Turk J Med Sci
34 (2004) 43-48

CLINICAL INVESTIGATION

Body Fat Distribution and Plasma Lipid Profiles of Patients with Multiple Sclerosis

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Received: 13.03.2003

Abstract: This study was performed to determine the body fat percentage, fat distribution and plasma lipid-cholesterol levels of patients with multiple sclerosis (MS). We compared the body fat percentage, distribution and lipid profile in 22 patients with definitive diagnosis of MS and age and height matched 16 healthy control subjects on normal diets. Poser criteria was used to determine the MS diagnosis. Body fat percentage and distribution were evaluated anthropometrically by measuring skin fold thickness from 7 different reference points of the body. The parameters of the body composition were obtained by using the equations of Durning, Womersly and Siri. Body fat distribution was calculated by using Mueller's formulation. The plasma levels of total cholesterol, high-density lipoprotein-cholesterol (HDL-C), low-density lipoprotein-cholesterol (LDL-C), very low density lipoprotein-cholesterol (VLDL-C) and triglycerides were measured spectrophotometrically in patients and healthy volunteers. The mean body fat percentage of male MS patients was significantly the lower than in the male controls ($P < 0.05$). Body mass index and lean body mass of MS patients did not differ from the controls of either sex. The ratio of central to peripheral body fat was lower in all MS patients. Although male patients had a lower ratio, the difference with the control group was not statistically significant. The ratio of upper to lower body fat in male patients was significantly higher than in the controls ($P < 0.05$). This difference was not present in the female population. Mean plasma total cholesterol levels were slightly higher in MS patients than in healthy volunteers, but this was not significant. Mean plasma HDL-C and LDL-C levels of the MS patients were not statistically different from the values of the controls. The levels of plasma VLDL-C and triglycerides of patients were significantly higher than the levels of healthy subjects ($P < 0.05$). Our results show that total subcutaneous fat stores of the body were diminished in male MS patients. Truncal and lower body fat of MS patients was reduced and upper body fat was increased when compared to the controls. Plasma levels of VLDL-C and triglycerides were also found to be higher in MS patients. It is considered that lipid metabolism can be influenced by MS. Further studies are needed to investigate how the fat storage process changes and to understand the importance of alterations in the plasma lipid profile in the course of MS.

Key Words: multiple sclerosis, lipid metabolism, body mass index, body composition

Introduction

Multiple sclerosis (MS) is a major demyelinating disease, with an unknown etiology, affecting white matter of the central nervous system and medulla spinalis (1,2). Many factors have been associated with its prognosis (3-14). Among these factors, feeding habits and body composition are especially important and these topics have been studied recently (6,7,14-19).

The negative effects of excessive animal fat consumption in MS patients were first determined by Swank et al. in 1950 (5-7). A patient was also reported who had a disorder of the fatty acid metabolism similar to that of MS (20). It has been thought that MS can alter the lipid metabolism and body fat storage and distribution (21-26). Inflammation in chronic illness is generally related with the alteration in body composition including weight loss, decreases in total body fat and increases in central fat deposition (27,28). The increasing production of interleukin-1 can at least in part be responsible for this kind of body composition alteration. Interleukin-1 might increase plasma triglycerides and LDL and cause abnormal

fat distribution by inhibiting lipoprotein lipase activity (27). It is also known that central fat deposition is associated with the atherogenic plasma lipid profile, including increases in LDL and triglycerides and decreases in HDL (29,30). Additionally, centripetal fat deposition and increases in total body fat negatively affect general health (21,31-36). This study was designed to assess the importance of abnormal fat distribution and deposition and plasma lipid profile changes in MS patients.

Materials and Methods

In this study, to determine the body fat percentage, distribution and plasma levels of total cholesterol, triglycerides, HDL-C, LDL-C and VLDL-C were evaluated in MS patients and healthy subjects of similar ages. Poser criteria were used by diagnosing definitive MS and the motor capacity of the patients was evaluated by Kurtzke expanded disability status scale (EDSS), in a range from 0.5 to 5.5. Diet in both groups was similar and contained normal amounts of animal fats. All persons in both groups were not taking drugs and were not suffering from any metabolic disorder that might affect plasma levels of lipid-cholesterol and body fat stores.

Body fat percentage and distribution were evaluated anthropometrically by measuring skin fold thickness from 7 different reference points of the body. The parameters of the body composition were obtained by using the equations of Durning, Womersly and Siri. Body fat distribution was calculated by using Mueller's formulation. Calibrated balance scales with divisions of 100 g and 0.5 cm were used for weight and height measurements. Body mass index (kg/m^2) was calculated by dividing the body weight by the square of the measured height. On all subjects, 7 skinfold measurements were obtained from the left side of the body with a skinfold caliper (Servier, France). All the measurements were made by the same physician (SÇ). Skinfold thickness measurements were performed on standard anthropometrical reference points such as the biceps, triceps, subscapular, abdomen, suprailiac, thigh and calf. Using the equations of Durning and Womersly, body density estimations were derived from skinfold thickness measurements. Parameters obtained by using the algorithm of the sum of 4 skinfold thickness measurements (biceps + triceps + subscapular + suprailiac) were sex specific (35-40). The formula of body density for males was 1.1631- (0.0632 x log Σ 4Sf) and for females. It was 1.1599 – (0.0717 x log Σ 4Sf). The equation given by Siri was used to estimate body fat percentage from the 4 skinfold thickness measurements. The Siri equation for estimation of body fat percentage is [4.95/(body density x 4.50)] x 100 (35). To evaluate the subcutaneous truncal fat mass, the following equation of Mueller was used: the ratio of central to peripheral fat distribution: [(subscapular + suprailiac + abdomen) / (biceps + triceps + thigh + calf)]. To estimate the upper body fat deposition, the ratio of upper to lower body skinfold thickness measurements was calculated by using the following equation; the ratio of upper to lower body fat distribution: [(biceps + triceps + subscapular) / (suprailiac + thigh + calf)] (22).

Blood samples from all subjects were collected from the antecubital vein between 08.00 and 10.00 hours. Plasma was separated by centrifuging blood at 4000 rpm for 15 min. Plasma total cholesterol level was measured by using the enzymatic end point method (Randox CH 201 kit). Plasma triglycerides were determined by the GPO-PAP method (Randox TR 212). Plasma HDL-C levels were assayed by the fully enzymatic cholorimetric method (Randox CH 2655). Plasma LDL-C and VLDL-C levels were calculated by using the Freidwold formula. An Olympus AV 800 spectrophotometer (Germany) was used for all lipid assays.

Statistical Analyses: Data are expressed as mean ± standard deviation of mean. The Mann-Whitney U test was used for statistical analyses.

Results

The mean ages of the male and female patients (n: 12/10) were 38.4 ± 2.6 and 35.7 ± 4.7 years, respectively. The mean ages of the healthy male and female volunteers (n: 8/8) were 39.3 ± 3.0 and 41.0 ± 4.1 years, respectively. The differences between the mean ages of males and females in both groups were not statistically significant. The mean height of patients was not statistically different from the healthy subjects of both sexes. The mean weight and body mass index (BMI) of male MS patients were found to be slightly lower than those of male healthy volunteers, which was not significant. Mean weight and body mass index were slightly higher in female patients compared to female controls, but the difference was not statistically

significant (Table 1). Mean height, weight and body mass index of MS patients were not significantly different from those of the control subjects (Table 1). The body fat percentage of male MS patients was significantly lower when compared to healthy male subjects ($P < 0.05$). In females there was no significant difference in body fat percentage between MS patients and healthy volunteers. The lean body mass of MS patients and healthy volunteers were similar in both sexes. The ratio of central to peripheral body fat distribution of female MS patients was significantly lower than that of the female controls ($P < 0.05$), but the same observation did not apply to the males. The ratio of upper to lower body fat distribution was significantly higher in male MS patients ($P < 0.05$). This parameter in female MS patients was slightly lower, but not significantly different from that in healthy subjects (Table 1). Mean duration of disease was 8.2 ± 3.1 years.

Mean plasma levels of total cholesterol, triglycerides, HDL-C, LDL-C and VLDL-C of progressive MS patients and healthy volunteers are given in Table 2.

The plasma levels of triglycerides and VLDL-C levels were significantly higher in progressive MS patients than those of the controls (Table 2). The mean plasma total cholesterol level of patients was found to be slightly higher in the patients group, but differences between the patients and controls were not statistically significant. Plasma HDL-C and VLDL-C levels were not different from those of the controls.

Table 1. Some anthropometric characteristics of MS patients and control subjects. (Mean values ± standard deviation of means)

Variable	Patient Group (n: 22)		Control Group (n: 16)		Statistical Analyses	
	Male	Female	Male	Female	In Males	In Females
	12	10	8	8		
Age (years)	38.42 ± 2.60	35.70 ± 4.7	39.3 ± 3.0	41.0 ± 4.1	NS	NS
Height (cm)	170.17 ± 5.71	157.60 ± 1.72	171.00 ± 9.54	159.14 ± 6.79	NS	NS
Weight (kg)	69.00 ± 12.44	61.80 ± 11.10	69.14 ± 12.23	58.57 ± 9.13	NS	NS
BMI (kg/m^2)	23.83 ± 3.77	24.85 ± 4.18	23.48 ± 2.26	23.63 ± 2.97	NS	NS
Body Fat Percent (%)	13.33 ± 3.84	21.89 ± 3.86	17.96 ± 1.15	21.81 ± 4.55	$P < 0.05$	NS
Lean Body Mass (kg)	59.63 ± 10.16	47.94 ± 6.89	58.05 ± 7.14	45.78 ± 6.86	NS	NS
Central/ Peripheral Body Fat	0.87 ± 0.20	0.57 ± 0.15	1.00 ± 0.17	0.87 ± 0.15	NS	$P < 0.05$
Upper/Lower Body Fat	1.02 ± 0.22	0.83 ± 0.22	0.82 ± 0.20	0.65 ± 0.18	$P < 0.05$	NS

Table 2. Plasma lipid profiles of progressive MS patients and healthy controls (Total cholesterol: T.Chol, Triglycerides: Trigly).

	Control Group		Patient Group		Statistical Analyses	
	Male	Female	Male	Female	In Male	In Female
T.Chol (mg/dl)	172.50 ± 35.38	177.25 ± 21.53	206.40 ± 20.43	192.33 ± 30.06	NS	NS
Trigly (mg/dl)	118.00 ± 27.93	101.00 ± 54.10	151.40 ± 37.90	241.00 ± 121.50	$P < 0.05$	$P < 0.05$
HDL-C (mg/dl)	64.00 ± 16.43	51.75 ± 14.22	57.60 ± 4.93	51.67 ± 8.04	NS	NS
LDL-C (mg/dl)	87.50 ± 23.87	101.25 ± 11.03	118.60 ± 19.03	87.67 ± 17.00	NS	NS
VLDL-C (mg/dl)	21.00 ± 7.62	24.25 ± 10.87	30.30 ± 7.40	48.17 ± 25.34	$P < 0.05$	$P < 0.05$
LDL-C/HDL-C	1.36 ± 0.36	1.95 ± 0.32	2.05 ± 0.28	1.69 ± 0.30	$P < 0.05$	NS

Discussion

Our results indicated that the mean body fat percentage of male MS patients, except for female patients, were significantly lower and the mean plasma levels of triglycerides and VLDL-C were found to be significantly higher than those of the controls ($P < 0.05$). These findings support the consideration that lipid metabolism and body fat mass changed in MS disease.

It is widely accepted that relative excess truncal and upper body fat is associated with atherosclerotic cardiovascular disease (29). Changes in body composition generally occur along with the activation of the immune system by chronic illness characterized by tissue injury and inflammation (29). Inflammation in chronic illness leads to the release of cytokines such as interleukin-1, and tumor necrosis factors responsible for alterations in body composition including weight loss, decreases in total body fat and increases in central fat deposition (27,28). The effect of interleukin-1 on abnormal fat distribution can be related with the inhibitory effect of lipoprotein lipase activity leading to increased levels of plasma triglycerides and LDL (27). It is also known that central fat deposition is associated with atherogenic plasma lipid profile including increases in LDL, triglycerides and decreases in HDL (29,30). The loss of body weight and fat in chronic illness can be strongly related with the lipolyses and connective tissue remodelity as well as an increasing of the protein turnover effect of the tumor necrosis factor (27). However, interleukin-1 beta also has an anabolic effect on connecting and visceral muscle tissue. Its anabolic effect can be related with stimulation of the production of platelet-derived growth factor, which cause a proliferation of fibroblasts and muscle cells (27). In other words, immobility is considered a causal factor for decreases in muscle mass (13,14,26). Formica et al. reported that nonambulatory patients with MS had reduced fat-free mass. It was emphasized that deficits in fat-free mass were associated with the severity of MS. The decrease in fat-free mass can be related to the development of the skeletal muscle atrophy in this illness. According to this hypothesis, MS leads to weakness resulting from atrophy of the skeletal muscles due to the reduction in total mitochondrial content per volume of contractile machinery (31). In this study, there was no significant difference in lean body mass between MS patients and control subjects. These findings were the opposite of the results expected.

Our results show that total subcutaneous fat stores of the body were diminished in male MS patients and truncal-lower body fat was reduced and upper body fat was increased when compared to the controls. These findings contradicted our expectations, as diminished daily motor activity is regarded as a predisposing factor to total body and truncal fat accumulation. However, Petejan et al. reported that the body fat percentage of MS patients was not lower than the normal ranges of a healthy population.

Some authors emphasized that lipid metabolism abnormalities are not only limited to the myelin sheet, but changes that affect the plasma lipid profile can also be seen in MS patients (8,15,19,20,41-49). In a limited number of studies, it has been suggested that the alteration in the plasma lipid profile is a causative factor for the progression of MS by interfering with the formation of MS plaques (6,7,12,14,41,46). The changes in plasma lipid profile can be considered the stimulating factor for the development of neurovascular pathologies, which are shown by near by MS plaques (12-14,19,42,45,46).

In previous studies, it has been shown that diets rich in saturated fat are strongly associated with the progression of MS (1,3,5-8,10,17,43,47). It was reported that a diet poor in animal fat, but rich in essential fatty acids was useful for preventing the progress of MS (5-8,13-15,18,41,47,49). Differences in plasma lipid profiles between MS patients and controls obtained in this study are not associated with the difference between the diet of MS patients and healthy controls because the diet compositions were similar in both groups. The other reason for the differences in plasma lipid profiles may be the difference in intensity and/or duration of motor activity between the 2 groups. It is known that lipid catabolism increases with metabolic activity severity due to physical activity, but we have not encountered any study evaluating the relationship between the alterations in plasma lipid and decreased motor activity in MS. The third reason for the changes in the plasma lipid profile of progressive MS patients may be due to alterations in the lipid metabolism (46). Some metabolic changes that can affect the lipid metabolism were reported in various studies (19,20,46). For example, elevated cerebrospinal fluid sorbitol and fructose concentrations, increases in plasma fatty acid levels and augmented plasma glutamic acid levels were

shown in MS (8,10,14,16,41). It is considered that these variations caused the increase in the NADPH / NADP ratio. NADPH is used for the biosynthesis of acetate, which is the precursor of both cholesterol and triglycerides. It is known that when a low amount of fat is taken in the diet, fatty acid biosynthesis is increased by excessive consumption of NADPH (48). Additionally, it was indicated that the main essential fatty acid, linoleic acid, fell in the red and white blood cells of MS patients (13,14). The other source of elevated plasma levels of triglycerides, VLDL-C and cholesterol, can be the cause of the demyelinization of MS plaques. Studies on lipid metabolism in MS patients have shown that some alterations in lipid content in the myeline cover of neurons exist (12-14,19,20,45,46). In the demyelination foci, total cholesterol and phospholipid content of myelin cover decreased (14). It was demonstrated that an elevated cholesterol concentration in cerebrospinal fluid in MS was considered the best indicator for demyelination in MS plaques (14,19). It was suggested that the activation of lipotrophin-endorphin metabolism-related lipase stimulation was responsible for the release of lipid contents of MS plaques (13,14). In additional, macrophage activation due to the existing reactive antibodies against auxiliary lipids (cholesterol, lecithin and phospholipid in galactocerebrosides and gangliosides) forms the other causal factor for the release the of the lipid content of demyelination foci (14,49). These preliminary reports indicate that alterations in the lipid metabolism could exist in MS patients.

Further studies are needed to investigate how the fat storage process changes and to understand the importance of alterations in the plasma lipid profile in the course of MS.

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