intake based on the food record. This software is commonly used to calculate the dietary intake for an individual.[23,24] In this study, the energy consumed will be analysed for macronutrients and micronutrients.

The assessors will be blinded during the assessment of the outcome, including baseline evaluation, after the intervention, and at the end of the maintenance phase, and they will be unaware of the group allocation. This is assumed to reduce the likelihood of influencing the enumerators' knowledge. Before the intervention, 2 postgraduate and 4 undergraduate students with minimum grade point average (GPA) 3.5 with working experience in the clinic or health centre from public health faculty, University Muhammadiyah, Aceh, will be chosen. They will have 2-day training on the questionnaire and the operational definitions, food record form, and Nutri survey application by the researchers. They will be also briefed on the instructions for tool calibration and measurements. During the training, in order to ensure the uniformity of outcome measurements, the assessors will need to demonstrate how to measure the blood pressure, body weight, BMI, and WC.

In this study, health message broadcasting will be carried out through WhatsApp application and personal phone calls to brief some medical problem-related interventions. At every 4 weeks, the participants in the intervention group will have face-to-face counselling, if required. To avoid any adverse event during the study, the research team will collaborate with the health department officer of Aceh Besar and Banda Aceh to monitor the study. The researchers will inform the officers if there are any respondents who feel unhealthy during the study and will transfer the worker to the health centre based on their recommendation.

The primary endpoint of this study is the reduction of blood pressure among EBP participants in the intervention group. While the secondary endpoints are the reduction of body weight, BMI, WC and energy intake among EBP participants in the intervention group. The researchers will also determine the participatory and engagement behaviour in the IF group during the maintenance phase.

The data of the participants will be kept in a locked cupboard by the principal investigator who will have access to the data, such as signed informed consent. The research team will be trained on data confidentiality before the intervention; therefore, they will need to code the data on enrolment after screening.

According to the Transparent Reporting of Evaluations with Nonrandomised Design (TREND) statement,[25] the characteristics of the respondents will include gender, age, marital status, education, health insurance, smoking behaviour, alcohol consumption and physical activity. The

outliers, double entries and missing values will be checked. The trial will present the mean, standard deviation, and *p*-value to evaluate the relationship between the groups. Subsequently, crude comparisons between the groups will be conducted using an independent t-test when the data is normally distributed or the Mann-Whitney test when it is not normally distributed at the baseline. The intervention effects will be measured using a generalised estimating equation (GEE) to control any potential confounding factors. Data will be analysed using SPSS 24. The research work is anticipated to be published within six months post-analysis.

Discussion

The text described a unique protocol of IF which is mimicking Muslim Sunnah fasting among people with EBP. The findings will contribute to reducing EBP. If proven to be effective, the IF method would be useful for developing an effective programme to prevent EBP among adults. Furthermore, this study also will provide evidence on whether and how comprehensive changes to the diet fasting at least in the intervention group can improve body weight, BMI, WC and energy intake. Successful interventions will be developed in future projects. The research findings will be disseminated to a wide audience, including the scientific community, through publications, discussion panels, and presentations at conferences. This study will also be highlighted to potentially be a reference for the development of a policy brief on blood pressure management in Indonesia.

This study obtained ethical approval from the University of Syiah Kuala Banda Aceh, Aceh, Indonesia. The protocol has been registered with clinicaltrials.gov, US National Library of Medicine (NCT04953650). The starting date at baseline was July 1 to September 16, 2021, with a total of 344 screened workers. The first day of intervention was September 27, 2021, and continued until March 13, 2022.

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Disclaimer: The text is based on a Ph.D. thesis.

Conflict of Interest: None.

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