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Correlation of Tyrosine Hydroxylase, Orexin, and NFL Concentration with Parkinson's Disease

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Abstract

The research aimed to identify serum biochemical variables that correlated to Parkinson's disease by the collection of 120 blood samples from healthy patients males coming to Ibn Sina Teaching Hospital in Mosul, from December to June 2023-2024, these samples were divided into several groups, Parkinson group, donated symbol P that included (30) samples divided into two subgroups according to age, P1 (50-65)years and P2 (66-80) years 15 blood sample for each, while Parkinson's family group donated symbol F, included (30) samples aged between (25-50) years, in addition to the Control group C that included (60) samples of Healthy people which divided into three subgroups, C1 (50-65) years, C2 (66-80) years, and C3 subgroup (25-50) years. These groups ' biochemical serum markers tyrosine hydroxylase, orexin, and neurofilament protein NFL had been compared. Results of this research showed a significant correlation as TH enzyme concentration decreased in patients' serum with Parkinson's disease in both groups P1, and P2 compared to the healthy group C1 and C2 ($p \leq 0.01$), also F group showed a significant decrease in the concentration of this enzyme compared to the healthy group C3, Besides there was a substantial difference in orexin hormone concentration level at probability level ($p \leq 0.01$)) in all groups, as hormone concentration decreased in P1subgroup patients compared to healthy C1 patients of the same age group, and this decrease increased in Parkinson's disease P2 patients compared to healthy C2. There was a significant increase in the serum's concentration of NFL protein in the P1 subgroup compared to the healthy C1 subgroup at a probability level ($P \leq 0.01$).

Keywords: *Neurofilament Protein, Orexin Hormone, Parkinson's Disease, Tyrosine Hydroxylase.*

Introduction

Parkinson s disease disorder occurs in the central nervous system and is characterized by gradual degeneration and death of dopaminergic neurons in the midbrain area called substantia nigra (SN) [1]. The final symptoms of this disease begin to appear when the percentage of dopamine neurons loss exceeds 50% as dopamine is a neurotransmitter that plays a major role in controlling movement and emotion. The motor pathological symptoms of Parkinson's disease (PD), include tremors, rigidity, slow movement, and instability [2]. Parkinson's disease was characterized also by Lewy bodies (LBs) existence, which are cytoplasmic inclusions containing alpha-synuclein protein, that are found in nerve cells of brain-affected areas [3, 4]. Tyrosine hydroxylase (TH) had an important role in reducing the biosynthesis of catecholamine, as it catalyzed the reaction to convert the amino acid L-Tyrosine to L-3,4-dihydroxy phenylalanine (L-dopa) in the central nervous system (CNS) and the adrenal medulla. After that, L-Dopa is converted to Dopamine (DA), which plays a role in the biosynthesis of epinephrine (Adrenaline) and norepinephrine (Noradrenaline) [5]. When the

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level of dopamine (DA) decreases, it leads to a constant imbalance in neurotransmitters and chemicals [6, 7]. Many studies confirm that orexin hormone plays a major role in Parkinson's disease and poor sleep, as it was noted that there is a decrease in orexin levels in the cerebrospinal fluid (CSF) in people with Parkinson's disease [8, 9]. Elevated NFL levels in people with PD can be interpreted as a biomarker and stable marker of axonal loss and dopaminergic axonal loss that occurs in the early stages of PD, and these studies have demonstrated for the first time the potential utility of plasma NFL as a biomarker, diagnostic and prognostic marker for early stages of PD [10, 11].

Materials and Methods

120 blood samples were collected from patients coming to Ibn Sina Teaching Hospital in Mosul, patients and healthy male people, during the period from December to June 2023-2024 AD, depending on the field supervisor and the doctor specialized in diagnosing disease cases and after obtaining official approval from the Nineveh Health Department. 5 ml of venous blood was drawn for each sample and placed in a Gel Tube and was centrifuged for 10 minutes to obtain serum for biochemical tests. The serum was transferred to an Eppendorf tube with a volume of 2.5 ml and duplicates were made from it. Then the samples were frozen (20) degrees. These samples were divided into several groups, Parkinson's group, donated symbol P that included (30) samples divided into two subgroups according to age, P1 aged (50-65) years and P2 aged (66-80) years 15 blood samples for each, while Parkinson's family group donated symbol F, included (30) samples aged between (25-50) years, in addition to Control group C that included (60) samples of Healthy people which divided into three subgroups, C1 (50-65) years old C2 (66-80) years and C3 subgroup (25-50) years.

Serum's Concentration of Biomarkers Determination

The analysis kit for TH enzyme, prepared by Bioassay technology and numbered E0720Hu, the kit for orexin hormone, prepared by Bioassay technology numbered E6966Hu, and the Kit for NFL was prepared by Bioassay technology numbered E4624Hu, had been used.

Statistical Analysis

The data were analyzed according to the simple experiment system and using a completely randomized design. The comparison was made according to the t-test under the probability level of 1%. The standard deviation and standard error were also included.

Results and Discussion

Tyrosine Hydroxylase (TH) Enzyme Concentration

Results showed that the concentration of the TH enzyme decreased in patient's serum of Parkinson's disease compared to the healthy group (Figure 1), as the decrease in the first group P1 (50-65) years was 7.06 compared to its concentration in the healthy group C1 8.75 at probability level ($p \leq 0.01$), while the decrease in the concentration of this enzyme in the second group P2 (66-80) years of patients was 5.09 compared to the healthy group C2 (7.27). Relatives family F group, also showed a decrease in the concentration of this enzyme compared to the healthy group C3, because the enzyme is a specific factor for dopamine generation, and there is a lot of evidence that dopamine deficiency is a pathological factor in neurodegeneration in Parkinson's patients [12]. The TH enzyme has a major role in the dopamine DA pathway in Parkinson's disease, and the presence of some genetic mutations in the family of patients has adverse effects on the TH-DA pathway and thus affects dopaminergic neurons, especially in early

Parkinson's disease in the serum of patients with this disease [13].

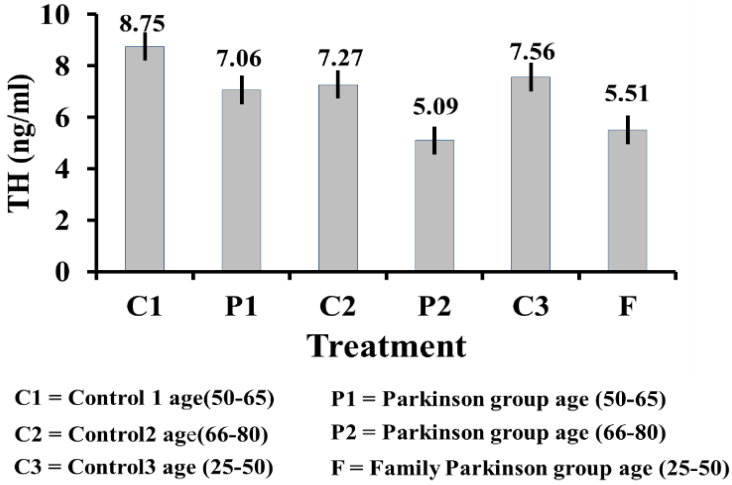

Figure 1. Comparison of Serum's TH Enzyme Concentration between Studied Groups

Serum's Orexin Hormone Concentration (HCRT)

Results of the current research, as shown in Figure (2), revealed that there was a significant difference in serum levels of orexin hormone concentration (HCRT) at probability level ($P \leq 0.01$) between Parkinson's disease patients, healthy people, and the relative family groups, as the concentration of this hormone decreased in Parkinson's patients P1, compared to the healthy group C1, and this decrease increased in Parkinson's patients P2, compared to the healthy group C2. This is consistent with the results of many studies, such as Huang *et al*. (2021), study, that revealed a significant decrease of this hormone levels in the serum and plasma of Parkinson's patients compared with the healthy group [14]. Besides Parkinson's family group, F showed a significant decrease compared with healthy control subgroup C3 at the same probability level and this decrease had been accepted by the study of Braun *et al*. (2024), who considered this decrease as a sign of complex Parkinson's disease and early incomprehensible symptoms with a group of non-motor symptoms, so it became clear that orexin has a role in Parkinson's disease [15].

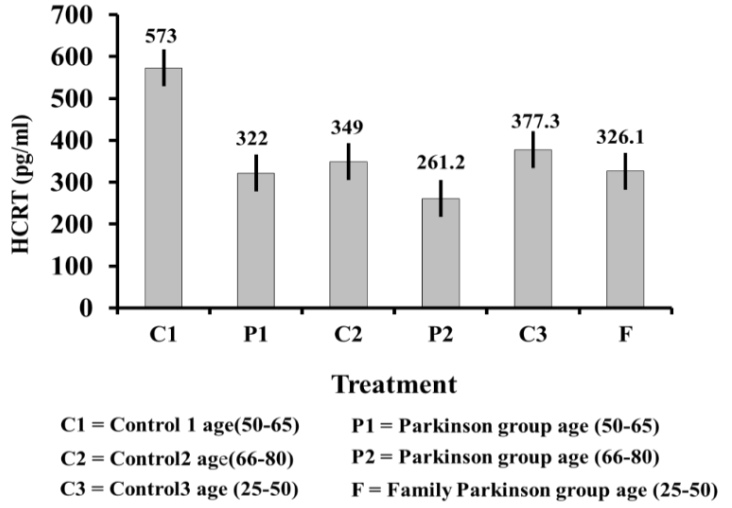

Figure 2. The Concentration of the Hormone HCRT in the Serum of the Studied Groups

Neurofilament Light Protein (NFL) Protein Concentration

Figure 3 shows that. NFL protein concentration had been significantly increased in the P1 group, compared with C1, at probability level ($p \leq 0.01$) The reason for this increase may be due to the greater damage of nerve axons as Osterveld *et al*. (2020), concluded [16]. The results also showed in Fig (3), that there is a significant increase in serum NFL concentration in group P2 compared to the healthy C2 subgroup because the levels of NFL protein concentration in the serum of Parkinson's disease patients increase annually faster with age [17]. It was also noted that the concentration of NFL showed an increase in both the patient and healthy groups, but the increase was greater and faster in the patients, which is consistent with the results of many studies, including the studies of [18,19]. The results also showed that there was a significant increase in serum's NFL protein concentration at probability level ($P \leq 0.01$) in the Parkinson's family F group compared with healthy C3 of the same age this increase in the Parkinson's family F may be considered as a sign before the onset of the disease, because the increase in NFL levels is related to the development of this disease across generations [18, 20].

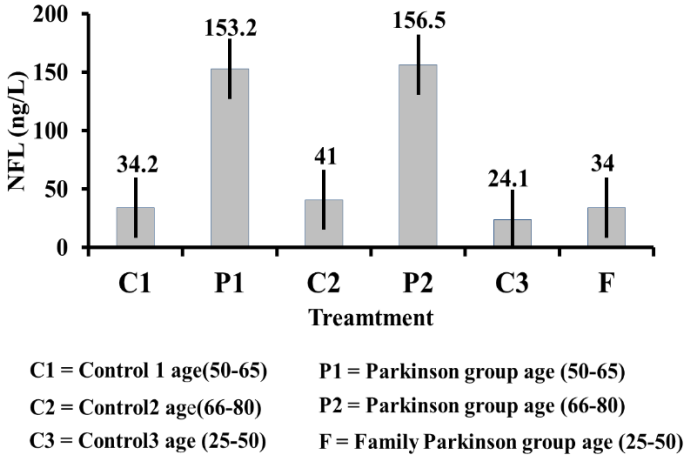

Figure 3. Comparison of Serum's NFL Concentration in Different Patient Groups Compared with Healthy Control Groups

Conclusion

Based on the results of this research that revealed significant differences in the serum concentration of TH enzyme, Orexin hormone and NFL Protein between Parkinson's patient groups, Healthy groups and relative family groups it is clear that there was a strong correlation between these biomarkers and Parkinson's stages development therefore these parameters considered as a good biomarker for Parkinson's disease and recommended to accomplished for Parkinson diagnosis.

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