Association of Gamma-GT Serum and Nerve Conduction Velocity of Nervus Peroneus Motor Vehicles on Diabetic Polyneuropathy Patients

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Abstract

Background and Objectives: Diabetic Polyneuropathy is one of the common complications of diabetes mellitus (DM) and can lead to foot ulcers or amputation. The pathophysiology of Diabetic Polyneuropathy includes several factors such as metabolic, vascular, autoimmune, oxidative stress and neurohormonal growth-factor deficiency. The recent studies have suggested the use of serum gammaglutamyl transferase (GGT) as an early marker of oxidative stress. Therefore, we investigated whether serum GGT may be useful in predicting Diabetic Polyneuropathy.

Methods: The study was conducted in patients with diabetic polyneuropathy who meet the criteria for inclusion and exclusion in neurological outpatient clinic and EMG room departments of Neurology Dr.Soetomo General Hospital Surabaya consecutively started in June 2014 to April 2015.

Result: We obtained 20 study subjects (8 subjects with increased serum levels of gamma GT and 12 subjects with normal serum levels of gamma GT). There was statistically no significant between serum levels of gamma GT with motoric nerve conduction velocity (NCV) of peroneal nerve (p = 0.582 ; Odds ratio 0.600).

Conclusion: There was no relationship between elevated levels of serum gamma GT with decreased motor nerve conductivity velocity peroneal nerve in patients with diabetic polyneuropathy.

Keywords: *Polyneuropathy, Gamma GT, Motoric, Nerve Conduction Velocity*

Introduction

Neuropathy is a classic complication of diabetes. Distal polyneuropathy is the most frequently progressive diabetic neuropathy that progressively manifests slowly, symmetrically with glove and stocking patterns [1]. Neuropathy is most common in diabetics patients age over 50 years, rarely happen in age under the 30s and very rarely in children [2].

Neuropathy is a major complication of diabetes that conduces in high morbidity rates. There is a strong association between hyperglycemia and progression of neuropathy reported in many studies. Oxidative stress plays an important role in the etiology and pathogenesis of diabetes. There is a change in the production of reactive oxygen species (ROS) in mitochondria and antioxidant defense systems of mitochondria [3]. Hyperglycemia, auto-oxidation of glycated proteins, increased production of reactive oxygen species (ROS), decreased antioxidant

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defense, increased lipid peroxidation and membrane degeneration are the main causes of apoptosis or necrosis, which is common in diabetes [4].

The process of oxidative stress causes damage to cells and occurs in several types of cells in the nerves, including neurons (in axons and nerve terminals), glial cells, vascular endothelial cells. There are many changes that trigger the activation and recruitment of macrophages, which causes an inflammatory mechanism of stress and cell death. Until there is a difference from cellular stress happened that causes cell dysfunction or death and shows clinical manifestations as a neuropathy [5].

Early detection of diabetic neuropathy is very important in diabetes patients because prevention could reduce morbidity and mortality, but there is no gold standard to diagnose polyneuropathy. The San Antonio consensus recommends that a diagnosis of polyneuropathy should be measured in at least one of the five categories that measured by symptom scores, physical examination scores, quantitative sensory testing (QST), cardiovascular autonomic function (cAFT) and electrodiagnostic [6]. Therefore, this study aims to determine the correlation of serum Gamma-GT levels and the nerve conduction velocity of Motor Peroneus Nerve in Diabetic Polyneuropathy Patients.

Methods

This study is cross-sectional to determine the association between serum Gamma-GT levels and motor peroneus nerve conduction velocity in type 2 of diabetes mellitus (DM) patients with polyneuropathy. This research was conducted between June 2014 to April 2015 in Nerves Unit of Dr. Soetomo General Hospital, Surabaya. The sample of the study was diabetic polyneuropathy patient who had outpatient treatment. The inclusion criteria were; patients suffering from diabetic neuropathy based on the Toronto criteria, <65 years old, were willing to participated in the study. As for the exclusion criteria were patients who have liver disorders, kidney disorders, heart problems, history of alcohol consumption, and obesity. The sampling technique of this study using consecutive sampling [7].

This research procedure begins when all the subjects included in the inclusion criteria and the responsible family of the patient are informed of the purpose, usefulness, and the risk of the study. At the end of the explanation, the subject or family was asked to read and ask questions about things that have not been understood. If they have understood and agreed, they were required to sign an approval letter [8]. Subjects who have signed the letter of consent recorded their identity and characteristics in the form. The data collection of research subjects was conducted by author and residents in training, with the following steps: a careful history, physical examination and neurologic, sample selection for appropriate cases of inclusion and exclusion criteria, recording of eligible samples and all clinical data required [9].

All the data collected was processed statistically using SPSS 22.0 (SPSS. Inc. Chicago IL). Univariate data analysis was used to describe each variable, either independent or dependent variable from case group and control group with frequency distribution table. The bivariate analysis was used to determine whether there a relationship between two variables, or can also be used to determine whether there a difference between independent variables with dependent variables by using chi-square test [10].

For interpretation of results, this study uses the degree of significance (α) of 5%, with a note if $p < 0.05$ then Ho is rejected, if $p > 0.05$ then Ho accepted [11]. While to know the amount of risk factor, then used Odd ratio analysis (OR) with interpretation as follows; if OR = 1 means that the variable suspected as a risk factor has no effect on the occurrence of an effect, if OR> 1 and the range of confidence interval do not include number 1, then the exposure is a risk factor of effect, if OR <1 and the range of confidence interval do not include number 1, then the exposure under study can reduce the occurrence of effects (preventing factors) [12].

Result

In this research, there were 20 subjects of DM polyneuropathy patient that consisting of 11 subjects with normal Gamma GT levels, the rest was not normal and from 20 subjects it was obtained an increase of NCV (nerve conduction velocity) by 8 subjects while the rest decreased. The mean age was 51.85 years with standard deviation ± 4.793 using the Kolmogorov-Smirnov test 0.548 ($p > 0.05$) indicating that the normal distribution

(Table 1).

Table 1. The relationship between age and and nerve conduction velocity (NCV) peroneus nerve motor

	Nerve Conduction Velocity	p
	Averange Std.Dev	
Age	51.85 ± 4.793	0.548

The overall subjects of the study were 20 subjects consisting of 4 men (20%) and 16 women (80%), wherein the group NCV (nerve conductivity velocity) decreased by 2 (50%) men and 6 people (37.5%) of women, whereas in the normal KHS group there were 2 (50%) male and 10 female (62.5%). The sex differences in each group were not statistically significant (p = 0.648) (Table 2)

Table 2. The relationship between sex , DM duration, TG serum duration and nerve conduction velocity (NCV) peroneus nerve motor

	Nerve Conduction Velocity		**p**
	Decreased	**Normal**	
Sex			0.648
Male	2 (50%)	2 (50%)	
Female	6 (37.5%)	10 (82.5%)	
DM duration			0.292
>10 Years	3 (60%)	2 (40%)	
<10 Years	5 (33.3%)	10 (66.7%)	
TG serum duration			
Normal	5 (55.6%)	4 (44.4%)	0.199
Increased	3 (27.3%)	8 (72.7%)	

In the subject group of DM polyneuropathy with decreased KHS has obtained 3 subjects (60%) who suffered DM >10 years and 5 subjects (33,3%) who suffer from DM <10 years, while patients with normal NCV got 2 subjects (40%) who suffered DM 10 years and 10 subjects (66.7%) who suffered from DM <10 years old. The percentage difference in lengths suffering from DM was not statistically significant (p = 0.292) (Table.2). The subjects of polyneuropathy DM with NCV decreased by 5 people (55.6%) with serum triglyceride (TG) level and 3 (27.3%) patients whose serum TG levels increased while the patients with normal NCV were 4 (44.4 %) with normal serum TG levels and 8 people (72.7%) whose serum TG levels increased. The percentage difference in serum TG levels was not statistically significant (p = 0.199) (Table 2).

Serum Gamma-GT levels with NCV decreased by 5 subjects (45.5%) that considered as normal and 3 subjects (33.3%) with elevated levels. While, serum

Gamma-GT level with normal NCV was 6 subjects (54.4%) as normal and 6 subjects (66,7%) with increasing rate. The association of serum Gamma-GT levels with nerve conduction velocity in diabetic polyneuropathy patients was not statistically significant with p = 0,582. The value of Odds ratios obtained was 0.600, with a confidence interval range of 0.097 - 3.720 (CI 95%) (Table 3).

Table 3. The relationship between serum Gamma GT levels and nerve conduction velocity (NCV) peroneus nerve motor

	Nerve Conduction Velocity		p	OR
	Decreased	Normal		
Gamma-GT serum level			0.582	0.600 (CI : 95% ; 0.097 – 3.720)
Normal	5 (45.5%)	6 (45.5%)		
Increased	3 (33.3%)	6 (66.7%)		

Discussion

Based on the theory, on normal subjects, age and sex might be affected NCV. Older subjects had longer latency, smaller amplitude, and slower NCV than the younger subjects. While in female is have a higher amplitude, and difference in latency in each extremity than male. In one study 15% of people with type 2 diabetes had symptoms of neuropathy and almost 50% obtained NVC deceleration. Another case-control study with electrocardiographic-Nerve Conduction Velocity (EMG-NCV) test obtained significant differences in age and sex in diabetic neuropathy patients compared to normal control. However, this study found no significant association between age, and sex of NCV in diabetic polyneuropathy patients [13]. This result was possible because of the research method used differently from previous studies.

The duration of DM patients also has an effect on the nerve conduction velocity, as in previous studies on the presence of complications of DM microvascular along with the length of DM associated with low nerve conductivity. Triglyceride levels also indirectly affect the nerve conduction velocity, hyperlipidemia is important in the development of diabetic polyneuropathy because elevated serum TG levels correlate with decreased myelin fiber density, independent of other variables such as age, DM length, DM control, and other variables [14].

In this study, there was no significant correlation between duration of type 2 diabetes and triglyceride levels with peroneus nerve conductive motor velocity in diabetic polyneuropathy patients. This was because there were differences in study design where this study using cross-sectional study that only shows the condition of the patient during the examination, while the process of poly polyneuropathy was a chronic process [15].

Theoretically, there is a close relationship between serum gamma-GT concentration and diabetic polyneuropathy in type 2 DM patients. This correlation also inversely proportional to nerve conductivity velocity [16]. It was mentioned that the higher serum gamma-GT the lower the speed of nerve conduction. In a study that comparing the group of type 2 DM with the normal group showed a significant increases in serum gamma-GT ($P < 0.001$) in all DM type 2 groups, whereas serum gamma-GT levels in diabetic polyneuropathy patients, were significantly increased compared to type 2 DM

patients with velocity normal nerve conduction (65.7 Vs 40.6 IU/L, P = 0.002). The results of this study did not statistically found a significant relationship between serum Gamma-GT levels and nerve conduction velocity of motor peroneus. This may be due to different types of studies with previous studies, patients with controlled blood sugar, and may require a larger sample [17].

Conclusion

Based on the result of the research, it can be concluded that there was no correlation between serum gamma-GT level and nerve conduction velocity of motor peroneus in diabetic polyneuropathy patients.

Ethical Clearance: The research process involves participants in the survey using a questionnaire 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 author reports no conflict of interest of this work.

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