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Research Paper

The Effect of Given Ferrous Sulfate, Ferrous Sulfate Plus Vitamin C and Ferrous Iron with Glucose Levels and Blood Hemoglobins in Pregnant Rats

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ABSTRACT

Background: Iron Nutrition Anemia is one of the nutritional problems in Indonesia that must get serious attention. One of the prevention of anemia is by giving iron, iron is more easily absorbed with vitamin C in the intestine compared to only drinking of iron. The aim of the study was to know effect of given ferrous sulfate, ferrous sulfate plus vitamin C and ferrous iron with glucose levels and blood hemoglobins in pregnant rats.
Methods: The study was conducted using experimental study with pre and post test control group design. The sample in this study were female white rat (*Rattus novergicus*), aged 2-3 months and body weight 200-250 grams, consisted of four groups (t1 = control group, t2 = giving Fe group, t3 = giving Fe + Vit C, t4 = giving elemental Fe), sample size 28 rats and 7 rats in each group. Giving Ferro Sulfate and Vitamin C done through a sonde in female *Rattus Novergicus* rats during pregnancy from the first day of pregnancy until the gestational age reaches 18th days. In female rat said to experience pregnancy with a gestational period ranging from 20-22 days. Giving doses in each treatment group were 200 mg ferrous sulfate, 100 mg vitamin C and 60 mg ferrous iron. Hypothesis test used one-way anova. A two-tailed *P*-value of <0.05 was considered statistically significant.
Results: Blood glucose levels before and after treatment in the control group and the group giving ferrous sulfate plus vitamin C had a significant decrease in blood glucose levels while blood glucose levels before and after treatment in the ferrous sulfate group and the ferrous iron administration group had a significant increase in glucose blood levels (p <0.05). Blood glucose levels in pregnant rats after being given ferrous sulfate, ferrous sulfate plus vitamin c, and ferrous iron which has the lowest blood glucose levels were the ferrous sulfate plus vitamin c group, and those that have the highest blood glucose levels were in the ferrous iron group. Comparison of blood glucose levels in each variable can be seen only the control group that had a significant relationship to the group giving ferrous sulfate (p <0.05). Blood hemoglobin levels before and after treatment in the control group had a significant decrease whereas in the group giving ferrous sulfate, the group giving ferrous sulfate plus vitamin C and ferrous iron experienced a significant increase in blood hemoglobin levels (p <0.05). Blood hemoglobin levels in pregnant rats after being given ferrous sulfate, ferrous sulfate plus vitamin c, and ferrous iron which have the highest hemoglobin levels were in the ferrous sulfate group. Comparison of blood hemoglobin levels in each variable can be seen only the control group that had a significant relationship to the group giving ferrous sulfate, ferrous sulfate plus vitamin C and ferrous iron.
Conclusion: This analysis confirmed iron can increase blood glucose for that consumption of iron supplements without any indication wit low hemoglobin is not recommended.

Keywords: Iron, Blood Glucose, Hemoglobin, Vitamin C

INTRODUCTION

According to Health Nutrition and Population Statistics in 2013, the incidence of anemia in pregnant women occurs in all countries both underdeveloped, developing and developed countries. The highest prevalence of anemia in pregnant women is in Congo, which is 67.3%, and Ethiopia 62.68%. Indonesia is one of the developing countries that has a fairly high prevalence of iron deficiency anemia which is 44.33%. [1]

One of the factors causing iron deficiency anemia is due to lack of iron intake in food consumed every day which is characterized by hemoglobin (Hb) levels not sufficient. In pregnant women iron deficiency anemia will increase the risk of giving birth to babies with low birth weight, miscarriage, premature birth, risk of bleeding before or during labor that can cause death of mother and baby. [2]

The iron given in this research is ferrous Sulfate and ferrous iron (Fe). Ferrous sulfate is a drug in the form of iron supplements that is used to treat or prevent low iron levels in the blood (for example, for anemia during pregnancy). Ferrous sulfate is a drug commonly given by health workers to pregnant women while ferrous iron is pure iron with the chemical symbol Fe. Ferro iron is actually not given to pregnant women, but because the basic ingredient of ferrous sulfate is ferrous iron, it will ferrous iron can affect blood glucose. [3]

Food sources rich in iron and folic acid are generally found in animal protein sources such as liver, fish and meat whose prices are relatively expensive and are not yet fully affordable by most people in Indonesia. Giving iron as an important effort in the prevention and control of iron deficiency anemia. Iron is given to a pregnant woman every day during her pregnancy or at least 90 (nine thirty) tablets. [4]

Increased blood hemoglobin levels, in addition to being able to be increased by the administration of phesic substances, can also be combined with the consumption of other nutrients such as vitamin C. Vitamin C is a vitamin that is as an antioxidant. Vitamin C can also facilitate the absorption of iron in the intestine because vitamin C can accelerate the transformation of ferric to ferrous which will be used in the erythropoesis process. [5]

Hyperglycemia often occurs during pregnancy and can cause several pregnancy complications, both for the mother and fetus. Previous research showed that around 16.9% of pregnant women in the world experience hyperglycemia. [6] Iron overload is a potential risk factor for type two diabetes. [3]

The aim of the study determine the effect of given ferrous sulfate, ferrous sulfate plus vitamin C and ferrous iron with glucose levels and blood hemoglobins in pregnant rats.

MATERIALS & METHODS

Study Design and Research Sample

The study was conducted using experimental study with pre and post test control group design. The sample in this study were female white rat (*Rattus novergicus*), aged 2-3 months and body weight 200-250 grams, consisted of four groups (t1 = control group, t2 = giving Fe group, t3 = giving Fe + Vit C, t4 = giving elemental Fe), sample size 28 rats and 7 rats in each group. The sample in this study had the inclusion criteria were normal blood glucose levels 100-200 mg/dl and was alive and healthy. Exclusion criteria in this study were weight loss of rats more than 10% after the adaptation period in the laboratory and rats died and were sick (appearance of dull hair, fall or baldness and less or inactive activity, abnormal exudate from the eyes, mouth, anus or genital).

Operational Definitions

The variables of this study included independent variable are given ferrous sulfate, ferrous sulfate plus vitamin C and ferrous iron, dependent variable are blood glucose level and hemoglobins.

Data Collection Technique

This study was approved by the Ethical Committee of Medical Faculty, Universitas Andalas with registered number No : 017/KEP/FK/2019. Giving Ferro Sulfate and Vitamin C done through a sonde in female Rattus Novergicus rats during pregnancy from the first day of pregnancy until the gestational age reaches 18th days. In female rat said to experience pregnancy with a gestational period ranging from 20-22 days. Giving doses in each treatment group were 200 mg ferrous sulfate, 100 mg vitamin C and 60 mg ferrous iron. Blood glucose and hemoglobins levels measured with spectrophotometer

Data Analysis

The quantitative variables were recorded as mean and standard deviation. Hypothesis test used one-way anova. A two-tailed *P*-value of <0.05 was considered statistically significant. Data were analyzed using the SPSS version 21.0.

RESULT

Differences in blood glucose and hemoglobin levels in pregnant rats (Table 1).

Table 1: Differences in blood glucose levels in pregnant rats

Group	Blood glucose level (mg/dl)		*p*
	Before intervention (Mean±SD)	After intervention (Mean±SD)	
Control	122.05±3.47	109.5±4.66	0.001
Ferrous sulfate	109.75±7.12	116.38±6.57	0.001
Ferrous sulfate plus vitamin C	111.23±8.82	93.96±6.71	0.001
Ferrous iron	109.75±7.12	191.03±4.65	0.003

Table 1 known blood glucose levels before and after treatment in the control group had a significant decrease (p = 0.001), in the ferrous sulfate group had a significant increase (p = 0.001), in the ferrous sulfate plus vitamin C group had a significant decrease (p = 0.001) and in the ferrous iron group had a significant increase (p = 0.003).

Table 2. Changes in blood glucose levels of pregnant rats in giving ferrous sulfate, ferrous sulfate plus vitamin C and ferrous iron

Group	Blood glucose level (mg/dl)	*p*
	Mean ± SD	
Control	-12.55±6.79	
Ferrous sulfate	6.63±9.02	0.001
Ferrous sulfate plus vitamin C	-17.26±14.32	
Ferrous iron	81.28±8.91	

Table 2 showed of the four groups the average change in blood glucose levels that occurred in pregnant rats after being given ferrous sulfate, ferous sulfate plus vitamin C and ferrous iron in the control group decreased (-12.55 ± 6.79), the ferrous sulfate plus vitamin group C decreased (-17.26 ± 14.32), while the ferrous iron group experienced a very high increase (81.28 ± 8.91) and the best results were in the ferrous sulfate group only because the ferrous sulfate group was the least experienced a change in increase (6.63 ± 9.02).

Table 3: Comparison of differences in blood glucose levels in each pregnant rat variable

Group	Control (p-value)	Ferrous sulfate (p-value)	Ferrous sulfate plus vitamin C (p-value)	Ferrous iron (p-value)
Control	-	0.194	0.001	0.001
Ferrous sulfate	-	-	0.001	0.001
Ferrous sulfate plus vitamin C	-	-	-	0.001
Ferrous iron	-	-	-	-

Table 3 known each group compared to the control group did not have a significant effect on the group giving ferrous sulfate, but the control group had a significant effect on the group giving ferrous sulfate plus vitamin C and the ferrous iron group, as well as the group giving ferrous sulfate had a significant effect on the group giving ferrous sulfate plus vitamin c and

ferrous iron groups, and ferrous sulfate plus vitamin c groups had a significant effect on ferrous iron groups.

Table 4: Differences in blood glucose and hemoglobin levels in pregnant rats

Group	Hemoglobin levels (mg/dl)		*p*
	Before intervention (Mean±SD)	After intervention (Mean±SD)	
Control	11.92±0.63	10.01±0.66	0.001
Ferrous Sulfate	11.75±0.43	14.01±0.62	0.001
Ferrous sulfate plus vitamin C	11.78±0.42	14.10±0.58	0.001
Ferrous iron	11.85±0.55	13.94±0.81	0.003

Table 4 showed blood hemoglobin levels before and after treatment in the control group had a significant decrease (p = 0.001), in the ferrous sulfate group had a significant increase (p = 0.001), in the ferrous sulfate plus vitamin C group had a significant increase (p = 0.001) and in the ferrous iron group had a significant increase (p = 0.003).

Table 5: Changes in hemoglobin levels of pregnant rats in giving ferrous sulfate, ferrous sulfate plus vitamin C and ferrous iron

Group	Hemoglobin levels (mg/dl)	*p*
	Mean ± SD	
Control	-1.91±0.54	0.001
Ferrous sulfate	2.25±0.83	
Ferrous sulfate plus Vit C	2.32±0.66	
Ferrous iron	2.09±0.94	

Table 5 showed of the four groups the average change in blood hemoglobin levels that occurred in pregnant rats after being given ferrous sulfate, ferrous sulfate plus vitamin C and ferrous iron which had the best results was in the group giving ferrous sulfate (2.25 ± 0.83), ferrous sulfate plus vitamin C (2.32 ± 0.66) and ferrous iron (2.09 ± 0, 94) due to the value of hemoglobin levels in the three groups both have an increase, and the value of the increase is also almost the same, but in the control group the hemoglobin level has decreased.

Table 6: Comparison of differences in hemoglobin levels in each pregnant rat variable

Group	Control (p-value)	Ferrous sulfate (p-value)	Ferrous sulfate plus vitamin C (p-value)	Ferrous iron (p-value)
Control	-	0.001	0.001	0.001
Ferrous sulfate	-	-	0.995	0.998
Ferrous sulfate plus vitamin C	-	-	-	0.978
Ferrous iron	-	-	-	-

Table 6 known each group compared to the control group had a significant effect on the ferrous sulfate group, the ferrous sulfate plus vitamin c group and the ferrous iron group, but the ferrous sulfate group did not have a significant effect on the ferrous sulfate plus vitamin c group and the ferrous iron group, so also in the group giving ferrous sulfate plus vitamin C had no significant effect on the group giving ferro iron.

DISCUSSION

The results of the study known Blood glucose levels before and after treatment in the control group and the group giving ferrous sulfate plus vitamin C had a significant decrease in blood glucose levels while blood glucose levels before and after treatment in the ferrous sulfate group and the ferrous iron administration group had a significant increase in glucose blood levels. Blood glucose levels in pregnant rats after being given ferrous sulfate, ferrous sulfate plus vitamin c, and ferrous iron which has the lowest blood glucose levels were the ferrous sulfate plus vitamin c group, and those that have the highest blood glucose levels were in the ferrous iron group. Comparison of blood glucose levels in each variable can be seen only the control group that had a significant relationship to the group giving ferrous sulfate. Blood hemoglobin levels before and after treatment in the control group had a significant decrease whereas in the group

giving ferrous sulfate, the group giving ferrous sulfate plus vitamin C and ferrous iron experienced a significant increase in blood hemoglobin levels. Blood hemoglobin levels in pregnant rats after being given ferrous sulfate, ferrous sulfate plus vitamin c, and ferrous iron which have the highest hemoglobin levels were in the ferrous sulfate group. Comparison of blood hemoglobin levels in each variable can be seen only the control group that had a significant relationship to the group giving ferrous sulfate, ferrous sulfate plus vitamin C and ferrous iron.

Previous study showed 27 mothers with pre-diabetes 17 of them consuming enough vitamin C, their blood glucose levels are lower than those of 10 pregnant women who consume less vitamin C that is having higher glucose levels. The higher the consumption of food sources of vitamin C, it could effect the lower the blood sugar levels. [7]

Another study found the routine administration of vitamin C during pregnancy does not improve blood glucose levels. [8] Blood glucose levels in the administration of ferrous iron have an average value (191.03 ± 4.65 mg/dl), the blood glucose level in this group were the highest value compared to other groups. In this group the blood glucose increased due to the administration of iron tablets every day or once a day, continuous administration of iron without any other substance given could cause an increase in iron storage in the liver (iron overload). This increase in iron stores in the liver can cause oxidative stress in pancreatic beta cells in pregnant rats. Disruption of pancreatic beta cells causes insulin deficiency resulting in increased blood sugar levels. [9]

This study is supported by another research that oxidative stress might contribute to the incidence of gestational diabetes. Lipid oxidation and DNA damage are likely to be the pathway between iron consumption and diabetes gestational. [10]

Decreased blood glucose levels that occur in the control group are caused because during pregnancy there will be a process of growth and development of the fetus, therefore it will affect physiological changes in pregnant women. Low blood sugar levels in pregnant women can also be caused because pregnant women lack nutrition, especially carbohydrates. [11]

In the group giving ferrous sulfate plus vitamin C blood glucose levels also fell due to the total vitamin C given was 150 mg/dl. Excess vitamin C could modulate the action of insulin so that in this group blood glucose decreased. Normal vitamin C needed by the body in a day is 85 mg/dl. [12]

Based on the results of research from all treatment groups giving ferrous sulfate only is the most recommended because the administration of ferrous sulfate has the least increase, and for the group of ferrous sulfate plus vitamin C we need to consider because the value of the glucose level is much decreased, so is the case with ferro iron administration is not recommended because it is proven in this study that ferro juice can increase blood glucose levels. [13]

Previous research known there was a significant increase in hemoglobin levels that is before being given treatment of hemoglobin levels in pregnant women averaged 10.32 gr% and increased to 11.23 gr% after treatment ($p = <0.001$). [14]

Based on the analysis of researchers giving ferrous sulfate, the combination of ferrous sulfate plus vitamin C and ferrous iron in all treatment groups has an influence on blood hemoglobin levels, this is due to the presence of iron content in ferrous sulfate which has a role in the erythropoesis process. In this study, when seen as a whole the administration of ferrous sulfate and ferrous iron did not have a problem with blood hemoglobin levels. Iron administration needs to be given to pregnant women because it can be seen from the control group, where the hemoglobin level in the control group is below normal hemoglobin levels. [15]

CONCLUSION

The conclusion of this study iron can increase blood glucose for that consumption of iron supplements without any indication wit low hemoglobin is not recommended. This study suggestion for the provision of iron supplements in pregnant women, consider again by adding vitamin C just enough to take iron supplements because in the iron supplement already contains vitamin C (iron supplements given under a government program).

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