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Serum Iron and Ferritin Level in Idiopathic Parkinson

Mehdi Farhoudi, Aliakbar Taheraghdam, Gholnar Abbasi Farid,
Mahnaz Talebi, Ali Pashapou, Jafar Majidi and Mohamad Goldust
Tabriz University of Medical Sciences, Tabriz, Iran

Abstract: Parkinson disease is a prevalent progressive neurodegenerative disorder, especially in western countries and among the elderly. This study aimed at evaluating serum iron and ferritin in patients with idiopathic Parkinson disease. In this case-control study, 50 patients with clinical diagnosis of idiopathic Parkinson disease (case group) were evaluated during a 12 month period. Fifty healthy persons (control group) recruited as well. Serum iron and ferritin levels were measured by biochemical and quantitative luminance methods, respectively in the case and control group. Fifty patients, 28 males and 22 females with the mean age of 64.53 ± 10.18 (40-84) years and 50 controls were enrolled. Serum iron levels were 70.22 ± 25.18 mg dL⁻¹ and 67.62 ± 39.53 mg dL⁻¹ in case and control group, respectively. Serum ferritin levels were 129.79 ± 137.67 ng dL⁻¹ and 109.87 ± 154.71 ng dL⁻¹ in case and control group, respectively. There was no significant difference between different grades of Parkinson disease considering the serum level of iron or ferritin. The current study showed that generally there is no significant difference between the patients with the idiopathic Parkinson disease and healthy controls in terms of serum iron and ferritin levels. The same results were attributable to different grades of the disease.

Key words: Parkinson disease, iron, ferritin, serum

INTRODUCTION

Parkinson is a progressive neurodegenerative disease occurring in all races with almost similar gender distribution (Sian-Hulsmann *et al.*, 2011). In America and Western Europe, its prevalence is 1-2 cases in every 1000 and it increases with age (Castiglioni *et al.*, 2010). The clinical manifestations include tremor, hypokinesia, rigidity, unnatural walking mode. This disease is divided into idiopathic, post encephalitis, pharmaceutical Parkinsonism and family Parkinsonism (Friedman *et al.*, 2009). In idiopathic Parkinsonism, pathologic studies indicate lack of pigmentation cell in black corpus and other centers of brain stem. Dopamine and acetylcholine are found in striped corpus and serve as neurotransmitter. In idiopathic Parkinson, it is believed that unbalance is observed between these two neurotransmitters because there is dopamine impairment in dopaminergic nigroaestrial system (Zukor *et al.*, 2009). Loss of dopaminergic neurons in substantia nigra can be referred to as characteristics of Parkinson disease (Mijajlovic *et al.*, 2008). Degeneration of these dopaminergic neurons is usually accompanied with iron accumulation in brain sensitive structures. Iron may increase as a result of its high penetration in brain parenchyma due to increasing manifestation of lactoferrin

and lactoferrin receptors in blood vessels and dopaminergic neurons in Parkinson (Hirsch, 2006). Also, iron may increase in microglia cells after phagocytosis of dopaminergic neurons. Therefore, incorrect regulating of iron resources may play a role in degenerative process of dopaminergic neurons (Gerlach *et al.*, 2006). Some other studies indicate role of iron and ferritin in Parkinson pathophysiology (Logroscino *et al.*, 2006; Wright *et al.*, 2004). In brain of patients suffering from Parkinson, level of iron and protein binding to iron is unnatural. Iron has been known as a cofactor of cellular oxidative damages (Felltschin *et al.*, 2003). Recent studies have introduced iron as a material leading to accumulation of α -synuclein in Loei corpus of those suffering from Parkinson (Hernandez *et al.*, 2002). Another role of iron is its capability in producing oxygen free poisonous radicals. It is proved that accumulation of iron in brain of those suffering from Parkinson is accompanied by ferritin increase. Moreover, it has been shown that iron and ferritins are substantially high in tissue of patients with Parkinson (Double *et al.*, 2000). In this disease, increasing of tissue iron may lead to saturation of points connected to iron in neuromelanin and develop a weak relation between iron and neuromelanin and therefore, increase the iron (Mirza *et al.*, 2000). Although, iron sediments in substantia nigra have been mentioned in several studies,

studying its relation with serum level of iron especially ferritin indicating iron resources in body is very limited (Chimonas *et al.*, 2006). This study aimed at analyzing iron and ferritin serum level in patients suffering from idiopathic Parkinson.

Chi-square test or Fisher's Exact Test considering conditions. Student t-test or One-way ANOVA test was used to compare qualitative variables. In all understudy cases, the results are known as statistically meaningful if $p \leq 0.05$.

MATERIALS AND METHODS

RESULTS

Subjects: In a case-control study conducted from March 2011 to March 2012 in neurology department of Tabriz Imam Khomeini Hospital, serum level of iron and ferritin was studied in 50 patients suffering from clinically established idiopathic Parkinson and 50 healthy individuals matched considering age and gender. Written consent was obtained from all the patients. Those classified in the control group also provided their written letter of consent.

One hundred persons were studied in following groups including 50 patients suffering from idiopathic Parkinson (group P, with mean age of 64.53 ± 10.18 (40-84) years old) and 50 healthy persons (group N, with mean age of 63.53 ± 9.78 (41-83) years old). Mean age in groups P and N was not statistically meaningful ($p \leq 0.621$). Serum level of iron was averagely 70.22 ± 25.18 (31-121) mg dL^{-1} and 67.62 ± 39.53 (7-146) mg dL^{-1} in groups P and N, respectively. There was no statistically significant difference between groups P and N ($P \leq 0.696$). Serum level of ferritin was averagely 129.79 ± 137.67 (7.4-621) ng mL^{-1} and 109.87 ± 154.71 (4-956.5) ng mL^{-1} in groups P and N, respectively (Table 1). There was no statistically significant difference between groups P and N in serum level of ferritin ($p \leq 0.498$). In the group including patients suffering from Parkinson, grades I, II, III and IV+V were 13, 12, 15 and 10 cases, respectively. Serum level of iron was averagely 71.62 ± 27.12 (34-112) mg dL^{-1} , 76.58 ± 22.63 (45-121) mg dL^{-1} , 67.33 ± 29.19 (31-113) mg dL^{-1} and 65.10 ± 20.49 (41-101) mg dL^{-1} in grades I, II, III and IV+V, respectively. In this regard, there was no statistically significant difference between the mentioned groups ($p \leq 0.714$). Serum level of ferritin was 103.70 ± 90.45 (7.9-310.3) ng mL^{-1} , 132.15 ± 174.09 (7.7-621) ng mL^{-1} , 157.50 ± 161.96 (7.4-481.1) ng mL^{-1} and 119.31 ± 109.72

Methods: Age, gender, records of diabetes mellitus, hypertension, high levels of blood cholesterol, ischemic heart disease, smoking, serum level of iron and ferritin, percentiles of serum level of ferritin and Parkinson grading were studied. Serum level of iron (by biochemical methods) and ferritin (by luminance quantitative method) was measured and compared in all individuals. Parkinson was graded according to Hoehen and Yahr Scale and serum level of iron and ferritin was compared in different grades.

Statistical analysis: SPSS™ 15 was used as statistical program. The resulted data have been stated as Mean±SD, frequency and percentage. Categorical variables were compared using contingency tables,

Table 1: Characteristics of the study population

Characteristics	Idiopathic Parkinson N = 50	Healthy individuals N = 50	p-value
Age	$64.53 \pm 10.18^*$	63.53 ± 9.78	0.621
Sex			
Male	28	25	0.542
Female	22	25	0.532
Diabetes mellitus	8(16) [#]	5(10)	0.342
Hypertension	17(34)	20(40)	0.328
Ischemic heart disease	6(12)	3(6)	0.242
Smoking	7(14)	6(12)	0.624
Serum iron	70.22 ± 25.18	67.62 ± 39.53	0.696
Serum ferritin	129.79 ± 137.67	109.87 ± 154.71	0.498

*Values are as Mean±SD, #values in brackets are percentage

Table 2: Level of iron and ferritin in different grades of Parkinson

Serum level (mg dL^{-1})	Grade I	Grade II	Grade III	Grade IV+V
Iron	71.62 ± 27.12	76.58 ± 22.63	67.33 ± 29.19	65.10 ± 20.49
Ferritin	103.70 ± 90.45	132.15 ± 174.09	157.50 ± 161.96	119.31 ± 109.72

Values are as Mean±SD

(14.2-366.2) ng mL⁻¹ in grades I, II, III and IV+V, respectively (Table 2). In this regard, there was no statistically significant difference between the mentioned groups, too ($p \leq 0.779$).

DISCUSSION

This research studied and compared serum level of iron and ferritin in patients suffering from idiopathic Parkinson and control group population. Average serum level of iron was not substantially different in a group suffering from idiopathic Parkinson and control group. Comparing serum level of ferritin demonstrated that there was no substantially significant difference between a group with Parkinson and healthy one. Several studies have conducted considering possible role of iron and its metabolism in Parkinson pathophysiology. However, most of the studies dealt with iron and ferritin level of brain tissue and there are very little studies regarding serum level of these two parameters (Shi *et al.*, 2010; Tribl *et al.*, 2009). Results of these few studies were not the same, too. Logroscino *et al.* (1997) compared serum level of iron, ferritin and transferrin in two groups suffering from idiopathic Parkinson and healthy subjects. This study reported serum level of all three factors in patients suffering from idiopathic Parkinson substantially less than those of healthy group. However, Logroscino *et al.* (1997) achieved different result in another study. They studied role of blood donation and its times in relation to risk of Parkinson incidence. This study initially supposed that increasing times of blood donation may decrease Parkinson incidence risk through reducing body iron sources. However, this result was not confirmed while there was found a substantial and reverse relation between serum level of ferritin and times of blood donation (Marder *et al.*, 1998). Annamaki *et al.* (2007) showed that there was no substantially significant difference between serum levels of iron and ferritin in patients suffering from Parkinson and healthy subjects (Annamaki *et al.*, 2007). Grau *et al.* (2001) studied and compared serum lactoferrin and ferritin in 23 patients with Parkinson and 15 healthy individuals. In this study, no substantially significant difference was observed between two groups (Grau *et al.*, 2001). Considering results of the above-mentioned studies, it is evident that most of the mentioned studies did not report any substantially difference between the group suffering from Parkinson and healthy subjects considering serum level of iron and ferritin. The results of this study are consistent with these findings, too. Patients age is one of the most important considerations regarding differences observed in serum level of iron. It has been demonstrated that serum level of

iron in aged subjects suffering from Parkinson is substantially higher than those of younger healthy subjects. But, it has no substantially significant difference with serum level of iron in aged healthy subjects (older than 65 years old) and even with those who are at the same age (Hunter *et al.*, 2008). The present study compares serum level of iron and ferritin at different levels of Parkinson disease (based on Hohen and Yahr Staging). No substantially difference was observed considering different stages of disease. In Grau *et al.* (2001) study 23 patients suffering from Parkinson classified according to Hohen and Yahr staging and level of ferritin was compared. Here, no substantially difference was observed, too (Grau *et al.*, 2001). In this study, just 20% of subjects, suffered from idiopathic Parkinson grade IV or V. In other studies few percents of patients suffered from advanced disease (Kaur *et al.*, 2003; Youdim *et al.*, 2004). Therefore, further studies on these patients with higher levels of severity of Parkinson may be helpful in achieving definite results.

CONCLUSION

This study concluded that generally there is no significant difference between the patients with the idiopathic Parkinson disease and healthy controls in terms of serum iron and ferritin levels. The same results were attributable to different grades of the disease.

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