The Role of Neudesin as a Novel Biomarker – in Iraqi Patients with Parkinson's Disease and Osteoporosis

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Abstract

Neuron-derived neurotrophic factor [NENF], a human plasma neurotrophic factor, also increases neurotrophic activity in conjunction with Parkinson's disease-related proteins in Neudesin. Although Neudesin (neuron-derived neurotrophic secreted protein) is a member of the membrane-associated progesterone receptor (MAPR) protein subclass, it is not evolutionary related to the other members of the same family. The expression of Neudesin is found in both brain and spinal cord from embryonic stages to adulthood, as w Neudesin levels in Parkinson's patients with osteoporosis disease and Parkinson's patients without osteoporosis disease, as well as the relationship between Neudesin levels, Anthropometric and Clinical Features (Age, Gender, BMI) and Serum Parathyroid Hormones vit D3, Ca and phosphorous, were studied in this study. Eighty individuals participated in this study. Osteoporosis is a risk factor for Parkinson's, and Osteoporosis is a risk factor for Parkinson's disease. In order to conduct this study, we selected patients from the Parkinson's Disease and Osteoporosis Center in Baghdad/ Alrisafa. G1 and G2 were (55-67) years old, (38-75) years old, and (55-66) years old, respectively. In all of the groups examined, the ratio of males to females has risen. Men are more likely than women to be diagnosed with Parkinson's disease, accounting for this disparity. Neudesin concentrations in G1 and G3 were substantially lower than those in G2 (P= ±0.0001), although G1's concentration was somewhat higher than G2's (0.803±0.091 ng./ml). A "cut-off value" for determining sensitivity and specificity to diagnose the condition was also determined in the study, which included examining the link between blood Neudesin levels and the classification of participants into cases and controls.

Key Words: Neudesin, Parkinson's Disease, Osteoporosis Disease.

DOI Number: 10.14704/nq.2022.20.4.NQ22140 **NeuroQuantology 2022; 20(4):423-428**

Introduction

People who have Parkinson's disease have a wide range of motor and non-motor symptoms and the hallmarks of rest tremor and bradykinesia, stiffness, and postural instability, which James Parkinson first described in 1817. (Jaukovic, 2008; Obeso, J.A, et 2017; Armstrong, MJ, 2020). As Parkinson's Disease (PD) progresses, the dopaminergic neurons in the substantia nigra pars compacta (SNpc) and the striatum (striatum) start to die off, which can have a big impact on a person's cognitive, psychological, and social abilities. Unfortunately, the exact cause of PD is still unknown (2020). PD is more common in men than women, with a statistical difference of about 50%. There is no clear reason for this difference. Men are more likely to get minor head injuries and be exposed to toxic chemicals at work, while women are more likely to get estrogen. Some researchers think this could be why women have a lower risk of getting cancer, while men have a higher risk.

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Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.
Received: 22 February 2022 **Accepted:** 27 March 2022

(Agyekum, H, 2018). With so much clinical and genetic data available, it can be difficult to sift through it all and find therapeutically relevant information (Balestrino, R & Schapir, A.H.V, 2020). The naturally unfolded-synuclein takes on a tertiary structure when it meets certain biochemical needs. PD-related neurodegeneration is caused by abnormal protein aggregation, oxidative stress, PD gene mutations, and overexpression of the PD gene, among other things. Another thing to know about-synuclein is that it can take on different species-specific conformational changes and aggregation depending on the conditions in which it is being made. The relative toxicity of its oligomeric and fibrillar forms has been debated.-synuclein also comes in different forms and species depending on the conditions of the experiment (Trudeau L.E., & N Burke Nanni, S 2018).

Both Osteoporosis and Parkinson's disease (PD) are connected with advanced age in terms of mortality and morbidity. The frequency of an individual increases throughout time, and the two may enhance one another's illnesses. Numerous studies have demonstrated that women with Parkinson's disease have progressive bone loss and an increased risk of pain, disability, and low energy fractures (Btstryt Ska, M, povoroznyuk at 2020); however, the precise mechanisms underlying Osteoporosis and its consequences in PD subjects remain unknown. Reduced BMD indices have been seen in Parkinson's disease (PD) persons. However, these findings are inconsistent and depend on gender, ethnic origin, and other features. Vertebral fractures are a common complication of systemic Osteoporosis in people with Parkinson's disease (Hosseinzadeh, A, Khalili 2018; Lee, J.Y., Lim, N.G, 2019).

According to a study group from the World Health Organization, people who have Osteoporosis have less bone mass, which makes their bones more fragile and more likely to break. This group came up with general criteria for diagnosing Osteoporosis based on dual-energy X-ray absorptiometry (Ukon, Y., Makino, T., Kodama, J 2019).

If you look at Neudesin, which is a member of the membrane-associated progesterone receptor (MAPR) protein subclass, you will see that it is not related to other members of the same family in terms of evolution. Neudesin is found in both the brain and spinal cord from the time a person is born until they are adults, as w. Neudesin's action is still unknown, but it was thought that NENF might help stabilize progesterone when progesterone membrane receptors activated it. This is because NENF is a member of the MAPR family and shares 40% structural homology with MAPR. However, more research is needed to ensure this is true (PGRMC1). In the hippocampal region, for example, progesterone was found to promote the growth of neural precursors through PGRMC1. This process is called five reductases, and it is essential to keep excitability and inhibition in balance. Progesterone metabolites also play a role in promoting neural precursor growth through PGRMC1.

Materials and Methods

Prospective research was conducted between February 2020 and July 2021 at the Specialized Center for Parkinson's with Osteoporosis Disease in Baghdad, Iraq. The research's design and participants: In this study, eighty volunteers were divided into three groups: There are fourteen patients in G1: Parkinson's disease and Osteoporosis, seven of them are male and seven of whom are female. Among the 36 Parkinson patients in G2: Parkinson without Osteoporosis, 28% are male and 8% female. G3 has 30 participants, 17 of whom are men, and 13 of whom are female controls. Male-to-female ratios in all patients have risen throughout time. Ten milliliters of venous blood were collected from the research subjects and a control group and put in a plain tube for 15 minutes at room temperature before being centrifuged at 4000 rpm for 10 minutes to extract serum, which was then refrigerated at (-20^{o}C) unless it was utilized right away. All of the above factors, Neudesin, PTH, Ca^{+2} Phosphorous, and Vit D3, must be considered. As weight (kg)/height (m) squared, we arrived at the individuals' BMIs (m^2).

Measurement of Serum Levels: To measure Neudesin levels, enzyme-linked immunosorbent assay (ELISA) kits (Human ENFE, ELISA Kit).

Results & Discussion

The table shows Neudesin concentrations in the three groups of patients (G1: Parkinson's with Osteoporosis, G2: Parkinson's without Osteoporosis, and G3: controls): (1). According to the results, the mean concentration of serum Neudesin for group 1 (1.376±0.122 ng/mL) was similar to that of group 3 (1.332±0.139 ng/mL), while the mean concentration of serum Neudesin for group 1 (1.376±0.122 ng/mL) was greater than

that of group 2 (0.803±0.091 ng/ml), as shown in figure 1. (1). More research is needed because no studies have looked into Neudesin's connection to Parkinson's disease or Osteoporosis. There was a significant (P=0.0001) correlation between the mean serum parathyroid concentrations in G1 (225.894±28.960ng/mL) and G3 (253.2755±1.616ng/mL), as shown in table (2), while the mean serum parathyroid concentrations in G1 (225.894±28.960ng/mL) were only marginally higher than those in G2 (199.952±18.749ng/mL). Because steroids make it hard for calcium to be absorbed from the intestines and reabsorbed from the kidney tubules, they can cause secondary hyperparathyroidism as a way to compensate for this. (Ohya, Y., Osaki, at 2018). Parathyroid hormone is another biological sign that can influence the course of PD symptoms (PTH). Furthermore, it appears that the intensity of PD symptoms is influenced by parathyroid gland function (Rocchitta, G, Migheli 2004). Table 2 shows that the mean serum calcium in G1 (10.562±0.465 mg/mL) was extremely significantly (P=0.0001) higher than the mean serum calcium in G3 (9.425±0.630 mg/mL), while the mean serum calcium in G1 (10.562±0.465 mg/mL) was somewhat higher than the mean serum calcium in G2 (10.249±0.670 mg/mL). PD's pathophysiology has been linked to various biochemical indicators, according to several research (Hirsch, E.C. 2013; Doherty, G.H. 2013). Calcium is an important part of how neurons work, how the depolarizing signal is sent, and how synapses work, all of which are linked to Parkinson's disease. (Cali, T. 2014). Furthermore, multiple studies have shown that calcium dysregulation is a contributing factor in developing Parkinson's disease. Dopaminergic neuronal death in the Substance Nigra (SNs) in the midbrain is caused by various molecular and neurological abnormalities, including autophagy and mitochondrial dysfunction, ER stress, and dysregulation of calcium hemostasis (Michel, P.P. 2016). In SNs, neuronal cell death is caused by losing calcium hemostasis. Mitophagy disruption, ER stress, mitochondrial malfunction, and synuclein aggregation may cause abnormal calcium hemostasis in DA neurons. The survival of DA neurons is reduced when calcium levels are either too high or too low. Calcium balance in DA neurons can be disrupted by various molecular diseases, such as an excess of NMDA receptor activation. Calcium elevations produce an overproduction of dopamine in DA neurons, resulting in autointoxication (hrani, S.S2020). Table 2 shows that the mean serum phosphorus in G1 (2.768 ±0.836 mg/dL) was slightly higher (P=0.0001) than the mean serum phosphorus in G3 (1.549 0 ±.784 mg/dL), while the mean serum phosphorus in G1 (2.768 ±0.836 mg/dL) was significantly lower (P=0.0001) than the mean serum phosphorus in G2 (6.991 ±11.396 mg/dL). Many studies have linked biochemical markers like phosphorus to PD and concluded that the difference in phosphorus serum levels between the two groups was insignificant (Chan, R. 2012). According to the study, there was a big difference in the amount of phosphorous in the blood of the two groups. Furthermore, low phosphorus levels were linked to a higher rate of Parkinson's disease (Tehrani, S.S, 2020). While the current research found a substantial variation in serum phosphorus levels between three gropes. Previous research has linked phosphorus in the blood to Parkinson's disease, with a very significant drop (p<0.001) compared to the control group. Table 2 shows that the mean serum vitamin D3 in G1 (25.013±2.044pg/mL) was slightly higher (P=0.0001) than the mean serum calcium in G3 (24.431±1.531pg/mL), and that the mean serum vit D3 in G1 (25.013±2.044pg/mL) was higher than the mean serum vit D3 in G2 (21.546±0.801pg/mL). If you do not know your blood vitamin D levels or remember things differently than you did, it is hard to make clear conclusions from this study. Furthermore, even though physical activity outside was used as a proxy for vitamin D status, there is strong evidence that physical exercise lowers the risk of Parkinson's disease, which could be a possible confounder in this study (Fang. X, 2018). It has not been proven that vitamin D levels are linked to the risk of getting Parkinson's disease. In contrast to the Finnish study, a study of more than 13,000 people in the United States found no link between vitamin D levels at the start of the study and the risk of Parkinson's disease 17 years later (Shrestha, S. 2016). Much previous research has shown that vitamin D 3 levels in the blood are linked to Parkinson's disease, with a huge difference (p 0.001) when compared to the control group (Order, A, and, Oada 2020), but this study found that vitamin D3 levels dropped in all three groups (p < = 0.0001 for all three groups). (Oader, A, and, Oada 2020).

Table 1. Serum levels of Neudesin in G1, G2 and G3

Parameter	Parkinson's disease & Osteoporosis patients n=14	Parkinson's disease without Osteoporosis patients n=36	Control N=30	P value
Neudesin (ng/mL)	1.376±0.122 (1.208-1.615)	0.803±0.091 (0.638-0.992)	1.332±0.139 (1.137-1.625)	0.0001^
^Significant difference among more than two independent means using ANOVA-test at 0.05 level.				

G1: Parkinson's disease & Osteoporosis patients.
G2: Parkinson's disease without Osteoporosis patients.
G3: Control.

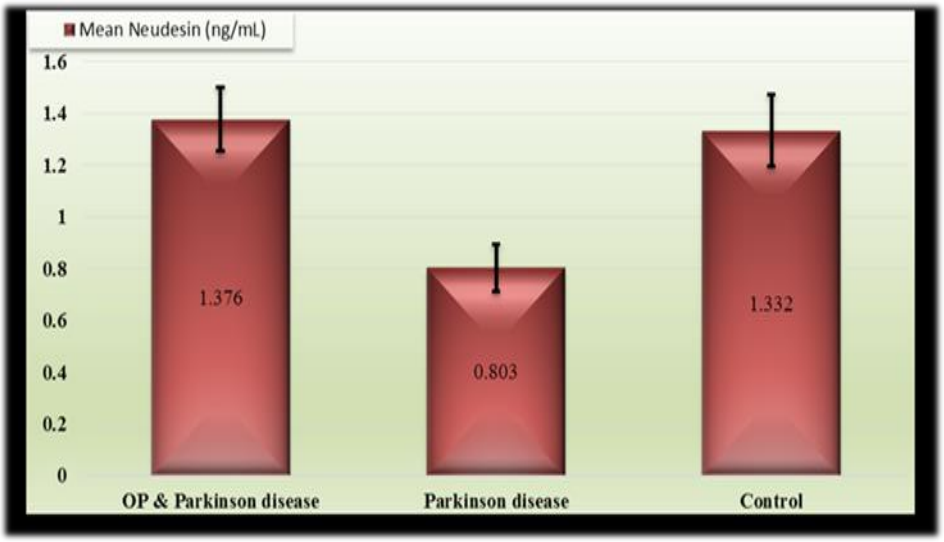

Fig. 1. Serum Neudesin hormone levels in G1: Parkinson's with Osteoporosis, G2: Parkinson's without Osteoporosis and G3: controls

Table 2. Serum levels of (PTH, Ca, phosphorus, and vit D3) in G1, G2, and G3

Parameter	Parkinson's disease & Osteoporosis patients n=14	Parkinson's disease without Osteoporosis patients n=36	Control N=30	P-value
Parathyroid(pg/mL)	225.894±28.960 (174.738-292.984)	199.952±18.749 (174.055-236.933)	253.275±51.616 (191.970-385.404)	0.0001^
Ca (mg/dL)	10.562±0.465 (9.675-11.060)	10.249±0.670 (6.932-11.165)	9.425±0.630 (8.182-10.444)	0.0001^
Phosphorus (mg/dL)	2.768±0.836 (1.389-4.592)	6.991±1.396 (5.138-9.780)	1.549±0.784 (0.586-3.547)	0.0001^
Vit D3 (ng/ml)	25.013±2.044 (22.676-27.625)	21.546±0.801 (19.788-22.939)	24.431±1.531 (22.722-27.561)	0.0001^
#Significant difference between two independent means using Students-test at 0.05 level.				
^Significant difference among more than two independent means using ANOVA-test at 0.05 level.				

Serum Neudesin Correlation Study

Serum Neudesin's association with the research population has analyzed clinical and biochemical indicators is outlined in the table (3). For G1 patients, serum Neudesin levels were negatively linked with age, calcium, vitamin D3, and parathyroid hormone (PTH). There was also a significant negative association between serum Neudesin levels and Age, BMI, and Vitamin D3.

Table 3. Correlation of Neudesin to clinical and biochemical parameters for G1 and G2.

		Parkinson's disease with Osteoporosis (G1)	Parkinson's disease (G2)
		Neudesin (ng/mL)	Neudesin (ng/mL)
Age (years)	r	- 0.430	- 0.142
	P	0.125	0.409
BMI (Kg/m2)	r	0.171	- 0.261
	P	0.559	0.124
Ca (mg/dL)	r	- 0.345	0.135
	P	0.227	0.433
Phosphorous (mg/dL)	r	0.315	0.136
	P	0.273	0.430
Vit D3 (ng/ml)	r	- 0.276	- 0.016
	P	0.340	0.927
Parathyroid (pg/mL)	r	- 0.416	0.274
	P	0.139	0.106
*Correlation is significant at the 0.05 level			

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