Evaluation of serum cortisol and dehydroepiandrosterone sulphate levels in parkinson patients with and without postural instability

Postural instabilitesi olan ve olmayan parkinsonlu hastalarda serum kortizol ve dehidroepiandrosteron sülfat düzeylerinin değerlendirilmesi

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ABSTRACT

Objective: Parkinson's disease (PD) is the second most common neurodegenerative disease. During PD many disorders occur in the neuroendocrine mechanism along with autonomic dysfunction. The aim of this study was to evaluate the values of cortisol and dehydroepiandrosterone sulphate (DHEAS) in idiopathic PD patients with postural instability (PI) in the medium and advanced stages of the disease.

Methods: Three groups were included in this study; patients with PI, patients without PI and control subjects. Each of the groups consisted of 30 patients. The fasting serum cortisol and DHEAS values of patients were obtained.

Results: Serum cortisol levels were significantly higher in patients with PI in the advanced stage of PD, whereas DHEAS levels were significantly higher in patients without PI in the early stage.

Conclusion: This situation was evaluated as the reflection of neuroendocrine response that occurred secondary to the progressive advancing neurodegeneration seen in PD patients. The data obtained may contribute to a better understanding of the pathophysiology of PD that in intermediate and advanced stages. In addition, our findings may help in establishing new treatment options for PD patients in the future. J Clin Exp Invest 2014; 5 (3): 376-380

Key words: Parkinson’s disease, postural instability, cortisol, dehydroepiandrosterone sulphate

INTRODUCTION

Parkinson’s disease (PD) has a chronic neurodegenerative and progressive period. During PD, in addition to common autonomic dysfunction, many changes occur in the neuroendocrine mechanism including circadian rhythm in the dopaminergic system of the central nervous system (CNS) [1].

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Postural instability (PI) generally shows an increase towards the chronic stage of the disease and affects daily life negatively by preventing patients from having independent motor skills. In previous studies it was reported that in the first two years of PD 34% of patients had PI, while in the tenth year of 71% had PI [2].

Cortisol and dehydroepiandrosterone (DHEA) are steroid type hormones that significantly affect energy metabolism, the immune system and stages of ageing. Although the importance of dehydroepiandrosterone sulphate, which is an esterified form of DHEA, has been identified in the elderly population, its physiologic effects have not been explained clearly yet. Neurosteroids are effective in the modulation of neurotransmitter activity, neurotrophic and neuroprotective functions. Consistent with this, a few studies have been conducted on neurodegenerative diseases and changes in the levels of neurosteroids to determine if there is an association among them [3].

In most previous studies cortisol levels were found to be high in PD patients. This situation has been considered as a process of advancing neurodegeneration in PD [4]. In contrast, the data about DHEAS, which is thought to be neuroprotective, are not clear enough [5,6].

The aim of this study is to evaluate serum cortisol and DHEAS values in idiopathic PD patients who have postural instability (PI) (Hoehn&Yahr stage 3-4) and who do not have PI (Hoehn&Yahr stage 1-2) by comparing them with a healthy group.

METHODS

Patients and laboratory methods

In this study a total of 90 people, who were divided into three groups consisting of 30 people, each were evaluated. The fasting serum cortisol and DHEAS levels of PD patients with PI (Hoehn&Yahr stage 3-4), PD patients without PI (Hoehn&Yahr stage 1-2) and the healthy control group were measured.

The patient groups and control group were distributed into available groups in terms of age and gender. The exclusion criteria for the patient groups were as follows: having any kind of endocrine disorder (Diabetes mellitus, Addison’s syndrome, hypothyroid, hyperthyroid etc.), secondary Parkinsonism, not being in the 40-80 age range, duration of PD of less than two years, use of anti-epileptic drugs, malignancy, polyneuropathy or having a psychiatric disease, chronic renal failure or having a cerebrovascular disease past history, motor disorder due to spinal trauma, and receiving dementia or corticosteroid treatment.

The samples were collected in the morning, at 08.00 am, into sample tubes containing clot activator and gel without anticoagulants. Cortisol and DHEAS were analyzed with a DXI 800 immunoanalyzer (Beckman Coulter Inc, USA) using chemiluminescent reactives. The obtained data were compared statistically by considering age and disease period among the groups. Ethical approval was obtained for this study.

Statistical analysis

Normal distribution of data was examined by the Shapiro-Wilk test. In the comparison of two groups (postinst-hassure) the Mann-Whitney U test was used when the data were not distributed normally. In the comparison of three groups, for normally distributed data single direction variance analysis, was used and for non-normally distributed data Kruskal-Wallis analysis was used. In case of finding a difference as a result of Kruskal-Wallis analysis, the nonparametric Student-Newman-Keuls test was used as a multiple comparison test. In comparison of categorical variables the Chi-square test was used and a p<0.05 value was considered statistically important. IBM SPSS Statistics 21.0 program was used for the statistical analysis.

RESULTS

No statistical difference was observed between the study groups in terms age, gender and disease period. The average age was found as 69.2 years in the group with PI, as 66.7 years in the group without PI and as 68.4 years in the control group (Table 1). In this study, serum cortisol levels in patients with PD were higher than those in the control group. Serum cortisol was found as 16.54 µg/dl in the group with PI (Hoehn&Yahr stage 3-4), as 11.69 µg/dl in the group without PI (Hoehn&Yahr stage 1-2) and as 10.13 µg/dl in the control group. According to these data the level of cortisol was found to be higher in the PD with PI group and this result was statistically significant (p=0.038). Moreover, the level of cortisol in the without PI group was found to be higher than that of the control group but this result was not statistically significant (p=0.207) (Figure 1).
Table 1. The demographic features of individuals in patient groups and control group

<table>
<thead>
<tr>
<th></th>
<th>Postural instability (+) (Hoehn&amp;Yahr stage 3-4) (n=30)</th>
<th>Postural instability (-) (Hoehn&amp;Yahr stage 1-2) (n=30)</th>
<th>Controls (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean ± SD)</td>
<td>69.2±10.9</td>
<td>66.7±7.9</td>
<td>68.4±8.2</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>16/14</td>
<td>16/14</td>
<td>17/14</td>
</tr>
<tr>
<td>Disease duration, years</td>
<td>5.5±3.2</td>
<td>4.5±2.1</td>
<td>-</td>
</tr>
</tbody>
</table>

**Figure 1.** The average serum cortisol values in patients and control group.

PI (+): PD patients with postural instability (Hoehn&Yahr stage 3-4)
PI (-): PD patients without postural instability (Hoehn&Yahr stage 1-2)

The level of DHEAS was found to be higher in patients with PD, as was so for cortisol, but it was lowest in the control group. The level of DHEAS in the group with PI (Hoehn&Yahr stage 3-4) was found as 94.12 µg/dl, in the group without PI (Hoehn&Yahr stage 1-2) as 99.01 µg/dl and in the control group as 61.55 µg/dl. However it was found, in particular, to be highest in the group without PI at a relatively early stage (stage 1-2) of PD and this result was also found to be statistically significant (p=0.046). Additionally it was found to be higher in the group with PI than in the control group and this result was found to be statistically significant (p=0.024) (Figure 2). According to these data the DHEAS levels were found to be higher in the relatively early stages of PD in the group without PI.

In this study, compared to the control group, both the levels of cortisol and DHEAS were found to be significantly higher in the PD patient group (p<0.05).

**Figure 2.** The average serum DHEAS values in patients and control group

PI (+): PD patients with postural instability (Hoehn&Yahr stage 3-4)
PI (-): PD patients without postural instability (Hoehn&Yahr stage 1-2)

**DISCUSSION**

When compared to the control group, the data from our study, suggest that cortisol levels are high especially in patients with PI in the moderate and severe stage (Hoehn & Yahr stage 3-4). This situation was evaluated as the reflection of neuroendocrine response that occurred secondary to the progressive neurodegeneration seen in PD. In patients with advanced disease, a tendency progress towards a rise in cortisol levels in response to chronic stress was observed. In addition, the level of DHEAS which is considered to be neuroprotective, was found to be the highest in the early stages of disease (Hoehn&Yahr stage 1-2). This finding suggests that neuroprotective mechanisms are more active in the early stage of PD.

Neuroinflammation along with oxidative stress, mitochondrial dysfunction and abnormal protein aggregation play an important role in PD pathophysiology. In classical neurodegenerative diseases like PD, a disorder occurs in the hypothalamo-hypophysyal-adrenal cycle and a change in cortisol level is observed [4,7,8]. In most studies a significant
increase in cortisol level was observed. It changes according to brain steroid condition, lifelong stress and disease. Increased steroid levels are known to be neurotoxic to the brain. It was reported that increased cortisol levels have a negative effect on the synthesis of many neurotransmitter including dopamine and serotonin by causing hippocampal atrophy and disorder cognitive functions [9].

It was reported 30 years ago that steroids are produced locally in CNS. The most commonly found neurosteroids in the CNS system are pregnenolone and DHEA [10]. Neurosteroids are effective in the modulation, neurotrophic and neuroprotective functions of neurotransmitter activity. As a result of this, they take part in many processes such as neural development, increasing synapse formation, plasticity, emotion-situation, memory, sexual behaviour, sleeping, digestion, aggression during stress, myelination and immune response [11].

DHEAS, which is synthesized in the glial cells locally, has a neuroprotective effect against free radicals that occur during the oxidative period in chronic neurodegenerative diseases like PD [6]. However, the information about neurosteroids is mostly dependent on studies done on animals and only a few clinical studies have been conducted on humans. In the study done on Parkinsonian monkeys with MPTP (1-methyl-4-phenyl-2,3,6 tetrahydro pyridine) lesion, it was shown that DHEAS regulated locomotor activity [12].

There are only a few studies that analyse neurosteroid synthesis changes in PD patients. In many studies the serum DHEAS levels of PD patients were found to be higher than those in control groups. It was reported that DHEAS plays a protective role in the hippocampus and neocortex region against the neurotoxic effects of glutamate analogues and corticoids. Also, it was shown that giving DHEAS decreases plasma cortisol levels and has the capacity to make structural changes in receptor proteins such as NMDA and dopamine [13,14]. In another study, patients with systemic lupus erythematosus that were given oral DHEAS administration for 3-6 months were shown to have decreased disease activity and a reduction in corticosteroid therapy treatments [15].

Many symptoms such as pain, change of mood and autonomic dysfunction can affect cortisol and neurosteroid level in PD patients. This situation was not dealt with in our study and was considered as a restrictive factor. In addition, the small number of patients included in the study can also be accepted as a restrictive factor.

Our study shows that there is a increase in the cortisol levels of PD patients in the advanced stage. The treatment aimed at reducing, increased cortisol levels can slow the speed of the disease in neurodegenerative diseases like PD. The level of DHEAS was found to be higher in the early phase of the disease. In order to understand the effect of DHEAS in PD patients better, more studies are needed in a large number of patients in which the disease is considered according to stages. As a result of this study we believe that the data obtained may contribute to a better understanding of the pathophysiology of the intermediate and advanced stages of PD. Also, our findings may help in establishing new treatment options for PD patients in the future.

REFERENCES