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The Association between Blood Glucose Control Measured with Serum HbA1c Level with Peroneal Motor Nerve Conduction Velocity in Patients with Type 2 Diabetes Mellitus with Polyneuropathy

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Abstract

Background and Objective. The poor control of blood glucose levels in patients with diabetes mellitus is a major risk factor from various complications of diabetes mellitus, such as polyneuropathy. One of the nerves that are often affected in the case of diabetic neuropathy is the peroneal nerve. This study aimed to determine the association between blood glucose level control measured with serum hemoglobin A1c (HbA1c) levels with peroneal motor nerve conduction velocity in type 2 diabetes mellitus patients with polyneuropathy.

Methods. The study was conducted on diabetic neuropathy patients who fulfilled inclusion and exclusion criteria in neurology unit and diabetes unit Dr. Soetomo General Hospital Surabaya on a consecutive basis from February to July 2013. The serum HbA1c level and nerve conduction velocity in peroneal motor nerve were examined; then, the results were grouped into two groups which were serum HbA1c <7% and ≥7% and NCV in normal and low peroneal motor nerve

Results. There were 26 subjects, consisting of 6 subjects with serum HbA1c <7% and 20 subjects with serum HbA1c ≥ 7%. There was an association between blood glucose level control measured by serum HbA1c levels and NCV in peroneal motor nerve with statistical significance of $p = 0.0018$ (Odd ratio 15; 95% IK 1.397 - 161.045).

Conclusion. There was an association between blood glucose level control measured by serum HbA1c levels with NCV in peroneal motor nerve in type 2 diabetes mellitus patients with polyneuropathy.

Keywords: polyneuropathy, HbA1c, nerve conduction velocity, diabetes mellitus

Introduction

Diabetes Mellitus (DM) is a group of metabolic disorders characterized by hyperglycemia, due to damage to insulin secretion, insulin work, or both. Factors that contribute to hyperglycemia include reduced insulin secretion, decreased glucose use, and increased glucose

production, and the etiology of diabetes mellitus. The number of patients with DM in the world has increased. Based on the Central Bureau of Statistics' data in Indonesia in 2003, from Indonesia's population above 20 years old of 133 million people, the number of DM patients in urban areas is 8.2 million and 5.5 million in rural areas¹. Based on the pattern of population growth, it is estimated that by 2030 the population over the age of 20 is 194 million; thus, it is estimated that there are 12 million people with diabetes mellitus in urban areas and 8.1 million in rural areas. Based on the observations in Surabaya (reported in 1993), the prevalence of symptomatic diabetic neuropathy was high (51.4%), and it will increase with the duration and severity of diabetes².

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Chronic hyperglycemia in diabetes is associated with damage, dysfunction, and failure of various organs, especially the eyes, kidneys, nerves, heart, and blood vessels. Poor control of glucose levels is a major risk factor for complications of diabetes mellitus. The incidence of diabetic neuropathy is related to male gender, irregular blood sugar control and hypertension in diabetes patients³. The American Diabetes Association (ADA) recommends the A1c target of less than 7%, while the American Association of Clinical Endocrinology recommends less than 6.5%. Efficient glucose control and monitoring using HbA1c can reduce complication of diabetes efficiently⁴.

The pathogenesis of diabetic neuropathy involves many factors such as metabolic, vascular, oxidative stress, and neurohormonal growth factor deficiency. Diabetic neuropathy results from complex interactions between metabolic factors directly related to hyperglycemia and structural changes such as degeneration of axonal and demyelination caused by microangiopathy⁵. This mechanism can involve a nerve called mononeuropathy or multiple called multifocal neuropathy. Both acute and chronic damage to peripheral nerve will result in anatomical and physiological changes in the peripheral nerve and will damage the structure consisting of myelin, axons, and buffer layers⁶.

In the case of polyneuropathy, the longest nerve fibers have the highest risk of exposure, while the short fibers are less risky. Polyneuropathy is a length-dependent neuropathy, because the longest nerve fibers in the body are those that travel from the lower back to the legs; thus, in case of polyneuropathy, the initial weakness or sensory impairment is the leg. The peroneal nerve in the limb contains motor and sensory fibers; thus, in the neuropathy of the peroneal nerve, the patient may experience both sensory weakness and impairment⁷. This study aimed to determine the association between blood glucose level control measured with serum HbA1c levels with NCV in peroneal motor nerve in type 2 diabetes mellitus patients with polyneuropathy.

Method

This research was a cross sectional study by using case-by-case sampling method (sampling from consecutive admission) until the samples were collected. The study was conducted in neurology unit, diabetes unit, and electromyography room of Dr. Soetomo General Hospital Surabaya on February - July 2013.

The subjects were selected according to the inclusion criteria including patients with type 2 diabetes mellitus who had polyneuropathy (Toronto Score ≥ 5), aged 45-70 years old and willing to participate in the research. The exclusion criteria were anemia, history of alcohol addiction, had impaired renal function, impaired liver function, complication of diabetic ulcers in the legs which complicated the examination of NCV (Nerve Conduction Velocity) in peroneal motor nerve⁸.

The variables of this study included independent and dependent variables. The independent variable is blood glucose level control measured by serum HbA1c levels. Meanwhile, the dependent variables was NCV in peroneal motor nerve.

The research material was a blood sample of the veins taken when the patient visited to the electromyography room in Dr. Soetomo General Hospital Surabaya before the neurophysiology examination. The research instrument used a patient data collection sheet. Examination of NCV in peroneal motor nerve was conducted with EMG tool in electromyography room of Dr. Soetomo General Hospital Surabaya with Caldwell brand and interpreted by EMG consultant neurologist. Serum HbA1c examination was performed in laboratory that has been certified internationally for HbA1c examination which was in Prodia clinic laboratory, Surabaya⁹.

Patients with type 2 diabetic polyneuropathy were screened based on the inclusion and exclusion criteria to obtain the research samples. The samples were then examined for serum HbA1c levels and NCV in peroneal motor nerve. After obtaining the data, it was performed a statistical test to determine the association between blood glucose level control measured with serum HbA1c levels with NCV in peroneal motor nerve in patients with type 2 diabetes mellitus with polyneuropathy. The data were analyzed using a software (SPSS 17) to find out whether there was an association between two variables by using chi square test¹⁰.

In this study, the normal value of NCV in peroneal motor nerve was >40 mm/msec according to the standards applied in the Electromyography room Dr. Soetomo General Hospital Surabaya by using the Caldwell tool. The analysis was divided into two groups: NCV in peroneal motor nerve >40 mm/sec (normal) and ≤ 40 mm/sec (slowing). Each patient in this study obtained two results of NCV in peroneal motor nerve:

the right and left side. For analysis purposes, if both sides obtained a normal result, it was considered normal. Meanwhile, if both sides or one side were slower, it was considered to experience a slowdown¹¹.

Result

The overall subjects of the study were 26 subjects consisting of 9 males (34.6%) and 17 females (65.4%), whereas in the HbA1c $\geq 7\%$ group, 7 (77.8%) males and 13 females (61.5%) (table 1). The gender difference in each group was not statistically significant ($p = 0.668$). Mean age of DM patients with polyneuropathy with HbA1c $< 7\%$ was 56.67 ± 6.861 years old while DM patients with polyneuropathy with HbA1c $\geq 7\%$ was 56.90 ± 5.486 years old (table 1). The mean age difference in each group was not statistically significant ($p = 0.693$).

From DM patients with polyneuropathy with HbA1c $\geq 7\%$, 9 (69.2%) were suffering from DM < 10 years old and 11 subjects (84.6%) suffered from DM ≥ 10 years (table 1). The difference in percentage of long-suffering DM was not statistically significant ($p = 0.645$). From DM patients with polyneuropathy with HbA1c $\geq 7\%$, 11 (73.3%) had normal serum TG level and 9 (81.8%) had high serum TG level (Table 1). The percentage difference in serum TG level was not statistically significant ($p = 1.000$).

In low NCV in peroneal motor nerve group, 6

subjects (66.7%) were males and 10 subjects (58.8%) were females (table 2). Different percentage of gender in each group was not statistically significant ($p = 0.668$). The association between long-suffering DM and NCV in peroneal motor nerve was shown in Table 2. In DM subjects with polyneuropathy with low NCV in peroneal motor nerve, 8 subjects (61.5%) suffered from long-standing DM < 10 years and 8 subjects (61.5%) suffered DM ≥ 10 years old. The difference in percentage of long-suffering DM in both groups was not statistically significant ($p = 1.000$).

The association between the serum triglyceride (TG) level and NCV in peroneal motor nerve was shown in Table 2. In DM patients with polyneuropathy with low NCV in peroneal motor nerve, 9 (60%) had normal serum TG levels and 7 (63.6%) had high serum TG levels. The difference in percentage of serum TG levels in both groups was not statistically significant ($p = 1.000$).

The association between serum HbA1c levels and NCV in peroneal motor nerve was shown in table 2. In DM patients with polyneuropathy with low NCV in peroneal motor nerve, there was 1 subject (16.7%) whose serum HbA1c levels were $< 7\%$ and 15 subjects (75%) whose serum HbA1c $\geq 7\%$. The percentage difference was statistically significant with $p = 0.018$. The value of odd ratio was 15, with a confidence interval range of 1,397 - 161,045 (95% CI).

Table 1. The characteristics of research subjects

	HbA1c level		Total N= 26	p
	< 7 % N = 6	$\geq 7\%$ N = 20		
Gender				
Male	2 (22.2%)	7 (77.8%)	9 (100%)	0.668
Female	4 (23.5%)	13 (61.5%)	17 (100%)	
Age	56.67 ± 6.861	56.90 ± 5.486		0.693
Period of suffering from DM				
< 10 years	4(30.8%)	9 (69.2%)	13 (100%)	0.645
≥ 10 years	2(15.4%)	11(84.6%)	13 (100%)	
Serum TG level				
Normal	4 (26.7%)	11 (73.3%)	15 (100%)	1.000
High	2 (18.2%)	9 (81.8%)	11 (100%)	

Table 2 The association between gender and nerve conduction velocity (NCV) in peroneal motor nerve

	NCV in peroneal motor nerve		Total n= 26	p
	Normal N = 10	Low N = 16		
Gender				
Male	3 (33.3%)	6 (66.7%)	9 (100%)	0.668
Female	7 (41.2%)	10 (58.8%)	17 (100%)	
Period of suffering from DM				
< 10 years	5(38.5%)	8(61.5%)	13 (100%)	1.000
≥10 years	5(38.5%)	8(61.5%)	13 (100%)	
Serum TG level				
Normal	6 (40%)	9 (60%)	15 (100%)	1.000
High	4(36.4%)	7(63.6%)	11 (100%)	
Serum HbA1c level				
< 7%	5(83.3%)	1 (16.7%)	6 (100%)	0.018
≥ 7%	5 (25%)	15 (75%)	20 (100%)	

Discussion

In the basic data characteristics of research subjects, there was no significant difference in several basic variables including gender and age. It needs to be taken into account because gender and age affect HbA1c values. A study revealed that males had a greater prevalence of DM than females (7.5% males, 3.4% females, $p < 0.001$). However, in elderly (> 66 years), it occurs in more females. Long-suffering from DM also affects HbA1c levels, as stated in the study that HbA1c levels significantly increased with duration of DM. In addition, it is stated that hypertriglyceridemia may decrease HbA1c. Age and gender can affect nerve conduction velocity, as stated that subjects with elder age have longer latency, smaller amplitude, and slower nerve conduction velocity than young subjects¹².

Females have a higher amplitude at the examination in the upper extremities, shorter latency of upper extremities, and longer latency in lower extremities than males. Long-suffering from DM also affects the velocity of the nerve conduction, as it is stated that

the occurrence of a microvascular complication of DM along with the duration of DM is associated with low nerve conduction velocity¹³. Triglyceride levels can also indirectly affect the velocity of nerve conduction. Hyperlipidemia is important in the development of diabetic polyneuropathy, as elevated serum triglyceride level correlates with decreased myelin fiber density which is independent of other variables such as age, DM length, DM control, and other variables. Therefore, this study attempted all subjects in relatively similar conditions, with the expectation of minimizing the influence of other factors that will affect the value of the variables studied¹⁴.

Other factors that affect HbA1c are anemia, impaired renal function, alcohol addiction as well as factors affecting nerve conduction velocity, such as kidney function impairment and alcoholism have been attempted to be controlled by researchers through several components of exclusion criteria. The results of this study statistically obtained a significant association between serum HbA1c levels with peroneal motor nerve conduction velocity. In DM patients with polyneuropathy

with low peroneal motor nerve conduction velocity, there was 1 subject (16.7%) whose serum HbA1c levels were <7% and 15 subjects (75%) with serum HbA1c levels \geq 7%. The percentage difference was statistically significant with $p=0.018$. The results of this study also obtained the value of Odds ratio of 15 with the range of confidence interval 1.397 - 161.045; thus, it is concluded that serum HbA1c \geq 7% is a risk factor for low peroneal motor nerve conduction velocity¹⁵.

It is in accordance with a study by Shekharappa et al., which mentions that there is progressive neuronal damage in DM patients triggered by poor blood glucose control, in which the researchers compared the nerve conduction velocity between DM patients and non-DM patients¹⁶. The wide range of confidence intervals in this study could be due to small sample size or basic data characteristics such as long-term suffering of DM, ranging from 1 year to 20 years, although in the analysis, the duration of DM is categorized into two groups¹⁷.

Conclusion

There was an association between blood glucose level control measured by serum HbA1c levels with peroneal motor nerve conduction velocity in type 2 DM patients with polyneuropathy.

Ethical Clearance: This research involves participants in the survey using sampling method that was accordant with the ethical research principle based on the regulation of research ethic committee. The present study was carried out in accordance with the research principles. This study implemented the basic principle ethics of respect, beneficence, nonmaleficence, and justice.

Conflict of Interest: The authors swear that there is no conflict of interest related with this paper.

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