RESEARCH ARTICLE

The Potential of Strawberry, Rome Beauty Apple, and New Combination on Fasting Blood as Supporting Diet Therapy in Patients with Type II Diabetes Mellitus

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Abstract

Strawberries (*Fragaria x ananassa*) and Rome beauty apples (*Malus sylvestris*) contain high antioxidants to reduce oxidative stress and improve the glycemic response with diabetes mellitus (DM) type II. This study aimed to analyze the effect of strawberries, Rome beauty apples, and their combination to decrease fasting blood glucose levels of type II DM patients. This experimental research used a randomized pre-post-test with a control group design. Subjects were 44 patients divided into four groups: K (control, not given the fruit), P1 (strawberries 200 g/day), P2 (apples 300 g/day), and P3 (the combination strawberries 100 g/day, apples 150 g/day) for 14 days in February–March 2019 in Surakarta. The inclusion criteria were DM patients aged 40–55 years who received oral antidiabetic drug therapy. Exclusion criteria were type II DM patients who, based on the doctor's diagnosis, had complications such as gastritis, hypertension, chronic renal failure, heart disease, liver disease, stroke, cancer, patients with consumption of antioxidant supplements. Mean of blood glucose level on K (149.82±39.125), P1 (141.00±38.079), P2 (128.73±31.841), and P3 (177.73±50.176). Analysis paired t test results showed a significant difference between before and after treatment (p=0.045). To find out which group was the most meaningful, the Bonferroni post hoc test. Decrease of fasting blood glucose levels with group K (−10.55, p>0.05), P1 (−30.18, p<0.05), P2 (40.27, p<0.05), and P3 (−32.91, p<0.05). ANOVA test was used to analyze, and the post hoc Bonferroni test with a control comparison was performed, resulting in p=0.028, in P2 and p>0.05 in P1 and P3. In conclusion, strawberries, Rome beauty apples, and their combination significantly decreased fasting blood glucose levels of type II DM patients, with the highest and most significant decrease in Rome beauty apples.

Key words: Apple, diabetes mellitus, diet therapy, strawberry

Potensi Stroberi, Apel *Rome Beauty*, dan Kombinasi Baru terhadap Gula Darah Puasa sebagai Penunjang Terapi Diet pada Pasien Diabetes Melitus Tipe II

Abstrak

Stroberi (*Fragaria x ananassa*) dan apel *Rome beauty* (*Malus sylvestris*) mengandung antioksidan tinggi untuk mengurangi stres oksidatif dan memperbaiki respons glikemik pada diabetes melitus (DM) tipe II. Tujuan penelitian adalah menganalisis pengaruh buah stroberi, apel *Rome beauty*, dan kombinasinya terhadap penurunan kadar glukosa darah puasa pasien DM tipe II. Jenis penelitian eksperimen dengan rancangan *randomized pre-post-test* dengan *control group design*. Subjek penelitian 44 pasien yang dibagi empat kelompok, yaitu K (kontrol tidak diberi buah), P1 (stroberi 200 g/hari), P2 (apel *Rome beauty* 300 g/hari) dan P3 (kombinasi stroberi 100 g/hari dan apel 150 g/hari) selama 14 hari pada bulan Februari–Maret 2020 di Surakarta. Kriteria inklusi adalah pasien DM usia 40–55 tahun yang mendapat terapi obat antidiabetik oral. Kriteria eksklusi adalah pasien DM tipe II yang berdasar atas diagnosis dokter mengalami komplikasi seperti mag, hipertensi, gagal ginjal kronik, penyakit jantung, penyakit hati, strok, kanker, dan pasien dengan konsumsi suplemen antioksidan. Kadar glukosa darah rerata pada K (149,82±39,125), P1 (141,00±38,079), P2 (128,73±31,841), dan P3 (177,73±50,176). Hasil analisis *paired t test* menunjukkan terdapat perbedaan yang signifikan antara sebelum dan sesudah perlakuan (p=0,045). Untuk mengetahui kelompok mana yang paling bermakna, dilakukan Uji *Post Hoc* Bonferroni. Penurunan kadar glukosa darah puasa pada K (−10,55; p>0,05), P1 (−30,18; p<0,05), P2 (−40,27; p<0,05), dan P3 (−32,91; p<0,05). Analisis dilakukan dengan uji ANOVA dan Uji *Post Hoc* Bonferroni dengan perbandingan kontrol menghasilkan p=0,028 pada P2 serta p>0,05 pada P1 dan P3. Simpulan, pemberian stroberi, apel *Rome beauty*, dan kombinasinya signifikan menurunkan kadar glukosa darah puasa pasien DM tipe II dengan penurunan tertinggi dan bermakna pada apel *Rome beauty*.

Kata kunci: Apel, diabetes melitus, stroberi, terapi diet

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Introduction

Diabetes mellitus defined as a syndrome of metabolic disease.[1] Metabolism of carbohydrates, proteins, and fats that are impaired in diabetes is caused by decreased insulin sensitivity, insulin secretion, or both, characterized by chronic hyperglycemia.[2] The number of people with diabetes mellitus in 2017 was 425 million. This number is expected to increase every year, and in 2045 it will reach 629 million.[3] Based on the report on *Riskesdas* 2018,[4] the prevalence of diabetes mellitus in Indonesia increased to 10.9% in 2018. This number increased by 4% compared to 2013. Prevention and management of diabetes mellitus are very important, that the necessary complementary alternative.[5]

Diabetes mellitus type II is caused by decreased insulin secretion or increase insulin resistance. It is related to reduced insulin secretion due to inflammation, metabolic stress, and genetic factors where β-cell dysfunction is the underlying factor.[6] Insulin resistance is caused by many factors, one of which is the oxidative stress factor. Oxidative stress is a condition of imbalance between free radicals and antioxidant systems, which causes decreased peripheral insulin sensitivity.[7] Reactive oxygen species (ROS) in the mitochondria result in increased endoplasmic reticulum stress and oxidative stress on β-cells that cannot respond to hyperglycemia. ROS also damages cellular components such as lipids, proteins, and DNA and triggers changes in transcription that increase insulin resistance.[8] Oxidative stress has an essential role in the development of DM type II. An external source of antioxidants can help address this oxidative stress. Therefore, the use of antioxidant agents is a promising new therapeutic strategy. Functional foods that have the effect of reducing blood glucose (hypoglycemic) levels are now considered as alternatives to drugs.[9] Routine intake of functional foods can improve sustained or chronic stress in diabetes mellitus through the antioxidant properties contained in functional foods.[10]

Strawberry antioxidants have hypoglycemic activity in diabetes mellitus.[11] Anthocyanins are part of the antioxidants in strawberries with very high levels, which affect lowering blood glucose levels, reducing blood vessel inflammation, and endothelial dysfunction.[12] Quercetin is a flavonoid found in fruits such as apples which functions as an anti-diabetic. This powerful antioxidant can prevent oxidative stress and delay the development of complications of diabetes mellitus.[13] This study was conducted to analyze the effect of administering strawberries, Rome beauty apples, and their combination to decrease patients' fasting blood glucose levels with diabetes mellitus type II.

Methods

This experimental study used a pretest-posttest control-group design. The subjects were diabetes mellitus type II patients at the public health centers in Kratonan, Ngoresan, Sangkrah, and Banyuanyar in the area of Surakarta city from February to March 2020. The inclusion criteria were patients with diabetes mellitus type II, male and female, aged 40–55 years who took only oral antidiabetic drugs, consumed fresh fruit, and communicated well. The subjects were measured for their body weight and height to determine their body mass index (BMI), a statistical index that describes nutritional status. The formula for calculating BMI is the weight (kg) divided by height (m²). BMI is classified as underweight (under 18.5 kg/m²), normal (greater than or equal to 18.5 to less than 24.9 kg/m²), overweight (greater than or equal to 25.0 to less than 27.0 kg/m²), and obesity (greater than 27.0 kg/m²).[14] BMI is used as a weight correction factor in calculating energy requirements. Then, the subjects were given education about the benefits of physical activity and a therapeutic diet using the diabetes mellitus leaflet and a list of food exchanges. The subjects who met the inclusion criteria at four health centers were randomized, which resulted in 44 people. Respondents were divided into four groups, group K (control group, not given the fruit), group P1 (given strawberries 200 g/day, obtained directly from farmers in Cemoro Kandang Strawberry Farm, Gondosuli village, Tawangmangu subdistrict, Karanganyar regency, Central Java province).

Group P2 (given Rome beauty apples 300 g/day) from farmers in Andonosari village, Pasuruan regency and group P3 (given the combination of strawberries 100 g/day and apples 150 g/day) for 14 days. The researcher explained the purpose and the procedure of the study before the subjects signed an informed consent form. The subjects fasted at least 8–12 hours before checking their fasting blood glucose levels. The

hexokinase method was used to measure fasting blood glucose levels on the first day before the intervention and the fifteenth day after the intervention. The examination was at the CITO Surakarta laboratory. It received accreditation from the National Accreditation Committee (KAN) LM-060-IDN using the INDIKO tool. The fruits were delivered to the respondents' houses every day for two times snacks, in the morning and afternoon for 14 days.

The SPSS version 22 program was used to process and analyze the data. The descriptive analysis of research variables was performed with frequency distribution tables and percentages, including gender, age, education, and BMI. The analysis of mean differences before and after the intervention was conducted using Paired t test. The analyses of differences in the effect of administering strawberries, Rome beauty apples, and their combinations were carried out using the one-way ANOVA test because the data were normally distributed. There was a significant difference ($p<0.05$) between the groups, so the posthoc test was performed to analyze the most different interventions in the strawberry, Rome apple, and combination groups with a confidence level of 95%. The Health Research Ethics Committee of Dr. Moewardi Regional General Hospital Surakarta has approved this research, with the ethical clearance number: 087/I/HREC/2020.

Results

Statistically, the distribution of research subjects between the control group, strawberries, Rome beauty apples, and the combination based on

Table 1 Characteristics of Subjects

Characteristics	n=44 (%)
Gender	
Female	10 (23)
Male	34 (77)
Age (years)	
40−45	9 (21)
46−50	11 (25)
51−55	24 (54)
Education	
Elementary school	16 (36)
Junior high school	10 (23)
Senior high school	16 (36)
University	2 (5)
Profession	
Housewife	22 (50)
Private employee	11 (25)
Entrepreneur	11 (25)
Body mass index	
Normal	24 (54)
Overweight	6 (14)
Obesity	14 (32)

the characteristics of gender, age, education, occupation, nutritional status showed no difference ($p>0.05$). Table 1 showed the female patients dominate the distribution of research subjects (34/77%). The subjects' age range in this study was 51−55 years (54%). The education was an elementary school and high school respectively(36%). Half of the subjects were a housewife. The average BMI scores in the control group were 25.28 kg/m², the strawberry group 24.65 kg/m², the Rome beauty apple group 25.50

Table 2 Comparison of Average Blood Glucose Levels Between Groups Before and After Intervention

Groups	Duration		Decrease Fasting Blood Glucose (Mean±SD) mg/dL	p^a
	On Day-0 (Mean±SD) mg/dL	On Day-15 (Mean±SD) mg/dL		
K	160.36±46.807	149.82±39.125	10.55±16.263	0.057
P1	172.09±28.648	141.00±38.079	30.18±29.253	0.004*
P2	170.73±41.478	128.73±31.841	40.27±23.018	<0.001*
P3	209.64±61.112	177.73±50.176	32.91±22.488	0.001*
p^b	0.080	0.045*	0.030*	

Note: *significant differences ($p<0.05$), K=control, P1=strawberries, P2=Rome beauty apples, P3=combination of strawberries and apples, a=paired t test, b=one-way ANOVA

Table 3 Comparison of Mean Difference of Fasting Blood Glucose Levels Based on Bonferroni Post Hoc Test

Groups		Mean Difference	p
K	P1	19.636	0.325
K	P2	29.727	0.028[*]
K	P3	22.364	0.176
P1	P2	10.091	1.000
P1	P3	2.727	1.000
P2	P3	7.364	1.000

Note: [*]significant differences (p<0.05), K=control, P1=strawberries, P2=Rome beauty apples, P3=combination of strawberries and apples, a=paired t test, b=one-way ANOVA

kg/m², and 25.36 kg/m². Most of the total study subjects had 54% normal nutritional status.

The results of the paired t test based on Table 2 showed that the groups administered with strawberries, Rome beauty apples, and their combination experienced a significant decrease in fasting blood sugar levels (p<0.05) after the intervention, but the control group experienced an insignificant decrease (p=0.057). A one-way ANOVA test was conducted to determine the presence or absence of significant differences between treatment groups. Table 2 showed that based on the one-way ANOVA test, there were no significant differences in the fasting blood glucose levels between the four groups at the pretest (p=0.080). Meanwhile, at the posttest, there were significant differences in each group (p=0.045).

Based on Table 3, it is known that the Bonferroni post hoc test results showed a significant decrease in fasting blood glucose levels between the control group and the Rome beauty apple group (p=0.028). On the one hand, the strawberry and the combination groups did not show significantly different results with p=0.325 and p=0.176, respectively. Based on the Bonferroni posthoc test results compared to the combination group, the strawberry group and the Rome beauty apple group obtained the same result (p=1.000).

Discussion

The results of the paired t test showed that the average decrease in blood glucose levels in Q

patients with DM who were given 200 grams of strawberries per day for 14 days was 30.18 mg/dL (Table 2). It is caused by anthocyanin content in strawberries which can reduce fasting blood glucose levels.[12] Strawberries contain anthocyanins 171.4 ppm wb/100 grams.[14] Anthocyanins control carbohydrate metabolism in the body by increasing PPARγ activation in the skeletal muscle and tissue, translocation, expression of glucose transporter 4 (GLUT4), and the secretion of adiponectin and leptin. Anthocyanins activate AMP-activated protein kinase (AMPK), which stimulates glucose uptake and insulin secretion by pancreatic β-cells and decreases RBP4 to increase insulin sensitivity. Anthocyanins also have the effect of inhibiting intestinal α-glucosidase, pancreatic α-amylase which slows glucose absorption after meals, thereby preventing postprandial hyperglycemia and increasing insulin secretion.[15]

The results of this study are similar to those of Putri et al.'s[12] study, which states that the administration of strawberry juice with a dose of 3.6 mL/200 gBW/day (made from 274 g of strawberries) for 14 days decreases fasting blood glucose levels of rats with DM type II (mean=163.82 mg/dL, p<0.05).[15] Administering a strawberry powder drink of 20 g/day (made from 330 g of strawberries) in obese subjects with insulin-resistant abdomen for 14 days did not significantly decrease blood glucose levels (mean=35 mg/dL, p>0.05). Increasing the dose to 40 g/day (440 g of strawberries) had a significant result (p<0.05) with an average decrease of 84 mg/dL.[16]

The average decrease in fasting blood glucose levels of patients with DM who were given 300 g of Rome beauty apples per day in this study was 40.27 mg/dL (Table 3). Apple Rome beauty contains quercetin 4,189/100 mg/kg.[17] This is caused by the content of quercetin in apples which has the effect of lowering blood glucose levels. Quercetin reduces blood sugar levels by inducing PPARγ expression, reducing intestinal glucose absorption, increasing glucose uptake in organs and tissues as well as insulin resistance, and reducing oxidative stress.[13] Quercetin has anti-hyperglycemic activity in diabetes.[18,19] Apple consumption has beneficial health effects, one of which is to manage diabetes mellitus type II. Polyphenols in apples have antioxidant activity and inhibit the activity of α-glucosidase.[20] Quercetin reduces oxidative stress by increasing

antioxidants, decreasing malondialdehyde and nitric oxide levels, and activating gene expression related to the PI3K/PKB signaling pathway, which modulates glucose metabolism resulting in a decrease in fasting blood sugar levels.[21]

The results of this study are in line with the study in the chronic disease management program (*program pengelolaan penyakit* kronis, *Prolanis*) group at the Genuk Public Health Center in Semarang with the intervention of *manalagi* apples for 14 days. They found that there were decreased fasting blood sugar levels in patients with diabetes mellitus type II who were given 200 g, 300 g, and 400 g of *manalagi* apples per day with a higher average decrease of 98.83 mg/dL, 124.33 mg/dL, and 150.16 mg/dL, respectively. The higher the dose of fruit is given, the higher its effect on decreasing fasting blood glucose levels will be.[22] Another similar study in hyperglycemic rats. The study found that giving *manalagi* apples to hyperglycemia rats at a dose of 20 g/200 gBW for 28 days could decrease their fasting blood glucose levels with an average decrease of 130.87 mg/dL.[23]

Giving a combination of 100 grams of strawberries and 150 grams of Rome beauty apples per day for 14 days in this study could significantly decrease fasting blood glucose levels of diabetes mellitus type II patients with $p<0.05$ and an average decrease of 32.91 mg/dL. The results of the Bonferroni post hoc test showed that the differences in the average fasting blood glucose levels between the P1 & P3 and P2 & P3 groups were not significantly different. It means that the P3 dose had the same effectiveness as P1 and P2 doses in reducing fasting blood glucose levels in patients with diabetes mellitus type II.

The decrease in fasting blood glucose levels in P3 is lower than P2. It is possible because the strawberries and Rome beauty apples are served in the form of fresh fruits so that the combination of fruit cannot be mixed evenly. As a result, the interaction of the phenolic compounds of the two fruits that produce a more hypoglycemic effect height cannot take place to the maximum. Besides, the composition of strawberries and apples is 50% of the P1 dose and 50% of the P2 dose. In comparison, the P3 dose was with a combination of 40% of strawberries and 60% of Rome beauty apples. The proportion of fruit combinations may not produce a more significant hypoglycemic effect than the effect of fruit without a combination (P1 and P2). The result showed a combination of juice with 20% of strawberries and 80% of apples had the highest hypoglycemia effect compared to other proportions, which are 30/70, 40/60, and 50/50.[24]

Phenols in apples contribute more to the α-amylase and α-glucosidase inhibitory activity in a combination of blueberries and apples. Fruit combination processing to juice has the potential to produce a more optimal interaction of phenolic compounds. It can release phenols bound into the water while maintaining antioxidant activity in the fruit to produce a higher hypoglycemic effect. The phenolic composition and pH influence the hypoglycemic effect of the fruit combination, and enzymes contained in the proportion of fruit combinations.[24]

Conclusions

Provision of strawberries and Rome beauty apples and their combination significantly decrease fasting blood glucose levels of patients with diabetes mellitus type II. Giving Rome beauty apples had a significant effect on reducing fasting blood glucose and LDL-C levels.

Conflict of Interest

There is no conflict of interest in this study.

Acknowledgments

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