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The Effect of Pumpkin Seeds (Cucurbita moschata) on Uric Acid Level in Hyperuricemia Patients

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ABSTRACT

Background: Hyperuricemia is a condition in which uric acid level exceeds normal threshold. The pumpkin seed extract contains flavonoids that can lower uric acid level. This study aims to analyze the effect of pumpkin seeds (*Cucurbita moschata*) capsules compared to allopurinol on uric acid level in hyperuricemia patients. **Methods:** This was an experimental research with a non-randomized control group pretest-posttest design. A total of 63 patients (32 intervention and 31 control) with hyperuricemia enrolled in this study through purposive sampling technique. The intervention group (IG) was given pumpkin seeds and control group (CG), allopurinol. Data were analyzed using paired and independent sample t-test. **Results:** The result of this study showed that uric acid level significantly decreased after the pumpkin seed capsule was provided (Mean changes=-0.33 mg,dl; P<0.001). However, allopurinol played a greater role in lowering uric acid levels (Mean changes=-0.92 mg/dl; P<0.001). The mean changes of uric acid between groups was also significant (P=0.039). In addition, some of the nutrition intakes showed a significant difference after the intervention. **Conclusion:** It can be concluded from the study that pumpkin seed capsules affected the decrease of uric acid level significantly, but the number was lower compared to allopurinol. In future studies, The dose of pumpkin seed should be considered.

Keywords: *Cucurbita; Plant extracts; Allopurinol; Hyperuricemia.*

Introduction

Hyperuricemia is a condition where uric acid level exceeds normal threshold in males with 7 mg/dl and females with 6 mg/dl (Madyaningrum *et al.*, 2020). Males do not have high levels of estrogen, so it is difficult for uric acid to excrete through urine, and as a result, the increase in uric acid level in males is higher than females (Rusman, 2021). The risk of developing gout can increase with age. This means that in the phase from young adult to senior adult, uric acid level is increasingly abnormal (Fadlilah and Sucipto, 2018). Based on basic health research, the prevalence of people with

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joint disease in Indonesia is 7.30% among people aged 15 and older (Riskesdas, 2018). People aged 75 and above are very susceptible to joint disease, which is 18.95%. According to the data from joint disease patients by provinces in Sulawesi in 2018, North Sulawesi province has the highest prevalence rate of joint disease, 8.35%, followed by Central Sulawesi province, 7.72% (Riskesdas, 2018). Based on the data from regencies/cities in Central Sulawesi in 2018, Palu City had the second highest prevalence rate of joint disease with 2,002 people (Riskesdas, 2018). In 2020, the city occupied the highest position on hyperuricemia, which was 2,824 people (Dinas Kesehatan Sulteng, 2020). Data obtained from the activity report by Bulili Health Center showed that there were 183 hyperuricemia patients in its working area. According to the profile of Kamonji Health Center, the prevalence of hyperuricemia patients in its working area was 1,829 (Kamonji Health Center, 2020).

Purine intake can affect uric acid levels because it is one of the compounds to form uric acid in our body. Therefore, consuming foods containing antioxidants such as quercetin, resveratrol, flavonoids, and vitamin C can inhibit negative effects of the purines (Fithri *et al.*, 2018). Functional foods can be used in medication (Daud *et al.*, 2021).

Functional foods like pumpkin seed capsules contain pumpkin seed flour which is dried under the sun for 7 hours, baked in the oven at 70-75 ^{0}C for 3 hours, and then formulated into powder and capsulated. Pumpkin seed capsules contain useful nutrients such as flavonoid compounds that can reduce uric acid levels. Flavonoids are a group of secondary metabolite compounds, and flavonoids can inhibit enzymes that play a role in the formation of superoxide anions, such as xanthine oxidase. Pumpkin seeds are rich in magnesium, zinc, amino acids, essential fatty acids, vitamin E, sterols, carotenoids, cryptoxanthin, monocyclic sesquiterpenoids, and trypsin inhibitors (Syam *et al.*, 2019). Research showed that pumpkin seeds extract produced positive flavonoids with an average of flavonoids which was 1.968% (Nurul Annisa Hafsiyah, 2021). Flavonoids are a group of secondary metabolite compounds. Flavonoids can inhibit enzymes that play a role in the formation of superoxide anions, such as xanthine oxidase. Xanthine oxidase is an enzyme that converts xanthine to uric acid. Based on this background, this study aims to investigate the effect of pumpkin seeds (*Cucurbita moschata*) on uric acid level in hyperuricemia patients in Palu City.

Materials and Methods

Study design

It was an experimental research with a non-randomized control group with pretest-posttest design.

Participants

This study included patients with hyperuricemia. Samples were obtained from the results of peripheral blood tests of 63 participants. The sampling technique used was purposive sampling. This study was divided into 2 groups, namely the intervention group (IG) and the control group (CG). The IG consisted of hyperuricemia patients who were given pumpkin seeds capsules treatment. The CG included hyperuricemia patients who were given allopurinol medication.

The inclusion criteria included the uric acid level that had to be high, 7-8.9 mg/dl for men and 6-7.9% mg/dl for women who were aged between 20-59 and did not take anti-hyperuricemia medication. The exclusion criteria were respondents' refusal to participate in this research. The dropout criteria were applied to the participants who consumed the pumpkin seeds extract or allopurinol <80% of the whole day during intervention.

Location of research

This study was conducted in the working area of Bulili Health Center and Kamonji Health Center in Palu City, Central Sulawesi Province, Indonesia.

Instruments and procedures

The instrument used respondent characteristics, 24-hour food recall questionnaires, and a test kit for measuring uric acid levels in peripheral blood and serum, which were provided by the Central Sulawesi Provincial Health Laboratory.

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The initial stage of this research was to conduct screening by taking peripheral blood samples from all the prospective respondents. The respondents, whose uric acid levels exceeded the normal threshold value (i.e., 7-8.9 mg/dl for male and 6-7.9 mg/dl for female or hyperuricemia), were given an explanation regarding the research procedures. If they agreed to participate in this study, they were asked to sign an informed consent. In the following stage, the respondents were divided non-randomly into two groups. The intervention group was given pumpkin seed capsules and the control group, allopurinol. The subjects were also asked about their daily nutrition intake using the 24-hour recall method. This was to observe nutritional intake change before and after the intervention. The intervention was carried out for 30 days by following the prior finding (Syam *et al.*, 2021). The dose for pumpkin seed capsule was 350 mg and 100 mg for allopurinol. Pumpkin seed capsules contain pumpkin seed powder. In making pumpkin seed flour before offering it to the participants, the seeds are dried under the sun for 7 hours, baked in the oven at 70-75 ^{0}C for 3 hours, and then made into powder and capsulated. The researcher then drew venous blood on day 31 to check the uric acid level and asked about the respondent's intake after the intervention.

Ethical considerations

The procedures received ethical approval with the number: 5427/UN4.14.1/TP.01.02/2022.

Data analysis

The analysis used in this study consisted of univariate and bivariate analyses. Univariate analysis is presented with distribution of frequency to describe the characteristics of participants and research variables. Bivariate analysis was performed using a paired and independent t-test to examine the difference before and after intervention in the respective groups as well as between independent groups. The analysis also was done to compare the mean change of respondents' intakes before and after intervention. The IBM SPSS for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA) was performed in all the data analysis process.

Results

Table 1 shows that most of the respondents are female in both groups, with 20 (62.5%) individuals in the IG and 23 (74.2%) individuals in the CG. From the number of female respondents, by menstrual status, most of the females (11 people, (34.3%)) experiencing menopause were in the IG and 15 (48.4%) participants were in the CG.

Respecting age category in both groups, most respondents were 47-59 year with 20 (62.5%) individuals in the IG and 23 (74.2%) in the CG. This was while on nutritional status category, respondents with normal status were mostly found in both groups, namely 14 (43.8%) in the IG and 11 (35.5%) in the CG. As the result, P-value was greater than 0.05 in all categories. This means that there was no significant difference between both groups, or the baseline data was homogeneous.

Based on **Table 2**, the uric acid level before intervention had an average value of 6.98±0.66 mg/dl in the IG. The average value decreased after the intervention of pumpkin seed capsules for 30 days to 6.65±0.83 mg/dl. In the CG, the uric acid level before intervention had an average value of 7.07±0.87 mg/dl. The average value also decreased to 6.14±1.04 mg/dl after allopurinol intakes for 30 days. The result of analysis after intervention showed a P-value of 0.03 which indicated that there was a difference in the decrease of uric acid level after intervention between both groups.

Table 2 shows that there was a significant increase in respondent's nutrients intakes after taking pumpkin seed capsules such as energy up to 1464.5 kcal/d from the initial value (P=0.01, vitamin C to 42.9 mg (P<0.001), and folic acid to 120.9 µg/d (P=0.03). Furthermore, the energy, carbohydrate, fat, vitamin C, and folic acid showed also significant differences between groups in which IG had higher values than the CG.

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Table 1. Respondents' characteristics.

Variables	Intervention		Control		P-value[a]
	n	%	n	%	
Sex					
Male	12	37.5	8	25.8	0.31
Female	20	62.5	23	74.2	
Menstrual status					
On menstruation	9	28.1	8	25.8	0.23
Menopause	11	34.4	15	48.4	
Age (y)					
20-33	4	12.5	2	6.4	0.29
34-46	8	25.0	6	19.4	
47-59	20	62.5	23	74.2	
Nutritional status					
Underweight	2	6.3	1	3.2	0.21
Normal	14	43.7	11	35.5	
Overweight	11	34.4	10	32.3	
Obese	5	15.6	9	29.0	
Medication compliance					
80-90	7	21.9	9	29	0.51
91-100	25	78.1	22	71	

[a]: *Chi square test.*

Table 2. The comparison of the uric acid levels and dietary intake parameters before and after the intervention within and between groups.

Groups	Intervention group	Control group	P-value[a]
Uric acid (mg/dl)			
Before	6.98±0.66[c]	7.07±0.87	0.06
After	6.65±0.83	6.14±1.04	0.03
P-value[b]	<0.001	<0.001	
Changes	-0.33±0.17	-0.92±0.17	0.003
Energy (kcal/d)			
Before	1329.4±372.5	1301.6±321.4	0.75
After	1464.5±354.8	1197.6±225.0	0.001
P-value	0.019	0.043	
Changes	135.1±17.7	-104±96.4	0.001
Carbohydrate (g/d)			
Before	196.3±89.7	174.4±71.6	0.29
After	225.0±80.1	182.7±45.9	0.01
P-value	0.08	0.55	
Changes	28.7±9.6	8.3±25.7	0.008
Protein (g/d)			
Before	50.4±17.9	52.9±21.3	0.60
After	45.9±15.1	40.2±11.0	0.09
P-value	0.22	<0.001	
Changes	-4.2±2.8	-12.7±10.3	0.08
Fat (g/d)			
Before	37.6±22.7	64.9±120.3	0.21
After	40.9±16.5	34.3±16.2	0.01
P-value	0.46	0.18	
Changes	3.3±6.2	-29.9±104.1	0.007

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Vitamin C (mg/d)			
Before	16.9±11.4	20.4±18.3	0.35
After	42.9±23.5	29.9±24.3	0.03
P-value	<0.001	0.03	
Changes	26.1±12.1	9.5±6.0	0.02
Calcium (mg/d)			
Before	133.9±90.9	250.0±402.2	0.11
After	144.6±74.7	147.7±204.9	0.93
P-value	0.60	0.23	
Changes	10.7±16.2	-102.3±197.3	0.79
Folic acid (µg/d)			
Before	92.4±58.2	81.2±27.4	0.37
After	120.9±51.9	93.9±42.8	0.02
P-value	0.03	0.19	
Changes	28.5±6.3	11.8±15.4	0.01

[a]: *Paired t-test;* [b]*: Independent samples t-test;* [c]*: Mean±SD.*

Discussion

Uric acid is a normal condition in human body but becomes dangerous if exceeds the normal limit. The mechanism that causes excess of uric acid in blood is when our body produces more uric acid but less excretion through urine (Yenrina *et al.*, 2008). If that case, medication is needed by patients with hyperuricemia. There are two medication principles for patients with hyperuricemia, namely reducing uric acid production and increasing its excretion (Permadi, 2006). Various forms of medication can be done such as the provision of drugs and diet settings. Drugs can be made of chemical, animal, and vegetable substances which can cure, relieve, or prevent disease and its symptoms with a right dose (Tjay and Rahardja, 2007).

Generally, drugs work with several mechanisms, including inhibiting and activating body enzymes, influencing transport processes, influencing microorganism biosynthesis, osmotic and neutralizing effects, and formation of bonding complexes. Allopurinol is a kind of drug which works by targeting enzymes. The inhibition process of allopurinol works on xanthine oxidase enzyme which forms uric acid (Sari *et al.*, 2018). This is while pumpkin seed capsules contain extracts rich in vitamin A, B, C, E, iron, zinc, carbohydrates, protein, fiber, fat, and other minerals which are beneficial and needed by our body (Syed *et al.*, 2019). Pumpkin seed capsule has become an effort to utilize biodiversity which is used as traditional/herbal medicine. It is anti-inflammatory and can inhibit the negative effects of purines. Pumpkin seed extracts also contains antioxidant called flavonoids. These flavonoids can inhibit an enzyme that forms superoxide anions, namely xanthine oxidase. It is an enzyme that converts xanthine to uric acid. Therefore, pumpkin seed capsules also reduce uric acid levels in respondents.

The pumpkin seed capsules caused changes in respondents' food intake after intervention. This study was in line with the research which showed that there was an increase in food intake in the underweight and stunted toddlers group in Banggai Regency after they were given pumpkin seed biscuits as supplementary feeding (Fandir *et al.*, 2022). Another study found the effect of pumpkin seed (*Cucurbita moschata*) biscuits on hemoglobin level and zinc status of pregnant women with Chronic Energy Deficiency (CED) in Bone Regency. According to the result of 24-hour dietary recall analysis, there was an increase in food intake of the respondents (Sukarya *et al.*, 2021). Pumpkin seed is a source of zinc, which can stimulate appetite and increase food intake in the subjects. Excessive purine intake in protein, as well as fat and simple carbohydrates, can lead to the increase in uric acid. Meanwhile, nutrients like flavonoid, vitamin C, calcium and folic acid can help to inhibit the negative effects of purine.

This study had several limitations. The researchers used a 24-hour recall method instead of

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the FFQ method. It is better to examine dietary habits rather than daily dietary intake. However, the authors failed to apply that method due to the lack of conditions during the research. This research also failed to control other potential factors that may affect uric acid. Despite the significant result of decreasing uric acid after pumpkin seed capsule intervention, the change was still lower than allopurinol. Future research should consider the use of the FFQ method, control the potential confounding, and add the pumpkin seed dose to get confident results.

Conclusion

It can be concluded from the study that pumpkin seed capsules affected the decrease of uric acid level significantly, but the number was lower compared to allopurinol. Future research should consider the use of the FFQ method, control the potential confounding, and add the pumpkin seed dose to get reliable results.

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Author's contribution

Mutmainnah, Syam A, Citrakesumasari, and Jafar N were involved in conceptualization, investigation, data analysis, drafting, editing, and reviewing the manuscript; and Palutturi S, Maria IL, and Mumang AA carried out editing and reviewing the manuscript.

Conflict of interest

The authors declared no conflict of interests.

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