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Original Article

Correlation of High Density Lipoproteins and Cerebral Vasomotor Reactivity in Healthy Individuals

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Abstract

Objective: Cerebral Vasomotor Reactivity (VMR) which reflects cerebrovascular autoregulation is impaired in stroke patients. Some risk factors for stroke such as hyperlipidemia affects endothelial layer of vessels and by disturbing of VMR make an important role in the occurrence of stroke. The aim of this study is to evaluate High-Density Lipoproteins (HDL) effects on VMR of cerebral vessels.

Materials and Methods: Sixty healthy male volunteers (<45 years old) without vascular risk factors history were evaluated in Tabriz Imam Reza Medical Center Northwest Iran, during a 12-month period. The participants were divided into three nearly equal groups with low HDL level (<40 mg/ml), normal HDL level (40-50mg/ml) and high HDL level (>40 mg/ml). The mean flow velocity of both middle cerebral arteries (MCA) was continuously measured by Transcranial Doppler (TCD) and VMR of MCA was calculated by breath-holding index (BHI).

Results: Mean BHI of left MCA in persons with low, normal and high HDL levels were 1.32 ± 0.44 %/sec, 1.47 ± 0.65 %/sec and 1.18 ± 0.48 %/sec respectively. Mean BHI of right MCA in low, normal and high HDL groups were 1.13 ± 0.35 %/sec, 1.39 ± 0.62 %/sec and 1.36 ± 0.55 %/sec, respectively. There was no statistically significant difference among these groups (p>0.05).

Conclusion: The current study showed that there was no statistically significant correlation between serum HDL level and BHI in left and right MCA of healthy persons.

Keywords: HDL, Vasomotor reactivity, TCD, Breath-holding index

Introduction

Stroke is a common neurological disabling disorder that is the second cause of mortalities in developing countries and the fifth cause of mortality in the United States [1,2]. Some risk factors such as age, sex hypertension, diabetes, smoking, obesity, coronary artery disease, contraceptive drugs, alcohol and hyperlipidemia participate in stroke incidence. According to epidemiological studies, by increasing in age the incidence of the disease is increased while the occurrence in men is more than women [3]. Hyperlipidemia affects vessels endothelium and leads to atherosclerosis [4]. Cerebral vessels Vasomotor Reactivity (VMR) that has a direct relationship with cerebral vessels auto regulation is the main factor in cerebral infarction [5]. Hyperlipidemia is one of the important factors that affect VMR,

so it seems that that to study the low-density level (LDL), high-density level (HDL) and atorvastatin on VMR is an important issue [6]. Several studies have been conducted on LDL and the effect of atorvastatin. However, there is no investigation about the effect of HDL on cerebral vessels vasomotor reactivity. Therefore, the present study was to point out HDL level effects in VMR of cerebral vessels in healthy individuals.

Materials and Methods

In this descriptive study, sixty healthy men under 45 years old without vessels risk factors like hypertension, diabetes, smoking, coronary and cerebral vessel disorder history from staff of Tabriz Imam Reza Hospital, northwest Iran and also medical students were studied. These individuals did not

consume drugs effective on vessels and they were prevented from drinking tea and caffeine. According to serum HDL level, individuals were divided into three groups including: 17 persons with HDL <40 mg/dl, 20 persons with normal HDL (40-50 mg/dl) and 23 persons with HDL >50 mg/dl. Breath holding index (BHI) test was employed to measure cerebral vessels VMR using Transcranial Doppler (TCD) ultrasonography (TCD system multidop X4, Germany). Individuals were positioned in lying down condition and a special hat was used for fixing of probes. Then, both left and right MCA signals were obtained in depth of 45–55 mm using 2MHZ probe through temporal windows. TCD system showed Mean Blood Flow Velocity (MBFV) of both arteries as two curves were pointed by different colors continuously. The basic amount of blood flow velocity after 5 minutes rest time was determined up to 30 seconds and it was considered as rest. Individual was asked to hold 30 seconds his breath after normal breath. The persons, who could not do that, were asked to hold breathing as much as possible. MBFV was recorded in last three seconds and it was considered as V_{max}. This procedure was repeated after 5 minutes rest and mean of these two values was used for calculation. In order to calculate BHI the following formula was employed:

$$BHI = \frac{V_{max} - V_{rest}}{Seconds\ of\ breath\ folding} \times 100$$

BHI is related directly on MBFV and shows the cerebral vessels blood flow velocity increase when breath-holding. Normal limit for BHI is $1/2 \pm 0/6$ percent per second.

A questionnaire was used to investigate daily activities through the week. Based on this questionnaire individuals were divided into A, B, C groups, daily activities result was offered according to the amount and hours of activities. Metabolic equivalent (MET) was obtained by calculation of individual metabolic activity on metabolic condition ratio in the rest period. MET indicated the level of calories consumption in complete rest period. Group A consisted individuals <3 MET activities, group B involves 3-6 MET and group C consists of > 6 MET.

Activities less than 3 MET involved cooking, reading and watching TV. Activities of 3-6 MET consisted of rapid walking, light and extension exercise and activities more than 6 MET involved sports such as tennis, mountain climbing and basketball [7]. Also, a special form was prepared for every subject and information about age, height, weight, body mass index (BMI) was registered. Individuals were filled written consent and the study was approved by ethical committee of Tabriz University of Medical Sciences (TUOMS).

Data were entered in SPSS software version 11.5 to be statistically analyzed and descriptive method was employed for data analysis. Also, one-way ANOVA and T-tests have been employed for quantitative comparison and chi-square test was used for qualitative comparison. In order to find out the existing correlation among variables, Pearson correlation coefficient and in case of necessity Spearman correlation were applied and to test data normality Klomogorov- Smirnov test was used. $p<0.05$ was considered significant.

Results

In total 60 healthy men were studied and were divided into three groups based on HDL serum level. Table 1 summarizes groups and variables; there is no statistical significant difference among parameters of groups.

Comparison of BHI level in three groups after omission of cases with 130 mg/dl LDL is shown in Table 2.

BHI and serum HDL levels

In the left MCA, the correlation between BHI level and serum HDL was not significant in total individuals (p=0.489, r=-0.094). Also, correlation between BHI level and groups by HDL 40 mg/dl (p=0.974, r=0.009) and HDL≥50 mg/dl (p=0.520, r=0.149) was not significant. In the right MCA, the correlation between BHI level and serum HDL was (p=0.178, r=0.178) and the difference in groups by HDL 40 mg/dl (p=0.462, r=-0.191), HDL<40mg/dl (p=0.055, r=0.447) and HDL≥50mg/dl (p=0.162, r=0.067) was not significant.

BHI & HDL40 mg/dl and HDL>40 mg/dl

In terms of left MCA, in group with HDL 40 mg/dl (p=0.974, r=-0.009) and HDL>40 mg/dl (p=0.467, r=-0.118) statistical meaningful correlation was not observed between BHI and serum HDL. In the right MCA, in first group (p=0.464, r=-0.191) and second group (p=0.417, r=0.129), there was no meaningful correlation between BHI level and serum HDL.

BHI & LDL ≤ 130 mg/dl and LDL >130 mg/dl

In the left MCA, there was no significant correlation between BHI level and serum HDL in group with LDL130 mg/dl (p=0.431, r=-0.122) and LDL>130mg/dl group (p=0.914, r=-0.035). In terms of right MCA, in first group (p=0.104, r=0.24) and second group (p=0.905, r=-0.039), there was no significant correlation between BHI level and serum HDL.

BHI & triglyceride ≤ 200 mg/dl and triglyceride > 200 mg/dl

In the left MCA, in group with triglyceride200 mg/dl (p=0.748, r=-0.051) and triglyceride>200 mg/dl group (p=0.547, r=-0.176), there was no significant correlation between BHI level and serum HDL. In the right MCA, there was no statistical meaningful correlation between BHI level and serum HDL in first group (p=0.096, r=0.251) and second group (p=0.926, r=-0.026).

Discussion

Investigations have showed that VMR impairment could occur in cerebral infarction patients [8,9]. HDL impacts on vasomotor function [10], plaque activation [11], clot formation [12], cellular viscosity, proliferation, apoptosis and cellular cholesterol homoeostasis. Also, it gains cholesterol from peripheral media and transfers it into the liver to biliary acid production [13]. In Kuvin et al, study, the relationship between HDL and peripheral vessels vasomotor function was investigated. It was concluded that peripheral vessels response on vasodilator factors was reduced in 40 > HDL compared with

Table 1: Studied parameter in three groups based on serum HDL

	HDL ≥40 mg/dl (n=17)	40 mg/dl>HDL>50 mg/dl (n=20)	HDL ≥50 mg/dl (n=23)	p-value
Age (year)	27.29±4.03	28.25±4.91	28.13±5.22	0.809
BMI (kg/m²)	24.79±1.94	24.44±3.94	23.13±2.82	0.191
Level of body activity				
A	14 (82.4%)	18 (90%)	22 (95.7%)	
B	2 (11.8%)	2 (10%)	1 (4.3%)	
C	1 (5.9%)	0	0	
LDL (mg/dl)	93.71±27.22	104.55±32.69	101.74±25.18	0.411
TG (mg/dl)	137.41±102.16	164.10±63.05	141.04±71.91	0.523
L-MCA BHI	1.32±0.44	1.47±0.64	1.18±0.48	0.240
R-MCA BHI	1.13±0.35	1.39±0.62	1.36±0.55	0.292

BHI: Breath Holding Index, BMI: Body Mass Index, HDL: High-density Lipoprotein, LDL: Low-density Lipoprotein, TG: Triglyceride

Table 2: BHI in three groups based on serum HDL excluding cases with LDL ≤130 mg/dl

	HDL ≤40 mg/dl	40 mg/dl>HDL <50 mg/dl	HDL≥50 mg/dl	p-value
L-MCA BHI	1.37±0.42	1.50±0.66	1.16±0.5	0.227
R-MCA BHI	1.13±0.36	1.45±0.65	1.42±0.54	0.226

BHI: Breath Holding Index, HDL: High-density Lipoprotein, LDL: Low-density Lipoprotein

40 HDL individuals. Also, HDL considered as flow-mediated (FMD) predictive factor. In this study, the relationship between FMD and HDL was strong in men. It was established that vessels basic diameter were different levels of HDL [10]. The Toikka et al, showed a similar relationship between HDL levels by peripheral vessels VMR [14]. According to the previous studies, there is a difference in BHI of individuals in BHI < 27s and BHI > 27s. Zovorea and Demarin showed that there is no difference between BHI in men and woman, however, it reduce by increasing in age [15].

Conclusion

According to our results, in a normal person, changes in HDL level do not have effect on VMR. It seems that by the passage of time, endothelium exposure to HDL and anatomic changes in the vessel can affect VMR. So study of elderlies may lead to different results.

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