Role of diet and antioxidants supplementation on progression and management of Parkinson's disease

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Abstract

Objective: To study the effect of anti-oxidative compounds on progression and management of Parkinson's disease (PD).
Design: An open randomized controlled trial.
Setting: The study was conducted in the neurology clinic of All India Institute of Medical Sciences, New Delhi, India.
Subjects: A total of 125 subjects were randomly selected out of which 35 patients either declined or dropped out.
Interventions: 90 PD patients were assigned randomly either to the case or control group. Coenzyme Q_{10}-90mg, Vitamin C-250mg & E-200 I.U./day were administered to the case group for six months duration and anthropometry, dietary intake, and neurological status were assessed at the beginning and end of the six months in both the groups.
Results: Difference in the total carbohydrate, protein and fat intake at the end of sixth month was found to be extremely statistically significant at $p > 0.001$. Unified Parkinson's disease rating scale (UPDRS) total scores of PD patients in the case group depicted slight decrease in total UPDRS scores from 29.17 $\pm$ 14. 01 at baseline to 24.58 $\pm$ 14.32 but the scores were not found to be statistically significant ($p > 0.05$).
Conclusions: It is reasonable to expect that diet and multiple antioxidant supplementation in PD patients should be able to prevent disease progression. However, large-scale clinical trails are required to confirm these trends and determine the exact dosages that are likely to be effective.

Keywords: Parkinson's disease, Supplementation, Antioxidants, Nutritional status.

Introduction

Parkinson's disease (PD) is the most common movement pathology, severely afflicting dopaminergic neurons within the substantia nigra (SN) along with non-dopaminergic, extra-nigral projection bundles that control circuits for sensory, associative, premotor, and motor pathways. Clinical, experimental, microanatomic, and biochemical evidence suggests PD involves multifactorial, oxidative neurodegeneration, and that levodopa therapy adds to the oxidative burden.[1,25] The SN is uniquely vulnerable to oxidative damage, having a high content of oxidizable dopamine, neuromelanin, polyunsaturated fatty acids, and iron, and relatively low antioxidant complement with high metabolic rate. Oxidative phosphorylation abnormalities impair energetics in the SN mitochondria, also intensifying oxygen free radical generation. These pro-oxidative factors combine within the SN dopaminergic neurons to create extreme vulnerability to oxidative challenge.[5, 9,39]

Disease progression is considered as the main risk factor for the development of these problems. Blocking disease progression with efficacious and safe neuroprotective agents therefore might be expected to prevent patients from reaching the stages of PD in which features develop that do not respond to current treatments.

Vitamin E appears to have the highest reduction potential followed in descending order by Vitamin C, ubiquinol, and glutathione.[6] Extensive dietary epidemiological studies associated female PD with less peanut consumption and male PD with less intake of salad dressings (both sources of Vitamin E), which are good sources of Vitamin E.[7,10.29] PD was found to be associated with reduced consumption of beta-carotene and ascorbic acid and not with Vitamin E intake while other researchers also found no associations with dietary intakes of Vitamin E and C rich foods.[14,16] The hypothesis that vitamin C spares vitamin E by regenerating it from the radical form was first proposed by Tappel[34] and proven by in-vitro studies of Packer *et a.*[26] An alternative explanation of the interaction *in vivo* between these vitamins suggests that vitamin C may not recycle vitamin E but serve to spare it by quenching radicals that would otherwise consume α - tocopherol.

Review of literature suggests that early PD patients treated with coenzyme Q10 without dopaminergic substitution to develop less disability and less decline in disease progression compared to placebo treated subjects. Therefore, long-term supplementation of this endogenously occurring compound is looked upon as a putative symptomatic and neuro-protective approach in PD. [8,28,30] Co-enzyme Q10 or ubiquinone is the vital cell membrane antioxidant and essential constituent of the ATP producing mitochondrial electron transport chain (ETC). It is a redox component present in all mammalian cell membranes. In the inner mitochondrial membrane ubiquinone plays a key role in shuttling electrons from complexes I and II to complex III of the respiratory chain. In extra mitochondrial membranes, ubiquinone may function in its reduced form as an antioxidant. Recent studies have demonstrated reduced activity of complex I of the electron transport chain in the brain and platelets in patients with PD. Platelet mitochondria from PD patients were found to have lower levels of coenzyme Q10 than mitochondria from age / sex – matched controls. There was a strong correlation between the levels of coenzyme Q10 and activities of complex I, II &

III. Oral coenzymeQ10 was found to protect the nigrostrial dopaminergic system in one-year-old mice treated with 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP), a toxin injurious to nigrostrial dopaminergic system. It was further found that oral coenzyme Q10 was well absorbed in parkinsonian patients and caused a trend toward increased complex I activity.[2, 3, 31, 32]

Thus, despite advances in modern therapy, patients with PD continue to experience unacceptable disability. The main challenge facing those involved in the management of patients with PD is the development of a neuro-protective therapy that can be administered early in the course of the disease and may play a role to slow, stop, or reverse disease progression. The present study was therefore undertaken on Indian PD patients to assess the role of antioxidant nutrients in PD prevention, progression and long-term management.

Materials and Methods

Subjects

An open randomized controlled trial was conducted on early PD patients (Hoehn & Yahr stage < 2.5) of both sexes, all ages and in all stages of disease, attending movement disorder clinic of department of neurology, All India Institute of Medical Sciences, New Delhi, India. Patients with dementia as tested on Diagnostic and Statistical Manual of Mental Disorders (DSM IV) were excluded from the study. 125 early PD patients were invited for the proposed study out of which 35 PD patients dropped out. The inclusion of study subjects in two groups was according to systematic random sampling method. PD patients were randomly assigned either to nutritional intervention i.e., case or non- nutritional intervention group i.e., control group (Table-1). The present study was performed after obtaining prior informed consent from the study subjects. Ethics committee of All India Institute of Medical Sciences, New Delhi, India approved the study. At the screening visit, after the nature, purpose, and potential risks and benefits of the study were explained to the subject, written informed consent was obtained. The subject underwent evaluation with a medical history, physical examination, and a battery of clinical assessments of PD.

Neurological Assessment

Complete diagnosis of PD was based on United Kingdom's Parkinson's disease (UKPD) Society Brain Bank Clinical Diagnostic Criteria (Hoehn and Yahr).[15] Briefly it was as follows:

Step 1: Diagnosis of Parkinson's Syndrome

Bradykinesia (slowness of initiation of voluntary movement with progressive reduction in speed and amplitude of respective actions and at least one of the following: -
Muscular rigidity
4-6 Hr. rest tremor
Postural instability not caused by primary visual, vestibular, cerebral or proprioceptive dysfunction.

Step 2: Exclusion Criteria for Parkinson's Disease

History of repeated strokes with stepwise progression of Parkinson's features
History of repeated head injury.
Oculogyric Crisis
Neuroleptic treatment at the onset of symptoms
More than one effected relative
Sustained remission
Strictly unilateral features after 3 years
Supranuclear gaze palsy
Cerebral signs
Early severe autonomic involvement
Early severe dementia with disturbances of memory, language and praxis
Babinski sign.
Presence of cerebral tumor or communicating hydrocephalus on CT Scan
Negative response to large doses of levodopa (if mal-absorption excluded)
MPTP exposure

Step 3: Supportive prospective criteria for Parkinson's disease; three or more required for diagnosis to definite Parkinson's disease.

Unilateral onset
Rest tremor present
Progressive disorder
Persistent asymmetry affecting the side of onset most
Excellent response (70 – 100%) to levodopa
Severe levodopa induced Chorea
Levodopa response for 5yrs. or more
Clinical course of 10yrs. or more

Anthropometric Measurements

A complete physical examination was performed in case and non-case patients. Weight was measured to the nearest kilograms and height to the nearest centimeters. At baseline, 3rd months, 6th months.

a) Body wt. in (kg.) b) Ht. in (m), Body weight & height was measured as per the standardized procedures.

Body mass index (BMI) BMI was measured as a ratio of weight in kilograms divided by height in meters squared (kg/m2). Cut-off criteria was as follows: Normal 18.0 - 22.9, Overweight 23.0 – 24.9 & Obese ≥ 25.[25,27,41]

Dietary Assessment

Dietary Assessment was done at baseline, 3rd and 6th months. It included calculation of nutrient information using a pre-tested 24h food recall performa consisting of three sections prepared according to the guidelines by National Institute of Nutrition, India. The first section of the performa dealt with the 24h nutrient intake, listing the details of morning tea, breakfast, mid-morning, lunch, evening tea, dinner and bedtime snack. The second section was meant for recording various food items usually not consumed daily. The consumption was recorded at baseline, monthly and at the end of sixth month. Data analysis of the dietary parameters was carried out using the standard values of Indian foods.[11,16]

MNA (Mini nutritional assessment)
The Mini Nutritional Assessment (MNA) test contained simple measurements and brief questions that could be completed in about 10 minutes.[35,36] MNA comprised, anthropometric measurements (weight, height and weight loss); global assessment (six questions related to life style, medication and mobility); dietary questionnaire (eight questions related to number of meals, food and fluid intake, and autonomy of feeding); and subjective assessment (self perception of health and nutrition). The sum of the MNA score distinguished between the following groups of PD patients: (a) those with adequate nutritional status: MNA > 24; (b) those at risk of malnutrition: MNA between 17 and 23.5; and (c) those with frank malnutrition: MNA < 17.

Assessment of Disease Progression
Assessment of disease progression by modified Unified Parkinson's Disease Rating Scale (UPDRS) [24] was done at baseline, 3rd month and 6th month. According to this scheme the disease was staged as follows:

1. Stage Zero: No signs of disease.
2. Stage One: PD symptoms on one side of the body only.
3. Stage Two: PD symptoms on both sides of the body. No impairment of balance.
4. Stage Three: Balance impairment. Mild to moderate disease. Physically independent.
5. Stage Four: Severe disability, still able to walk or stand unassisted.
6. Stage Five: Wheelchair bound or bedridden unless assisted.

Recommendations for Coenzyme Q_{10} administration
Coenzyme Q_{10} capsules, 30mg each were advised to consume thrice a day, Vitamin C-250 mg per day and Vitamin E-200I.U. one capsule per day for a period of six months by the patients in the case group.

End Point
Primary end Point
Change in UPDRS part III after six months.

Secondary end Point

1. Change in UPDRS part I & II
2. Modified Hoehn & Yahr staging, Schwab and England activities of Daily living scale.
3. Change in nutritional status

Statistical Analysis
Data was recorded on a pre-designed performa. The performas were thoroughly reviewed for any incomplete information before entering the data on an excel spreadsheet. All the entries were rechecked for any incomplete information. Since all the study variables were continuous, the distribution of each of the variable was checked. For the variables following approximate *normal distribution, mean* and *standard deviation* was computed, while for non-normally distributed variables summary statistics were computed by median and range. *Student's t-test* was used to compare the mean values in two groups. *Pearson correlation matrices* were calculated to derive relationship between PD stage and scores of mini nutritional assessment, mini nutritional assessment scores and quality of life and daily dietary sugar intake and stage of PD. Statistical tests used were two-tailed and *p values* were derived. *P-values* smaller than 5% were considered statistically significant.

Results

The mean age of the study subjects was 63.4± 6.6 y and 62.9 ± 5.4 y for nutritional intervention and non- nutritional intervention group. The mean (SD) duration of PD was 3.6 (5.3) years (1-7 years). The most common concomitant diseases were dyslipidemia in 52% of patients, arterial hypertension in 28% and diabetes in 18% of PD patients. Mean body weight increased from 56. 4 ± 11 kg at baseline to 58.8 ± 7 kg at the end of the sixth month in the case group, while in the control decreased from 57.7 ± 11 kg to 56.1 ± 9 kg. It was also found that in the nutritional-intervention group PD patients mean body mass index (BMI) in kg/m^2 also improved slightly from 22.19 ± 4 at the baseline to 23.14 ± 3 at the end of the sixth month, and BMI (kg/m^2) scores in the non-nutritional intervention group declined from 22.06 ± 5 to 21.45± 4 at the end of the sixth month. Therefore the above results revealed results that nutritional status of PD patients changed over time, and BMI was also found inversely proportional to duration of disease. No change in mean knee height (47.2, 46.8 cm), mid-arm circumference (22.5, 22.9cm) and calf circumference (29.5, 29.8 cm) in the case group at baseline and at the end of sixth month. It was also observed that in the case group at baseline maximum number of patients had normal BMI 18.5-25$kg/m^{2,}$ which remained almost the same at the end of the sixth month. On the contrary in the control group number of undernourished patients increased and normal BMI decreased at the end of the sixth month. It was also assessed that nutritional status of PD patients changed over time, and BMI was also found to be inversely proportional to duration of disease (Table 2).

Table 1: Number of Parkinson's disease patients invited and declining in the study

	Case	Control	Total
Invited	67	58	125
Declining	17	18	35
Participated	50	50	100
Data presented on	45	45	90
Participation rate	75%	86%	80%

Table 2 Age and anthropometry of Parkinson's disease patients

		Age (yrs.)		Weight (kg.)		Height (cm.)	
		Base Line	6 months	Base Line	6 months	Base Line	6 months
Control	Mean	62.9	62.9	57.7	56.1	161.7	161.7
	SD	5.4	5.4	11	9	19	19
	N	45	45	45	45	45	45
Case	Mean	63.4	63.4	56.4	58.8	159.4	159.4
	SD	6.6	6.6	11	7	16	16
	N	45	45	45	45	45	45

		Knee Ht. (cm)		BMI (kg./m^2)		Mid Arm Circumference (cm.)	
		Base Line	6 months	Base Line	6 months	Base Line	6 months
Control	Mean	48.4	48.4	24.18	23.6	22.8	23.2
	SD	5	5	4	3	3	3
	N	45	45	45	45	45	45
Case	Mean	47.2	46.8	22.15	22.95	22.5	22.9
	SD	4	4	4	3	3	3
	N	45	45	45	45	45	45

		Calf Circumference (cm.)	
		Base Line	6 months
Case	Mean	29.5	29.8
	SD	3	3
	N	45	45
Control	Mean	30.49	30.49
	SD	3.2	3.2
	N	45	45

In the beginning PD patients mean daily carbohydrate energy (en)% at baseline ranged between 54-58 en%, protein 11 en% and total fat 32-33 en%. Carbohydrate intake assessed at baseline were lower then the World Health Organization (WHO) recommendations of dietary allowances of 55-65en%, protein intake was found to be within the range of 11-15% and total fat 32-33en% much above the above the recommended range of 15-30%. Macronutrient intake increased steadily as per desirable dietary recommendations at the end of third month in the case group and at the end of the trial carbohydrate intake favorably increased to 65 en%, total protein 14 en% and total fat intake declined to 39 en%. Mean macro-nutrient intake levels attained at the end of sixth month fairly met the desirable recommendations for Indian elderly PD patients (Table 3).Difference in the total carbohydrate, protein and fat intake at the end of sixth month was found to be extremely statistically significant at *p value* less than 0.001 (Table 4). Extremely statistically significant values were observed at the end of sixth month in the case and control group for energy, carbohydrate, protein and fat ($p>0.001$).

Mean daily intake of micronutrients, fatty acids and fibre also improved in the case group. At baseline, estimated values of saturated fatty acids (SFA) were 13.91 en%, monounsaturated fatty acids (MUFA) 10.43% and polyunsaturated fatty acids (PUFA) 8.11 en%, with the recommended dietary allowances (WHO, 2003), for SFA < 10%, MUFA < 10% and PUFA 6-8en%, respectively. As a consequence of dietary counseling at the end of third months SFA became 7.5 en%, MUFA < 7.5 en% and PUFA 5.9 en%. Desirable range of n-3 and n-6 fatty acid of 1-3 en% and 5-8 en%, was achieved at the end of 90 days in the supplementation group. Average daily dietary fibre intake estimated at the beginning was found to be 9g, much below than the desirable limits, but later increased greatly to 24g ($p < 0.001$). Intake of average daily dietary vitamin C increased drastically in the case group from 43 $\pm$ 26 mg to 75$\pm$ 44 mg at the end of third month reaching to a maximum desirable intake of 111$\pm$ 28mg at the end ($p< 0.001$), the recommended dietary intake of vitamin C is 90mg/day (Panel on Dietary antioxidants and related compounds, 2000) while in control group intake decreased. In the control group, the observed intake at baseline and sixth month was 63mg and 48mg respectively, which are quite below the mean daily dietary recommendations. Mean daily dietary vitamin E intake in the case group at baseline was 6mg/day and after six months increased to 9mg per day, the levels were much below 15mg/day, the recommendations given by Panel on Dietary antioxidants and related compounds (2000), although patients stressed on consumption of vitamin E rich foods rich foods as advised. Out of 45 PD patients in case group, most of the patients were well nourished (62%) and remaining were undernourished. In the control group, at baseline 35% were undernourished and at the end of the sixth month the number increased to 40% (Table 4). In the control group energy intake was observed to be declining as carbohydrate, protein, fat and other micronutrients and fatty acids intake were below the

recommended dietary allowances. Undernourished PD patients in the case group showed significant improvement in macro and micronutrient intake.

Table 3 Mean daily macronutrient, mineral and vitamin intake by Parkinson's disease patients.

		Energy (K Cal)			**Protein (g)**			**Protein (en%)**		
		Base line	3rd month	6th month	Base line	3rd month	6th month	Base line	3rd month	6th month
Control	Mean	1546	1398	1420	48	48	43	11	14	11
	SD	542	242	364	18	18	11	2	2	2
	N	45	45	45	45	45	45	45	45	45
Case	Mean	1526	1574	1675	42	61	59	11	16	14
	SD	405	443	95	16	21	5	4	3	3
	N	45	45	45	45	45	45	45	45	45

		Fat (g)			**Fat (en%)**			**Carbohydrates (g)**		
		Base line	3rd month	6th month	Base line	3rd month	6th month	Base line	3rd month	6th month
Control	Mean	55	62	53	32	39	41	180	162	188
	SD	12 45	12	17	3 45	9	6	101	141	51
	N		45	45		45	45	45	45	45
Case	Mean	56	47	39	33	33	23	206	192	272
	SD	21 45	19	9	3 45	4	2	56	59	17
	N		45	45		45	45	45	45	45

		Carbohydrates (en%)			**Vitamin A (μ g)**			**Vitamin D (μ g)**		
		Base line	3rd month	6th month	Base line	3rd month	6th month	Base line	3rd month	6th month
Control	Mean	58	58	52	943	1013	948	5	5	5
	SD	7 45	7	9	273	701	449	1	1	3
	N		45	45	45	45	45	45	45	45
Case	Mean	54	57	65	1075	1063	1180	5	5	5
	SD	6 45	6	9	783	801	210	3	3	2
	N		45	45	45	45	45	45	45	45

		Vitamin E (mg)			**Vitamin C (mg)**			**Thiamine (mg)**		
		Base line	3rd month	6th month	Base line	3rd month	6th month	Base line	3rd month	6th month
Control	Mean	6	5	5	63	53	48	1	1	1
	SD	1	2	2	16	18	34	0	0	0
	N	45	45	45	45	45	45	45	45	45
Case	Mean	6	8	9	43	75	111	1	1	1
	SD	2	2	2	26	44	28	0	0	0
	N	45	45	45	45	45	45	45	45	45

		Riboflavin (mg)			**Niacin (mg)**			**Vitamin B_6 (mg)**		
		Base line	3rd month	6th month	Base line	3rd month	6th month	Base line	3rd month	6th month
Control	Mean	1	1	1	12	12	12	1	1	1
	SD	0	0	0	2	2	1	0	0	0
	N	45	45	45	45	45	45	45	45	45
Case	Mean	1	1	1	13	12	14	2	2	2
	SD	0	0	0	3	3	3	0	0	0
	N	45	45	45	45	45	45	45	45	45

		Vitamin B_{12} (μ g)			Calcium (mg)			Iron (mg)		
		Base line	3rd month	6th month	Base line	3rd month	6th month	Base line	3rd month	6th month
Control	Mean	5	6	5	524	514	501	8	9	8
	SD	4	2	3	238	137	235	4	2	3
	N	45	45	45	45	45	45	45	45	45
Case	Mean	6	6	7	589	783	814	7	9	10
	SD	4	5	5	347	508	238	4	5	5
	N	45	45	45	45	45	45	45	45	45

		Zinc (mg)			Fibre (g)		
		Base line	3rd month	6th month	Base line	3rd month	6th month
Control	Mean	8	8	8	12	10	2
	SD	2	1	2	6	2	3
	N	45	45	45	45	45	45
Case	Mean	8	8	8	14	11	24
	SD	2	3	2	8	7	6
	N	45	45	45	45	45	45

		Saturated Fatty Acids (g)			Monounsaturated Fatty Acids (g)			Polyunsaturated Fatty Acids (g)		
		Base line	3rd month	6th month	Base line	3rd month	6th month	Base line	3rd month	6th month
Control	Mean	16	16	18	11	9	8	4	4	5
	SD	2	4	3	3	2	2	1	0	2
	N	45	45	45	45	45	45	45	45	45
Case	Mean	24	15	14	18	12	14	4	9	11
	SD	3	3	2	1	2	3	0	2	3
	N	45	45	45	45	45	45	45	45	45

Table 4 Percentage of total energy (en%) from carbohydrates proteins and fats in Parkinson's disease cases.

		Carbohydrate en%				
		Base Line	6th Month	Difference	P Value	Statistical Significance
Case	Mean	54	65	- 66. 00	<	Extremely
	SD	6	9		0.0001	SS
	N	45	45			

		Protein en%				
		Base Line	6th Month	Difference	P Value	Statistical Significance
Case	Mean	11	14	- 17. 00	<	Extremely
	SD	4	3		0. 0001	SS
	N	45	45			

		Fat en%				
		Base Line	6th Month	Difference	P Value	Statistical Significance
Case	Mean	33	23		<	Extremely
	SD	3	2	17.00	0. 0001	SS
	N	45	45			

Nutrition intervention in the supplementation group increased intake of functional foods, rich in antioxidants, vitamins and minerals. Intake of cereals was observed to be increased by 17%, pulses and legumes by 48%, milk and its products by 59%, meat, fish and chicken and egg by 58%, green leafy vegetables consumption by 76%, other seasonal vegetables 55% and fruits by 24%. The increased intake of various food groups was compensated by decrease in total fat as emphasis was given on fat quality than quantity and reducing intake of sugar by 45% and 50% respectively (Table 6).

PD patients tend to consume high amount of fat in order to obtain high energy to overcome general body weakness and observed slowing of body movements (78%). Average

intake of fruits and vegetables of 2 servings a day at baseline in both the case and control groups was below five servings per day recommended as part of healthy diet. Later, in case group mean intake was increased to on average 9 servings per day. It was also observed that patients belonging to high income groups consumed 1-2 servings of fruits daily, while middle income group patients consumed 1-2 servings of fruits 2-3 times in a week.

Table 5: Mean daily food intake by Parkinson's disease patients

		Cereals (g)			**Pulses & Legumes (g)**			**Milk & its Products**		
		Base line	3rd month	6th month	Base line	3rd month	6th month	Base line	3rd month	6th month
Control	Mean	158	168	162	27	29	29	157	161	182
	SD	54	124	64	18	18	11	34	42	61
	N	45	45	45	45	45	45	45	45	45
Case	Mean	168	174	198	24	41	47	141	318	348
	SD	105	23	22	16	11	3	54	23	22
	N	45	45	45	45	45	45	45	45	45

		Meat Group (g)			**Green Leafy Vegetables (g)**			**Other Vegetables (g)**		
		Base line	3rd month	6th month	Base line	3rd month	6th month	Base line	3rd month	6th month
Control	Mean	29	22	27	28	39	32	80	62	88
	SD	12 45	12	17	13 45	19	6	101	141	51
	N		45	45		45	45	45	45	45
Case	Mean	32	60	78	22	73	92	56	82	215
	SD	21 45	9	4	10 45	14	7	56	59	17
	N		45	45		45	45	45	45	45

		Fruits (g)			**Fats & Oils (g)**			**Sugar (g)**		
		Base line	3rd month	6th month	Base line	3rd month	6th month	Base line	3rd month	6th month
Control	Mean	58	58	52	79	73	82	49	54	59
	SD	7 45	7	9	7	11	9	7	9	6
	N		45	45	45	45	45	45	45	45
Case	Mean	82	149	178	75	47	41	48	37	24
	SD	6 45	6	8	9	2	2	7	3	2
	N		45	45	45	45	45	45	45	45

Mini nutritional assessment (MNA) revealed that in the beginning out of 90 PD patients, 29 were well nourished, 7 under-nourished and 29 at the risk for malnutrition. Identification of PD patients at risk for malnutrition is most important by MNA, because changes in weight and albumin levels occur later. Almost all the patients (91%) consumed three meals a day, 51% reported moderate anorexia. 25 out of 90 patients reported weight loss between 1-3 kg in last three months. Most of the patients (74%) had no feeding difficulty. Majority of PD patients (65%) were uncertain of their nutritional state. In comparison with the other people of same age none considered their health status better than others of the same age.

Most of the PD patients (90%) consumed more than one serving of dairy product (milk, cheese, curt) every day and all of them had two or more servings of legumes or eggs per week. None consumed meat, fish, and poultry every day. PD patients consumed up to 5 servings of fruits or vegetables per day. Consumption of water, juice, coffee, tea, milk ranged above (5 cups for more than half of the patients (65%). Frequency of occurrence of nutrition related conditions was compared between PD patients at the risk of under-nutrition and well nourished. Significant statistical significance ($p<0.001$) was found in the reported problems of weight loss, anorexia, constipation and feeding difficulty.

As a result of nutritional intervention and antioxidants supplementation initial PD patients MNA scores of 17-23.5 (at risk of malnutrition) and below 17 MNA scores (undernourished) together decreased from 39% to 37% in the. In the control group combined scores of patients at risk of malnutrition and undernourished increased from 38% to 40% in the case group. Age and anthropometry of Parkinson's disease patients by nutritional status are presented in Table 6 and mean daily macronutrient, mineral and vitamin intake by Parkinson's disease patients by nutritional status are given in Table 8.

Table 6: Age and anthropometry of Parkinson's disease patients by nutritional status

			Age (yrs.)	Weigh t (kg.)	Height (cm.)	Knee ht. (cm.)	Mid Arm Circumference (cm.)	Calf Circumference (cm.)
CASE	Normal	Mean	58.6	59.4	161.1	48.4	22.5	28.5
		SD	7.1	5.7	10.2	2.8	3	2.8
		N	28	28	28	28	28	28
	Under Nourish	Mean	67.4	52.3	158.7	47.3	21.9	27.1
		SD	6.6	3.9	8.3	1.9	2.5	2.7
		N	17	17	17	17	17	17

Table 7: Mean daily macronutrient, mineral and vitamin intake by Parkinson's disease patients by nutritional status

			Energy (K Cal)			Protein (g)			Protein (en%)		
			Base line	3rd month	6th month	Base line	3rd month	6th month	Base line	3rd month	6th month
CASE	Normal	Mean	1484	1431	1720	49	47	49	13	13	11
		SD	202	83	62	12	12	8	0	2	3
		N	28	28	30	28	28	30	28	28	30
	Under Nourish/ At risk	Mean	1250	1549	1427	40	61	46	13	14	13
		SD	121	146	93	6	9	4	1	0	2
		N	17	17	15	17	17	15	17	17	15
CONTROL	Normal	Mean	1429	1323	1241	48	54	42	15	16	13
		SD	54	122	64	18	14	8	1	1	2
		N	29	29	27	29	29	27	29	29	27
	Under Nourish/At risk	Mean	1341	1323	1241	38	37	43	11	11	14
		SD	78	49	132	13	12	20	1	0	2
		N	16	16	18	16	16	18	16	16	18

			Fat (g)			Fat (en%)			Carbohydrates (g)		
			Base line	3rd month	6th month	Base line	3rd month	6th month	Base line	3rd month	6th month
CASE	Normal	Mean	56	47	56	34	30	29	196	205	205
		SD	20 28	9	27	0	4	7	66	29	17
		N		28	30	28	28	30	28	28	30
	Under Nourish /At risk	Mean	40	61	46	33	35	33	169	204	189
		SD	12	14	12	3	2	2	41	30	19
		N	17	17	15	17	17	15	17	17	15
CONTROL	Normal	Mean	54	54	42	33	29	27	184	184	189
		SD	12 29	12	17	3	9	6	10	14	51
		N		29	27	29	29	27	29	29	27
	Under Nourish /At risk	Mean	38	37	43	33	27	27	187	206	184
		SD	11	7	13	3	2	7	21	20	12
		N	16	16	18	16	16	18	16	16	18

			Carbohydrates (en%)			Vitamin A (µ g)			Vitamin D (µ g)		
			Base line	3rd month	6th month	Base line	3rd month	6th month	Base line	3rd month	6th month
CASE	Normal	Mean	52	57	60	1015	963	1280	4	5	5
		SD	16	6	8	783	801	210	3	2	2
		N	28	28	30	28	28	30	28	28	30
	Under Nourish /At risk	Mean	54	51	54	915	1063	1022	4	3	5
		SD	12	4	3	783	801	214	1	2	2
		N	17	17	15	17	17	15	17	17	15
CON	Normal	Mean	52	60	60	803	913	918	3	3	4
		SD	7	7	9	219	201	399	1	1	1
		N	29	29	27	29	29	27	29	29	27

T	Under	Mean	56	62	59	823	903	878	3	2	3
R	Nourish	SD	2	4	3	119	226	319	1	1	1
O	/At risk	N	16	16	18	16	16	18	16	16	18
L											

			Vitamin E (mg)			**Vitamin C (mg)**			**Thiamine (mg)**		
			Base line	3rd month	6th month	Base line	3rd month	6th month	Base line	3rd month	6th month
		Mean	6	8	9	83	75	101	1	1	1
C	Normal	SD	2	2	2	56	44	68	0	0	0
A		N	28	28	30	28	28	30	28	28	30
S	Under	Mean	6	6	8	71	59	58	1	1	1
E	Nourish	SD	2	4	3	1	2	2	1	0	1
	/At risk	N	17	17	15	17	17	15	17	17	15
C		Mean	6	5	5	67	59	48	1	1	1
O	Normal	SD	1	2	2	16	18	34	0	0	0
N		N	29	29	27	29	29	27	29	29	27
T	Under	Mean	5	6	5	41	39	48	1	1	1
R	Nourish	SD	2	2	1	3	2	2	1	0	1
O	/At risk	N	16	16	18	16	16	18	16	16	18
L											

			Riboflavin (mg)			**Niacin (mg)**			**Vitamin B_6 (mg)**		
			Base line	3rd month	6th month	Base line	3rd month	6th month	Base line	3rd month	6th month
		Mean	1	1	1	13	12	14	2	2	2
C	Normal	SD	0	0	0	3	3	3	0	0	0
A		N	28	28	30	28	28	30	28	28	30
S	Under	Mean	1	1	1	11	12	12	2	2	2
E	Nourish	SD	0	0	0	4	1	3	0	0	0
	/At risk	N	17	17	15	17	17	15	17	17	15
C		Mean	1	1	1	11	10	12	1	1	1
O	Normal	SD	0	0	0	2	2	1	0	0	0
N		N	29	29	27	29	29	27	29	29	27
T	Under	Mean	1	1	1	10	9	9	1	1	1
R	Nourish	SD	0	0	0	2	2	1	0	0	0
O	/At risk	N	16	16	18	16	16	18	16	16	18
L											

			Vitamin B_{12} (µ g)			**Calcium (mg)**			**Iron (mg)**		
			Base line	3rd month	6th month	Base line	3rd month	6th month	Base line	3rd month	6th month
		Mean	6	6	7	553	703	814	7	9	10
C	Normal	SD	4	4	3	347	301	228	4	5	5
A		N	28	28	30	28	28	30	28	28	30
S	Under	Mean	5	6	5	813	789	804	7	9	10
E	Nourish	SD	3	5	2	347	453	138	4	5	5
	/At risk	N	17	17	15	17	17	15	17	17	15
C		Mean	5	4	5	574	564	501	8	7	8
O	Normal	SD	3	2	2	198	231	238	4	2	3
N		N	29	29	27	29	29	27	29	29	27
T	Under	Mean	4	3	3	572	552	511	8	7	7
R	Nourish	SD	2	2	1	167	212	198	3	4	2
O	/At risk	N	16	16	18	16	16	18	16	16	18
L											

			Zinc (mg)			**Fibre (g)**		
			Base line	3rd month	6th month	Base line	3rd month	6th month
CASE	Normal	Mean	8	8	8	14	11	18
		SD	2	3	2	8	7	6
		N	28	28	30	28	28	30
	Under Nourish /At risk	Mean	7	8	8	15	18	17
		SD	2	3	2	4	7	7
		N	17	17	15	17	17	15
CONTROL	Normal	Mean	8	8	8	7	8	8
		SD	2	1	2	3	2	3
		N	29	29	27	29	29	27
	Under Nourish /At risk	Mean	16	16	18	9	8	8
		SD	2	4	3	3	2	2
		N	16	16	18	16	16	18

			Saturated Fatty Acids (g)			Monounsaturated Fatty Acids (g)			Polyunsaturated Fatty Acids (g)		
			Base line	3rd month	6th month	Base line	3rd month	6th month	Base line	3rd month	6th month
CASE	Normal	Mean	15	15	14	12	12	14	4	7	9
		SD	3	3	2	1	2	3	0	2	3
		N	28	28	30	28	28	30	28	28	30
	Under Nourish /At risk	Mean	14	14	13	10	14	15	4	6	7
		SD	2	2	3	3	2	2	1	0	2
		N	17	17	15	17	17	15	17	17	15
CONTROL	Normal	Mean	16	15	17	11	7	8	4	5	5
		SD	4	4	3	3	2	2	1	0	2
		N	29	29	27	29	29	27	29	29	27
	Under Nourish /At risk	Mean	18	18	17	10	8	8	4	4	5
		SD	2	4	2	3	3	2	1	1	2
		N	16	16	18	16	16	18	16	16	18

PD was managed mainly through dopamine replacement therapy - pharmaceutical agents aimed at replacing dopamine in the brain or mimicking its actions at dopamine receptors. Most commonly used is the dopamine precursor levodopa in combination with carbidopa (Sinemet® and Sinemet CR). The vast majority of patients experienced benefits during 1-2.5 years of medication (95%). Typically, after 2-5 years on levodopa drugs the (84%), patient's reported responses to be becoming erratic. Dyskinesias, a feature characterized as excessive and uncontrollable movements developed (73%) and nausea was a persistant problem (68%). Other adverse effects found to develop were: sleep disturbances (79%), "freezing" and inability to move (32%), mental confusion (67%), hallucinations (59%), dystonia (47%) and low blood pressure episodes (17%). Sleep disturbances were common in PD patients, affecting as many as 59% of patients during the course of the disease. Decreased frequency of bowel movements, two or less per week, occurred in 41% of patients with PD. However, difficulty completing a bowel movement, with straining and incomplete evacuation, called difficulty defecating was more common, occurring in 59% of people with PD. Many people had both constipation and difficulty defecating, and it's important to distinguish between them as their treatments differ. In some people with PD, perhaps 5%, constipation and difficulty defecating resulted in fecal impaction, bloating, discomfort and pain. 45% had no depression, 40% had mild-to-moderate depression, and 15% had severe depression.

Mean monthly frequency (in terms of assigned scores) of specific food intake indicated that the consumption of fats and oils was significantly higher among obese individuals. In males in the overweight category, the intakes of paneer (cottage cheese) and fast foods were also significantly higher ($p < 0.05$). On the other hand intakes of mustard oil and vegetables were significantly less frequent in obese PD patients ($p < 0.05$). A positive trend in the frequent consumption of sugar, sweets, and fried foods with increasing PD was seen at the end of the study.

Mean daily energy intake by the presence of various side effects was also estimated in comparison to the recommended dietary allowances for Indians. The reported energy intake was much lower than the desirable recommended intakes. Nutritional intervention markedly

improved daily energy intake in PD patients with anorexia from 989 kcal to 1398 kcal (40%), 1077 kcal to 1559 kcal with weight loss (45%), 1092 kcal to 1531 kcal with feeding difficulty (40%) and 1217 kcal to 1498 kcal (23%), while patients with neuro-psychological problems did not show marked improvement in mean daily energy intake (7%).

Discussion

In the present study we investigated anthropometric measurements in PD patients population, but due to lack of available anthropometric data of elderly Indian PD patients assessed data could not be compared. The nutritional strategies were found to be effective as the mean body weight increased. The finding that in the case group at baseline maximum number of patients had normal BMI of 18.5-25kg/m^2 which remained almost the same at the end of the sixth month needed further interpretation. On the contrary in the control group number of undernourished patients increased and normal BMI decreased at the end of the sixth month.

Therefore, anthropometric indices of fat and muscle advocated as measures of nutritional status were successfully used. Its usefulness as an indicator of nutritional status is dependent on the availability of current local and anthropometric data should be collected in healthy older age groups.[26,38] PD patients were found to report weight loss greater than 10 pounds compared with controls, and the weight loss was correlated with the stage of disease.[10]

The observation that PD patients belonged to middle income group clearly indicated that they were able to afford a well- balanced diet, but either due to ignorance regarding nutritive value of foodstuffs or due to disease based feeding complications PD patients were not found to be consuming a well-balanced diet (Table 4 & 5). Moreover, swallowing disorders, impaired hand to mouth co-ordination, nausea, excessive saliva production, and delayed gastric emptying time may all have contributed to reduced energy intake in PD patients in the present study.

The aim of the study was to identify possible diet-related protective factors and risk factors for Indian PD patients. On the basis of specific food-items PD patients mean daily intake of cereals, pulses, milk and its products, green leafy vegetables and fruits was not adequate as per daily dietary recommendations. Consumption of fats & oils and sugars & sweets was enormous, ranging between 72-82g and 48 - 59g, respectively.

As, dietary data from India on nutritional status of older people is scarce. The report of National Nutrition Monitoring Bureau (NNMB, 1996 and 97) on status of diet and nutritional status in elderly population was compared. It was observed that the mean intake of cereals and millets together were 445g and 357g in males and females respectively was much higher then the reported intakes by PD patients in our study (Table 6). The consumption of pulses, green leafy vegetables and other vegetables was less than recommended dietary intakes in both the sexes.

Further recently available data from nutritional survey of older people conducted by National Nutrition Monitoring Bureau, India, (1997, 2002)[23] report the average intake of cereals showed an increase with decrease in income levels. In the case of other foods, particularly milk and milk products, and fats and oils, the consumption improved with increasing income. The intake of cereals and millets, pulses and legumes, green leafy vegetables were less than recommended dietary allowance in all the income groups while that of fats and oils and sugar and jaggery was satisfactory in all groups, except slum dwellers. But, in our study it was observed that PD patient's fruit and vegetable intake was reduced and sugar, fat and oil intake considerably irrespective of the socio-economic status (Table 6). The observed daily caloric intake of PD in the intervention group was found to be lower then the recommended intake. Therefore, caloric reduction was kept under scrutiny during the course of study in the case group. It was observed that considerable personal discipline was required by study subjects to adhere to the dietary regimen and lowering of lipid calories was taken as an integral part of this strategy, because lipids are the foremost substrates for per oxidative attack coming from endogenous oxidative overload. In addition, review of literature indicated that high animal fat consumption generally results in a pro-inflammatory shift in the tissues due to the preponderance of long-chain omega-6 content. Parkinson's patients in the case group were therefore well advised to rebalance their dietary fatty acid sources by minimizing saturated fats and increasing long-chain omega-3 intakes while reducing their total caloric intake.

The finding that increased intake of calories of animal fats is associated with PD is biologically consistent with the hypothesis that oxidative reactions play a key role in the pathogenesis of PD. Lipid is one of the major sources of oxygen radicals through the lipid per oxidation pathways.[1,13] Diets with high lipid content have shown toxic effects on tissue function in different regions, including the brain, enhancing levels of oxidative stress. The excessive production of free radicals may depend not only on compounds with a specific toxicity, such as 1-methyl-4-phenyl-1, 2,3,6-tetrapyridine (MPTP) and pesticides, but also on the susceptibility of the ageing brain to oxidative stress. For example, structural changes in cellular membranes produced by both diet and age may shift the cholesterol – phospholipid ratio or the unsaturated fatty acid content, which increases the susceptibility of neurons to oxidative stress.[18] A cohort study in England depicts cardiovascular disease was a predominant cause of death among patients with parkinsonism, when compared with general population.[4] Thus, our findings are consistent with the hypothesis that cardiovascular disease and parkinsonism might share the common pathology.

Alternatively, fat intake might be a surrogate for other dietary or lifestyle variables; fat and oil intake is generally associated with a diminished intake of fruits and vegetables, which are the main sources of dietary antioxidants. Fat intake may also be related to some toxic compounds related

to cooking procedures. Micronutrient inadequacies are common among elderly, even in the most developed countries. With the nutritional transition towards higher fat, lower fiber diets, attention to maintaining and increasing intakes of traditional fruits vegetables and whole grains is of considerable importance. The expert committee of the Indian Council of Medical Research (1998), taking into consideration the nutrient requirements has recommended that for the prevention of chronic diseases every individual should consume at least a minimum of 300g of vegetables and 100g of fruits. The link between high fruit and vegetable intake and reduced rate of PD progression may be partly explained by antioxidant protection. In the recent past, the importance of antioxidants in restricting the damage that reactive oxygen radicals can cause to the cells and cellular components has been receiving considerable attention. Raw and fresh vegetables like green leafy vegetables, carrots, fresh fruits including citrus and tomato have been identified as a good source of antioxidants. Antioxidants in fruits and vegetables may reduce rate of PD progression by modulating DNA damage and lipoprotein oxidation.[9,12,17,19]

The paradox that PD patients lose weights as their energy intake increased suggested that the weight loss is caused by increased energy expenditure. This argument is supported by clinical observations that PD patients have higher energy expenditures than controls.[19] Higher resting energy expenditure in some PD patients was found to be related to severe muscle rigidity. Furthermore body mass index of PD patients was inversely correlated with their clinical dyskinetic severity and in separate study, significant weight gains were observed in PD patients after pallidotomy which was associated with some cardinal manifestations.[21] On the other hand. Diets rich in fat have a particularly high content of calories because fat is an energy dense nutrient and the patients in non-nutrition intervention group might have consumed more dairy fats because they have higher energy expenditure due to the disease. However, this is unlikely because the association between dairy fats was stronger after adjustment for total caloric intake. It is also unlikely that PD patients in non-nutrition intervention group increased their caloric intake, specifically eating from dairy fats, a well known risk factors for several diseases related to ageing. Fat intake might be a surrogate for other dietary or lifestyle variables; animal fat intake is generally associated with a diminished intake of fruit and vegetables, which are the main sources of dietary antioxidants. Fat intake might even be related to some toxic compound linked to preparation of food.

Although appetites for sugar and fat are inborn human characteristic, but 76% of PD patients reported to have altered appetites for sugar and fat which could be a regulatory mechanism developed to deal with insufficiency and undernutrition. There is much evidence for the view that the brain is one of the major regulators of the dietary behaviour. Fats and sweets seem to appeal to emotions and are the dominant object of food aversions and cravings. Clinical disturbances in the control of food intake such as bulimia nervosa and the binge eating disorder also involve cravings for energy-dense, sweet or fat rich foods.[37] Sweet and fat rich foods have assumed a dominant place in the food supply, they are energy dense, good –tasting, inexpensive and convenient to use. Alternatively, fat intake might be a surrogate for other dietary or lifestyle variables and is generally associated with a diminished intake of fruits and vegetables, which are the main sources of dietary antioxidants.[20,22]

We considered the possibility that presence of other chronic diseases or their therapy might have differentially affected the dietary habits of PD patients. We considered the possibility that presence of other chronic diseases or their therapy might have differentially affected the diet habit of PD patients. It is reasonable to expect that dietary discipline and CoQ and vitamin E & C supplementation should be able to prevent disease progression and prove to be a valuable and cost effective approach. However, the exact dosages that are likely to be effective have yet to be determined through large-scale clinical trails to confirm these trends. Thus, the thoroughness of this approach will provide data, which would enable better management and healthcare plans to be developed for PD patients.

Conflict of Interest: None.

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