Molecular Aspects of Zinc Intake (Zn) and Selenium (Se) on Glycosylated hemoglobin (HbA1c) in patients with type 2 Diabetes Mellitus (DMT2)

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Abstract

Diabetes mellitus (DM) is a metabolic disease characterized by hyperglycemic. HbA1c is the result of the examination for glycemic control Zinc and Selenium are metaloenzim factors. play a role in the mechanism and regulation of insulin synthesis This study aims to explore the relationship between zinc and selenium with HbA1C in patients with type 2 diabetes mellitus. Cross sectional study to patients W1th type 2 diabetes rnellilus. Samples numbered 108 people conducted at several hospitals In Bandung from years 2011 to 2013. The sample was done by purposive sampling. Zinc and Selenium are collected by SOFF. HbA1c rs measured by the method of affinity chromalugrc1phy. Data were analyzeu by Fisher's Exact test and Spearman correlation (p <0.05) The study showed that there was a significant relationship between Zinc Selenium and HbA1c were s1gnifica~t1y (p <0.001). There is a relationship between Zinc and Selenium with HbA1c, so the management of diet with intake of Zinc and Selenium is needed in the regulation of patients with type 2 diabetes rnelhtus.

Keywords: Intake Zinc, intake Selenium, levels of HbA1c

1. INTRODUCTION

Diabetes Mellitus (DM) is one or the chronic degenerative diseases that the prevalence continues to increase by year to years.[1] OM is also a group of metabolic diseases by charactensties chronic hyperglycemia due to a defect m msuhn secretion, insulin or both.[2] The type 2 diabetes pathogenesis based on impaired insulin secretion by pancreatic beta cells and impaired insulin action due to insensitivity (resistance) to insulin target tissues. Shaw showed, the wortdwide prevalence of diabetes in the adult population aged 20-70 years was 6 4% in 2010, affected 287 million adults and is expected to increase to 7.7% and affected 439 million adults in 2030.~ The prevalence of OM in Indonesia rs expected lo increase from 5.1 % in 2000 to 6.3% in the year 2010.' Furthermore, Missmanagement could lead to complications and increased morbidity and mortality pasien." Glycosylated hemoglobin or (HhA1c) rs one of the laboratory tests for blood sugar control. s Persistent hyperglycemia causes glycosytation of the protein hemoglobin. It is estimated by the percentage of glycosylated hemoglobin glycation of hemoglobin (HbA1c). which are used clinically since 30 years ago to assess the degree of chronic hyperglycemia in patients with mild severe of OM.' Its value indicates the

average level of sugar in the period of 3 months; disglycemia helpful to know the characteristics of the study population because it is simple compared to oral glucose tolerance test (OGTT). In diabetes, one percent increase in HbA 1c associated with 20-30% that it would lead to increase in mortality and morbidity of the cardiovascdiscasular.[7,8]

DM management is necessary to seek the *way* the blood sugar levels closely to normal. The main pillars Is a medical nutrition therapy. Medical nutrition therapy, or better known as diet *of* meal arraniements for persons with OM is a very important factor In controlling blood suqar. Dietar; management generally still rarely pay attention to the availability and adequacy of the trace elements and bioactives food. Dieticians tend more priority to macro-nutrients such as carbohydrates. fats and proteins .Trace minerals are important for the body speofically in patients with type 2 diabetes. Dietary management generally still rarely *pay* attention to the availability and adequacy of the trace element minerals and bioactive food.

Minerals such as Zinc and Selenlurn including types of trace minerals, In the body there Is a small amount, but it has a play very vital role.[1~] This mineral belongs to a group of minerals that works as an antioxidant metaioenznn w~1ich can prevent rree radicals, increase insulin receptor sensitivity thereby potenl1ally preventing the degenerative disease [11]

Zinc for example is an clement essential for the synrhes.s, storage clnd secretion of insulin It is a component of several enzymes Zinc ha;, atso an important role in rnaintalning the balance function of mul!t1ple networks and have an important role in modulating system imun.'i Body'i; ability lo synthesize and secrete Insulin is affected by zinc in tho body, because it is involved in the mechanism of regulation and synthesis of insulin receptors "

Selenium serves as part of a protem known as S~lenoprutein. Solcnoproterin plays a role as a defensive mechanism to 0X1dative stre:,s, to regulation or thyroid hormone acuvily, and for the redox status of vitamin C and other molecules. However, note that the "therapeutic window· Sc limited. a1,d the adverse effects on health may occur due to excessive intake of Se (supra nutriuonal) or below the level required to toxicity." Selenium acts as an antioxrdant and contributes m regulating cell membrane integrity and lowering the risk of oxidative damage."' High-Se diet can stimulate the release of glucagon, promotes hyperglycemia, or can cause excess of gluthathion peroxidase-1 and other antioxidants Sdenoprotein resulting in insulin resistance and obesitas. [15] This study aims to explore the relationship between zinc and selenium with HbA1c in patients with type 2 diabetes mellitus.

2. METHODS AND MATERIALS

This study is cross sectional study design, which was implemented in January 2011 Io December 2013. The experiment was conducted at several hospitals m Bandung. Research was used all patients by type 2 diabetes who did endocrine outpatients clinic at Hospital in Bandung and incorporated Diabetes Association Members (Persadia). The samples was taken as many as 108 patients. They were obtained by purposive sampling with the following inclusion cntenas: Patients with type 2 diabetes who have a history or results of HbA tc. age <65 years. did not have a blood disorder,

as been getting nutrition education, without the complications of the disease, not regnant and was willing to be the subject of research by signing informed consent.

The eating habits questionnaire was colledted by Food Frequency Questionnaire (FFQ). This data were analyzed by Nulri survey. Nutrition intake of trace minerals such Zn, Se was collected by Food Frequency Questionnaire (FFQ). HbA1c was measured by affinity chromatography method. Processing and analysis the data was used by computer software with a significance level of p <O 05 and 95% confidence level. Data were analyzed in univariate and bivariate format. The corelation between independent variables and !he dependent variable was analyzed by non-parametric statistical analysis the Fisher Exact, Spearman correlation (p <0.05). This study has pproved by ethical clearance

3. RESEARCH RESULT

3.1 Characteristics of Samples

The study sample characteristics Include age. educational background, employment, and others in this study it is presented m Table 1.

Table 1. Distribution of the characteristics of the study sample by gender

SamplesCharacteristics	Categoryby Sox					
	Bo~		Girt		Total	
	n	%	n	%	N	%
Age						
<50 years	5	11.6	7	12,7	12	11.1
2:50 years	38	88.4	48	87,3	96	86,9
Educationlevel						
Elementary	8	18,6	52	80,0	60	55,5
Hlaher	35	81,4	13	20,0	48	44.5
Occupation						
Work	23	53,5	64	98,5	87	80,6
Unemeloy	20	46.5	1	1,5	21	19,4
Family OM History						
Yes	25	58,1	23	35,9	48	44,4
No	18	41.9	42	64,6	60	55,6
Duration suffer OM						
<5 year	19	44,2	31	47,7	50	46,3
2:5 year	24	55,8	34	52,3	58	53.7
Medical therapy						
Yes	39	90.7	59	90,8	98	90,7
No	4	9.3	6	9,2	10	9.3
Exercise (Sport)						
Yes	15	34,9	11	90,8	26	24,1
No	28	65.1	54	9,2	62	75.9
NutritionalStatus						
Normal	25	58,1	28	43,1	53	49,1
Malnutrition=	18	41,9	37	49,2	55	50,9

3.2 Intake of Zinc, Selenium and levels of HbA1c samples

Based on finding, Zinc intake showed it achieved at a mean of 8.3 ± 2.62 mg, with a minimum intake value of 5.2 and a maximum of 18 mg. The recommended dietary allowance level (RDA) of less than 80% by 56 (61.5%). The intake of selenium ~showed on lhe average position of 74.62 t 15 46 ug With a rmrumum intake value of • 41 and a maximum of 104 ug that can be seen in Table 2. The findings suggest that most of the patients were in the intake of zinc is not ideal to meet the recommended ~ nutrient required by RDA.

Table 2. Distribution of the intake of zinc, selenium intake and levels of HbA1c samples.

Variabel	Statistical analysis		
	;>:±SD	Min	Max
Zinc Intake (mg)	8,3 i 2,62	5.2	18
Baik (>80% RDA)	35 (38,5%)		
Kurang (80%RDA)	56 (61,5%)		
Selenium Intake (µg)	74,62 ± 15,46	41	104
Good (<"80% RDA)	91(100%)		
Less {<80%RDA)	0(0%)		
HbA1c Level(%)	8,4 i 2,17	5,7	15,4
Controlled (:S7%)	32(35,2%)		
Uncontrolled (> 7%)	59 (64.~"/o)		

Based on the study of HbA1c levels showed thal il achieved at the mean of 8.4 *l* 2, 17 percent which the achievement of a minimum value *of'.:,.!* and a maxlmurn of 15.4 percent. This showed that the majority or patients are at high HbA1c levels or uncontrolled regulation.

3.3 Relationship intake of zinc and selenium intake with levels of HbA1c

Based on the data analysis of the relationship intake zinc, selenium with HbA1c levels obtained the data as it is presented in Table 3 below.

Table 3. Relationship intake of zinc and selenium intake with levels of HbA1c

variabel	n	r	P
Zinc intake and HbA1c level	108	-0,482	0,001*
Selenium intake and HbA1c level	108	-0.863	0.001•

**) Kore/asi Spearman p<0,05*

Results of correlation analysis on samples of zinc intake patients with type 2 diabetes showed that zinc intake was significantly associated with HhA1c levels (r = -0.482, p <0.01). The present invention provided an indication of improvement zinc intake which meets the nutritional adequacy (RDA) can reduce HbA1c levels in patients with

type 2 diabetes. Selenium ,intake also showed significantly association with HbA 1c els (r: -0.863, p <0.05). Results of this analysis indicated that an increased intake f selenium in accordance with the level of adequacy of the advice showed a decrease of the levels of HbA1c.

3.4 Effect of intake of zinc, selenium on HbA1c

Based 011 regression analysis of the effect of the intake of zinc, selenium cigainst HbA1c levels of data obtained as follows: Levels of HbA1c = 13.6 - 0.44 (zinc mtake) - 3.03 (selenium Intake), wi'h coefficient R = 0.773 or 77.3% HbA1c is determined by lhe intake of zinc and selenium, rest influenced by other factors, namely obedience berdiit, drug consumption. exercise. heredity, habits and eating patterns (p <0.001).

4. DISCUSSION

This study has shown a significantly association between the intake of zinc with HbA1c levels. despite a weak ncgahve relationship (r: -0 4). This study also showed a statistically significant association between the intake of Selenium with HbA 1 c levels (p <0.001). These results were consistent with research conducted by Jayawardena el *al.,* 2012. lhat the better grades of zinc ,n lhe blood, then the mdividual will be in the regulatory status of OM were better, but lower when compared with the regulations on me individual non OM. ·e Song study, patients with type 2 diabetes who given ;ro-z (flour and "me) !or 3 months was able to reduce HbA1 c levels in bermakna [1]

Zin.; (Zn) Is an essential rmcronutnent that 1s needed for more than 300 different cellular processes. including DNA. protein synthesis, enzyme activity, and intracellular signaling. Require compartmentalization ol cellular homeostasis Zn into intracellular organelles, which are closely regulaled through the inteqrntion of transport mechanism [16] Zinc works as an anboxrdant to protect intracellular oxidation process produces free radicals wnich wlll also work as a synthesizer, storing and secreting a protective role insulin.[19] Zinc affect on damage pancreatic beta cells. Lack of zinc affects the beta cells of the pancreas in response lo the call of the body to produce and secrete insulin. lowers insulin secretion and improve insulin resistance.[20] If the pancreas docs not produce and secrete enough insulin ln the body's glucose levels remain high. so !hat with continued high levels or glucose in the body of the regulation of blood sugar ts not good.[71]

The role of zinc as an antioxidant is inhibition of ROS via the reduction of glucose toxicity by Zn. Zinc stimulates transcription of metatlothionein. Metallothionein itself have antioxidant effects. Zinc provides protection agarnst free radical attack immune mediators (immune-mediated free radical attack) lo protect sulfhydryl groups (SH) against oxidation. Also participaticn in the inhibition of the production or free radicals (Haber Weiss cycle) to compete with the transition metal. Zrnc contributes to stabili,dng SH by protecting proteins from oxidation. II also reduces direct and radical O_2 .OH . H_2O_2, and the level of xanthine oxidase. thereby improving mitochondrial function. This radical decline decrease lead to lipid peroxidation. Zinc also stimulates the activity ol insulin promoter PDX-1. and rnhibrts the activity of xanthine oxidase, thus reducing lipid peroxidation. [7?]

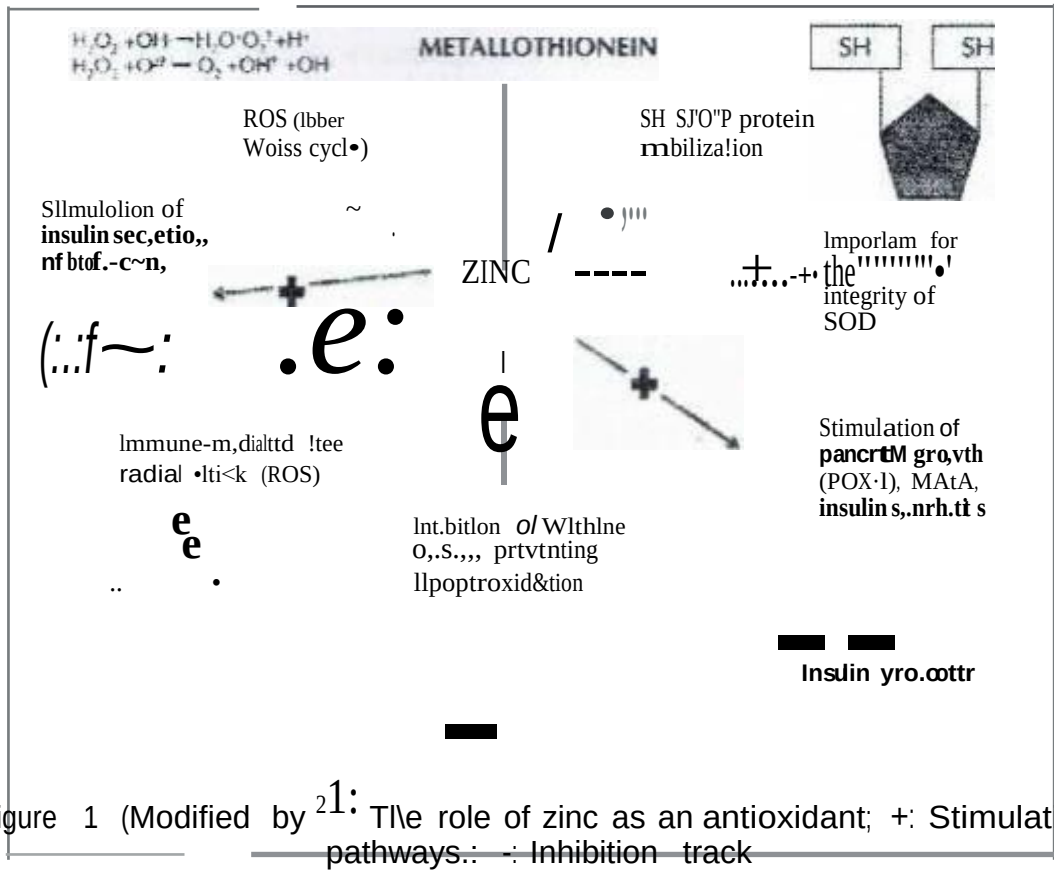

Figure 1 (Modified by [21]: Tl\e role of zinc as an antioxidant; +: Stimulation pathways.: -: Inhibition track

Research on intake of selenium (Se) in patients with diabetes, previous findings Indicated tr1.-.t contrary lo the possibihty of a relabonshlp between the level of control of diabetes and changes in the levels of this mineral. Se intake in this study was measured and the relationship between the intake and the metabolic control of di::ihetAs, as determined by glycosyiated hemoglobin (HbA1c). A negalive correlation between the intat-e 01 se ano NUA1C was touno. oome swuies :snuw,uw,:;, [73] selenium levels in the diabetic grouµ compared with the non diabetes. Subjects of research data showed that selenium plays a role in regulation of beta cell-specific target genes and potentially push the overall improvement in the function of U1e island Langerhans.[24] On the other hand, has shown that high levels of selenium are associated with the prevalence of diabetes.

In addition due Lo the intake of zinc and selenium that already meet adequacy. HbA1c levels were also influenced by other factors, including the use of pharmacological therapy The results showed that nearly all of the samples (90%) using the pharrnacoloqic therapy. Oral hypoglycemic drugs and injection drug given Lo patients with diabetes mellitus can reduce HbA1c between 05 Lo 3.5% .[25]

5. CONCLUSIONS AND RECOMMENDATIONS

This study showed an association between the intake of zinc and selenium with HbA1c levels in patients with type 2 diabetes mellitus (T2DM). It is suggested that the management of diet in patients with type 2 diabetes that it needed to pay attention to

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e intake of zinc and Se in sufficiency recommended with respect to obtain a ontrolled HbA 1 c levels. Futher research It is needed to be examined gluthathion eroxidase-1 and selenoproteins other antioxidantS such as Copper {cu) which esulted in insulin resistance and obesity.

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7. AUTHOR CONTRIBUTIONS

All authors partlcipatec in data collection, participated In the study design. statrsncal analysis and preparation of the manuscript All authors gave final approval for publication. There Is no conflect interest with any company in this research