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Serum Lipid Concentrations in Iranian Veterans with Combat-Related Chronic Posttraumatic Stress Disorder

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Objective: Several studies demonstrated changes in serum lipid concentrations in chronic post traumatic stress disorder (cPTSD) patients. The purpose of this study was to assess serum lipid concentrations in soldiers with cPTSD and compare it with chronic major depressive disorder (cMDD) patients.

Methods: We measured serum lipid concentrations in patients with cPTSD (n=40) and cMDD (n=40) and compared the results. The patients were all male (30-48 years old) and had an illness history of more than 2 years prior to conducting the study. The groups were matched regarding their body mass index (BMI) and duration of symptoms. Laboratory investigations and psychiatric evaluations were carried-out 5 days after admission. Serum lipid concentrations were measured by enzyme assay (EA).

Results: cPTSD group showed significantly greater mean cholesterol concentrations (227.3 ± 69.7 mg/dL) than the cMDD group (190.7 ± 35.4 mg/dL) (p=0.004). Mean high density lipoprotein cholesterol (HDL-C) concentrations for cPTSD patients (66.6 ± 17.6 mg/dl) was significantly lower than HDL-C level in cMDD patients (76.5 ± 19.7 mg/dL) (p= 0.02). In contrast, mean low density lipoprotein cholesterol (LDL-C) concentrations for cPTSD patients (118.9 ± 60.1 mg/dL) was significantly higher than LDL-C level in cMDD patients (76.5 ± 25.2 mg/dL) (p= 0.000). Although similar differences was noticed on triglycerides concentration (cPTSD; 220.2 ± 79.0 and cMDD; 201.0 ± 61.8), it was statistically non-significant (p= 0.23).

Conclusion: Our findings suggest that cPTSD patients are at high risk of developing arteriosclerosis and vascular incident secondary to low levels of HDL-C and high levels of LDL-C.

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Introduction

Serum lipid concentrations have been studied in different psychiatric disorders. Increased concentrations of serum cholesterol and triglycerides have been found in patients with panic disorder, obsessive compulsive disorder, generalized anxiety disorder, aggressive and antisocial behaviors (1-6). Low concentrations of cholesterol and lipoproteins have been found in patients with schizophrenia and suicidal behavior (7). However, studies on chronic major depressive disorder (cMDD) showed no changes in serum cholesterol or triglycerides (8,9).

Posttraumatic stress disorder (PTSD) is a relatively new diagnostic category. In the Diagnostic and Statistical Manual of Mental Disorder (DSM-IV), three clusters of PTSD symptoms are listed: Trauma re-experience, avoidance and increased arousal. To fulfill the criteria for PTSD, a person must also have been exposed to an extreme and life threatening stress (10).

Studies have reported an association between stressful situations and increased concentrations of serum lipids (11). There are also reports of cerebrovascular disease in

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Vietnam War veterans who had developed PTSD (12). In Vietnam and Persian Gulf wars, the autopsy of veterans who died young, revealed extraordinarily advanced arteriosclerosis (12,13).

The main purpose of the present study was to investigate the concentrations of serum cholesterol, triglycerides, low density lipoprotein cholesterol (LDL-C) and high density lipoprotein cholesterol (HDL-C) in Iranian veterans with combat related PTSD and compare them with the similar parameters in patients with cMDD.

Materials and Methods

The group of patients with combat related cPTSD included 40 men. The age of the patients was 30 to 48 (mean= 36). Because in previous studies it has been shown that patients with cMDD had no changes in serum lipids, the control group was chosen from these patients (8,9). The control group consisted of 40 men suffering from cMDD with the age range of 32 to 47 (mean= 40). Groups were matched on demographic characteristics, BMI, nicotine dependency and duration of the illness. None of the patients had other psychiatric or medical disorders (presence of a co-morbid medical or psychiatric disorder was an exclusion criteria). All of the patients had undergone psycho-pharmacotherapy with SSRI antidepressants or benzodiazepines prior to the study. Because neither SSRIs nor benzodiazepines have been found to influence serum lipid concentrations, they were not considered as exclusion criteria (14).

Psychiatric Assessments

Using DSM-IV criteria, 2 independent psychiatrists carried out the assessments. The agreement rate between the two assessors was 97%. A diagnosis of MDD was established if beck depression inventory (BDI) was more than a cut of point of 14. The duration of the illness in both groups was more than 2 years prior to the study. All laboratory investigations, psychiatric and medical assessments were performed within 5 days of hospitalization to match patients' diet and activity.

Biochemical investigations

Blood samples were collected in the morning (between 8-9 AM) after an overnight fast of twelve and half hours. The blood was taken from forearm vein by a standard commercial kit (Pars-Azmon, Iran) and collected in a tube without added anticoagulant. Serum concentration of LDL, HDL and triglyceride were measured by enzyme assay (EA) immediately after taking the samples. Serum LDL-C concentrations were calculated by following formula: LDL-C = cholesterol - (HDL-C + triglycerides /5) (15). If triglycerides concentrations were more than 400 mg/dl, LDL-C was assessed separately in the laboratory.

Statistical Analysis

Considering the fact that lipids value follows a normal distribution curve, the data were analyzed by t-test using SPSS software (SPSS for windows 13.0, Chicago, IL, USA). A *P*-Value of <0.05 was considered statistically significant.

Results

Patients with cPTSD showed significantly higher mean cholesterol concentrations (227.3 ± 69.7) than the cMDD group (190.7 ± 35.4) ($p=0.004$). Our results also showed that mean HDL-C concentrations in patients with cPTSD (66.6 ± 17.6) was significantly lower than the mean HDL-C concentration in patients with cMDD (76.5 ± 19.7) ($p = 0.02$). In contrast, the mean LDL-C concentrations was significantly higher in cPTSD group than cMDD group (118.9 ± 60.1 vs.76.5 ± 25.2) ($p= 0.000$).

Although cPTSD patients had higher mean concentrations of triglycerides (220.2 ± 79.0) than cMDD patients (201.0 ± 61.8), this was not statistically significant ($p = 0.23$) (Table 1).

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Tab 1. Mean concentration of cholesterol, low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol(HDL-C) and triglycerides in Iranian veterans with combat-related chronic posttraumatic stress disorder (cPTSD) and chronic Major depressive disorder (cMDD)

Serum lipids	cPTSD(n=40)	cMDD(n=40)	P-value
Cholesterol(mg/dl)	227.3 ± 69.7	190.7 ± 35.4	0.004
Triglycerides(mg/dl)	220.2 ± 79.0	201.2 ± 61.8	0.238
HDL-C (mg/dl)	66.6 ± 17.6	76.5 ± 19.7	0.021
LDL-C(mg/dl)	118.9 ± 60.1	76.5 ± 25.2	0.000

Discussion

Our findings show that there is a high serum level of cholesterol and LDL-C and low serum level of HDL-C in patients with combat related PTSD. This is significantly higher than what are seen in patients with major depressive disorder.

Our findings are in accordance with the results of studies performed on Vietnam veterans suffering from PTSD (12,13). In their studies on Vietnam veteran, however, researchers did not separately measure the serum level of LDL-C and HDL-C. They also had a sample size with a mean age of 44. Because serum lipid concentrations have been shown to increase with age (16), we chose our case group from a younger population (mean age= 36).

Solter et al. and karlovic et al. found that elevated concentrations of serum lipids are associated with combat-related cPTSD (17,18). They also showed that increased concentrations of cholesterol and LDL-C appear to be correlated with increased arousal symptoms of cPTSD (18). Karlovic et al. found no differences in serum lipid concentrations of Croatian veterans with combat-related PTSD and those who had PTSD and co morbid MDD. But they found that those veterans with a diagnosis of PTSD had higher lipid concentrations than veterans with MDD or healthy control subjects (19).

Low levels of HDL-C and high levels of LDL-C are well known risk factors for arteriosclerosis and vascular incidents (20). Epidemiological studies in Vietnam veterans have shown a high prevalence of cerebro-vascular and cardiovascular disease especially in PTSD patients (12,13).

In addition to the increased lipid concentration in PTSD, there are many other biological alterations such as hypersensitivity of steroid receptors, alterations in cortical and hypothalamic- pituitary- adrenal axis (21). Southwick et al found that abnormalities of noradrenergic functional regulation are related to the long–term neurobiological consequences of severe and uncontrollable stress. They also explored the pathological relationship between PTSD and other anxiety disorders (22). It has been shown that PTSD patients have enhanced sympathetic nervous system activity. Agonists of noradrenergic system can induce symptoms of PTSD (23) while, β -adrenergic antagonists appear to be effective drugs in psycho pharmacotherapy of PTSD (24).

McCann et al. found a correlation between increased activity of noradrenergic system and increased levels of cholesterol. They showed that increased catecholamine levels can activate lipoprotein lipase, which increases the concentrations of free fatty acids in the serum. These fatty acids are transformed into cholesterol and triglycerides in the liver (25).

There was several limitations in our study; the authors did not concentrate on the serum level of other stress markers such as catecholamine or cortisol. Our samples consisted of only male patients and those with combat related PTSD. Our result therefore, can not be generalized to female population and those who have developed PTSD in a situation not related to war.

In conclusion, our findings highlight an increased risk of arteriosclerosis in patients with PTSD.

Further research projects, especially those which can involve female patients and civilians, are required to investigate the biochemical abnormalities in patients with PTSD. This will help the clinicians to reduce the chance of adverse vascular events in this population.

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