THE EFFECT OF MULTI-MICRONUTRIENT SUPLLEMENT COMPARED TO IRON FOLIC ACID TABLET TO IMPROVE IMUNOGLOBULIN G (IgG) LEVEL AMONG ANEMIC PREGNANT WOMEN IN SECOND TREMESTER

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ABSTRACT

The need for nutrients intake during pregnancy is very important to determine the quality of a child in the future. Several micronutrients take a key role for stimulating the immune system . Zinc is the most important one. This study aims to evaluate the effect of multi micronutrient (MMN) on immunoglobulin G levels of the anemic pregnant women in Second trimester, compared to iron folic acid (IFA). A single blind randomized controlled trial was conducted in Surabaya City. The samples size of 30 pregnant women were randomly allocated into two groups or 15 pregnant women in each group. Control group received iron folic acid , and the treatment group received multi micronutrient UNIMMAP formula. Either IFA or MMN was consumed daily for one month. Statistics analysis was done using Chi square test on data (age, education, income), paired t test , independent t test and the data are not normally distributed then use Mann Whitney. The results showed no significant difference in immunoglobulin G level between the two groups. It can be concluded that the administration of multiple micronutrients (MMN) cannot increase immunoglobulin G in pregnant women with anemia, this is probably due to consumption of macro nutrients that are poor compared to daily needs during pregnancy.

Key word: *Multi micro nutrient, Iron Folic Acid, Immunoglobulin G.*

INTRODUCTION

The period of pregnancy is a very important period because at this time the quality of a child is determined. Fulfillment of optimal nutrition at this time will affect the growth and development of the fetus as well as the health of the mother, if the nutritional intake of pregnant women is not sufficient, there is a possibility that growth disorders will occur in the mother and the fetus she is carrying and a decrease in the immune system in the body(1).

Immunoglobulin G is one of the immune systems found in almost all human body fluids. IgG has the basic structure of immunoglobulins consisting of 2 H heavy chains and 2 L light chains. In normal people IgG is 75% of the total amount of immunoglobulins. In normal people IgG is 75% of the total amount of immunoglobulins. Immuno globulin g functions against antigens, either viruses or bacteria, that enter the body that can cause infection(2). The Fc portion

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of IgG has a variety of biological processes starting with an immune complex that results in the destruction of foreign antigens. The immune complex consisting of cell and antibody binding to the Fc receptor on the *killer* cell initiates a cytolytic (*antibody dependent cell-mediated cytotoxicity* = ADCC) response aimed at cell-enveloped antibodies. Immune complexes that interact with lymphocytes at Fc receptors on platelets will cause platelet reactions and aggregation. Fc receptors play a role in the transport of IgG through placental cells from the mother to the fetal circulation[(3)]. So that in newborns igG comes from the mother who protects the baby against infection[(3)]. In studies conducted by experimental animals by giving zinc with the right dose of 0.25 mg can increase the production of immunoglobulin G[(4)].

As part of a global strategy to prevent micronutrient shortages in pregnant women, the United Nations Children's Fund (UNICEF) recommends the use of multi-micronutrients (MMN) for prenatal supplements as a pilot program in developing countries. Multi micronutrients contain 15 types of vitamins and minerals that are most important for pregnant women including vitamin A, vitamin E, vitamin D, vitamin B1, vitamin B2, niacin, vitamin B6, vitamin B12, folic acid, vitamin C, Fe, zinc, copper, selenium, and iodine. This study aims to find out the effect of multi-micronutrient administration compared with iron fo Acid (IFA) to the levels of immunoglobulin G in anemic second trimester pregnant women.

MATERIAL AND METHOD

This type of research is an experimental study with a single blind randomized controlled trial design. In this study, using two groups, namely the treatment group and the control group. The treatment group was given multi-micronutrient (MMN) containing 15 kinds of mineral vitamins which refer to the formula from the United Nations International Multiple Micronutrients Preparation (UNIMMAP). While the control group was given a blood supplement containing 60 mg iron and 400 μg folic acid or abbreviated as Iron Folic Acid (IFA) which is usually used in the program. The intervention was given for 1 month with a daily dose (one tablet a day). The research subjects were pregnant women who met the following inclusion criteria: agreed as respondents in the study, gestational age 12-24 weeks and had no history of chronic disease. Screening was carried out on 227 pregnant women, 151 in the Rangkah community health center and 76 community health centers in Tanah Kalikedinding.From screening with inclusion criteria, it was obtained subpopulation of 50 pregnant women. Then performed a second screening by measuring hemoglobin levels using an HB meter. From the second screening, it was found that the sub-population of anemia pregnant women were 40 samples. The pregnant woman stated that she resigned from the study of 8 people and did not want to take 2 supplements so that the sample was randomly divided into 2 groups consisting of 15 treatment groups and 15 control groups. Immunoturbidimetric assay in Parahita Laboratory to measure the level of immunoglobulin G.

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The intervention was given using multi micronutrient (MMN) and iron folic acid (IFA) prepared in tablet form which was put into a bottle with the same shape and color. Given to pregnant women after completing the initial blood draw. Supervision of supplement consumption by asking pregnant women every day and at the end of the study a check was carried out on the supplements given whether they had been drunk or not, otherwise they were excluded from the study. The initial data for pregnant women taken in this study were age, education, occupation, nutritional status, and income obtained from questionnaire interviews. Pre nutritional intake using a 24 hour food recall. Initial blood draw for immunoglobulin G levels prior to intervention. After the intervention was completed, a second blood was taken to measure the level of immunoglobulin G and asked about nutritional intake for 24 hours post food recall. The data obtained will be carried out by statistical tests with the chi square test on education, employment and income data, paired T-test to see the differences before and after the intervention, independent sample T test to see the differences between the treatment and control groups if the data is not distributed normal then use mann whitney. This research was conducted after obtaining a Certificate of Ethical Worthiness from the Health Research Ethics Commission of the Faculty of Dentistry , Airlangga University Number: number 517 / HRECC.FODM / VII / 2019.

RESULTS AND DISCUSSION

Characteristics of Research Subjects

Subjects who followed until the end of the study were 15 subjects in the treatment group and 15 subjects in the comparison group respectively.

Table 1. Characteristics of Research Subjects

Variable	Group		p
	Control	Treatment	
Age			
17-25	5 (33,3%)	5 (33,3%)	0,231
26-35	9 (60%)	7 (46,7%)	
36-45	1 (6,7%)	3 (20%)	
Education			
Elementary school	0 (0,0%)	2 (13,3%)	
Junior high school	2 (13,3 %)	1 (6,7%)	0,109
senior high school	13 (86,7 %)	9 (60%)	
university equivalent	0 (0%)	3 (20%)	
Profession			
IRT	12 (80%)	12 (80%)	
General employees	2 (13,3%)	2 (13,3%)	0,572
Traders	0 (0%)	1 (6,7%)	
Honorary	1 (6,7%)	0 (0%)	

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Nutritional status			
Less LILA <23,5	1 (6,7 %)	4 (26,7%)	0,231
Normal LILA ≥ 23,5	14 (93,3 %)	11 (73,3%)	
Income			
Height> 2.500.000	12 (80%)	8 (53,3%)	0,383
Medium 1.500.000 - 2.500.000	2 (13,3%)	6 (40%)	
Low <1.500.000	1 (6,7%)	1 (6,7%)	

Based on the analysis, there was no significant difference (p> 0,05) in the characteristics of pregnant women between the treatment and comparison groups (Table 1).

Nutritional intake

In this study, a multiple recall was carried out twice, then the results of the recall were translated into nutrients. Assessment of nutritional intake includes intake of protein, carbohydrates, fat , zinc, iron and folic acid as well as the percentage of RDA for each nutrient.

Table 2. Average Nutritional Intake of Pregnant Women

sVariable	Group				p
	Control	% AKG	Treatment	% AKG	
Protein (g)					
Pre	46,28 ± 17,91	66,07	51,83 ± 23,69	74,06	0,233
Post	48,86 ± 16,30	69,75	61,05 ± 44,30	87,16	0,623
Carbohydrates (g)					
Pre	142,86 ± 51,24	34,94	160,66 ± 68,32	41,37	0,496
Post	149,18 ± 59,20	46,53	146,30 ± 109,91	46,11	0,670
Fat (g)					
Pre	34,94 ± 15,35	53 , 44	41,37 ± 19,38	61,42	0,691
Post	46,53 ± 42,07	52.23	46,11 ± 35,19	68,46	0,394
Zinc (mg)					
Pre	4,38 ± 1,86	36,46	5,66 ± 3,50	47,08	0,530
Post	4,52 ± 1,51	37,69	5,61 ± 5,39	46,73	0,764
Fe (mg)					
Pre	4,46 ± 1,65	16,46	4,52 ± 2,00	16,70	0,050 *
Post	4,14 ± 1,32	15,30	6,08 ± 2,68	23,79	0,594
Folic acid					
Pre	90,22 ± 39,91	14,98	97,53 ± 50,54	16,22	0,100
Post	78,10 ± 40,99	12,97	148,52 ± 118,98	24,70	0,458

Note: RDA = nutritional adequacy rate , * Mean p <0,05

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The t-test results for the mean nutritional intake of pregnant women showed no significant difference (p > 0.05)), only in the intake of zinc, there was a significant difference (p <0.05) (Table 2). The average nutrient intake in the treatment group and comparison group was largely still less than the RDA. The results of the analysis of the level of nutrient consumption showed that there was no difference in intake between the treatment group and the comparison group for each nutrient (p> 0.05).

Immunoglobulin Levels

Table 3 . Simultaneous immunoglobulin G levels before and after the intervention

Immunoglobulin G levels	Control (IFA)		Treatment (MMN)	
	Before	After	Before	After
Average	1360,1	1322,4	1316,2	1302,6
Standard deviation	234,7	234,1	251,3	237,3
Minimum	1036	1034	942	1022
Maximum	1763	1756	1756	1739
P- *value paired t test*	0,115		0,379	
P- *velue independent T test*	0,625 *			
	0,819 **			

Note: * before treatment ** after treatment

The analysis showed that using the *paired t test* showed that there was no difference in the levels of immunoglobulin G before and after the intervention in the control group (p = 0,115> 0,05). In the treatment group also showed no difference in immunoglobulin G levels before and after the intervention (p = 0,379> 0,05). D ari results of independent testing of T-test showed no difference between the control group and the treatment group before (p = 0,625 > 0,05) and after (p = 0,819 > 0,05) intervention.

Nutritional intake

The results of the analysis of food intake showed that the mean intake of nutrients in the two groups was not statistically different except for zinc intake (p <0,05). Most of the intake of pregnant women is in the low category. protein, carbohydrates, fats, Fe, zinc, and folic acid have a very important role in the formation of hemoglobin. Zinc plays a role with protein in the formation of Immunoglobulin G. M. Humans who are deficient in zinc micronutrients are at risk of experiencing immune response disorders because zinc is a mitogen for lymphocytes so that zinc deficiency can result in decreased proliferation activity of lymphocytes[5].

The condition of zinc deficiency is often encountered along with the weak ability of immunity to maintain immunity[6]. In addition to inhibiting the metabolism of nutrients, zinc deficiency in plasma also causes a decrease in hypersensitivity reactions to disease entry

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accompanied by decreased phagocytosis activity and cytokine production[7]. The reduced production of cytokines, especially T helper (TH1) cells, interferon, leukocytes, and B lymphocytes, will facilitate the activity of other pathogens that enter the body's defense system. In long-term zinc deficiency, this can damage the system for regulating The activity, thereby increasing the risk of opportunistic infections[6].

The results of this research[8] stated that low-than-required zinc intake during pregnancy has 1.6 times more risk of developing anemia and a decreased immune system compared to pregnant women whose zinc needs are met.

Immunog lobuline levels G

The mean immunoglobulin G level in the treatment group before the *multi micronutrient* intervention was 1316,2 ± 251,3 gl / dl. after the intervention the average immunoglobulin G levels were 1302,6 ± 237,3 gr / dl. From these results it can be said that the administration of *multi micronutrients* could not increase the level of immunoglobulin G. Because there was a decrease in the average level of immunoglobulin G after giving *multi micronutrients* to the treatment group around 36,20 gr / dl. The mean of immunoglobulin G levels in the control group before intervention with *iron folic acid* was 1360,1 ± 234,7 g/dl. After the intervention, the average immunoglobulin G levels were 1322,4 ± 234,1 g/dl. From these results it can be said that *iron folic acid* administration cannot increase immunoglobulin G levels. There was a decrease in immunoglobulin G levels after giving *iron folic acid* to the treatment group by about 52,33 gr / dl.

The differences in immunogolulin G in the treatment group and the control group after the intervention showed that the decrease in immunogolulin G levels in the treatment group was lower than the decrease in immunogolulin G levels after the intervention in the control group. Then when viewed from one by one from the entire treatment group and the control group, there was an increase in immunoglobulin levels in 6 people (40%) of respondents in the treatment group. Whereas in the control group the increase in immunogolulin G levels was only 1 person (6,7%). However, the results of statistical tests with *independent T tests* showed that there were no differences in the levels of immunoglobulin G between the control group and the treatment group ($p = 0,498 > 0,05$).

Some micronutrients that have links with the immune system one of which is zinc. In humans, zinc deficiency has a relationship with impaired immune response because zinc is a mitogen for lymphocytes so that zinc deficiency can result in decreased proliferative activity of lymphocytes[5]. Marees states that zinc influences the innate and adaptive immune system, with zinc supplementation reversing the negative effects of zinc deficiency, including impaired immune cell development, impaired immune response mediated by T-cells, and being able to prevent allergies and autoimmunity, or even suppression of allogenic reactions[9]. Research

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conducted by Hojyo stated that the administration of zinc which forms ZIP10 (Zrt and Irt-like protein 10) functions as a regulator of B-cell receptor signaling (BCR) which is needed to regulate the humoral immune response[10]. In a study conducted by experimental animals by giving zinc with the right dose, namely 0.25 mg, it can increase the production of immunoglobulin G[4]. In the study, there was no significant increase in immunoglobulin G levels due to inadequate protein consumption as shown in table 1 . Protein deficiency has an impact on the immune response in the body, because the immune system is greatly influenced by protein consumption, the more severe the protein deficiency, the lower the immune system in the body[5].

CONCLUSION

There was no difference in decreasing immunoglobulin G levels in pregnant women with trimester II anemia between those who were given multi micronutrients compared with iron folic acid. How to maximize the effectiveness of immunoglobulin G supplementation in pregnant women is by eating foods according to the adequacy of what she recommends according to gestational age.

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