Research Article

Parkinson's Disease and Serum Cholesterol Levels: A Case Control Study
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Summary

Background: Several recent prospective, population-based studies suggest a role of lipid and cholesterol metabolism in the pathogenesis of Parkinson's disease (PD). This study is to test the hypothesis that lower serum cholesterol levels may be associated with PD.

Methods: The total serum cholesterol, LDL-C, HDL-C, and VLDL-C levels of 107 patients with idiopathic Parkinson's disease and 106 control subjects were obtained. In both groups, subjects with known hyperlipidemia and smokers were excluded. All patients were evaluated according to the Unified Parkinson's Disease Rating Scale and staged according to the Hoehn and Yahr scale. The collected data of PD patients and control subjects were compared using two-sample t-tests and Pearson's Chi-Square tests.

Results: The mean serum total cholesterol level was 189 ± 30.7 mg/dL in the PD group and 199.3 ± 20.2 mg/dL in the control group (p= 0.983). The mean VLDL-C level was 13.2 ± 2.8 for patients, and 24.9 ± 3.2 for control group (p = 0.155).

Conclusion: Although the mean total cholesterol level and VLDL-C level were lower in the patient group, this study did not show any statistically significant difference between PD patients and the control group.

Key words: Parkinson's Disease, Pathogenesis, Serum cholesterol levels

Özet

Amaç: Yakın zamanda yapılan toplu dayalı prospektif çalışmalarında, Parkinson Hastalığı (PH) ’ın patogenezinde serum lipid ve kolesterol seviyelerinin rol alabileceği bildirilmiştir. Bu çalışma, düşük kolesterol seviyelerinin PH’na eşlik edebilceği hipotezini test etmek amacıyla yapılmıştır.


Bulgular: Serum total kolesterol seviyeleri Parkinson grubunda 189 ± 30.7 mg/dL ve kontrol grubunda 199.3 ± 20.2 mg/dL bulundu (p= 0.983). Ortalama VLDL-K seviyeleri hasta grubunda 13.2 ± 2.8 mg/dL ve kontrol grubunda 24.9 ± 3.2 mg/dL (p = 0.155) bulundu.

Sonuç: Bu çalışma, her ne kadar, hasta grubunda total kolesterol ve VLDL-K seviyeleri kontrol grubuna göre düşük olsa bile istatistiksel olarak anlam taşımadığını göstermiştir.

Anahtar Kelimeler: Parkinson Hastalığı, Patogenez, Serum Kolesterol seviyeleri
INTRODUCTION

Parkinson disease (PD) is the second most common neurodegenerative disorder, caused by a selective degeneration of dopaminergic cells in the substantia nigra\(^{(1)}\). The exact mechanism that underlies the selective dopaminergic cell death in Parkinson's disease is as yet unknown, but mitochondrial dysfunction and oxidative stress are thought to play a major role\(^{(2)}\). Several recent findings also suggest a role of lipid and cholesterol metabolism in Parkinson's disease pathogenesis. Cholesterol is a major component of neuronal cell membranes and synapses and essential for maintaining their structure and function\(^{(3)}\).

Three recent case-control studies\(^{(6,9)}\) suggest that higher serum cholesterol levels may be related to lower prevalence of PD. Three independent prospective studies provided further support for the hypothesis that higher serum cholesterol may be associated with a lower future risk of PD\(^{(2,4,14)}\).

We designed a case–control study to determine the relationship between serum cholesterol concentrations and the occurrence of PD.

MATERIAL AND METHODS

Consecutive PD patients who presented at the Bakirkoy Research and Training Hospital for Neurological and Psychiatric Disorders Movement Disorders Outpatient Clinic were recruited for the study. Control subjects were recruited from the spouses or relatives of the patients. All PD patients met the published criteria of idiopathic PD\(^{(18)}\).

The subjects previously diagnosed with hyperlipidemia and who had used or were still using statins and smokers were excluded in both groups. Also, subjects with severe dementia (Mini-Mental State Examination score \(\leq 20\)), depression (Hamilton Scale for Depression score \(\geq 16\)), diabetes mellitus or secondary Parkinsonism were excluded\(^{(20)}\). All patients were evaluated according to the Unified Parkinson's Disease Rating Scale and staged according to the Hoehn and Yahr scale. Lipid profiles measured in fasting state and levels of total cholesterol, low-density lipoprotein cholesterol (LDL-C), very low-density lipoprotein cholesterol (VLDL-C), total triglyceride and high-density lipoprotein cholesterol (HDL-C) levels were obtained. All the cholesterol concentrations were determined uniformly at the same laboratory, using the same blood sample for each subject. The study protocol was reviewed and approved by the institutional review board and written informed consent was obtained from all participants. Statistical analysis was performed using two-sample t-tests and Pearson's Chi-Square tests.

RESULTS

The study group consisted of 107 PD patients (56 male, 51 female) with a mean age of 66.4 ± 8.4. The control group consisted of 106 subjects (53 male, 53 female) with a mean age of 62.2 ± 8.5. The disease duration was 6.4 ± 8.4 years and UPDRS score was 32.4 ± 12.8 in the patient group (Table-1).
Table 1: Summary characteristics of cases and controls

<table>
<thead>
<tr>
<th></th>
<th>CASE</th>
<th>CONTROLS</th>
<th>ALL PARTICIPANTS</th>
<th>p-values*</th>
</tr>
</thead>
<tbody>
<tr>
<td>( Number of participants/ % )</td>
<td>107 (50.2)</td>
<td>106 (49.8)</td>
<td>213 (100)</td>
<td></td>
</tr>
<tr>
<td>Age (year) (SD)</td>
<td>66.4 ± 8.4</td>
<td>62.2 ± 8.5</td>
<td>64.2 (± 8.8)</td>
<td>p=0.945</td>
</tr>
<tr>
<td>Male ( % )</td>
<td>56 (52.3)</td>
<td>53 (50.0)</td>
<td>109 (51.1)</td>
<td>p=0.886</td>
</tr>
<tr>
<td>Women ( % )</td>
<td>51 (47.6)</td>
<td>53 (50.0)</td>
<td>104 (48.8)</td>
<td>p=0.910</td>
</tr>
<tr>
<td>Disease duration (year) (SD)</td>
<td>6.4 ± 8.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>UPDRS score (SD)</td>
<td>32.4 ± 12.8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hoehn and Yahr Stage (I-II-III-IV)</td>
<td>(16-32-35-24)</td>
<td></td>
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</tbody>
</table>

SD: Standard deviation, * p ≤ 0.05 is statistically meaningful.

The mean serum LDL-C level was 128.2 ± 31.1 mg/dL in the PD group and 119.5 ± 35.2 mg/dL in the control group (p=0.445). The mean serum VLDL-C levels were 13.2 ± 2.8 and 24.9 ± 3.2 mg/dl in the patient and control group respectively (p=0.155). The total triglyceride levels were 113.2 ± 54.4 and 124.0 ± 78.2 in the patient and control group respectively (p=0.551) (Table-2).

The serum level of total cholesterol, VLDL-C, HDL-C and triglyceride were lower in the patient group. On the other hand, LDL-C level was higher in the patient group. There was not any statistically significant difference between PD patients and the control group.
Table 2: Serum cholesterol concentrations of cases and controls

<table>
<thead>
<tr>
<th>CHOLESTEROL TYPE (mg/dl)</th>
<th>CASE (SD)</th>
<th>Controls (SD)</th>
<th>p-values *</th>
</tr>
</thead>
<tbody>
<tr>
<td>HDL cholesterol (mg/dl)</td>
<td>47.6 (±11.3)</td>
<td>54.9 (±17.7)</td>
<td>p = 0.274</td>
</tr>
<tr>
<td>LDL cholesterol (mg/dl)</td>
<td>128.2 ± 31.1</td>
<td>119.5 ± 35.2</td>
<td>p = 0.445</td>
</tr>
<tr>
<td>VLDL cholesterol (mg/dl)</td>
<td>13.2 ± 2.8</td>
<td>24.9 ± 3.2</td>
<td>p = 0.155</td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>189 ± 30.7</td>
<td>199.3 ± 20.2</td>
<td>p = 0.983</td>
</tr>
<tr>
<td>TRIGLYCERIDE</td>
<td>113.2 ± 54.4</td>
<td>124.0 ± 78.2</td>
<td>p = 0.551</td>
</tr>
</tbody>
</table>

SD: Standard Deviations
* p ≤ 0.05 is statistically meaningful.

DISCUSSION
Evidence is accumulating that alterations in fat metabolism are involved in the pathogenesis of neurodegenerative diseases, including Parkinson's disease [11,17]. Results from a recent meta-analysis showed an increased risk of Parkinson's disease in carriers of the APOE ε2 allele [7], which is associated with lower plasma levels of total cholesterol [8]. Decreased cholesterol synthesis was observed in skin fibroblasts from patients with Parkinson's disease [10], and lower levels of total cholesterol have been described in Parkinson's disease patients compared with controls [15,17]. Lower cholesterol levels also have been associated with higher mortality in the elderly [13] and higher risk of Alzheimer's disease [12].

In our study, VLDL-C and total cholesterol levels were lower in the patient group, and LDL-C level was higher. Although the mean total cholesterol level and VLDL-C level were lower in the patient group, the serum levels of all cholesterol types were not statistically significantly different between PD patients and the control subjects. A recent study by Huang et al reported that lower LDL-C is associated with increased risk of PD in Japanese–American men after age-adjustment [4]. Interestingly, a recent study of the Rotterdam cohort also found an association of lower total cholesterol and increased PD risk, but only in women [2]. The same study also pointed out that a higher dietary intake...
of unsaturated fatty acids was associated with a decreased risk of PD and the dietary habits were assessed before onset of PD(2). Although LDL-C was found to be low among men in some studies and among women in other studies, there was not any statistically significant difference between men and women in VLDL-C, LDL-C and total cholesterol levels in our study.

In a case-control study the authors also evaluated the use of statins, and found much higher percentage of use of statins in the control versus PD subjects (PD men 20.3% vs. control men 38.0%; PD women 12.7% vs. control women 30.6%). They speculated about the protective effect of statins on degenerative diseases as "if the association of lower LDL-C with PD is itself the critical mechanism, then the higher use of statins in the controls versus cases reflects the different biology of the two groups rather than a protective effect on PD of the cholesterol-lowering agents" (6). Patients using statin and smokers were excluded from the patient and control groups in order not to affect the results. Another remarkable study showed the evidence that lower total serum cholesterol also may be associated with modestly faster progression of PD symptoms(5).

Several recent findings also suggest a role of lipid and cholesterol metabolism in Parkinson's disease pathogenesis. Cholesterol is a major component of neuronal cell membranes and synapses and essential for maintaining their structure and function(11). Results of in vitro studies suggest an association between lipids and the localization and structure of the alpha-synuclein protein, the major component of the pathologic Lewy bodies found in brains of patients with Parkinson's disease(19).

Lower serum levels of total cholesterol have been described in patients with Parkinson's disease compared with controls(17). Moreover, serum cholesterol is the most important determinant of serum levels of coenzyme Q10, a powerful antioxidant and mitochondrial electron acceptor, that has shown beneficial effects in animal studies and initial trials on Parkinson's disease(16).

Our study is not prospective. On the other hand, a prospective study with large cohort suggested that PD risk neither was significantly related to history of hypertension, hypercholesterolemia, or diabetes(3). Even in this study, the authors reported PD risk may modestly decline with increasing blood cholesterol levels. As a conclusion, although the mean total cholesterol level and VLDL-C level were lower in the patient group, our study did not show any statistically significant difference between PD patients and the control group. However, whether low serum cholesterol may have a role in the pathogenesis of PD must be investigated future.

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