

The role of pepaya fruit extract (*Carica papaya. L*) As a complemter therapy on the change of hemoglobin content in the white rat (*Rattus norvegicus*) anemia

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Abstract

Background: Anemia is a common health problem that occurs throughout the world, where 50% of cases of anemia are caused by iron deficiency. One alternative for preventing anemia is to use papaya fruit extracts that contain antioxidants good for the body and blood profile levels but are underutilized.

Objective: To determine the effectiveness of papaya fruit extracts as an alternative to increasing hemoglobin levels in anemic white rats.

Methods: This type of research method used is True Experimentation. The research design used was a pretest and post-test control group design. With a sample size of 16 divided into 2 groups, namely the intervention group given papaya fruit extract and the control group given aquadest. Data analysis using Friedman and Post hoc Wilcoxon.

Results: Increased hemoglobin level after papaya fruit extract in the treatment group was 1,120 g / dl ($p < 0.05$).

Conclusion: Papaya fruit extract significantly influences hemoglobin level.

Keywords: papaya fruit, hemoglobin, anemia

Introduction

Anemia in postpartum mothers is a medical condition where the number of red blood cells or hemoglobin is less than 11gr% ^[1] Hemoglobin is an oxygen-carrying substance in red blood cells with normal levels of 12-16 gr% ^[2]. Physiologically anemia occurs when there is a lack of hemoglobin due to the disruption of the formation of red blood cells due to reduced levels of iron in the blood ^[3].

Hemoglobin is a red pigmented protein found in red blood cells and functions to carry oxygen from the lungs to be carried throughout the body. Hemoglobin bond with oxygen is called oxyhemoglobin. The structure of hemoglobin consists of iron and globin proteins. Iron contains hem pigments and globin proteins contain four amino acid chains consisting of alpha, beta, delta and gamma chains ^[2].

Anemia can be caused by impaired red blood cell formation or increased loss of red blood cells through chronic bleeding, sudden bleeding or excessive lysis of red blood cells. Anemia is mostly caused by iron deficiency factor which is characterized by low hemoglobin levels and a decrease in ferritin levels. All anemia results in a decrease in hematocrit and hemoglobin values and all symptoms are ultimately related to a reduction in the transport of oxygen to cells and organs thereby disrupting the function and health status ^[4].

The prevalence of anemia in developed countries reaches 14%, and 51% in developing countries. According to the World Health Organization (WHO) the incidence of anemia in postpartum mothers is 56%. In India maternal mortality due to anemia reaches 19%, from cases of anemia in postpartum mothers 65% -75%. Indonesian demographic and health survey data (IDHS) in 2015 stated that the maternal mortality rate in Indonesia was 305 per 100,000 live births. In Indonesia, mortality in postpartum mothers due to anemia reaches 30% ^[5].

Postpartum mothers are prone to anemia, because of a loss of blood during labor. Fatigue, physical disability, postpartum blues and decreased cognitive abilities are factors that influence anemia in postpartum mothers ^[4]. Causes of anemia include hemolysis, bleeding, bone marrow suppression, nutrient deficiency including iron deficiency, folic acid, pyridosine, vitamin C. Anemic mothers will complain of symptoms such as weakness, fatigue, lethargy, fatigue, frequent dizziness and dizzy eyes, petals pale eyes, lips, skin and palms ^[3].

To meet the needs of iron, postpartum mothers need to take iron supplements. Giving Fe tablets to postpartum mothers is recommended by the government for up to 40 days after delivery. The body's response to the administration of Fe tablets was monitored through improved hemoglobin values with a minimum increase of 0.3 g / dl. In addition to giving Fe tablets, puerperal women were also given high doses of vitamin A (200,000 IU) which were consumed one tablet after delivery and one tablet the next day at the latest on the 42nd day after delivery, and all midwives had received a Hb test with the purpose that they could carry out routine test of both pregnant women and postpartum mothers ^[6]. However, the iron contained in supplements if taken in large doses and for a long time can cause damage to the intestinal lining, body abnormalities, shock and liver failure ^[7].

Papaya contains several chemical compounds or secondary metabolites, namely saponins, alkaloids, tannins, flavonoids, triterpenoids and quinones ^[8]. In several studies, chemical compounds from papaya can affect human blood profiles, namely hemoglobin, leukocytes, and platelets. Terpenoids and alkaloids affect bone marrow hematopoiesis thereby increasing the number of leukocytes, platelets and hemoglobin levels. Flavonoids have an effect on platelets by preventing platelet aggression, whereas saponins have the ability to interact with erythrocyte membranes resulting in

hemolysis [9, 10, 11].

Papaya fruit extract is given by sonde to make it more effective for 14 days in accordance with the time needed for rat blood cells in the process of replication after experiencing iron deficiency. Subjects in this study used white rats (*Rattus norvegicus*) to see the role of papaya extract on changes in hemoglobin levels.

Material and Method

This type of research is a pure experimental (true experiment) with a randomized pre-post-test control group design that aims to compare the two groups allocated by random means by testing. Experimental animals in this study were divided into two groups: the group giving papaya extract and the control group. Giving papaya fruit extract in liquid form given for 14 days.

Research result

Table 1: Test the normality of data in the intervention and control groups before and after the behavior

Variable		Group			
		Intervention		Control	
		Statistics	p-value	Statistics	p-value
Hemoglobin	Pre	0.726	0.004	0.954	0.753
	Post 1	0.884	0.206	0.964	0.847
	Post 2	0.875	0.169	0.939	0.604

The above table shows that the results of Shapiro Wilk's data normality test can be known that the hemoglobin p-value obtained is significant value <0.05 or the distribution of data is not normally distributed, so the Friedman and Post hoc Wilcoxon tests were performed.

Table 2: Analysis of hemoglobin levels in the intervention and control groups

Hemoglobin Levels	Intervention	Control
	Mean±SD	Mean±SD
Pre	10.5±0.36	10.5±0.29
Post 1	12.4±1.27	13.5±0.88
Post 2	13.0±1.08	13.7±1.08
P value	0.001	0.002

Friedman test

Based on table 2 the significance value obtained is <0.05. Thus, it can be concluded that "there are at least two different measurements". To find out which measurements are different, a Wilcoxon post hoc analysis is performed, as follows:

Table 3: Analysis of hemoglobin levels in the intervention and control groups

Hemoglobin	P value	
	Intervention	Control
Pre - post 1	0.012	0.012
Pre - post 2	0.012	0.012
Post 1 - post 2	0.176	0.779

Post Hoc Wilcoxon

Based on table 3 using the Wilcoxon test, p = 0.012 was obtained for the pre-post 1 and pre-post 2 groups, while for the post 1 and post 2 groups 0.176. Thus, it can be drawn statistically and clinically, hemoglobin levels before treatment and different from hemoglobin levels after one

week's treatment. Statistically and clinically, hemoglobin levels before treatment differ from hemoglobin levels after two weeks of treatment. Statistically and clinically, hemoglobin levels after one-week treatment were no different from hemoglobin levels after two weeks of treatment.

Discussion

Analysis of the Effect of Giving Papaya Fruit Extract on Changes in Hemoglobin Levels

The results of measurements of the effect of treatment on the first measurement, it can be concluded that treatment can increase hemoglobin levels. The hemoglobin level that was given the treatment had a hemoglobin level of 1.120 g / dl higher than the control group the difference was significant different (p = 0.001). That is because of the addition of papaya fruit extracts which are rich in antioxidants, vitamin C and Fe. This is similar to the research conducted by Desvy Yulianti using papaya fruit extract and is able to increase hemoglobin levels.

The erythrocyte age of rats is half of the erythrocyte age in humans that is 60 days and the 14 days used for papaya fruit extract is the time required for rat red blood cells in the process of replication after experiencing iron deficiency, so that changes in hemoglobin levels can be seen thereafter [12]. Increased hemoglobin levels as a result of this research are quite high, it can be caused by several factors including the conditions of the research subjects, such as gender and iron deficiency conditions, the tools used or because of the content of other substances present in papaya extract which helps the process of formation of red blood cells.

The experimental animals used in this study were female while in the research conducted by Anita Yulianti was male. The experimental animals used in the study conducted by Sasikala, Abirami and Bushara were healthy animals while in this study the animals were treated with iron-deficient treatment as conducted by Ning-Ning Siaw. Iron deficiency conditions will further increase the absorption of iron by the body.

The difference in the increase in hemoglobin levels that are high enough can also be caused by the tools used. Tools that are not standardized regularly can cause bias in the analysis process. In the diet there are iron levels. Iron is a micro mineral that is very important in the formation of hemoglobin. Stages of hem synthesis begin in the mitochondria, in the mitochondrial matrix, acid aminolevulinic synthase (ALAS) catalyzes the first step of the hem synthesis pathway, which is called a condensation reaction between glycine and succinyl coenzyme A (CoA) which produces d aminolevulinic acid (ALA). ALA is transported to the cytosol where the next step takes place. ALA dehydrate converts 2 ALA molecules into monopyrrole, pofobilinogen (PBG). The next two enzymatic steps, involving PBG deaminase and uroporphirinogen III synthase, convert 4 PBG molecules to cyclic tetrapyrrole, uroporphirinogen III. Then decarboxylation to form coproporphyrinogen III (CoPIII), which is transported to the mitochondria by an unknown mechanism [13, 14].

In this study it can be seen that in the control group there was also a significant increase in hemoglobin levels this was due to the same feeding to the intervention group and the condition of iron deficiency.

Papaya fruit extract contains flavonoid compounds. Papaya fruit flavonoid compound is a polyphenol compound that

acts as an antioxidant, which in blood cells can act as a reservoir of hydroxyl radicals and superoxide so that it protects membrane lipids and prevents cell damage. flavonoid compounds resulting from papaya extract can increase the process of erythropoiesis (formation of erythrocytes) in the bone marrow and have an immunostimulatory effect^[12].

Flavonoids are substance compounds containing polyphenolic compounds derived from plants (herbs). Flavonoids are potential antioxidants to ward off free radicals. Flavonoids have strong antioxidant activity which is an excellent hydrogen donor. Flavonoids have better antioxidant activity than vitamin C (ascorbic acid), vitamin E (tocopherol) which is a major antioxidant in the body^[15].

The intake of antioxidant compounds from papaya fruit extract numbers of free radical attacks on blood cells can be minimized and the process of blood cell formation can be increased, so that hemoglobin levels can be maintained. In addition, Desvi Yulianti's research results showed that the active ingredient of flavonoids can increase hemoglobin levels^[16].

Conclusion

Based on the results of research and discussion that has been described previously about the administration of papaya extract as an alternative to increasing hemoglobin levels in rats, it can be concluded to have an effect on increasing hemoglobin levels.

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