Oxidant /Antioxidant Status in Newly Diagnosed Patients with Parkinsonism :Effects of Therapy

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الخلاصه

لتقييم تأثيرات العلاج الثابت على حالة الاكسده(مستوى المالونديليهايد)/ مضادات الاكسده (مضادات الاكسده الكليه) في مرضى باركنسون المشخصين حديثا"بالمقارنه مع مجموعة ضبط من الاصحاء.

ادخل لهذه الدراسه 38 من مرضى باركنسون المشخصين حديثا.احليت هذه الحالات من عياده للامراض العصبيه من تشرين الاول 2009 ولغاية شباط 2011.ادخل للدراسة ايضا اربعون من الاشخاص الاصحاء من اعمار واجناس مقاربه لمجموعة المرضى كمجموعة ضبط. في البدايه سحبت عينات من الدم من مجموعة المرضى قبل بدء العلاج ومجموعة الضبط وتم قياس مستوى المالونديليهايد ومضادات الاكسده الكليه في مصل الدم كما وتم حساب دلالة كتلةالجسم باستخدام معادله خاصه. بعدها وضع المرضى على علاج ثابت وبجرعه موحده لمدة ثلاثة اشهر بعدها تم سحب عينةدم ثانيه من مجموعة المرضى وقياس نفس المفردات المذكوره اعلاه.

كان هنالك ارتفاع معنوي في مستوى المالونديليهايد وانخفاض معنوي في مستوى مضادات الاكسده الكليه في مصل الدم في مرضى باركنسون بالمقارنه مع مجموعة الضبط. بعد فترة العلاج بقي الارتفاع المعنوي في مستوى المالونديليهايد والانخفاض المعنوي في مستوى مضادات الاكسده الكليه في مصل الدم بالمقارنه مع مجموعة الضبط.

لم يكن هنالك اختلاف معنوي في مستوى المالونديليهايد ومضادات الاكسده الكليه في مرضى باركنسون في مرحلة ماقبل وبعد العلاج.

هنالك علامات فرط الاكسده عند مرضى باركنسون المشخصين حديثا وان العلاج بمضادات باركنسون المحدده في هذه الدراسه كان ذا تأثير لايذكر على التحول في حالة الاكسده/مضادات الاكسده.

Abstract

To assess effects of a fixed therapy on the oxidant (malondialdehyde "MDA" levels)/ antioxidant status (Total antioxidant status "TAS")in newly diagnosed patients with Parkinson disease in comparison to healthy controls.

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Thirty eight newly diagnosed patients with Parkinson disease were included in this study. they were referred cases from neurologist Clinic from October 2009 to February 2011. included also in the study 40 apparently healthy age and sex matched subjects as a control groups. A blood samples were taken initially from the patients before starting therapy and the controls and assay of serum MDA and TAS were done. Body mass index (BMI) were calculated according to a certain equation. Patients then were put on fixed therapy for 3 months after which another blood samples were taken and assay of the same parameters were done.

There was a significantly elevated serum MDA and a significantly lowered serum TAS levels in newly diagnosed patients with Parkinson disease in comparison to healthy controls. After therapy patients still having a highly significant difference in the levels of serum MDA and TAS in comparison to controls.

There was insignificant difference in the serum levels of MDA and TAS between patients in the pre-therapy and post-therapy stages.

Newly diagnosed patients with Parkinson disease having signs of oxidation stress, and that the specific anti-parkinsonian therapy used in this study have no significant effect on the shifted oxidant/ antioxidant status.

Keywords: Parkinson's disease, MDA, TAS, effect of anti-parkinsonian therapy.

Introduction

Parkinson's disease (PD), is a major chronic neurodegenerative condition of the elderly[1]. Although most patients with PD appear to have no strong genetic determinant, epidemiologic evidence points to a complex interaction between genetic vulnerability and environmental factors[2].

Oxidative stress (OS) has been implicated as a major mechanism in the pathogenesis of PD. There are several factors that predispose brain tissue to high oxidative damage susceptibility. The brain consumes a large amount – approximately 20% of total

body oxygen, although it represent less than 2% of total body weight[3]. A further compromising factor is that the brain is relatively deficient in protective mechanisms because it has markedly reduced levels of glutathione,glutathione peroxidase and tocopherol compared to the liver[4].

Malondialdehyde (MDA) is the most generally used index of lipid peroxidation in the appreciation of the role of oxidative stress in disease and it is often assayed with thiobarbituric acid (TBA) procedure[5,6]

The aim of this study was to assess, oxidant status (represented by serum MDA), antioxidant status (represented by serum total antioxidant status TAS), in newly diagnosed patients with PD and the effect of 3 months of a fixed therapy on such parameters in comparison to healthy controls.

Patients and methods

This study included 38 newly diagnosed patients with PD according to clinical criteria[7]. They were 28 males and 10 females, they were referred cases from a private neurological clinic from October 2009 to February 2011. Clinical disability of the patients ranged from I to II according to the Hoehn and Yahr rating scale [1]. Patients with other diseases or on drug therapy were excluded from the study. Included in the study also 40 apparently healthy, age and sex matched subjects as a control group. They were 29 males and 11 females. For the patients group after diagnosis, a blood samples were taken and assay of serum MDA and TAS were done. Patients then put on a fixed regimen as follows:

levodopa 250mg+carbidopa 25mg (Sinemet-MSD-USA) 1/2 tablet 6 times /day

Bezhexol (Parkizole- Hikma-Jordan) 2mg tab 1 tablet 3 times /day

Bromocriptine (Parlodil-Novartis-Swiss) 2.5mg tab 1 tablet 2 times/day

They were given for 3 months after which another blood samples were taken and assay of the same parameters were done.

For the control, a blood samples were taken and also assay of serum MDA and TAS levels were done.

For both patients and controls, BMI were calculated according to the following equation:

BMI= Weight (Kg) / Height (m^2) [8]

The characteristic of the patients and controls are given in table 1.

Statistical analysis:

Standard statistical methods were used to determine the mean and standard deviation (SD).Unpaired t-test was used to compare the results of different biochemical parameters of patients with PD with the controls. Paired t-test was used to compare the results of different biochemical parameters among patients with PD before and after therapy. P-value ≤ 0.005 was considered to be statistically significant[9].

Methods: Serum MDA level was measured using TBA assay method[6] .TAS assay was according to the method discovered by Miller et al [10] ,using a kit supplied by Randox company (UK).

Results

Table 2 showed that patients with PD had an elevated serum level of MDA and a low blood level of TAS in comparison with healthy controls.

There was insignificant differences between the levels of MDA and TAS in patients with PD at pre-therapy and post-therapy stages (Table 3).

By comparison of the serum level of MDA and TAS in patients with PD at post-therapy, and controls, there was a significantly elevated MDA and a significantly lowered TAS levels (Table 4).

Table 1: The characteristics of controls and patients with Parkinson's disease .

Group	Parameter	Mean ± SD
Control Number=40	Age (years)	62.55 ± 6.17
	BMI (Kg/m^2)	21.75 ± 1.68
Patients Number=38	Age (years)	60.59 ± 7.81
	BMI (Kg/m^2)	21.81 ± 1.89

Table 2: Comparison between mean serum levels of MDA and TAS in patients with parkinson's disease in the pre-therapy stages and controls.

Parameters	Control Mean± SD	Patients pre-therapy stage Mean± SD	P-value
MDA (µmol/L)	1.14 ± 0.12	1.93 ± 0.18	S
TAS (mmol/L)	1.74 ± 0.13	1.15± 0.11	S

S: statistically significant differences using unpaired t-test.

Table 3:Comparison between mean serum levels of MDA and TAS in patients with parkinson's disease in the pre-therapy and post- therapy stages.

parameters	Patients pre-therapy stage Mean± SD	Patients Post- therapy Stage Mean± SD	P-value
MDA (µmol/L)	1.93± 0.18	1.88 ± 0.16	NS
TAS (mmol/L)	1.15 ± 0.11	1.17± 0.09	NS

NS: statistically non-significant differences using paired t-test.

Table 4: Comparison between mean serum levels of MDA and TAS in patients with parkinson's disease in the post-therapy stages and controls.

parameters	**Control Mean ± SD**	**Patients post- therapy Mean ± SD**	P-value
MDA (µmol/L)	1.14 ± 0.12	1.88 ± 0.16	S
TAS (mmol/L)	1.74 ± 0.13	1.17± 0.09	S

S: statistically significant differences using unpaired t-test.

Discussion

In recent years there has been increasing evidence suggesting that OS plays an important role in the pathogenesis of PD[11,12]. In PD the increased dopamine synthesis demanded by surviving nigral neurons increase the production of free radicals [13]. Koutsillieri et a[l(12)], concluded that OS plays a significant role in generating cell death signals including apoptosis in patients with PD.

This study revealed an elevated serum MDA levels in patients with PD at diagnosis in comparison to healthy controls. This is in agreement with the study conducted by Younes Mhanni et al [14]. They reported a significant elevation in the mean TBA concentration in both levodopa treated and untreated patients with PD compared to control group. Our findings also goes with the findings of Sanyal et al [15] who reported that the plasma MDA levels are significantly higher in PD patients in comparison to controls. In contrast Molina et al [16], reported that serum MDA levels did not differ significantly in patients with PD in comparison to healthy controls, and suggested that high serum lipid peroxidation rates constitute a risk factor for younger onset PD in predisposed individuals. Increased levels of MDA in peripheral blood in patients with PD may indicate a systemic reaction to chronic oxidative stress in the brain.

With regard antioxidant status, this study reported that TAS levels were lower in patients with PD. Many research workers reported a significant decrease in the activity of catalase protective enzyme in erythrocytes of patients with PD compared to healthy controls[14,17,18]. King et al [19] studying the concentration of antioxidant vitamins A, C and E in elderly patients with Parkinson's disease reported that there is no evidence that a deficiency of the antioxidants contributes to the onset or progress of PD. In our study determination of TAS is a tool used to evaluate the general antioxidant defense status. It has the advantage of measuring the overall antioxidant status regardless of individual variations in the elements of the antioxidant defense system[10].

This study also revealed, insignificant effect of a fixed therapy (Sinemet, Parkizole and Parlodil) on the shift occurring in the

oxidant / antioxidant status in patients with PD. This might indicate that lipid peroxidation level is not influenced by anti- Parkinsonism therapy in patients with PD which is the same conclusion reported by Molina et al[16].On the other hand Buhmann et al., [20] reported no significant changes in plasma lipoprotein oxidation, but an increase in plasma autoxidation and a decrease in plasma antioxidant in patients with PD treated with levodopa.

This might be the first study in assessing the effect of a fixed therapy on total antioxidant status in newly diagnosed patients with PD.

In conclusion: Newly diagnosed patients with PD having signs of oxidation stress, and that the specific anti-Parkinsonian therapy used in this study have no significant effect on the shifted oxidant/ antioxidant status.

References

1. Hoehn MM; Yahr MD. Parkinsonism: onset, progression and mortality. Neurol 1967;17:427-442.
2. Quinn I; Bahtia K; Brown P; Cordivari C; Hariz M; Lees A et al. M; Lees A et al. Movement disorders In: Clarke C; Howard R; Rossor M; Shorron S (eds). Neurology A Queen Square Textbook 1st edition 2004. Wiley –Blackwell Ltd. pp:155-164.
3. Floyd RA; Carney JM. Free radical damage to protein and DNA: Mechanisms involved and relevant observations on brain undergoing oxidative stress. Ann Neurol 1992;32:S22-S27.
4. Floyd RA; Zaleska M; Harmon HJ. Possible involvement of iron in oxygen free radicals in aspects of aging in brain. In: Free radicals in molecular biology: Aging and disease. Armstrong D et al (eds). New York: Raven press, 1984.pp:143-161.
5. Gawat S; Wardas M; Niedworok E; Wardas P. Malondialdehyde (MDA) as a lipid peroxidation marker. Wiadlek 2004; 57:453—455.
6. Lefevre G, Beljean-Leymarie M; Beyerle F; Bonnefont-Rousselot D; Cristol JP; Therond P etal. Evaluation of lipid peroxidation by measuring thiobarbituric acid reactive substances. Ann Biol Clin 1998;56(3):305-319.

7. Hughes AJ; Ben-Shlomo SE; Daniel SE; Lees AJ. What features improve the accuracy of clinical diagnosis in Parkinson's disease. A clinicopathological study. Neurol 1992;2:1142-1146.
8. Leermarkers EA; Dunn AL; Blair-SN. Exercise management of obesity. Med Clin North Am 2000;84:419-425.
9. Kirkwood BR. Essential of medical statistics 1st edition-Blackwell Scientific Publication, Oxford 1989.pp43-56.
10. Miller NJ; Rice-Evans C; Davies MJ; GopinathanV; Milner A. A novel method for measuring antioxidant capacity and its application to monitoring the antioxidant status in premature neonates. Clin Sci 1993; 84:407-412.
11. Jenner P; Olanow CW. Oxidative stress and the pathogenesis of Parkinson's disease. Neurol 1996;47 (6 suppl 3):S161-S-170.
12. Koutsilieri E; Scheller C; Grunblatt E; Nara K; Li J; Riederer P. Free radicals in Parkinson's disease. J Neurol 2002;249 (suppl 2):1-5.
13. Clane DB; Langston JW. Etiology of Parkinson's disease. Lancet 1983;2:1457-1459.
14. Younes-Mehnni S; Frih-Ayed M; Kerkeni A; Bost M; Chazot G. Peripheral blood markers in oxidative stress in Parkinson's disease. European Neurol 2007;58(2):78-83.
15. Sanyal J; Bandyopadhyay SK; Banerjee TK; Mukherjee SC; Chakraborty DP; Ray BC et al. plasma levels of lipid peroxides in patients with Parkinson's disease. European Rev Med Pharmacol Sci 2009;13:129-132.
16. Molina JA; Jimenez-Jimenez FJ; Fernandez-Calle P; Lalinde L; Tenias JM; Pondal M et al. Serum lipid peroxides in patients with Parkinson's disease. Neurol Sci Letters 1992; 136(2):137-140.
17. De la Torre R; Casado A; Lopez- Fernandez E; Carrascosa D; Casado MC; Venarucci D etal. Human aging brain disorders: role of antioxidant enzymes. Neurochem Res 1996;21(8):885-888.
18. Abraham S; Souandarajan CC; Vivekanandhan S; Behari M. Erythrocyte antioxidant enzymes in Parkinson's disease. Indian J Med Res 2005;121:111-115.

19. King D; Playfer JR; Roberts NB. Concentrations of vitamin A,C and E in elderly patients with Parkinson's disease. Postgrad Med J 1992;68:634-637.
20. Buhmann C; Arlt S ; Kontush A; Moller- Bertram T; Sperber S; Oechsner M et al. Plasma and CSF markers of oxidative stress are increased in Parkinson's disease and influenced by antiparkinsonism medication. Neurobiol Disease 2004;15:160-170.