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Effect of high-protein milk on lipid profiles and blood glucose in young adult

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ABSTRACT

Background: *High-protein milk is a complex food that contains several potentially bioactive compounds that might affect blood glucose and cholesterol. Epidemiological data indicate that high-protein milk consumption is associated with a decrease in the prevalence of metabolic disorders or maintaining metabolic health.* ***Objective:*** *This study aimed to analyze the effect of high-protein milk on cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides, and fasting blood glucose.* ***Methods:*** *This study used an experimental trial with the designed randomized controlled trial. The subjects were divided into two groups: 24 subjects in the treatment group and 23 subjects in the control group. The treatment group was given high-protein milk and nutritional education for 90 days. The control groups were given nutritional education.* ***Results:*** *The results showed that blood glucose did not have a significant difference between the two groups ($p>0.05$), but it decreased 1.75±3.6 mg/dl after high-protein milk intervention. Blood cholesterol and LDL showed significant differences between the two groups ($p<0.05$). HDL and triglycerides showed no significant difference between the two groups ($p>0.05$).* ***Conclusion:*** *Intervention of high-protein milk could significantly reduce cholesterol and LDL levels and reduce blood glucose after 90 days of intervention in the young adult age group. High-protein milk can be a recommendation to prevent metabolic syndrome.*

KEY WORDS: *fasting blood glucose; high-protein milk; lipid profiles*

INTRODUCTION

Metabolic syndrome represents a clustering of different metabolic abnormalities. Metabolic syndrome prevalence is present in approximately 25% of all adults with increased prevalence in advanced ages. Adult age is one phase in an individual's lifespan after adolescence [1,2]. The level of metabolic stability of the adult body is the result of a balance between the level of body protein breakdown and protein synthesis. The role of nutrition in adulthood is to increase and/or maintain a normal weight, prevent disease, and improve health status. In adulthood, a person needs to maintain normal blood glucose, cholesterol, body weight, and blood pressure levels [3,4]. Epidemiological data indicate that high-protein milk consumption is associated with a decrease in the prevalence of metabolic disorders or maintain metabolic health [5,6].

Milk protein contains two major protein components, namely casein protein and whey protein. Casein and whey have unique physicochemical and biological properties [7]. In milk, casein is major protein, contributed around 80% of total ptotein found in milk, while whey composed 20% of protein [8]. Biological components of whey protein are α-lactalbumin (α-LA,

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20%); β-lactoglobulin (β-LG, 50%); serum albumin (BSA, 10%); immunoglobulins (10%); and protease peptones (<10%) [7,9]. Whey protein has high protein quality and branched-chain amino acid (BCAA) proportions. Whey protein can act as an antioxidant, antihypertensive, antitumor, hypolipidemic, reduce cholesterol, increase muscle mass, antiviral, antidiabetic, and antibacterial [10,11].

A study by Pal [8] found that the protein content in milk could reduce total cholesterol and LDL after 12 weeks of intervention. The Intervention of fermented milk containing whey protein could reduce triglyceride levels, increase HDL, reduce systolic blood pressure and reduce the atherogenic index after 8 weeks of intervention [12]. A study by Nagaoka [13] showed that peptides derived from β-LG have a better hypocholesterolemic effect than β-sitosterol in test animals. β-LG can also act as an anti-microbial and anti-carcinogenic.

Whey protein can maintain uptake of glucose in the blood and increase insulin sensitivity. Drinking milk containing protein or consuming whey with carbohydrates can increase plasma insulin as a mechanism to decrease blood glucose or maintain blood glucose levels within normal limit [14,15]. Whey protein is absorbed faster than casein and can reduce postprandial glucose response. Whey protein enters the jejunum faster than casein, especially in the form of degraded peptides [16,17].

Several studies from animal trials, healthy individuals, and type 2 diabetes mellitus individuals show that dairy whey proteins may significantly decrease the postprandial glucose response because of the insulinotropic effect of its amino acids [14,18,19]. Another study found that the consumption of peptides and intact whey protein reduced the glucose response in a dose-dependent manner in healthy subjects [20]. Several studies have proven the benefits of milk protein in improving or maintaining a normal blood lipid profile and blood glucose [12,11,21]. However, the mechanism of high-protein milk contributing to blood glucose and cholesterol is still poorly understood in young adults. This study aimed to analyze the effect of high-protein milk on blood glucose levels and cholesterol.

METHODS

Study design and participants

This study was performed as a single-blind randomized controlled trial, which investigated the effects of high-protein milk on lipid profiles and fasting blood glucose. Participants were randomized to begin the study, either the intervention or the control group by simple randomization. This research was conducted from January to April 2017. All participants provided written informed consent and the study was approved by the Ethics Committee of the Faculty of Medicine, University of Indonesia No.162/UN2.F1/ETIK/II/2017.

The population in this study were students at IPB University. Inclusion criteria were aged 18-30 years and in good health. The exclusion criteria were lactose intolerance, allergy to milk or protein, having a history or suffering from chronic disease (coronary heart disease, hypertension, atherosclerosis, kidney problems), participation in other studies, and routinely consuming cholesterol-lowering drugs/supplements/hormonal therapy. The minimum sample size in this study was calculated using the formula for estimating the sample size of two independent groups according to Lemeshow [22] obtained 24 subjects in the treatment group and 23 subjects in the control group.

Measures

High-protein milk. This study was conducted for 90 days of intervention. This study was divided into two groups; the treatment group and the control group. The treatment group was given high-protein milk products (Appeton, Kotra Pharma (M) Sdn Bhd) and nutritional education interventions personally. In the treatment group, participants consumed high-milk protein products at a dose of 3x50 grams or 150 grams/per person/day without changing the participant's daily diet. Once a week the product was distributed to participants by providing a compliance form. Daily milk consumption was recorded on the compliance form provided by the researcher. The nutrient composition of the product is shown in **Table 1**. The control group was not given a product and was given a personal nutrition education intervention. Nutrition education interventions consist of 6 materials on nutrition

knowledge including balanced nutrition guidelines, good snacks, the importance of breakfast, the benefits of milk, good physical activity, and the benefits of vegetables and fruit. The aim of the nutrition education intervention in both groups was to improve the nutrition knowledge of the subjects so that there would be a common perception of nutrition in the two groups.

Lipid profiles and blood glucose levels. Lipid profile and blood glucose measurements were carried out 2 times during the study; before and after 90 days of intervention in each group. Before taking blood, the subject fasted for 10-12 hours, and only consume water. Blood samples were taken from the subject as much as 5 ml from a vein. Blood samples were taken by a health analyst from the Regional Health Laboratory of Bogor City. Lipid profiles were measured by using the enzymatic colorimetric test method and blood glucose measured by ELISA method at the Regional Health Laboratory of Bogor City.

Data analysis

All analyses were conducted using SPSS Ver. 23. The first data analysis was a descriptive measurement of several parameters such as individual characteristics. Some of the measures analyzed include mean and standard deviation. Paired t-tests were used to see differences in each group before and after the intervention. Independent t-test for analysis of differences between treatment and control groups. Significance was established at $p< 0.05$.

RESULTS

Characteristics of subjects

The number of applicants during open recruitment was 78 people, then screening was carried out based on inclusion and exclusion criteria, 60 applicants met the criteria and 18 applicants declined to participate in the study. The reason for refusing to participate in this

Table 1. Nutrients composition of high-milk protein

Nutrients	Total of nutrients/100 g	Total of nutrients/ day (150 g)	Average percentage of nutrient adequacy/day	
			Male	Female
Energy (kcal)	400	600	22	27
Carbohydrates (g)	52	78	21	25
Fiber (g)	5.6	8.4	22	26
Protein (g)	30	45	73	80
Fat (g)	10	15	16	20
Amino acid				
Leucine (g)	2.6	3.9	-	-
Lysine (g)	2.8	4.2	-	-
Arginine (g)	1.0	1.5	-	-
Valine (g)	1.9	2.9	-	-
Isoleucine (g)	1.6	2.4	-	-
Phenylalanine (g)	1.2	1.8	-	-
Treonine (g)	1.3	1.9	-	-
Methionine (g)	0.8	1.2	-	-
Histidine (g)	0.8	1.2	-	-
Triptopan (g)	1.0	1.5	-	-
Glutamic acid (g)	5.6	8.4	-	-
Proline (g)	2.6	3.9	-	-
Aspartic acid (g)	2.1	3.1	-	-
Serin (g)	1.6	2.4	-	-
Tyrosine (g)	1.6	2.4	-	-
Alanine (g)	0.8	1.2	-	-
Glycine (g)	0.5	0.7	-	-
Cysteine (g)	0.4	0.6	-	-

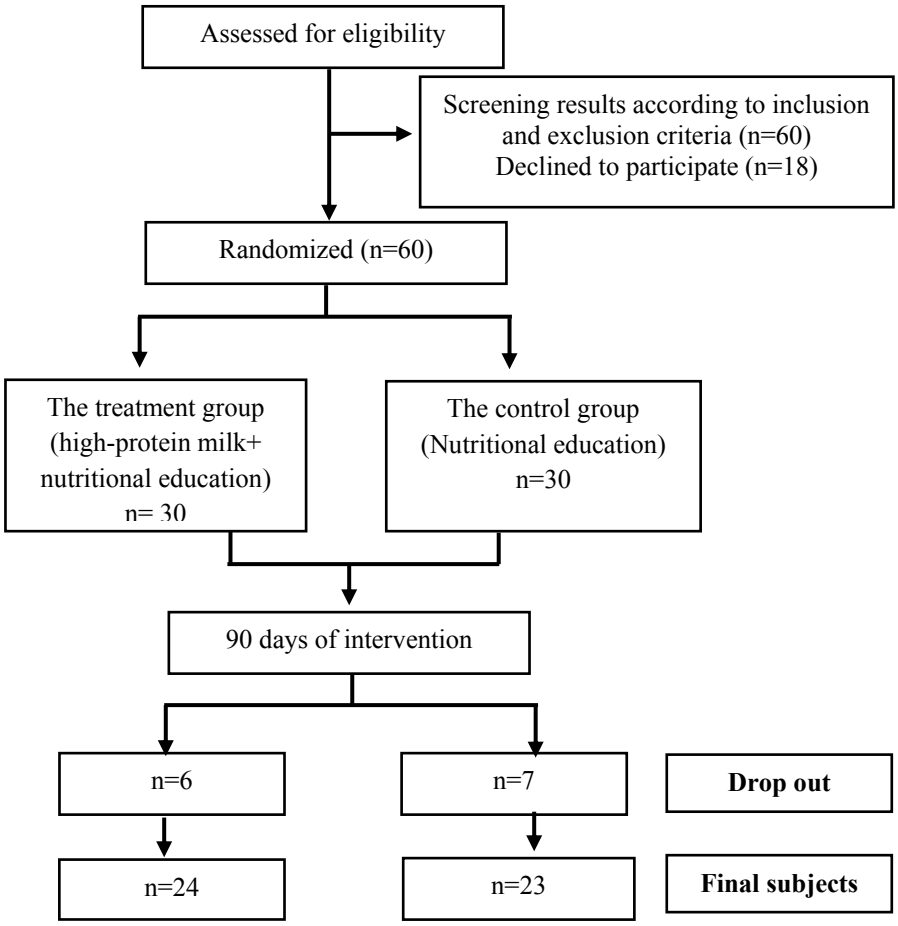

Figure 1. Research Flow

study was that the intervention time was too long and certain personal needs. Randomization was carried out and obtained 30 subjects in the treatment group and 30 subjects in the control group. During the study, several subjects dropped out because some had allergies to the milk they were given, were sick and some had passed the education given. The final subjects of this study were 24 subjects in the treatment group and 23 subjects in the control group (**Figure 1**).

Characteristics of subjects observed in this study did not differ significantly ($p>0.05$) between the two groups (**Table 2**). Subjects in the study were mostly women, both in the treatment group (62.5%) and in the control group (83%). Most subjects between the ages of 18-24 years were 79.2% in the treatment group and 95.7% in the control group. There were no significant differences in body weight, height, BMI, and blood pressure between the treatment group and the control group ($p>0.05$), the treatment and control groups had the same subject characteristics.

Effect of high-protein milk on lipid profiles and fasting blood glucose

There was no significant difference in HDL and triglyceride levels between the treatment and control groups ($p>0.05$). The results of the paired t-test show that there were significant differences in cholesterol levels between the treatment and control groups ($p<0.05$), with a mean decrease of 11.3 mg/ml in the treatment group and an increase of 1.6 mg/ml in the control group. LDL levels significant difference between the treatment and control groups ($p<0.05$), with a mean decrease of 9.9 mg/dl in the treatment group and an increase of 4.4 mg/dl in the control

Table 2. Distribution of subject characteristics

Variable	Subject characteristics		p[1]
	Treatment	Control	
Gender[2]			0.12
Male (n, %)	9 (38)	4 (17)	
Female (n, %)	15 (62)	19 (83)	
Age (year, mean±SD)	22.7 ± 2.2	22.3 ± 1.9	0.46
18-24 (n, %)	19 (79)	22 (96)	
25-30 (n, %)	5 (21)	1 (4)	
Weight (kg, mean±SD)	44.4 ± 4.2	43.7 ± 4.3	0.59
Height (cm, mean±SD)	161.0 ± 7.9	157.6 ± 6.7	0.11
BMI (kg/m^2, mean±SD)	17.0 ± 0.9	17.6 ± 0.7	0.12
Blood pressure (mmHg, mean±SD)			
Systolic	108.0 ± 10.0	108.2 ± 9.7	0.52
Diastolic	70.9 ± 7.0	70.3 ± 5.3	0.06

[1] independent t-test; [2] Mann-Whitney test; BMI = body mass index

Table 3. Lipid profile and fasting blood glucose subjects

Variables	Groups		p[1]
	Treatment	Control	
HDL (mg/dl)			
Baseline	52.3 ± 15.1	54.6 ± 10.6	
Endline	51.9 ± 7.3	52.4 ± 7.7	
p[2]	0.89	0.39	
Δ	-0.4 ± 13.3	-2.2 ± 12.7	0.63
Trygliceride (mg/dl)			
Baseline	79.3 ± 26.9	77.3 ± 22.4	
Endline	81.3 ± 24.4	85.7 ± 20.9	
p[2]	0.74	0.04	
Δ	2.1 ± 29.8	8.4 ± 18.7	0.39
Cholesterol (mg/dl)			
Baseline	170.1 ± 28.9	169.9 ± 19.3	
Endline	158.9 ± 25.8	171.6 ± 21.5	
p[2]	**0.02***	0.642	
Δ	-11.3 ± 21.3	1.6 ± 16.3	**0.02***
LDL (mg/dl)			
Baseline	100.0 ± 26.5	98.2 ± 18.9	
Endline	90.0 ± 22.4	102.6 ± 22.7	
p[2]	**0.03***	0.37	
Δ	-9.9 ± 20.8	4.4 ± 23.3	**0.03***
Fasting blood glucose (mg/dl)			
Baseline	87.3 ± 2.5	85.3 ± 2.3	
Endline	85.4 ± 2.5	86.5 ± 2.3	
p[2]	**0.03***	0.76	
Δ	-1.8 ± 3.6	0.2 ± 3.4	0.06

[1] independent t-test; [2] paired t-test; *significant; Δ = delta
HDL = high density lipoprotein; LDL = low density lipoprotein

group. The average changes in fasting blood glucose levels after the intervention did not show a significant difference between the treatment and control groups (p>0.05). **Table 3** shows that after the intervention there was a significant decrease of 1.8 mg/dl (p<0.05) in the treatment group, but still in normal value (<126 mg/dl). In the control group, there was no significant difference in fasting blood glucose after intervention (p>0.05).

DISCUSSION

The dairy product provided was high-protein milk, the main component is whey protein and contains complete amino acids. Dairy proteins have the potential to suppress postprandial lipaemia due to their insulinotropic effects, as insulin is known to inhibit hormone-sensitive lipase and the release of free fatty acid (FFA). After the intervention for 90 days, HDL levels in the treatment group tended not to change, although there was a decrease of 0.4 mg/dl in the treatment group and 2.2 mg/dl in the control group. Fekete [23] stated the same results that giving milk containing whey protein to overweight respondents had no effect on HDL levels. The provision of milk protein for a longer time is likely to provide more in-depth information about the effect of milk protein on HDL levels.

After the intervention of high-protein milk, triglyceride levels did not change significantly. The results of research by Tahavorgar [24] showed that after intervention 65 grams of whey protein after 12 weeks could not reduce triglyceride levels. The effect of feeding milk containing whey protein on triglyceride levels is not well known. Triglyceride metabolism is influenced by several factors including chylomicron secretion in the intestine, very-low density lipoprotein (VLDL) secretion in the liver, and lipoprotein uptake by the tissue, and the possibility of whey protein influencing any of these stages.

After the intervention of high-protein milk, cholesterol levels decreased significantly ($p<0.05$), but were still at normal levels. The results of this study were in line with the research conducted by Fekete [23] that giving milk containing whey protein to respondents could reduce blood cholesterol. A study conducted by Pal [8] showed that intervention with whey protein after 12 weeks in respondents could reduce cholesterol levels. This might be caused by the β-Lactoglobulin component in milk protein can inhibit cholesterol absorption through changes in micellar cholesterol solubility in the intestine and inhibit the expression of genes involved in fatty acids.

The average changes in cholesterol levels of subjects in the treatment group led to a better improvement in lipid profile compared to the control group. The same conclusion by Fekete [23] with an experimental research design that consumption of whey protein (56 g / day) for 8 weeks can improve lipid profiles. A cohort study by Kim [25] involving 2,103 respondents that milk consumption can reduce the risk of metabolic syndrome. There are several mechanisms of milk protein in improving lipid profiles which inhibit the expression of genes involved in intestinal fatty acids and cholesterol synthesis and absorption, catabolic enhancement through the excretion of tricarboxylic acid cycle compounds, and stimulate bacterial activity in the intestine which results in higher short-chain fatty acids, which plays a role in lipid metabolism [26-29]. The results of this study indicate that high-protein milk especially those containing whey protein can improve or maintain normal blood lipid profile levels in adults young.

Amino acids (Ile-Ile-Ala-Glu-Lys) from β-LG have been shown to have hypocholesterolemic activity in test animals and their mechanism of action is related to the inhibition of micellar solubility from cholesterol, which causes suppression of cholesterol absorption by direct interaction between cholesterol in micelles and tryptic peptide inside the jejunal epithelium. A study conducted by Nagaoka [13] proved that peptides derived from β-LG have a better hypocholesterolemic effect compared to β-sitosterol in test animals. β-LG can also act as an anti-microbial and anti-carcinogenic.

Cholesterol levels can be influenced by several factors including nutrient intake. Cholesterol levels are associated with fat, carbohydrate, and protein intake because these three nutrients can become acetyl CoA which is a cholesterol-forming ingredient in the body. Individuals who cannot control their cholesterol intake will cause an increase in cholesterol levels in the blood. This is due to the inability to regulate cholesterol homeostasis by reducing cholesterol absorption in the intestine or reducing cholesterol synthesis [30-32].

Consumption of milk containing protein can stimulate insulin secretion. Insulin has an effect on the metabolism of carbohydrates, fats, and proteins, including stimulation of glucose absorption, glycogen synthesis, lipid absorption, triglyceride synthesis, and protein synthesis and inhibits protein breakdown, lipolysis, and gluconeogenesis. Therefore, stimulation of secretion by milk protein contributes to metabolic effects on tissues and plays a role in muscle mass anabolism [33]. The

results of the study by Tahavorgar [24] suggested that giving milk containing whey protein after 12 weeks of intervention could reduce fasting blood glucose levels but there were no significant differences between the control groups. The research conducted by Harna [34] showed that intervention of high milk protein can decrease postprandial glucose levels in the treatment group compared than in the control group.

Insulin response after consuming whey protein has been demonstrated in several studies. This suggests that whey protein has the potential as insulinotropic. The insulinotropic mechanism of whey protein is likely due to bioactive peptide content, specific amino acids, and incretin hormone activation (especially glucose-dependent insulinotropic polypeptide or GIP) which is released when consuming whey protein [19,35]. The bioactive peptide content in milk protein is related to blood glucose through the activity of enzymes involved in regulating glucose. There have been no in vivo studies that report the benefits of milk protein hydrolysates on dipeptidyl peptidase-IV (DPP-IV) activity and α-glucosidase inhibitory activity in humans. Milk protein hydrolyzate has been shown to have an effect on serum blood glucose through insulinotropic mechanisms. The branched-chain amino acids (BCAA) component in milk protein also has a role in regulating blood glucose. Free amino acids can directly act on the level of β cells to release insulin through various mechanisms including membrane depolarization and mitochondrial signaling that affects insulin secretion [36-38].

CONCLUSIONS

The intervention of high-protein milk has a beneficial effect on health and can be a recommendation to prevent metabolic syndrome. High-protein milk given to young adults can reduce cholesterol, LDL, and blood glucose levels, and maintain lipid profile and fasting blood glucose within normal limits. Further study on the effects of high-protein milk in people with metabolic syndrome is needed.

Declaration of conflicting interests

No potential conflict of interest was reported by the authors

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