J Neural Transm (2000) 107: 177–181

Journal of Neural Transmission

Serum levels of coenzyme Q_{10} in patients with Parkinson's disease

F. J. Jiménez-Jiménez[1], **J. A. Molina**[2], **F. de Bustos**[3], **A. García-Redondo**[3], **C. Gómez-Escalonilla**[2], **A. Martínez-Salio**[2], **A. Berbel**[2], **A. Camacho**[2], **M. Zurdo**[1], **B. Barcenilla**[1], **R. Enríquez de Salamanca**[4], and **J. Arenas**[3]

[1] Department of Medicine-Neurology, University of Alcalá, Alcalá de Henares, Madrid,
[2] Department of Biochemistry, and
[3] Neurology, Hospital Universitario Doce de Octubre, Madrid,
[4] Department of Medicine, University Complutense, Madrid, Spain

Received July 14, 1999; accepted August 3, 1999

Summary. We compared serum levels of coenzyme Q_{10} and the coenzyme Q_{10}/cholesterol ratio in 33 patients with Parkinson's disease (PD) and 31 matched controls. The mean serum coenzyme Q_{10} levels did not differ significantly between the 2 study groups. Coenzyme Q_{10} levels were not correlated with age, age at onset, duration of the disease, scores of the Unified Parkinson Disease Rating Scale (UPDRS) or the Hoehn and Yahr staging in the PD group. The coenzyme Q_{10}/cholesterol ratio had a significant correlation (although low) with duration of the disease ($r = -0.46$), total UPDRS score ($r = -0.39$), motor examination of the UPDRS ($r = 0.45$). These values were not influenced significantly by therapy with levodopa or dopamine agonists. The normality of serum coenzyme Q_{10} and coenzyme Q_{10}/cholesterol ratio suggest that these values are not related with the risk for PD.

Keywords: Parkinson's disease, oxidative stress, coenzyme Q_{10}, mitochondrial function, serum levels.

Introduction

The pathogenesis of the neuronal degeneration of neurons in the pars compacta of the substantia nigra in patients with Parkinson's disease (PD) remains unknown. Several studies suggested the presence of oxidative stress in the substantia nigra of PD patients (reviewed by Jiménez-Jiménez et al., 1998a), although the significance of these findings is unclear.

The activity of the complex I of the mitochondrial respiratory chain is decreased in the substantia nigra of PD patients. However, the results of studies measuring mitochondrial complexes in peripheral tissues such as muscle, platelets, and lymphocytes, are controversial (reviewed by Jiménez-Jiménez et al., 1998b; Schapira, 1994).

Coenzyme Q_{10} (CoQ_{10}) is the electron acceptor for mitochondrial complexes I and II and a powerful antioxidant (Ernster and Dalner, 1995). Shults et al. (1997) reported correlation between mitochondrial CoQ_{10} levels and activities of complexes I and II/III, and decreased mitochondrial CoQ_{10} levels in platelets from parkinsonian patients. In addition, Matsubara et al. (1991) found decreased serum CoQ_{10} levels in PD patients.

The aim of this study was to assess the serum levels CoQ_{10} in a large series of patients with PD compared to a control population, in order to elucidate whether low serum levels of this antioxidant could play a role as risk factor for PD.

Patients and methods

We assessed the serum levels of CoQ_{10}, and the CoQ_{10}/cholesterol ratio in 33 patients with PD recruited from outpatients attended in the Neurology Departments of 2 urban Hospitals. They fulfilled diagnostic criteria for PD (Hughes et al., 1992) and were evaluated with the Unified Parkinson's Disease Rating Scale (UPDRS) (Fahn et al., 1987) and the Hoehn and Yahr staging (1967). Thirtheen patients were untreated, while the other 20 were treated with antiparkinsonian drugs alone or in combination including levodopa (18 cases), bromocriptine, pergolide or ropinirole (14 cases), and deprenyl (5 cases).

The control group comprised 31 healthy patients. Informed consent was obtained in each case. The clinical features of both groups are summarized in Table 1.

The following exclusion criteria were applied both to patients and controls: A) Ethanol intake higher than 80 g/day in the last 6 months. B) Previous history of chronic hepatopathy or diseases causing malabsorption. C) Previous history of severe systemic disease. D) Atypical dietary habits (diets constituted exclusively by one type of foodstuff, such as vegetables, fruits, meat, or others, special diets because of religious reasons, etc) F) Intake of drugs which modify lipid absorption. G) Therapy with vitamin supplements in the last 6 months.

Table 1. Clinical data and results of PD patient and control groups. Data of quantitative variables are expressed as mean ± SD. *PD* Parkinson's disease, *ADL* activities of daily living

	PD-patients n = 33	Controls n = 31
Clinical data		
Age (years)	66.5 ± 12.3	64.7 ± 8.0
Female	18	19
Male	15	12
Age at onset of PD (years)	61.1 ± 12.8	
Duration of PD (years)	5.4 ± 5.2	
Scores of the Unified PD Rating Scale (UPDRS)		
Total (items 1–31)	30.2 ± 13.9	
ADL subscale (items 5–17)	12.3 ± 7.9	
Motor subscale (items 18–31)	15.6 ± 7.4	
Hoehn and Yahr stage	2.3 ± 0.9	
Coenzyme Q_{10} levels (nmol/L)	1,157 ± 344	1,219 ± 424
Coenzyme Q_{10}/cholesterol ratio	0.23 ± 0.06	0.23 ± 0.05

Venous blood samples were taken from each fasted patient or control between 8.00 and 10.00 a.m. The blood samples were collected on ice and centrifuged. The serum specimens were frozen at −30°C and protected from light exposure with aluminum foil until analysis. The determinations were performed blindly.

Serum levels of CoQ_{10} were determined by high performance liquid chromatography with electrochemical detection. The method used was that of Langedijk et al. (1996) with some modifications. Since $CoQH_2$ (reduced form of CoQ_{10}) is easily oxidized to CoQ_{10} (ubiquinone) from the moment of the sample extraction, we evaluated the total CoQ_{10} (sume of CoQ_{10} and $CoQH_2$). When samples were extracted, precautions were not taken to prevent oxidation of $CoQH_2$ to CoQ_{10}, so the ratio $CoQH_2/CoQ_{10}$, could not be determined. Sample preparation was the same as Langedijk et al. (1996). The stationary phase was a reverse phase column (HR-80 RP-C_{18}, 80 × 4,6 mm. ESA Inc). The mobile phase was prepared dissolving 7 gr. of $NaClO_4.H_2O$ in 1,000 ml of methanol/propanol/$HClO_4$ 70%, 700.8:200:0.2 (vol/vol), and the flow rate was set at 0.8 ml/min. The programed conditions for the electrochemical detector and the post-column valve were the same too. The system was enterely controlled by a computer (Kromasystem 2000, Kontron Instruments). Injections were made in a 50 µl injection valve (Model 7161, Rheodyne, Cotaty, USA) with a 100 µl syringe from Hamilton (Bonaduz, Switzerland). The calibration method used ubiquinone as external standard. The within-run coefficients of variation for CoQ_{10} and $CoQH_2$ were, respectively, 5 and 3.2%, and the day to day precisions were 9.2 and 6.3%. CoQ_{10} recovery ranged between 88 and 93%. The measurements of CoQ_{10} were expressed in nmol/L.

The determinations of serum cholesterol were carried out in a Hitachi 717 autoanalyzer with in vitro diagnostic kits (Boehringer Mannhein, Mannhein, Germany).

The results were expressed as mean ± SD. The statistical analysis used the Biostatistical Packet of "R-Sigma Data Base" (Horus Hardware) (Moreu et al., 1990), and included the two-tailed student's t test, ANOVA, and calculation of Pearson's correlation coefficient when appropriate.

Results

The results are summarized in Table 1. The mean serum levels of CoQ_{10} and the CoQ_{10}/cholesterol ratio did not differ significantly from those of controls. CoQ_{10} levels were not correlated with age, age at onset, duration of the disease, scores of the Unified Parkinson Disease Rating Scale (UPDRS) or the Hoehn and Yahr staging in the PD group. The CoQ_{10}/cholesterol ratio had a low but significant correlation with duration of the disease ($r = -0.46$), total UPDRS score ($r = -0.39$), motor examination of the UPDRS ($r = -0.45$). These values were not influenced significantly by therapy with levodopa or dopamine agonists, although patients treated with deprenyl had lower serum CoQ_{10} levels (Table 2).

Discussion

CoQ_{10} is well known for its role as election carrier in the lipid phase of mitochondrial membrane. The low potential required for its oxidation or reduction makes it possible to fulfil its pivotal role in the mitochondrial electron transport chain (Lagendijk et al., 1996), particularly in complexes I and II. For this reason it performs a crucial role in the energetic metabolism.

CoQ_{10} is present in all human tissues, it is transported in the circulation by lipoproteins and, as cholesterol, is synthesized by the mevalonate pathway.

Table 2. Influence of antiparkinsonian treatment on serum coenzyme Q_{10} levels and coenzyme Q_{10}/cholesterol ratio (mean ± SD)

	Coenzyme Q_{10} (nmol/L)	Coenzyme Q_{10}/cholesterol ratio
Levodopa		
yes (n = 18)	1,128 ± 285	0.22 ± 0.06
no (n = 15)	1,128 ± 421	0.23 ± 0.05
Dopamine agonist		
yes (n = 14)	1,096 ± 287	0.22 ± 0.06
no (n = 19)	1,231 ± 386	0.23 ± 0.04
Deprenyl		
yes (n = 5)	1,007 ± 91*	0.19 ± 0.06
no (n = 28)	1,201 ± 369	0.23 ± 0.05

*$p < 0.05$ when compared with controls

Plasma cholesterol concentrations are well correlated with CoQ_{10} (Lagendijk et al., 1996). For this reason, in the present study, serum cholesterol concentrations were measured, and the CoQ_{10}/cholesterol ratio was calculated.

The data of the present study show that, when compared with controls, PD patients had similar serum CoQ_{10} levels and CoQ_{10}/cholesterol ratios. These data do not rule out the possibility that there may be regional deficiencies of CoQ_{10} in some areas of the brain. CoQ_{10} was not related with the analized clinical features of PD. CoQ_{10}/cholesterol ratio showed low but significant correlations with duration and severity of the disease. Therapy with levodopa or dopamine agonists did not influence these values. The reasons for the lower serum levels of CoQ_{10} in patients treated with deprenyl are unknown, but the small number of patients under this treatment limits the validity of this observation.

The normality of serum levels of CoQ_{10} and CoQ_{10}/cholesterol in PD patients found in the present study is in disagreement with the previous report by Matsubara et al. (1991), and suggests that serum CoQ_{10} levels are apparently unrelated with the risk for PD.

Acknowledgments

This work was supported in part by a grant of the Comunidad de Madrid (Exp. 08.5/0005/1997) and by the "Fundación Neurociencias y Envejecimiento".

References

Ernster L, Dallner G (1995) Biochemical, physiological and medical aspects of ubiquinone function. Ann Neurol 42: 261–264

Fahn S, Elton RL, and members of the UPDRS Development Committee (1987) Unified Parkinson's Disease Rating Scale. In: Fahn S, Marsden CD, Goldstein M, Calne DB (eds) Recent developments in Parkinson's disease, vol II. McMillan, Florham Park, pp 153–163

Hoehn MM, Yahr MD (1967) Parkinsonism: onset, progression and mortality. Neurology 17: 427–442

Hughes AJ, Ben-Shlomo SE, Daniel SE, Lees AJ (1992) What features improve the accuracy of clinical diagnosis in Parkinson's disease? A clinicopathological study. Neurology 42: 1142–1146

Jiménez-Jiménez FJ, Ortí-Pareja M, Gasalla-González T (1998a) Epidemiología, etiología y patogenia de la enfermedad de Parkinson. In: Jiménez-Jiménez FJ, Luquin MR, Molina JA (eds) Tratado de los trastornos del movimiento, chap 10. IM&C, Madrid, pp 223–258

Jiménez-Jiménez FJ, Ortí-Pareja M, Molina JA (1998b) Alteraciones mitocondriales en las enfermedades neurodegenerativas. In: Jiménez-Jiménez FJ, Molina JA, Arenas J (eds) Enfermedades mitocondriales. Rev Neurol 26 [Suppl 1]: S112–S117

Langedijk J, Ubbink JB, Vermaak WJH (1996) Measurement of the ratio between the reduced and oxidized forms of coenzyme Q_{10} in human plasma as a possible marker of oxidative stress. J Lipid Res 37: 67–75

Matsubara T, Azuma T, Yoshida S, Yamagami T (1991) Serum coenzyme Q_{10} level in Parkinson syndrome. In: Folkers K, Littarru GP, Yamagami T (eds) Biomedical and clinical aspects of coenzyme Q. Elsevier Science, Amsterdam, pp 159–166

Moreu E, Molinero LM, Fernández E (1990) R-Sigma: Base de datos bioestadística para un ordenador personal. Horus Hardware, Madrid

Schapira AHV (1994) Mitochondrial dysfunction in neurodegenerative disorders and aging. In: Schapira AHV, DiMauro S (eds) Mitochondrial disorders in neurology. Butterworth-Heinemann, Oxford, pp 227–244

Shults CQ, Haas RH, Passov D, Beal MF (1997) Coenzyme Q_{10} levels correlate with the activities of complexes I and II/III mitochondria from parkinsonian and nonparkinsonian patients. Ann Neurol 42: 261–264

Authors' address: Dr. F. J. Jiménez-Jiménez, C/ Corregidor José de Pasamonte, 24, 3-D, E-28030 Madrid, Spain, e-mail: Fjimenezj@meditex.es