



The effect of increasing blood glucose level on several atherogenic factors with biomolecular in diabetes mellitus type II patients

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ABSTRACT

Hyperglycemia in type 2 diabetes results in excessive production of superoxide in mitochondria damage, poly ADP ribose polymerase activity and inhibition of glyceraldehyde-3 Phosphate Dehydrogenase. These give raise to complicated reaction in the form of polyol pathway. Protein Kinase C (PKC) activation, increasing hexosamine Advanced Glycation End Products (AGES). Expression of several molecules intracellular Adhesive Molecules-1 leads to endothelial dysfunction. This study aims analyzing several atherogenic factors arising from the increase of blood glucose level in people with diabetes mellitus of type 2. Observational research with comparative sectional study in patient with diabetes mellitus of type 2 aged 30 – 60 years has been conducted. Sample of the research were conducted at 70 participants. Examination of PARP and ICAM-1 were conducted by Linked Immunosorbent Assay (ELISA) technique. Data were analyzed statistically by using t-test and chi-square. The mean of PARP activity in the type 2 DM group was 457 ± 81.34 Unit/ μ l, in non DM group it was 214 ± 75.54 Unit/ μ l. Mean of ICAM-1 concentration in DM group of type 2 was 670.93 ± 192.44 ng/ml and in non DM group it was 360.01 ± 137.56 ng/ml. concentration in DM group of type 2. There was a significant correlation between the increasing of PARP activity and the increasing of ICAM-1 concentration. In addition, there was also a significant correlation between PARP activity. ICAM-1 is atherogenic factors.

Keywords: type 2DM, hyperglycemia, endothel, PARP, ICAM-1.

INTRODUCTION

Type 2 DM is a degenerative illness that has become a significant concern in Indonesia and the rest of the world. The number of cases of type 2 DM are expected to increase very year. A patient who has type 2 DM shows abnormality in both insulin secretion and its effect [1,2]. There are 3 main reasons for the increasing number of type 2 DM patients, improved prosperity change to peoples, and reduced physical activity type 2 DM is characterized by uncontrolled hyperglycemia (glucotoxicity) with HbA1c levels $> 7\%$ and 2 hours postprandial blood glucose ≥ 200 mg/dl. The uncontrolled level of blood glucose damage the beta cells this causing a decline in insulin secretion [3,4,5]. Without treatment, the patient will suffer chronic complications, including microvascular, macrovascular and tissue damage. Insulin resistance and beta cell dysfunction are the main cause of hyperglycemia in DM type 2. High intracellular glucose and excessive mitochondrial superoxide production cause DNA damage. Damaged DNA activities poly ADP ribose polymerase (PARP) which in turn inhibits glyceraldehyde-3-phosphate dehydrogenase (GAPDH). GAPDH is essential for intracellular glycolysis. As a consequence complications in DM type 2 including effects on the polyol pathway, PKC activation through DAG, and the formation of advanced glycosylation End products (AGEs) [6,7,8]. Those reactions will increase the formation of ROS consequently expression of molecular

that cause damage to tissue increase [9,10]. Expression of Intracellular Adhesive Molecules-1 (ICAM-1), inactivates NO. In the end it induced endothelial dysfunction [11,12].

These changes affect the polyol pathway, activate protein kinase C, increase flux through the hexosamine pathway and formation of advanced glycation end product, expression of intracellular adhesive molecule -1 and nitric oxide. The end result is endothelial dysfunction [13,14,15]. The aim of this study was to observe several atherogenic factors that are affected by the increased blood glucose levels in diabetes mellitus type 2 patients. Atherogenic factors is ICAM-1 concentration.

EXPERIMENTAL SECTION

Observational research was conducted using a cross sectional study comparative on patients with type 2 DM aged 30 – 60 years old, 19 males and 16 females. The study group comprised 35 patients with type 2 DM who has postprandial blood glucose ≥ 200 mg/dl, and HbA1c level $\geq 7\%$, either the patients hospitalized at the polyclinics Internal medicine RSUP. M Djamil Padang. The control group was 35 non-DM volunteers.

Sample was taken with random block on patients type 2 DM who were hospitalized in general medicine Dr. M. Djamil hospital, Padang. Type 2 DM patients consist of 19 males and 16 females. Each patient is undergoing conducting anamnesis involving interview, smoking habit, gender, blood glucose checkup, weight, height, hip and wise circumference. Hereafter, blood glucose and HbA1c checkup were conducted. People without DM function as a comparator who got the same treatment as the patients with blood glucose level post prandial ≤ 200 mg/dl and HbA1c $\leq 7\%$. Each sample and comparator underwent vena blood taken procedure for 10 ml to measure the HbA1c level with variant hemoglobin testing system technique. In order to check up blood glucose checkup, PARP, ICAM-1 were given the form of serum.

The blood glucose of each patient was examined using an enzyme method and HbA1c level with variant hemoglobin testing system technique. PARP activation, ICAM-1 and NO level are checked with Enzyme Linked Immunosorbent Assay (ELISA) technique. Statistical analysis used t-test and chi-square.

RESULTS AND DISCUSSION

Table 1. The Characteristic of Research's Subject

Characteristic of research's subject	type 2 DM Mean \pm SD	Non DM Mean \pm SD	p
Age (years)	51,66 \pm 5,06	49,77 \pm 5,27	0,13
Body Mass Index, BMT (kg/m ²)	25,00 \pm 2,31	24,21 \pm 2,69	0,19
Blood glucose fast (mg/dl)	191,60 \pm 35,47	93,37 \pm 7,18	< 0,001
Blood glucose 2 hours PP (mg/dl)	367,77 \pm 70,68	125,06 \pm 16,01	< 0,001
HbA1c(%)	11,19 \pm 2,04	6,02 \pm 0,56	< 0,001

Table 2. The Average of PARP Activities on Patient with DM of type 2 and Non DM

Group	n	PARP activity (Unit/ μ l) Mean \pm SD	p
Type 2 DM	35	457 \pm 81,34	0,01
Non DM	35	214 \pm 75,54	

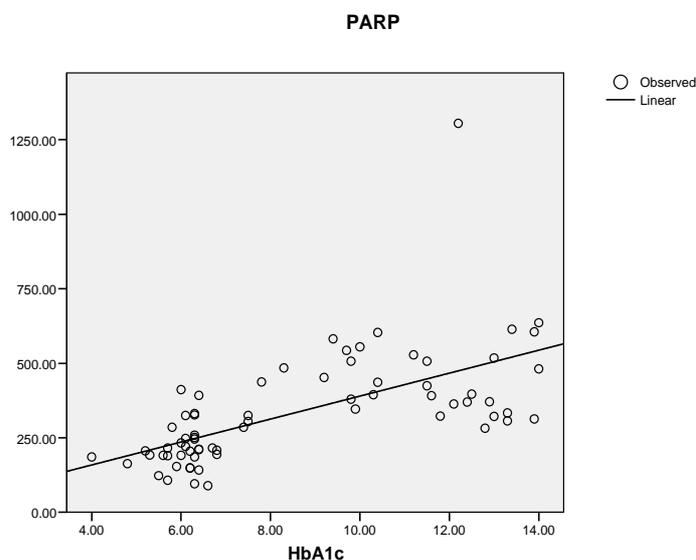


Figure 1. Correlation HbA1c with PARP activity

Table 3. The Average of ICAM-1 Level on Patients with Type 2 DM and Non DM

Group	n	Cocentration ICAM-1 (ng/ml) Mean ± SD	p
Type 2 DM	35	670,93 ± 192,44	< 0,001
Non DM	35	360, 01 ± 37,56	

There was a significant difference in NO level between patients with DM type 2 and the control non DM group ($p \leq 0,001$). A significant correlation between the increasing in PARP activity and ICAM_1 level were shown in figure 2 and 3 respectively.

The advanced of PARP level due to the increasing of Intracellular glucose levels that causes superoxide on mitochondria increase (Reusch, 2003., Brownlee, 2005). This condition leads to the destruction of DNA mitochondria and DNA nucleus [12,13]. PARP is a marker of DNA damage by catalyzing the poly-ADP-ribosylation on several core proteins as histon. The result of other researches (Reusch, 2003., Monnier *et al*, 2006) show that the increase of ICAM-1 level on patients with DM of type 2 DM occurred due to the vascular destruction as a result of excessive superoxide. The excessive superoxide in mitochondria damages the DNA, which in turn activates the PARP. The activation of PARP inhibits GAPDH that lead to PKC activation. The increase of PKC activity increases the ICAM-1 level. Glucose level in blood and in related to the damage to the corpus system as a result of repeatedly elevated glucose leads that follow food consumption.

From the result of the research, it is concluded that there were average increase of PARP activities and ICAM-1 level, on patients with DM of type 2 compared to the control of non DM. There is a significant correlation between the increasing of PARP activities with ICAM-1 level.

The result of the research could be used as guidance in conducting the treatment to patient with DM of type 2. PARP inhibitor or GAPDH activator could be developed as a treatment so that DNA damage in patients with DM type 2 doesn't inhibit the glycolysis pathway not cause *atherogenesis* factor.

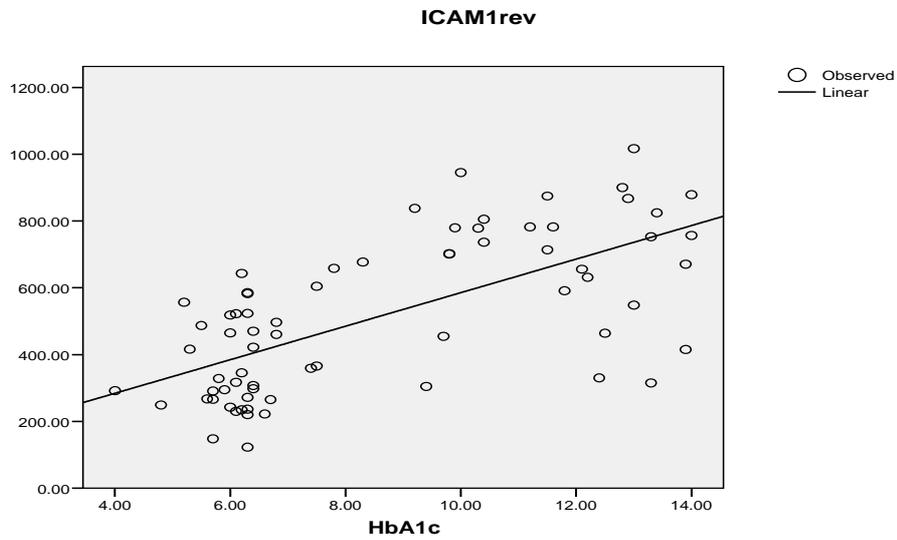


Figure 2. Correlation between HbA1c with ICAM-1 concentration

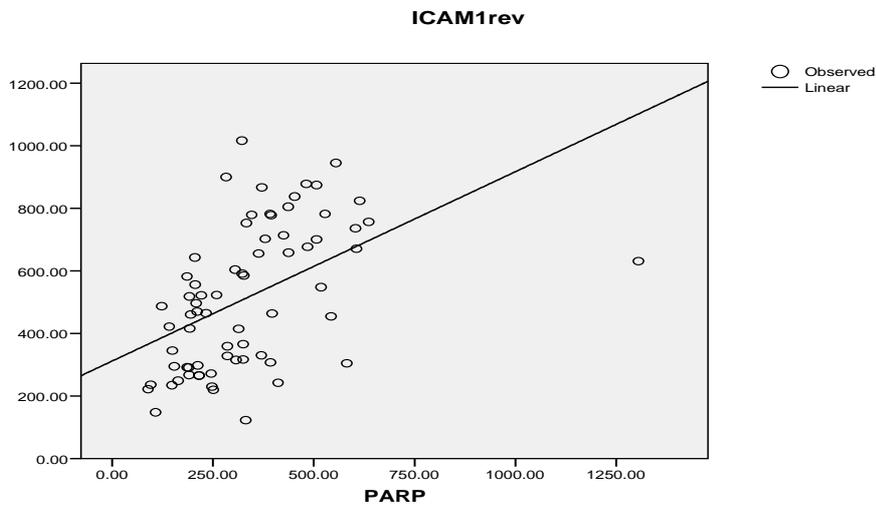


Figure 3. Correlation between PARP activity with ICAM-1 concentration

CONCLUSION

Increasing blood glucose caused increasing PARP activity, where atherogenic factor was ICAM-1 concentration.

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