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Original Article

Pharmacology Section

Clinical Response of Levodopa Carbidopa Combination in Patients with Idiopathic Parkinsonism

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ABSTRACT

Introduction: Parkinson's disease is the most common form of a group of progressive neurodegenerative disorders. The use of levodopa as dopamine – replacement therapy is highly effective in ameliorating the symptoms of the disease and remains the standard drug with which other therapies are compared.

Aim: To study the change in Unified Parkinson's Disease Rating scale (UPDRS) scores in patients receiving levodopa and carbidopa treatment (levodopa- carbidopa combination).

Materials and Methods: Study was conducted in Department of Neurology, Government Medical College, Trivandrum, India on 75 patients. All patients diagnosed with Idiopathic Parkinson's disease (PD) satisfying inclusion criteria were enrolled into the study. Informed written consent was taken from all patients. Baseline UPDRS scores were recorded followed by reassessment at the end of six month. Data was analysed using paired t-test with help of SPSS-16 statistical software.

Results: Baseline UPDRS was collected and after 6 months of treatment, it was reassessed. Baseline total score was 49.8; the follow-up score was 39.5. A decrease in score was seen in various components of UPDRS.

Conclusion: Upon statistical analysis this difference was found to be significant, which implies that, there is improvement in patient's condition. Improvement was noted in Mentation, behaviour, mood, activities of daily living and motor functions. Hence there is positive treatment response for levodopa carbidopa therapy in patients with idiopathic PD.

Keywords: Activities of daily living, Neurodegeneration, UPDRS

INTRODUCTION

Neurodegeneration is a process in which there is progressive loss of structure and function of neurons, including neuronal death. Many late-onset neurodegenerative diseases, including Parkinson's disease and Huntington's disease, are associated with the formation of intracellular aggregates by toxic proteins [1]. The aetiology is multifactorial and consists of an interaction between environmental factors, genetic predisposition, oxidative stress and proteosomal dysfunction [2]. It is characterized by presence of tremor, rigidity, bradykinesia, and postural instability [3]. Levodopa is highly effective in ameliorating the symptoms of Parkinson's disease (PD). Levodopa has been the most widely used treatment for over 30 years [4].

Levodopa is associated with significant complications such as the "wearing off" effect, levodopa-induced dyskinesias and other motor complications. Hence catechol-o-methyl-transferase inhibitors, dopamine agonists and nondopaminergic therapy are alternative modalities in the management of PD and may be used concomitantly with levodopa or one another. The neurosurgical treatment, focusing on deep brain stimulation is reviewed [5]. The Unified Parkinson's Disease Rating Scale (UPDRS) is used in the evaluation of patients with Parkinson's disease. The UPDRS is the most commonly used scale in the clinical study of PD [6]. Over the past 25 years the UPDRS has become a standardized tool in the clinical evaluation of patients with PD. In the present study an attempt was being made to use UPDRS as a response monitoring tool in idiopathic PD.

AIM

To monitor treatment response of levodopa and carbidopa in idiopathic Parkinson's disease in Neurology department of Government Medical College, Thiruvananthapuram, India.

MATERIALS AND METHODS

Prospective observational study was conducted between May 2013 to September 2014. Patients diagnosed with idiopathic PD by the neurologist were included. A sample size of 75 was taken. UPDRS [7] was used as a tool to monitor the change in treatment response.

Sample size calculation

The response rate of levodopa among patients with PD is 57% [8]. This finding is used to calculate the sample size of current study.

$N = Z_{\alpha}^{2}PQ/ d^2$

$N = (1.96)^2 X 57 X 43 / (11.4)^2$

N = 75

N = sample size

P = incidence proportion of treatment benefit

Q = 100-P

d = precision, 20% of P, $Z\alpha = 1.96$ if $\alpha = 0.05$

Inclusion and exclusion criteria

Patients of either sex, with idiopathic PD diagnosed by Brain Bank criteria were included in the study. Patients taking drugs as a part of Parkinson-plus syndromes and other movement disorders and not giving consent were excluded. Ethical clearance was obtained from The Human Ethics Committee of the institution.

Study tools

1. Informed written consent form.
2. Structured proforma.
3. UK Parkinson's disease society Brain Bank clinical diagnostic criteria.
4. Unified Parkinson's Disease Rating Scale (UPDRS).

Study procedure

Confidentiality and anonymity of the patient's information was maintained during and after the study.

All the patients satisfying the inclusion criteria were enrolled in the study. A written informed consent was obtained from the patient/

guardian/ relative. All the relevant information regarding the patient were obtained and recorded in the structured proforma. Baseline UPDRS score was recorded, followed by reassesment at the end of 6 months.

STATISTICAL ANALYSIS

UPDRS was used as a primary data collecting tool. The mean initial baseline score and the mean score after 6 months of treatment were compared using paired t-test with a significance level of 5%. All categorical variables were represented as proportions and quantitative variables as mean (SD). Data was entered in excel 2013. Analysis was done with SPSS version 16.

RESULTS

Prospective evaluation of 75 patients who were receiving levodopa and carbidopa combination (carbidopa 25mg, levodopa 100mg) in Neurology outpatient department of our institution, from May 2013 – September 2014 was carried out and the data were analysed.

Age distribution

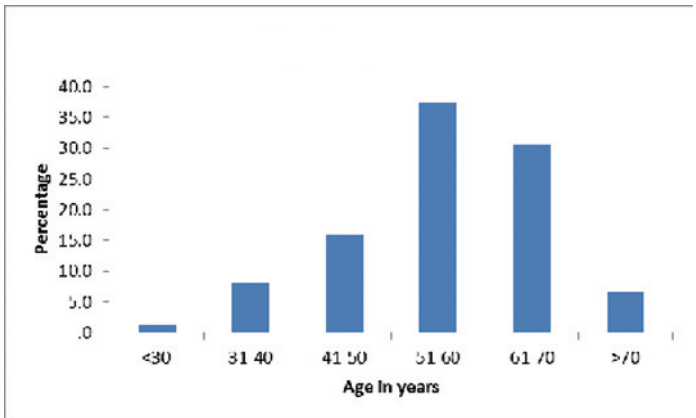
The age range of study population was 21 to 84 years. Mean age of the patients was 56.5 years. Number of cases were maximum (37.3%) in the age interval of 51-60 years [Table/Fig-1].

Sex distribution

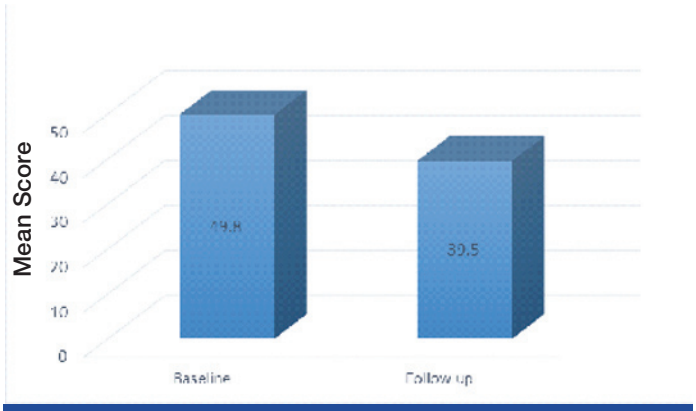
Among the 75 patients observed, 38 were females and 37 males. Percentage of female patients is 50.7 and male patients are 49.3.

UPDRS

Baseline UPDRS score was recorded for 75 patients. The mean value being 49.8, with a standard deviation of 17.1. After 6 months of treatment follow-up score was recorded. The mean value was 39.5, with a standard deviation of 15.4. Analysis shows that difference is statistically significant with a p-value of <0.001 [Table/Fig-2].



[Table/Fig-1]: Age wise distribution of study population.



[Table/Fig-2]: UPDRS total score.

UPDRS part I - Mentation, Behaviour and Mood

UPDRS is divided into 4 main parts; part 1 includes evaluation of mentation, behaviour and mood. Baseline score of part 1 was recorded for 75 patients. Mean value was 2.8, with a SD of 1.8. Follow-up score was recorded after 6 months, mean value was 2.2, with a SD of 1.6. The difference is statistically significant with p-value of <0.001 [Table/Fig-3].

UPDRS part II - Activities of daily living

Part 2 of UPDRS includes evaluation of ADL. Baseline score of part 2 was recorded for 75 patients. Mean value was 13.7, with a SD of 5.4. Follow-up score was recorded after 6 months, mean value was 10.1, with a SD of 5.3. The difference is statistically significant with p-value of <0.001 [Table/Fig-4].

UPDRS part III - Motor examination

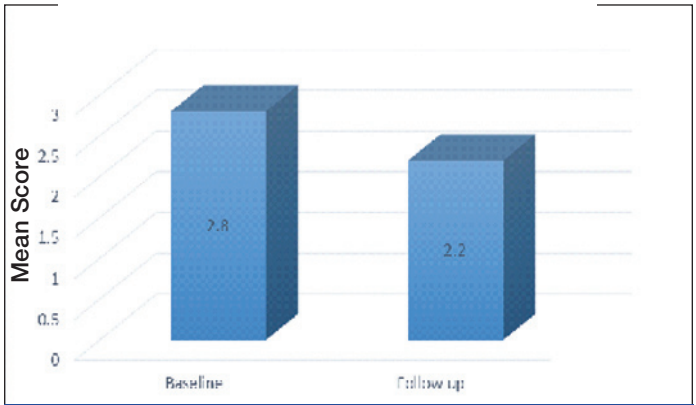
Part III of UPDRS includes motor examination. Baseline score of part 3 was recorded for 75 patients. Mean value was 27.7, with a SD of 11.3. Follow-up score was recorded after 6 months, mean value was 22.6, with a SD of 10.8. The difference is statistically significant with p-value of <0.001 [Table/Fig-5].

UPDRS part IV - Complications of therapy

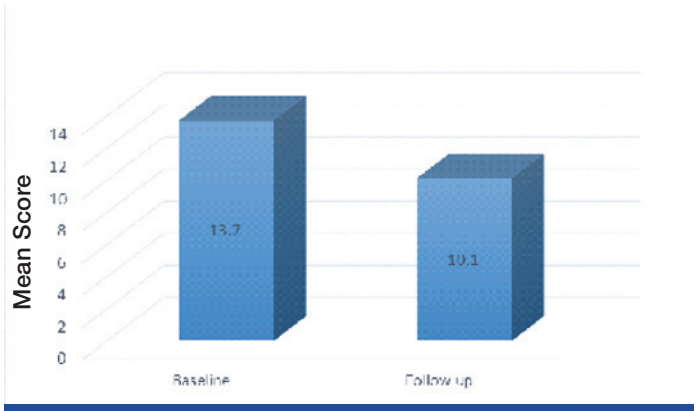
Part IV of UPDRS evaluates complications of therapy. Baseline score of part 4 was recorded for 75 patients. Mean value was 5.5, with a SD of 2.1. Follow-up score was recorded after 6 months, mean value was 4.6, with a SD of 1.9. The difference is statistically significant with p-value of <0.001 [Table/Fig-6].

DISCUSSION

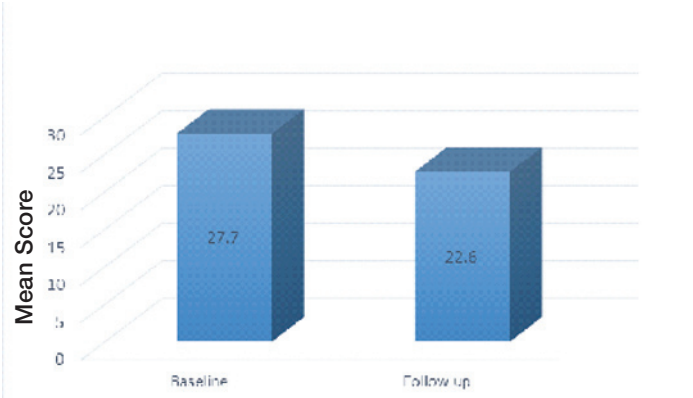
Neurodegeneration is a process in which there is progressive loss of structure and function of neurons, including neuronal death. Parkinson's Disease (PD) is the second most common neurodegenerative disorder after Alzheimer's disease [9]. In the present study change in Unified Parkinson's Disease Rating Scale (UPDRS) scores in patients receiving levodopa and carbidopa treatment was assessed.



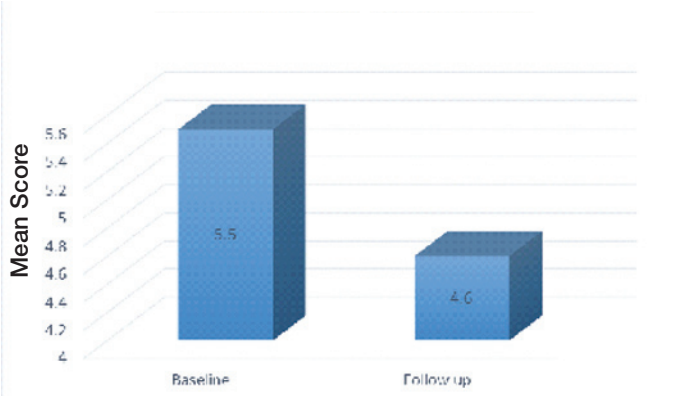
[Table/Fig-3]: UPDRS part I - Mentation, Behaviour and Mood.



[Table/Fig-4]: UPDRS part II - Activities of daily living.



[Table/Fig-5]: UPDRS part III - motor examination.



[Table/Fig-6]: UPDRS part IV - complications of therapy.

Age plays a significant role in the aetiology, clinical response and prognosis of PD. In the present study age range of study population was 21 to 84 years. Mean age of the patients was 56.5 years. Number of cases were maximum (37.3%) in the age interval of 51-60 years. There is a male predominance seen in world wide prevalence of PD. In the present study 75 patients were included, 37 were males and 38 females.

The UPDRS is the most commonly used scale in the clinical study of Parkinson's Disease [10]. The UPDRS is made up of the following sections [10].

Part I: Evaluation of Mentation, behaviour, and mood.
Part II: Self-evaluation of the Activities of Daily Life (ADL).
Part III: Evaluation of motor function.
Part IV: Evaluation of complications of therapy.
A study was conducted by S Molloy et al., among patients with PD in 2005 [11]. In that study 31 patients with PD were included. Mean age of these patients was 77.1 years. In the present study age range of study population was 21 to 84 years. Mean age of the patients was 56.5 years. Number of cases were maximum (37.3%) in the age interval of 51-60 years.

There is a male predominance seen in world wide prevalence of PD. In a study conducted by S Molloy et al., 31 patients were included; among them 24 were males and 7 females [11]. In a study by Rajesh Pahwa et al., [8] 87 patients were included, among them 47 were male, and 40 females [8]. In the present study 75 patients were included, 37 were males and 38 females.

In a study by Rajesh Pahwa et al., in North America on extended release levodopa/carbidopa, 87 patients were included [8]. Baseline mean UPDRS part I was 1.6. After 6 months of treatment, mean UPDRS part I score was 1.2. The difference was statistically significant with p-value of 0.01. In the present study, baseline mean UPDRS part I was 2.8. After 6 months of treatment, mean UPDRS part I score was 2.2. The difference was statistically significant with p-value of < 0.001.

UPDRS part II consists of evaluation of ADL. In a study by Rajesh Pahwa et al., Baseline mean UPDRS part II was 10.3 [8]. After 6 months of treatment, mean UPDRS part II score was 7.5. The difference was statistically significant with p-value of < 0.0001. In a study by Parkinson Study Group [12], baseline mean UPDRS II was 8.3. After 23 months of treatment, mean UPDRS part II score was 2.2 with a p-value of 0.001. In the present study, baseline mean UPDRS part II was 13.7. After 6 months of treatment, mean UPDRS part II score was 10.1. The difference was statistically significant with p-value of <0.001.

UPDRS part III consists of evaluation of motor examination. In a study by Rajesh Pahwa et al., Baseline mean UPDRS part III was 25.9. After 6 months of treatment, mean UPDRS part III score was 17 [8]. The difference was statistically significant with p-value of < 0.0001. In a study by Parkinson Study Group [12], baseline mean UPDRS III was 22.0. After 23 months of treatment, mean UPDRS part III score was 7.3 with a p-value of < 0.001. In the present study, baseline mean UPDRS part III was 27.7. After 6 months of treatment, mean UPDRS part III score was 22.6. The difference was statistically significant with p-value of <0.001.

UPDRS part IV consists of evaluation of complications. In a study by Rajesh Pahwa et al., baseline mean UPDRS part IV was 0.5 [8]. After 6 months of treatment, mean UPDRS part IV score was 0.4. The difference was not statistically significant with p-value of 5.3. In the present study, baseline mean UPDRS part IV was 5.5. After 6 months of treatment, mean UPDRS part IV score was 4.6. The difference was statistically significant with p-value of <0.001.

LIMITATION

- This study was a prospective observational study. For better assessment of treatment response, a randomised controlled trial is preferable.
- Study period was short. So delayed adverse effects and eventual neurodegenerative effects were not monitored.
- Sample size is small. Larger numbers of patients are needed for proper assessment of treatment related complications.

CONCLUSION

Inspite of treatment complications, levodopa carbidopa therapy remains the gold standard in treating idiopathic parkinson's disease. as its beneficial efffects outweighs side effects.

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