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Pengaruh Infused Water Kombinasi Buah (Apel, Nanas, Strawberry, Mentimun) terhadap Tekanan Darah dan Kadar Gula Darah Puasa Pasien Sindroma Metabolik

The Effects of Combined Fruit-Infused Water (Apple, Pineapple, Strawberry, Cucumber) on Blood Pressure and Fasting Blood Glucose in Patients with Metabolic Syndrome

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ABSTRAK

Latar Belakang: *Infused water buah (IWB) mengandung antioksidan dan kalium yang dapat menghambat atau memecah rantai reaksi radikal, bersifat antihiperglikemia dan antihipertensi, namun belum terbukti secara ilmiah pada pasien sindroma metabolik (SM).*
Tujuan: *Menganalisis pengaruh IWB terhadap tekanan darah dan kadar GDP pasien SM.*
Metode: *Rancangan berupa Randomized-Control Trial dengan pre-posttest kontrol-grup. Responden sebanyak 24 orang dari Puskesmas Cakranegara diambil secara consecutive sampling dan secara acak dibagi menjadi 2 kelompok yaitu kelompok kontrol (diberikan konseling gizi) dan perlakuan (diberikan konseling gizi + IWB terdiri dari apel, mentimun, nanas dan strawberry dalam 250 ml air selama 14 hari). Pengukuran tekanan darah dan kadar GDP responden dilakukan sebelum dan setelah perlakuan. Analisa deskriptif menggunakan Chi Square, sedangkan uji beda menggunakan uji t-test, Mann-Whitney dan Wilcoxon.*
Hasil: *Responden akhir yang terlibat sebanyak 22 orang. Pada kelompok perlakuan (n=11), rerata tekanan darah sistolik menurun 5,4 mmHg (p=0,140), tekanan darah diastolik menurun 0,9 mmHg (p=0,792), dan GDP meningkat 9,2 mg/dL (p=0.929). Tidak ada perbedaan bermakna pada variabel tekanan darah sistolik (p=0,448), diastolik (p=0,835), dan GDP (p=0,599) antara kedua kelompok setelah intervensi.*
Kesimpulan: *Konsumsi IWB tidak berpengaruh signifikan pada perubahan tekanan darah sistolik, diastolik dan GDP pasien sindroma metabolik.*

Kata Kunci: *Infused Water Buah, Tekanan Darah, Kadar Gula Darah Puasa, Sindroma Metabolic*

ABSTRACT

Background: Fruit-infused water (FIW) contains antioxidants and potassium as a antihyperglycemic and antihypertension via inhibition or break the chain of radical reaction but has not been proven in patients with MS.
Purpose: To evaluate the effects of FIW on blood pressure and fasting blood glucose (FBG) in patients with MS.
Methods: This was a Randomized-Control Trial (RCT) with pre-posttest control group design. 24 patients of Cakranegara Health Center who fulfilled the criteria were randomly divided into control (given counseling only) and treatment (counseling + FIW consists of apple, cucumber, pineapple and strawberry in 250 ml water for 14 days) groups. Blood pressure and FBG were measured before and after intervention. Chi Square was used for descriptive analyze, whereas T-test, Mann Whitney and Wilcoxon was used for differences in means.
Results: In the treatment group (n=11), systolic and diastolic mean levels were decreased by 5.4 mmHg (p=0.140) and 0.9 mmHg (p=0.792) respectively. However, FBG levels were increased by 9.2 mg/dL (p=0.929). There were no differences on systolic (p=0.448), diastolic (p=0.835) and FBG (p=0.599) between two groups.
Conclusion: FIW consumption are unable to improve blood pressure and FBG levels on metabolic syndrome.

Keywords: Fruit-Infused Water, Blood Pressure, Fasting Blood Sugar Level, Metabolic Syndrome

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INTRODUCTION

The global prevalence of metabolic syndrome is estimated to be around a quarter of the world's population (more than 1 billion) and the prevalence in Indonesia is 21.66%.[1,2]. About 20-25% of the world's adult population suffers from metabolic syndrome, and tends to increase the risk of heart disease by 3 times[3]. Data from the World Heart Organization (WHO) in 2016 showed that 54% of the highest causes of death in the world were due to non-communicable diseases, of which 49.5% (15.2 million of 30.7 million deaths) were due to ischemic heart disease and stroke, which are increasing in Indonesia. Indonesia[4,5].

Metabolic syndrome is a metabolic disorder that includes central obesity, hyperglycemia, hypertriglyceridemia, hypertension and low HDL cholesterol levels and the diagnosis is made if you experience at least 3 of these symptoms[6]. Obesity is associated with an increase in free fatty acids that induce oxidative stress resulting in an increase in ROS and is a major cause of insulin resistance and the development of diabetes mellitus[7]. The increase in intra-abdominal fat accumulation in obesity may impair the secretion of various adipositokines including leptin, adiponectin, resistin, tumor necrosis factor (TNF-a) and interleukins (IL-1 and IL-6) which are important factors in energy regulation, thereby triggering the development of metabolic syndrome[8]. Hyperglycemia accompanied by hypertension is associated with an increased risk of cardiovascular disease through molecular mechanisms, namely increased formation of Advanced Glycation End Products (AGEs), oxidative stress, and inflammation[9].

Antioxidants can work by 2 mechanisms, namely inhibiting / preventing ROS and as chain breakers of radical reactions[10]. Apart from natural sources, antioxidants can also come from chemical synthetics, which can cause side effects in the form of inflammation to liver damage if used long term, and are carcinogenic in experimental animals[11]. Therefore, people tend to choose the consumption of food and drinks from natural ingredients. Infused water is a method of soaking ingredients (fruit, vegetables, and spices) for a certain period of time to remove their phytochemical compounds[12]. The benefits that can be obtained from plant extraction through infused water are mainly related to the presence of several phenolic components (flavones, flavanones, anthocyanins, isoflavones and catechins) and antioxidants such as carotenoids (provitamin A), tocotrienols and vitamin E (tocopherol) and vitamin C (ascorbic acid)[13].

In vivo studies have shown that the phloretin content in apples inhibits the formation of carboxymethyl-lysin (CML) and suppresses the expression of AGEs receptors (RAGE), which mediate inflammation and insulin resistance[14]. Strawberries contain ellagic acid which is known to inhibit the conversion of α-amylase, αglucosidase, and angiotensin I enzymes so that it can control hyperglycemia and hypertension[15]. In addition to being a source of vitamin C and flavonoids, bromelain in pineapple has been shown to interfere with neutrophil binding sites for Pselectin (an endogenous lectin) so that it can reduce cell glycation and inflammation in diabetes and other inflammatory conditions[16,17]. Saponins in cucumber have an antihyperglycemic mechanism by preventing glucose absorption in the brush border membrane of the small intestine[18].

In a previous study, giving cucumber infused water to hypertensive elderly was proven to lower blood pressure in 14 days[19]. In addition, a significant decrease in adult male blood pressure occurred when given infused water with a combination of kiwi, watermelon and red wine[20]. A case study reported that postprandial blood sugar levels of T2DM patients decreased significantly after giving fruit infused water for 10 days[21]. The fruit infused water method has been widely practiced and developed in the community, but its benefits have not been studied, especially for improving blood pressure and fasting blood sugar parameters in patients with metabolic syndrome.

METHODS

Research Subject

The research method was a Randomized Control Trial (RCT) with a pre-posttest control-group design. The study was carried out for 14 days of treatment on 5-19 February 2020. The research respondents were outpatients at Cakranegara Health Center, Mataram City, NTB who met the criteria for metabolic syndrome based on the patient's medical records in the last 1 year, aged 18-60 years, and able to carry out activities. normal. Metabolic syndrome patients with acute infection, taking antioxidant supplements, pregnant or lactating, taking insulin injections, smoking and drinking alcohol were not included in this study. The number of respondents needed was calculated using the Lemeshow formula. The minimum number of respondents were 11 people per group with a loss to follow-up calculation of 10%, so the number of respondents were 12 people per group. Respondents were randomly divided into two groups, namely the treatment group (n=12) who received nutrition counseling and 250 ml of fruit infused water once a day; and the control group (n=12) only received nutrition counseling. Food intake and physical activity of respondents became confounding variables controlled by monitoring food intake through recording food intake (food record) and measuring physical activity using the short-form International Physical Activity Questionnaire (IPAQ).

All respondents were given nutritional counseling according to individual needs with the help of leaflets containing information related to diet for metabolic syndrome and the distribution of daily meals as well as sample menus. Respondents were given a daily food intake log book to be filled out at every meal/drink, accompanied by an explanation of how to fill it out. Research officers conducted daily monitoring and cross checks on the notebook, and analyze food intake using Nutrisurvey software. The respondent's daily food intake

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was then calculated on average with the exception of holidays, banquets and fasting.

Physical activity assessment questionnaire using short-form IPAQ which has been tested for reliability and validity in 12 countries as an instrument for measuring physical activity for ages 15-69 years[22]. IPAQ measured physical activity during leisure time, gardening and domestic activities, physical activity at work and transportation[23].

The diagnosis of metabolic syndrome followed the International Diabetes Federation (IDF) criteria, which is having a waist circumference (LP) 90 cm (men) or 80 cm (women) and is accompanied by two other criteria, namely: GDP 100 mg/dl, blood pressure 130/85 mmHg, triglycerides 150 mmHg or have a history of treatment for hypertension, HDL cholesterol 40 mg/dl (men) and 50 mg/dl (women) or have a history of treatment for dyslipidemia[24]. Determination of the diagnosis was carried out by the researcher according to the doctor's direction based on the recorded patient's medical record data, so that a diagnosis of hyperglycemia, hypertension and/or dyslipidemia was obtained. Based on the secondary data, the researcher made a visit to the respondent's house to measure the waist circumference. Respondents with a waist circumference of 90 cm (for men) or 80 cm (for women) will continue to provide informed consent and ask for their consent to become respondents. The consent form and research protocol have been approved by the Ethics Committee of RSUD dr. Moewardi Surakarta, Central Java with letter number 089/I/HREC/2020.

Dietary Intervention

The fruits used in this study were 50 g apples, 20 g strawberries, 30 g pineapples, and 50 g cucumbers, which were obtained from the Bertais main market, Mataram City with the following specifications: Manalagi apple type, fresh, clean and without defects, bright light green colo., weight ±100 g/piece; fresh strawberries, ripe, red, shiny skin appearance; fresh local pineapple, ripe yellow skin; and fresh cucumber, clean green skin. Pineapple fruit is washed, then peeled, then rinsed with other fruits with mineral water. All fruits were sliced thinly using a multifunction slicer and then soaked in 250 ml of mineral water. Storage is carried out in a refrigerator at a temperature of ± 100C for 9 hours. The fruit infused water drink is filtered and poured into tightly closed bottles to be distributed to respondents in the morning. Respondents were asked to immediately spend the given infused water.

Oxidative stress is one of the factors causing insulin resistance and the development of metabolic syndrome which can be controlled by the intake of antioxidants and potassium in the diet[25,26,27] . The fruit combination infused water sample test was carried out as a preliminary test to determine the antioxidant activity and potassium levels of the drink which were then analyzed for their effect on the respondents' blood pressure and fasting blood sugar levels. Antioxidant activity was analyzed using quantitative DPPH (2,2-diphenyl-1picrylhydrazyl) method, the principle of which is to measure DPPH radical scavenging by antioxidants from a compound using UV-Vis spectrophotometry and expressed by IC_{50} (Inhibitory Concentration). IC_{50} values are categorized as very strong if less than 50 ppm, strong if 50-100 ppm, moderate 100-150 ppm and weak 151-200 ppm, very weak if > 200 ppm[28]. Potassium analysis was carried out quantitatively using atomic absorption spectrophotometry with a wavelength of 766.5 nm. The test results were carried out with 2 repetitions (duplo). Testing of antioxidant activity and potassium levels of fruit infused water samples was carried out at the Pratama Chem-Mix Laboratory, Jogjakarta, Central Java.

Outcome

The variables measured in this study were fasting blood sugar and blood pressure before and after the intervention. Patients were asked to fast for at least 8 hours for blood sampling the following morning for examination of GDP and blood pressure. Blood pressure checks were carried out at the Cakranegara Health Center by trained nurses with 2 repetitions for each respondent by giving 5-minute break after the respondent arrived. The tools used are aneroid sphygmomanometer GEA brand and stethoscope. The patient is asked to sit in the chair provided with the back upright and the legs not crossed. The location for checking blood pressure is in the antebrachial region with the stethoscope placed in the cubital fossa above the brachial artery of the left arm.

Examination of fasting blood sugar levels is carried out by nurse officers and laboratory assistants at the Health Testing and Calibration Laboratory of the NTB Provincial Government. The respondent's venous blood sample was taken as much as 2 ml and analyzed using the Enzymatic Colorimetric (GOD-PAP) method.

Statistic Analysis

Univariate analysis to determine the descriptive description of variable characteristics includes non-parametric data expressed by frequency and percentage (%), while parametric data is expressed by mean ± standard deviation. Bivariate analysis used independent t-test to determine differences between groups in the systolic blood pressure variable, while the Mann-Whitney test was used on diastolic blood pressure and GDP. Paired t-test was used to analyze the difference in mean before and after the intervention of systolic blood pressure variables, while the Wilcoxon test was used to analyze diastolic blood pressure and GDP. Significant value was stated with $p<0.05$. Normality of the data using the Saphiro Wilk test and declared normally distributed if $p> 0.05$.

RESULTS AND DISCUSSION

General Characteristics of Respondents

A total of 24 respondents participated in this study but 2 people dropped out at the end of the study due to an accident (1 person) and went out of town (1 person) so that the total respondents were 22 people, namely 11 people in the treatment group and 11 people in the control group. The treatment group had almost the same general characteristics as the control group (Table 1). Almost all respondents were women except 2 (18.2%) men who were randomly assigned to the treatment

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group. The treatment group had a lower mean BMI and waist circumference than the control group although they were not significantly different (p>0.05). Moderate physical activity was found in 54.5% of respondents in the treatment group and 72.7% of respondents in the control group. In general, the respondents' physical activity did not differ in the two groups (p=0.490).

IC_{50} Antioxidant Activity and Potassium Levels in Infused Water Fruit

Antioxidant activity in laboratory test studies using the DPPH IC_{50} method, namely the ability of the sample compound to reduce 50% of free radicals. The smaller the IC_{50} value, the stronger the antioxidant activity of the sample. The results of the IC_{50} antioxidant activity test and the quantitative test for potassium levels are presented in Table 2.

Infused Water Combination of Fruits Has No Effect on Blood Pressure and GDP

Before the intervention, the mean blood pressure and GDP of the respondents in the treatment group and the control group were not statistically different (p>0.05). Specifically, for GDP, the treatment group had a mean of about 40 mg/dl lower than the mean of the control group. After drinking the combination fruit infused water for 14 days, blood pressure decreased but GDP increased (Table 3). The mean systolic blood pressure in the treatment group was not significantly different from the control group (p=0.448). There was no significant difference in the mean diastolic blood pressure (p=0.835) and GDP (p=0.599) in the treatment group compared to the control group.

Research on the benefits of fruit infused water combined with apple, pineapple, strawberry, and cucumber in patients with metabolic syndrome has never been done before. Food testing was carried out to determine the antioxidant activity and potassium levels contained in the infused water using the composition of the fruit. The total weight of the fresh fruit combination is 150gram with the results of the nutritional value analysis using nutrisurvey are 57.1 kcal energy, 0.7 g protein, 0.5 g fat, 13.9 g carbohydrate, 2.5 g fiber and 192.4 mg potassium. The weight of the fruit used is equivalent to the recommended diet for fruit consumption for patients with diabetes mellitus in one unit of food exchange. The selection of the type of fruit used in this study was based on consideration of availability throughout the season, easy to obtain and contains phytochemicals that act as antihyperglycemia, antihypertensive and dyslipidemia improvement in previous studies[19,29,30,31]. The composition of the combination fruit is expected to further increase its antioxidant content compared to only 1 type[12]. The test results showed that the antioxidant content of fruit infused water was included in the very low category with an IC_{50} value of 11,341.25 ppm (> 200 ppm). When compared with several previous studies, the antioxidant activity value of infused water is stronger than Rome Beauty apples (IC_{50}: 49.870.8 ppm), manalagi apples (IC_{50}: 36,848.9 ppm), kiwifruit juice (IC50: 37.400.66 ppm), and apple cider (IC_{50}: 51,797.75 ppm), but lower than pineapple juice (IC_{50}: 126.70 ppm), strawberry juice (IC_{50}: 31.45 ppm) and cucumber extract (IC_{50}: 189.26 ppm)[28,32,33,34–36]. Soaking in water can dissolve antioxidants contained in fruit such as ascorbic acid (vitamin C) and flavonoids[37]. The level of dissolved potassium in 250 ml of infused water based on laboratory tests is only 71.8 mg (37.3% of the fresh fruit content), while the daily requirement of potassium for adults is 4700 mg/day.

The fruit water infused intervention for 14 days reduced systolic blood pressure by 5.4 mmHg and diastolic by 0.9 mmHg but not statistically significant and not different from the control group (p>0.05). This is not in line with several previous studies, namely through giving cucumber infused water to the elderly with hypertension significantly lowering blood pressure[38]. Another study by Putranto by giving infused water a combination of red wine, watermelon and kiwi in healthy adult male respondents can reduce systolic blood pressure by 13.72 mmHg and diastolic by 11.57 mmHg significantly[20]. Administration of high polyphenol fruit juice as much as 500 ml/day in healthy adult subjects showed a decrease in blood pressure after 6 weeks of intervention[39]. Meanwhile, giving pomegranate juice to hypertensive subjects for 2 weeks was shown to reduce systolic and diastolic blood pressure[40]. Another study showed different results, namely the administration of orange juice in hypertriglyceride and hypercholesterolemic subjects and apple cider in healthy adult subjects did not show a significant decrease in blood pressure[41,42]. In this study, a non-significant decrease in blood pressure could be due to the condition of the subject being different from the previous study. The antihypertensive effect of some fruit juices is related to their bioactive components such as polyphenols, vitamins, minerals and nitrates[43]. Insulin resistance is associated with increased expression of vascular adhesion molecules, oxidative stress, inflammation, and decreased vascular nitric oxide levels, which can increase vascular stiffness leading to persistent hypertension[44]. The content of active compounds that are antioxidants and potassium levels in fruit infused water are not strong enough to control hypertension in metabolic syndrome. In one study, consumption of food sources of potential antioxidants by 1 mmol/day reduced the risk of hypertension by 1.3% (in men) and 1.8% (in women)[45]. In addition, several studies have shown that increasing potassium intake to as needed in the 75-125 mmol (2900-4700 mg/day) range can effectively lower blood pressure[27]. The application of the DASH (Dietary Approached to Stop Hypertension) diet which contains potassium up to 4.7g/day for 2 weeks has been shown to significantly reduce blood pressure in hypertensive patients[46]. Potassium can help lower blood pressure through several mechanisms, namely increasing natriuresis, releasing Nitric Oxide (NO), endothelium vasodilation through the sodium sodium pump pathway in the plasma membrane, to muscle relaxation through inhibition of the sympathetic nervous system[43].

GDP levels after administration of infused water for 14 days did not differ between groups (p=0.599). Antioxidants in fruit can come from water-soluble

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vitamins (vitamin C) and several active compounds and flavonoids in fruit, namely phloretin (apple), ellagic acid (strawberry), bromelain (pineapple) and saponins (cucumber). Research shows that giving 200 grams of apple juice/day for 7 days reduces postprandial blood sugar levels in T2DM patients but not significantly[47]. Meanwhile, in experimental animal studies, rats that received a high-fat diet for 17 weeks showed significantly more than doubled blood glucose levels, but the administration of 75 mg/kg phloretin showed lower fasting blood glucose levels[14]. In chronic hyperglycemia, there is excessive formation of reactive oxygen species (ROS) and reactive carbonyl species (RCS), and/or defective antioxidant defense mechanisms, as well as glucose auto-oxidation resulting in the formation of free radicals. In this study, the respondent's food intake was controlled by nutritional counseling, while the respondent's physical activity was not changed (activity as usual). The respondent's carbohydrate intake can affect blood sugar levels related to the nature of the food and the process of digestion and absorption in the small intestine, namely viscosity, form of food, cooking and processing methods, type of starch (amylose or amylopectin), presence of anti-nutritional substances and fiber, fat and protein. protein[48]. The average carbohydrate intake of respondents did not differ between groups and was in the less category (<80% requirement) with fiber intake of 7.6 grams/day or about 1/3 of the requirement. Research shows that a high-fiber diet reduces insulinemia by 10% and insulin resistance by 13%[49]. The fiber content in fruit infused water cannot help meet individual fiber needs, because what is consumed is only fruit juice-soaked water. Fiber can improve insulin resistance by increasing individual glucose homeostasis, regulating hormonal responses, modulating inflammatory cytokines, increasing the glycemic index of foods, reducing the risk of obesity and changing the gut microbiota[50]. Consumption of fruits and vegetables has been shown to reduce the risk and incidence of metabolic syndrome, especially because of the presence of vitamin C and fiber in it[51]. In addition, fiber in fresh fruit can produce gut microbiota that can lower blood pressure through regulation of SCFA receptors, namely GPR41 and Olfr78[52]. This shows that the consumption of fresh fruit is more recommended than replacing it with infused water.

This study can be empirical evidence showing that in cases of hyperglycemia and hypertension accompanied by central obesity, consumption of fruit infused water does not provide a significant improvement effect, especially in reducing blood pressure and GDP. Some of the limitations of this study were that it did not examine the stress/psychological conditions, as well as exposure to free radicals of the respondents and did not test the energy content, macronutrients, glycemic index values and soluble fiber in fruit infused water. Further research can be done by increasing the portion of fruit infused water consumption and extending the intervention time by controlling the respondent's fiber intake so as to allow an improvement in blood pressure and GDP in metabolic syndrome.

CONCLUSION

Consumption of 250 ml of fruit infused water (apple 50 g, pineapple 30 g, strawberry 20 g, and cucumber 50 g) with a potassium content of 71.8 mg and antioxidant activity IC_{50} 11,341.25 ppm for 14 days did not show any improvement in blood pressure components. systolic and diastolic and fasting blood sugar levels of patients with metabolic syndrome significantly.

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