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Research Article

The Relationship Between Phase Angle Obtained from the Maximum Reactance and Fasting Glucose, Hemoglobin A1c in Type 2 Diabetes Mellitus

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Abstract

Aim: The phase angle obtained from the maximum reactance (PA max) is a better potential indicator than the phase angles obtained from multiple frequencies. Our aim in this study is to investigate the correlation of PA max with fasting glucose and hemoglobin A1c in Type-2 Diabetes Mellitus (T2 DM).

Material and Methods: The study was conducted prospectively, two groups were formed as T2 DM (n=75) and healthy controls (n=32) and their demographic variables were examined. Right hand, left hand, right leg, left leg, hand leg and leg leg segment measurements were taken with electrical impedance method and phase angle was obtained at maximum reactance. Correlations with fasting glucose, hemoglobin A1c and other variables were examined.

Results: Fasting glucose, glycated hemoglobin A1c, age, body mass index, body fat percentage were found to be significantly higher in the T2 DM group compared with the healthy group. However, RH PA max, RL PA max, LL PA max, H_L PA max, and L_L PA max values were found to be significantly lower than in the healthy group. In T2 DM group, hemoglobin A1c was found significantly negative correlated with PA max in all segments, while fasting glucose is negatively correlated with all segments except LH Pamax.

Conclusion: PA max is significantly reduced by the impaired glycemic index in T2 DM and is a potential marker reflecting metabolic status.

Keywords: Phase angle, diabetes mellitus, fasting glucose, hemoglobin A1c

INTRODUCTION

Type-2 Diabetes Mellitus (T2 DM) is a chronic metabolic disease characterized with hyperglycemia associated with decreased insulin secretion or effect. The International Diabetes Federation drew attention to the fact that approximately 571 million adults (20-79 years old) were diagnosed with diabetes in 2021, of which 95% were T2 DM (1,2). The prevalence of T2 DM in Turkey has increased significantly with each passing day, reaching 13.7% (3). Serious micro and macrovascular complications may develop if hyperglycemia cannot be controlled (4). There is a need to investigate the negative effects of the uncontrolled glycemic index at the metabolic and cellular level.

Recently researchers started to use bioimpedance analysis (BIA) to examine the metabolic status of T2 DM. BIA is a non-invasive, inexpensive, and easy-to-apply method that measures body compositions and cellular health levels based on the electrophysiological characteristics of the human organism (5). It provides data on muscle and fat mass, total protein and mineral ratios, intracellular and extracellular fluid amount and hydration status (6). Along with these, phase angle (PhA) is a commonly used BIA parameter in clinical studies. It gives useful information

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about cellular health and shows the electrical activity and functioning of cell membranes. PhA is closely related to the metabolism of the human body (7). It can vary according to the age, sex, ethnicity, physical activity, and health status of an individual.It is mainly between 3-15 degrees (8,9). High levels of PhA indicate increased reactance and low resistance, which reflects healthy or intact cell mass. Low levels are associated with decreased energy storage and a decline in the selective permeability of cell receptors at the cellular level (10).

PhA is used as a diagnostic and prognosis indicator in diabetes mellitus, sepsis, malignancies, cirrhosis, and renal diseases (11-14). Significant relationships were found between the use of oral hypoglycemic agents and low phase angle in elderly diabetic male patients (15). In hemodialysis patients, PhA is found to be lower in diabetic nephropathy patients compared to non-diabetic hemodialysis patients, and PhA is also found to be an independent marker for heart failure (16). It is also associated with diabetes mellitus complications, progression, and disease duration (17).

Recently, the phase angle obtained from maximum reactance (PA max) has become more objective in clinical studies. Because PA max is the best indicator of the body's electrical resistance and reactance. It is easily obtained from BIA instruments and it is calculated by the arc-tangent formula of the ratio of reactance (Rc) to resistance.It has the potential to replace multi-frequency analysis variables (11).

PhA and PA max is directly related to the cell membrane. However, PA max is independent of the PhA obtained from multi frequencies and better reflects metabolic status and glycemic regulation. There are limited studies investigating the relationship between impaired glycemic index and PA max in T2 DM patients. Our aim in this study is to examine the relationship between fasting glucose and hemoglobin A1C (HbA1C) and PA max.

MATERIAL AND METHOD

This single-center, prospective study was approved by the Kırsehir Ahi Evran University Faculty of Medicine Clinical Research Ethics Committee (Date: 07.06.2022, Decision No: 2022-11/112). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.Informed consent forms were obtained from all patients.Our study included 107 participants, 75 had T2 DM and 32 were healthy controls. The study was conducted between August and October 2022. Venous blood samples from the forearm of all participants were obtained in the morning after at least 8-10 hours of fasting. The blood collected in non-anticoagulant gel tubes was centrifugedat 2000 g for 10 minutes after coagulation for 30 minutes. Studies were performed on an autoanalyzer (AU 5840; Beckman Coulter, California., USA) using routine laboratory methods. Fasting glucose levels were examined. Glycated hemoglobin (HbA1c) level was studied from blood samples taken into K2EDTA tubes. HbA1c was measured using high-performance liquid chromatography (HPLC) (Premier Hb9210; Trinity Biotech, Co.Wicklow, Ireland). Variables were compared between groups.

Bioimpedance analysis

The study was performed using a Tanita MC-780MA device in both groups after 8-10 hours of fasting (Tanita Europe BV Hoogoorddreef 56e 1101 BE, Amsterdam, The Netherlands). The height, sex, and age of the participants were entered into the analyzer. Participants were asked to stand on the analyzer with bare feet in such a way that the electrodes on the scale were in contact with the soles of the feet. At the same time, they were asked to hold the handpieces with their bare hands such that the electrodes on the handpieces were touching the palms of their hands, and to wait in an upright position, motionless and steady until the results appeared on the screen. Age, sex, body weight (kg), body mass index (BMI), muscle and fat percentage of the groups were examined. Maximum reactance PA max was obtained from six different segments: right hand (RH), left hand (LH), right leg (RL), left leg (LL), hand-leg (H_L), and leg-leg (LL). used as a variable.

The PAmax variables obtained from each segment were compared between the groups. In addition, the correlation of PAmax values with fasting glucose, HbA1C, age, BMI, muscle (%) and fat ratios (%) were examined.

Exclusion Criteria

The presence of malignancy, bone marrow or primary diseases, anemia, pregnancy, acute or chronic infection, smokers, conditions causing acute metabolic disorder, cardiac arrhythmia, and pacemakers were excluded from the study.

Statictical Analysis

Statistical analyzes of the study were performed using Statistical Package for Social Sciences for Windows (IBM SPSS version 28.0, Armonk, NY, USA) software. The normality assumption of continuous variables was tested with Kolmogorov-Smirnov and Shapiro-Wilk tests. Homogeneity of variances was done by the Levene homogeneity test. Descriptive statistics of the variables are given as Arithmetic Mean±Standard Deviation. In the study, group comparisons were made using the Independentet t test. Relationships between variables were examined by Pearson correlation analysis. The sample size of the study was calculated by using Priori power analysis. Tail (s)=Two, Effect size d=0.6, α=0.05, Power (1-β err prob)=0.85, Allocation ratio N2/N1=1 taken while calculating the sample size. Priori power analysis while calculating the sample size of the study was performed with the G*Power 3.1.9.7 (Franz Foul, Unversitat Kiel, Germany) program.

RESULTS

The distribution of genders by groups is homogeneous (p>.05). Descriptive statistics of the groups and group comparisons are given in Table 1. Age, BMI and body fat (%) ratios of T2 DM are significantly higher than the healthy group (p<.001). However, T2 DM group's H_L PA max (p=.002), RL PA max (p<.001), LL PA max (p<.001), RH PA max (p=.015), L_L PA max (p<.001) values were lower than the healthy group. These values are statistically significant. In addition, the body muscle (%) ratios of healthy individuals are higher than Type 2 DM (p<.001). HbA1C and fasting glucose values were higher in T2 DM group (p<.001).

Correlations between PA max and other variables in the T2 DM group are given in Table 2. According to these results, there is a negative significant correlation between the age of the patients and H_L PA max, RL PA max, LL PA max, RH PA max, LH PA max and L_L PA max. There is no statistically significant relationship between BMI and segmental PA max (p>.05). There is a positive correlation between muscle (%) values and H_L PA max, RL PA max, LL PA max, RH PA max, LH PA max, L_L PA max. Fat (%) ratios were negatively correlated with H_L PA max, RL PA max, LL PA max, RH PA max, LH PA max and L_L PA max, H_L PA max, RL PA max, LL PA max, RH PA max, LH PA max and L_L PA max were negatively correlated with HbA1c .There was a negative correlation between fasting glucose and H_L PA max, RL PA max, LL PA max, RH PA max, L_L PA max.The relationship between LH PA max and fasting glucose was not statistically significant (p>0.05).

Table 1. Demographic, biochemical and PA max variables of the groups

Variables/Groups	Healthy n=32(29.9%)	T2 DM n=75(70.1%)	p
Gender, Male, n(%)	15(46.9%)	28(37.3%)	0.357#
Age	29.96±10.38	57.52±10.34	<0.001*
BMI	23.51±3.96	30.50±5.22	<0.001*
Fasting Glucose	97.03±8.32	183.16±67.82	<0.001*
HbA1C	5.41±0.29	8.54±2.02	<0.001*
Muscle (%)	75.08±7.05	65.43±7.65	<0.001*
Fat (%)	20.93±7.40	31.10±8.04	<0.001*
H_L PA max	6.23±0.78	5.70±0.77	0.002*
RL PA max	5.97±0.88	5.04±0.92	<0.001*
LL PA max	5.87±0.84	4.92±0.85	<0.001*
RH PA max	6.84±0.84	6.38±0.87	0.015*
LH PA max	6.65±0.76	6.36±0.72	0.070*
L_L PA max	6.04±0.82	5.06±0.85	<0.001*

*: independent t test, #: chi-square test
DM: diabetes mellitus, BMI: body mass index, HbA1C: glycated hemoglobin, PA max: phase angle at the maximum reactance value
H_L: hand_leg, RL: right leg, LL: left leg, RH: right hand, LH: left hand, L_L: leg_leg

Table 2. Correlation findings between segmental PA maxs and other variables in Type-2 DM

Variables	Fasting Glucose	HbA1C	Age	BMI	Muscle(%)	Fat(%)
H_L PAMAX	-0.274**	-0.330**	-0.356**	-0.006 NS.	0.320**	-0.318**
RL- PAMAX	-0.368**	-0.433**	-0.477**	-0.133 NS.	0.358**	-0.356**
LL- PAMAX	-0.385**	-0.469**	-0.515**	-0.141 NS.	0.384**	-0.383**
RH- PAMAX	-0.346**	-0.363**	-0.316**	-0.029 NS.	0.321**	-0.320**
LH- PAMAX	-0.188NS.	-0.230*	-0.221*	0.094 NS.	0.236*	-0.233*
L_L- PAMAX	-0.398**	-0.485**	-0.532**	-0.164 NS.	0.404**	-0.402**

*: correlation is significant at the 0.05 level, **: correlation is significant at the 0.01 level, N.S.: non-significant correlation
DM: diabetes mellitus, BMI: body mass index, HbA1C: glycated hemoglobin, PA max: phase angle at the maximum reactance value
H_L: hand_leg, RL: right leg, LL: left leg, RH: right hand, LH: left hand, L_L: leg_leg

DISCUSSION

Studies have been made between PhA and impaired glycemic index in diabetes, but it has been limited to PA max. However, PA max is the best indicator of cell receptor integrity and health. It is a parameter independent of various frequencies adopted by BIA devices (18). In our study, PA max levels were found to be significantly lower in the T2DM group compared to the healthy group (Table 1), PA max tended to decrease as fasting glucose level and HbA1C levels increased (Table 2). According to these results, we can say that an impaired glycemic index negatively affects cell receptor integrity and cellular health level.

In a study including patients with T1 DM, T2 DM, and control subjects, Buscemi et al. showed that the total body PhA obtained at 50 kHz was lower in the diabetes group (19). Buffa et al. received the phase angle from a single frequency using the standard positions of the outer and inner electrodes on the right hand and foot. They showed the presence of a lower phase angle in diabetic patients compared to healthy controls, and reported that this is a diagnostic and prognostic marker (20). In a study conducted by Jun et al, PAmax measured in the RA, LA, RL, and LL were found to be significantly lower in patients with T2 DM regardless of sex compared with the control group (11).

In our study, HbA1C decreased significantly in all segments in T2 DM group, and fasting glucose significantly decreased PA max in all segments except LH (Table 2). Ditmar et al. reported that phase angle is an indicator of catabolism in T2 DM and is negatively correlated with HbA1C (17). In their study including 321 patients with T2 DM, Choi et al. reported that phase angle measured at 50 kHz had an independent relationship with fasting glucose and HbA1C (21).

Age factor negatively affected PAmax in all segments as in HbA1c (Table 2). Buscemi et al. found a significant and independent relationship between age and PhA in a study that included patients with T1 DM and T2 DM (19). Jun et al. also found that the phase angle decreasesd as the age of patients with diabet increased and the duration of the disease increased (22).

In addition, it was revealed that while muscle percentage had a positive effect on PA max in T2 DM, fat percentage had a negative effect (Table 1). Other studies reported an increase in fat ratio and a decrease in muscle mass due to hyperglycemia (23). PA max tended to increase when muscle mass increased or fat mass decreased. Studies have found that PhA is positively correlated with muscle content and negatively correlated with fat ratios (24,25).

Studies with PhA in diabetes have generally been carried out at certain frequencies and in a limited number of segments (17,19-21). In our study, however, PA max was obtained independently of frequencies and was significantly lower in all segments except LH compared to the healthy group. This result may show that PA max reflects the metabolic status better in Type-2 DM and may be an important marker in diagnosis and prognosis. In addition, we are aware that fasting glucose and HbA1C as well as age and fat percentage negatively affect PAmax. Age is a non-changeable risk factor. However, by regulating blood glucose and reducing fat percentages, PA max levels can be increased and cellular health levels can be improved. We suggest investigating the factors affecting PAmax and the use of PAmax in the examination of metabolic status, diagnosis, and prognosis in type-2 DM.

CONCLUSION

PA max is a potential marker that can be easily obtained from BIA devices independently of multiple frequencies and reflects the metabolic status in T2 DM. Impaired glycemic index, age, and body fat percentage significantly reduce PA max. It can be used as a diagnostic and prognostic marker in clinical practice.

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Conflict of Interest: *The authors have no conflicts of interest to declare.*

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