

# Observation of Parkinson's Disease Cases with Special Reference to Effectiveness of Different Group of Anti-Parkinsonian Drugs

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## ABSTRACT

**Background & Aim:** Parkinson's disease (PD) is the second most common neurodegenerative disorder after Alzimers disease. Over the years it is being managed with pharmacotherapies which includes L-dopa, dopamine agonists, MAO inhibitors, COMT inhibitors and amantadine with variable efficacy. Aims and objectives: of the study is to know the effectiveness of different groups of antiparkinsonian drugs and their comparison. **Materials and Methods:** A cross-sectional study was done taking 30 patients of PD more than 50 years of age attending to the Geriatric and Medicine OPD S.C.B. Medical College Cuttack Odisha. PD was diagnosed by using Parkinson's disease society brain bank criteria {PDBBC}. Cases were to followed up at an interval of 2 to 3 Months interval. Written informed consent both in English and local odia language was obtained from all patients prior to the study. Statistical analysis was done by using SPSS version 21. **Results:** Mean age of study population was  $65 \pm 6.95$  and out of which 80% (24) were males, 20% (6) were females. Resting tremor was present in 100% of cases. Rigidity and bradykinesia were present in 80% of cases. Initially LD and CD combination therapy was prescribed to all patients. On subsequent follow up motor symptoms was improved in 86.7% (26) patients. Smooth response and fluctuations were observed in 70% (21) and 73.3% (22) patients' respectivel. With the use of anticholinergic drugs like trihexiphenidyl either alone or in combination with LD + CD tremor was improved in 100% cases. Rigidity improved in 75% of cases but bradykinesia was not improved. The combination of LD+ CD wearing off, sudden off and random off were 38.1% (8), 14.29% (3), 28.57% (6) patients respectively. **Conclusions:** Parkinson's disease should be diagnosed early and treatment must be initiated as soon as possible. Levodopa and carbidopa may be prescribed initially to the PD patients. When motor complications develop COMTI or DA can be added.

**Keywords:** Parkinson's disease, Lew bodies, Levodopa, Carbidopa, rigidity, tremor.

## INTRODUCTION

Parkinsons disease (PD) is the second most common neurodegenerative disorder after Alzimers disease.<sup>[1,2]</sup> It is considered the most frequent movement disorder. Its cardinal features were first described by James Parkinson in 1817. The usual age of onset is after 50 years and upto 80 years and decrease after the age of 90. Clinically movement disorder of PD are mostly motor symptoms like akinesia, rigidity, tremor at rest.<sup>[3]</sup> Symptoms are mostly due to the loss of dopaminergic neurons in the substantia nigra pars compacta which leads to severe deficiency of dopamine in putamen and caudate nucleus. Cytosolic Lew bodies are the hallmark of PD which are characterised by aggregated alpha synuclein. There are different stages of PD from stage 1 to stage 6.<sup>[4]</sup> Stage 1. Alpha synnucln aggregation usually occurs

in dorsal motor nucleus of vagus and glossopharyngeal nerve or olefactory bulb. Stage 2. -alpha synuclein extend to medulla oblongata, the pontine tegmentum and the locus coeruleus. Stage 3.- substantia nigra and amygdala are involved. Stage 4.- there occurs marked degeneration in dopaminergic neurons of substantia nigra. Stage 5 and 6.- Lew bodies and neuritis occurs in neocortex which causes many cognitive symptoms. Braak's work showed about the non-motor presentations of PD like smell dysfunction, constipation, rapid eye moment (REM) sleep disorder and depression.<sup>[5]</sup> The onset of PD is incidious and slowly progressive. Tremor precede bradykinesia and rigidity. Initially signs are asymmetric or unilateral and become bilateral or symmetrical as the disease progress. Gradually the typical resting tremo, rigidity, and slowness of movement occurs. Diagnostically motor symptoms of PD characterize the disease andnon-motor symptoms also signifiye debilitating features.<sup>[6-11]</sup> In advanced PD patient may develop fluctuating confusion , disorientation , visual hallucinations . This visual hallucination is proposed as a diagnostic feature of PD and consequence of disease

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progression.<sup>[12]</sup>This progress to more severe psychosis and dementia.<sup>[13]</sup>

The present study was undertaken to know the effectiveness of different groups of antiparkinsonian drugs and their comparison.

**MATERIALS AND METHODS**

A cross-sectional study was done taking 30 patients of PD more than 50 years of age attending to the Geriatric and medicine OPD S.C.B. Medical college cuttack Odisha between May 2016 to April 2017. PD was diagnosed by using parkinsons disease society brain bank criteria {PDBBC} Written informed consent both in English and local odia language was obtained from all patients prior to the study. Details of the patient were recorded in a proforma according to age, sex, symptomssign. All patients were undergoing detailed clinical examination followed by routine and biochemical tests including CBC, blood sugar, blood urea, serum creatinine, serum electrolytes, urine routine/microscopic, liver function tests, and thyroid function tests. MRI of brain was done in all patients. All PD patients were prescribed antiparkinsonian drugs as per usual doses. Cases were followed up at an interval of 2 to 3 Months interval.

**Parkinson’s Disease Society Brain Bank Criteria:**

- Criteria required for establishing the presence of Parkinsonism

**Bradykinesia**

- Plus one of these three.
- Rigidity
- Resting tremor, Postural instability

- Exclusion criteria for Parkinson’s disease  
Repeated stroke or step wise progression repeated head injury encephalitis oculogyric crisis, recent neuroleptic treatment, relevant toxic exposure, >1 affected relative, sustained remission of symptoms,

unilateral signs after 3 years, supranuclear gaze palsy, cerebellar signs, severe early autonomic failure, severe early dementia, pyramidal signs, mass lesion or hydrocephalus on CT scan, no response to levodopa.

- Positive criteria for parkson’s disease (3 or more required)

Unilateral onset, rest tremor, progressive disorder, persistent asymmetry, excellent (70-100%) response to levodopa, Severe levodopa induced dyskinesia. Patients having no tremor were advised for MRI to exclude brain stroke, tumour or demyelination.

**Statistical Analysis**

Statistical analysis was done by using SPSS version 21. Data was expressed as mean, median and percentage and ranges were calculated for continuous variables. Chi square test and Fischer exact test were used to compare categorical variables. Kruskal Wallis test and ANOVA test were applied on quantitative data and comparison of stasttical difference of normal variables among different groups. A p-value of < 0.05 is considered as significant.

**RESULTS**

Total 30 Parkinsons Disease cases were taken for the study. Mean age of study population was 65 ± 6.95 and out of which 80% (24) were males, 20% (6) were females. Among the motor symptoms resting tremor was present in 100% of cases. Rigidity and bradykinesia were present in 80% of cases. Among the non-motor symptoms delirium was in 93.3% (28) cases, decline in cognitive function was 73.3% (22), demyelination was 30% (9) cases. Autonomic dysfunctuions like postural hypotension and urinary bladder dysfunction were 16.7% (5) and 20% (6) cases respectively. [Table 1]

**Table 1: Age wise distribution of clinical signs**

Clinical features	< 60 years N (%)	> 60 years N (%)	Total N (%)	P values *
Tremor Absent Present	0(0) 9 (30.0)	0(0) 27 (70.0)	0(0) 30 (100)	
Rigidity Absent Present	5 (55.6) 4 (44.4)	1 (4.8) 20 (95.2)	6 (20.0) 24 (80.0)	0.005
Bradykinesia Absent Present	3 (33.3) 6 (66.7)	3 (14.3) 18 (85.7)	3 (20.0) 24 (80.0)	0.329
Depression Absent Present	1 (11.1) 8 (88.9)	1 (4.8) 20 (95.2)	2 (6.7) 28 (93.3)	0.517
Cognitive Decline Absent Present	6 (66.7) 3 (33.3)	2 (9.5) 19 (90.5)	8 (26.7) 22 (73.3)	0.003
Dementia Absent Present	9 (100) 0 (0)	12 (57.1) 9 (42.9)	21 (70.0) 9 (30.0)	0.029
Postural hypotension Absent Present	9 (100) 0 (0)	16 (76.2) 5 (23.8)	25 (83.3) 5 (16.7)	0.286

Urinary dysfunction				
Absent	9 (100)	15 (71.4)	24 (80.0)	0.141
Present	0 (0)	6 (28.6)	6 (20.0)	

**Fischer exact test was used**

**Table 2: Response to levo-dopa & carbidopa combination**

Clinical features	Number	Percentage
Motor symptoms		
Improve	26	86.7
Not Improve	4	13.3
Non- Motor symptoms		
Improve	24	80
Not Improve	6	20
Fluctuations		
Improve	8	26.7
Not Improve	22	73.3
Dyskinesia		
Improve	5	16.7
Not Improve	25	83.3
Smooth response		
Present	21	70
Absent	9	30

**Table 3: Fluctuations seen in levodopa with carbidopa combination treatment**

Fluctuations		Number	Percentage
Wearing off	Present	8	38.1
	Absent	13	61.9
Sudden off	Present	3	14.29
	Absent	18	85.71
Random off	Present	6	28.57
	Absent	15	71.43
Dose failure	Present	3	14.29
	Absent	18	85.71
Delayed on	Present	7	33.33
	Absent	14	66.67
Freezing	Present	10	47.62
	Absent	11	52.38

**Table 4: Dyskinesia with different treatment combinations**

Treatment Combination	Present N (%)	Absent N (%)
LD & CD	9 (40.9)	13 (59.1)
LD & CD & DA	5 (41.7)	7 (58.3)
LD & CD & MAO	2 (16.7)	10 (83.3)
LD & CD & COMT	1 (8.3)	11 (91.7)
LD & CD & Amantidine	1 (8.3)	11 (91.7)

**Table 5: comparison of on time**

Treatment group	On time (in hours)Mean +- SD	P value
LD Monoecherypy	20.33 +- 1.22	< 0.001
LD with DopamineAgonist (DA)	23.21 +- 0.77	
LD with MAO	23.67 +- 0.42	
LD with COMT	23.68 +- 0.46	

**Table 6: comparison of off time**

Treatment group	Off time (in hours)Mean +- SD	P value
LD Monoecherypy	3.0 +- 1.11	< 0.001
LD with DopamineAgonist (DA)	1.25 +- 0.58	
LD with MAO B	0.78 +- 0.26	
LD with COMT I	0.62 +- 0.47	

Initially Levodopa (LD) and Carbidopa (CD) combination therapy was prescribed to all patients. On subsequent follow up motor symptoms was improved in 86.7% (26) patients. Smooth response and fluctuations were observed in 70% (21) and 73.3% (22) patients respectively. Dyskinesia was

present in 83.3% (25) cases without improvement. [Table 2]

With the use of anticholinergic drugs like trihexiphenidyl either alone or in combination with LD + CD tremor was improved in 100% cases. Rigidity improved in 75% of cases but bradykinesia was not improved. The combination of LD+ CD

wearing off, sudden off and random off were 38.1% (8), 14.29% (3), 28.57% (6) patients respectively. Freezing was present in 47.62% (10) and no response was in 14.29% (3) cases. [Table3].

Combination therapy of LD + CD, LD + CD + DA (dopamine Agonist), LD+ CD + MAO-BI(Monoamine-Oxidase-B Inhibitor),LD + CD + COMT (Catechol-O-methyltransferase) and LD + CD + Amantidine the dyskinesia disappeared in 59.1%, 58.3%, 83.3%, 91.7% and 91.7% cases respectively. [Table 4] In our study comparison of ON- time by LD monotherapy, LD with DA, LD with MAOBI, and LD with COMTI is shown in [Table 5]. The comparison of OFF- time with LD monotherapy, LD with DA, LD with MAOBI, and LD with COMTI is shown in [Table 6].

## DISCUSSION

Total 30 PD patients were taken for the study the mean age of study population was 65.07 ± 6.95 and most of them were males. Resting tremor was present in 100% cases but rigidity and bradykinesia was present in 80% of cases. Depression and cognitive decline were present in 93.3%, 73.3% cases respectively. This depression is the most common neuropsychiatric disturbance in PD among non-motor symptoms as per the observation of Brain Bridge Rusdin et al.<sup>[14]</sup> Anxiety was present in 60% of cases in our study and this is another common non- motor symptom as per other few studies.<sup>[15,16]</sup> Initially almost all patients received LD + CD, on subsequent follow up most symptoms improved in 86.7% cases which is in accordance with other published observation.<sup>[17-19]</sup> Smooth response and fluctuations were 70% and 73.3% cases respectively in our study. Dyskinesia was observed in 83.3% cases and did not improve. Cotzias and colleagues had treated 16 PD patients with oral levodopa 3-16 g /day had showed remarkable improvement in tremor, akinesia, rigidity but agranulocytopenia was observed in 4 patients. Another study showed that 20% cases showed improvement in akinesia but 30% had no improvement.<sup>[20]</sup> In our study patients taking LD + CD wearing off, sudden off, random off, freezing were 38.1%, 14.9%, 28.57%, 47.62% respectively but dyskinesia was present in 40.9% cases taking LD+CD & 41.7% taking LD + CD + DA but it was least who had taken LD + CD + COMTI and LD + CD + Amantidine which was only 11%. The COMTI entacapone acts mainly on extracerebral COMT and does not cross blood brain barrier but tolcapone inhibits both extracerebral and cerebral COMT and so affects the synthesis and metabolism of dopamine in the brain When combination of LD + CD + Trihexiphenidyl was given tremor was improved in 100% cases, even the resistant tremor also. In our study in LD monotherapy off time was 3.0±1.11 (p<0.001) but combination of LD + DA the

off time was reduced by 1.75 to 2 hours with the mean off time of 1.25 ± 0.589 (p<0.001). Dopamine agonists were initially used as an adjunctive therapy to LD in advanced PD patients with motor complications as per the observation of Rinne et al.<sup>[21]</sup> As per our study LD+ MAO- B Inhibitors off time was reduced by 2.25 hours with mean off time of 0.78±0.26 (p< 0.001) which is in accordance to observation by other few studies.<sup>[22,23]</sup> Both selegiline and rasagiline have shown to have antiparkinsonian effects particularly in reducing off time. With LD + COMTI off time reduced by 2.75 hours with the mean off time of 0.62±0.47 (p<0.001).

## CONCLUSION

Parkinsons disease should be diagnosed early and treatment must be initiated as soon as possible. Levodopa and carbidopa may be prescribed initially to the PD patients. When motor complications develop COMTI or DA can be added. Subsequently when the motor symptoms become worse MAO-B inhibitors may be added if not administered before. For dyskinesia Amantidine can be added.

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