

# Frequency of Improvement in Muscular Rigidity after Pallidotomy in Medically Refractive Parkinsonian Patients

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## ABSTRACT

**Objective:** To find out frequency of improvement in muscular rigidity after Pallidotomy in Parkinsonian patients who are medically refractory.

**Material and Methods:** This prospective descriptive study conducted in Neurosurgical Unit II, Punjab Institute of Neuro-Sciences, LGH, Lahore, during the period of one year from March 2015 to February 2016. They were evaluated before admission by history and thorough examination and then investigated with a CT scan and MRI of the brain. This study included patients as young as 30 years to as old as 65 years. Those patients who had trauma, stroke, demyelination or lesion in basal ganglia were excluded from the study.

**Result:** 75 patients were included in the study with no lost to follow up. At the time of presentation, baseline rigidity graded as 3 in 37 (49.3%) and grade 4 in 38 (50.67%) patients. Reduction in rigidity at  $\geq 25\%$ , was considered significant improvement. At 3 months follow up 49 (65.3%) patients had UPDRS grade 1 while 26 (34.7%) had (Unipied Parkinson's Disease Rating Score) UPDRSS grade 2 and no patient shown UPDRS grade 3 or 4. Out of 37 patients who had UPDRS grade 3 at baseline, 32 had grade 1 while 5 had grade 2 after Pallidotomy. Out of 38 patients, who had UPDRS grade 4 at baseline, 17 had UPDRS grade 1 while 21 had UPDRS grade 2 after pallidotomy. The difference was calculated to be significantly high ( $p < 0.001$ ).

**Conclusion:** Pallidotomy is one of the successful surgical procedures to reduce Parkinsonian muscular rigidity.

**Keywords:** Parkinson's disease, dyskinesia, rigidity, medically refractory, UPDRS (Unified Parkinsons Disease Rating Score).

## INTRODUCTION

Parkinson's disease (PD), after the name of English surgeon, James Parkinson, is a progressive and degenerative disease of dopamine producing neurons in different areas of the brain.<sup>1</sup> It is characterized by bradykinesia, muscular rigidity, tremors, gait and postural instability. Its motor component becomes prominent when more than 50% loss of dopamine producing neurons occurred in Substantia nigra. This neuronal loss resulted in decreased amount of dopamine, the neurostimulator.<sup>2</sup>

The incidence of PD is different globally because of different factors like structural difference in population, the patient's survival in a population, case ascertainment, data collection and methodology used

to define the patient's disease.<sup>3</sup> It affects 1% of the population older than 60 years. Incidence of PD in different population is 11.4 to 15.5 cases per 100,000 populations per year and age-adjusted incidence rate 7.2 to 15.3 per 100,000 persons per year.<sup>4</sup> It not only involves motor system of the body, but non motor systems like autonomic dysfunction, neuropsychiatric disorders, thoughts changes, cognition, mood disorders, sensory and sleep problems also involve.<sup>5</sup> There is no definite etiology which resulting in Parkinson's disease but some factors have a definite association in the pathophysiology of PD. These factors are patient's genetics, environment (living in rural areas, consume well water), aging, chemical exposure (especially to herbicides and pesticides) and

lifestyle.<sup>6</sup> Exposure to pesticides can increase the risk as much as 80%, which is subjective to period of exposure.<sup>7</sup>

This study was done to observe the effects of pallidotomy on Parkinsonian rigidity in whom the medical therapy causes adverse effects like dyskinesia by using Unified Parkinson's Disease Rating Score Part 22 (rigidity component). This will help us to calculate statistical data for this surgical procedure in our region as there is no related study available previously and also observes the beneficial effects and related risks and complications.

## MATERIALS AND MEDTHODS

### Study Design

This study was conducted in Neurosurgical Unit II, Punjab Institute of Neurosciences, Lahore General Hospital, Lahore, during the period of one year from March 2015 to February 2016.

### Inclusion Criteria

There were 75 patients enrolled in this study, including both genders. Patients who are refractory to medicines (Levodopa and Carbidopa), who are 30 to 65 years old and who have muscular rigidity of grade 2 to 4 included this study.

### Exclusion Criteria

Those patients who have muscular rigidity due to stroke or infarction, demyelination, trauma or lesion in the basal ganglia were excluded from the study.

### Data Collection Procedure

Seventy five patients admitted via outpatient department in Neurosurgery Unit II fulfilling the inclusion criteria. Patients diagnosed on history, clinical examination, CT scan and MRI brain. They were asked to sign informed consent for the surgical procedure and using their data in research. All patients were operated by the same surgical team and muscular rigidity was measured pre- and post-operatively by using Unified Parkinson Disease Rating Score part 22.

Along CT and MRI brain other baseline investigations like CBC, LFTs, RFTs, blood sugar level, X-ray chest and ECG were also done for surgery's purpose.

### Data Analysis

Data was analyzed by using SPSS version 21.0

statistical package. Continuous data (age, UPRDS grade) were presented as mean and standard deviation. While, categorical variables (gender and improvement) were presented as frequency and percentage. Data was stratified for age, gender, duration of PD, baseline UPRDS grade and duration of medical treatment to deal effect modifiers. Post-stratification, the chi - square test was applied. p-value  $\leq 0.05$  was considered as significant.

### Follow-up

Patients were asked to remove stitches on 7 post-operative days. Patients were called for follow up after 3 weeks and then after 3 months to assess reduction in muscular rigidity by using UPDRS part 22 and hence assess the frequency of effectiveness of Pallidotomy.

## RESULTS

The patients included in this study were of 30 years to 65 years. The mean age of patients was  $54.32 \pm 7.23$  years presented in **Table 1**. According to results, the

**Table 1:** Mean age of the patients.

Age of patient (years)	N	75
	Mean	54.32
	SD	7.23
	Minimum	30
	Maximum	65

prevalence was more common in male patients (n = 55, 73.3%) as compared to females (n = 20, 26.7%). Male to female ratio was 2.75:1. The mean duration of diagnosis of Parkinson's disease was  $6.52 \pm 2.62$  years illustrated in **Table 2**. The minimum duration was 1 year, while maximum duration was noted 15 years. The mean duration of treatment was  $5.05 \pm 2.07$  years.

**Table 2:** Duration of disease.

Duration(years)	N	75
	Mean	6.52
	SD	2.62
	Minimum	1
	Maximum	15

The minimum duration of disease was 1 year, while maximum duration was 9 years. At the time of presentation, the baseline UPDRS score for rigidity was 3 in 37 (49.3%) patients while 4 in 38 (50.67%) patients (**Table 3**). In our study, all (100%) patients

reduction of rigidity was noted in all patients regardless of age and gender and duration shown in **Table 6**. 46 patients were treated for  $\leq 5$  years and 29 patients for  $> 5$  years, all shown improvement in reduction of rigidity at follow up.

**Table 3:** Distribution of UPDRS grade at baseline.

Grade	Number	Percentage
3	37	49.33
4	38	50.87

showed reduced rigidity with Pallidotomy after three months of follow-up (**Table 4**). At 3 months follow-up

**Table 4:** Reduction in rigidity.

Improvement in rigidity		Frequency	Percentage
	Yes	75	100%
	No	0	0%
	Total	75	100%

**Table 5:** Comparison baseline rigidity grades with follow-up grades.

		Follow-up UPDRS Rigidity Grade				Total
		1	2	3	4	
Baseline UPDRS rigidity grade	1	0	0	0	0	0
	2	0	0	0	0	0
	3	32	5	0	0	37
	4	17	21	0	0	38
Total		49	26	0	0	75

49 (65.3%) patients had UPDRS grade 1 while 26 (34.7%) had UPDRS grade 2 and no patient shown rigidity of UPDRS grade 3 or 4 (**Table 5**). Out of 37 patients who had UPDRS grade 3 at baseline, 32 had grade 1 while 5 had grade 2 after Pallidotomy and out of 38 patients who had UPDRS grade 4 at baseline, 17 had UPDRS grade 1 while 21 had UPDRS grade 2 after Pallidotomy. The difference was calculated to be significantly high ( $p < 0.001$ ). Improvement in

**Table 6:** Comparison of improvement with baseline UPDRS rigidity grade.

		Improvement		Total
		Yes	No	
Baseline UPDRS rigidity grade	1	0	0	0
	2	0	0	0
	3	37	0	37
	4	38	0	38
Total		75	0	75

## DISCUSSION

Parkinson's disease is a degenerative and progressive disease of dopamine producing neurons. It is characterized by bradykinesia, tremors, muscular rigidity and postural instability. It was treated surgically in initial period, but at the high rate of complications.<sup>8</sup> In 1960, Levodopa was introduced which remarkably reduced symptoms of Parkinson's disease.<sup>9</sup> It was noted that after a certain period of time levodopa causes abnormal movements of the body known as dyskinesia. These dyskinetic movements were very cumbersome for patients and for caretaker as well. With the passage of time, frequency and severity of dyskinetic movements increases, which led the patients either to wheelchair bound or bed bound. To coup this adverse effects pallidotomy was reintroduced with more accuracy and precision and with advanced neuromonitoring and imaging.<sup>10</sup>

Pallidotomy is a technically demanding procedure, but its results are good. Its treatment goals are to prevent dyskinesia, reduced rigidity of muscles and improve quality of life of the patients. Parkinson's disease is slow and progressive degenerative disorder. It takes years to develop motor symptoms, though the process of degeneration started years back. As shows in this study that 18 patients ( $n = 75$ , 24.0%) have the disease for 5 years, 16 patients (21.3%) for 6 years, 9 patients (12.0%) for 7 and 8 years each, 4 patients (5.3%) for 9 years, 7 patients (9.3%) for 10 years and 3 patients (3.9%) have for 1, 12 and 15 years each.

Clinical manifestations appeared when more than 50% dopaminergic neuronal loss occurred.<sup>12</sup> The Parkinson's disease progresses in stages. In the Braak staging system<sup>13</sup> stage 1 is pre-symptomatic stage, in this stage cell loss has occurred but not in insignificant number to cause symptoms. In stage 2, a cell loss occurred in olfactory bulb resulted in a decreased sense of smell along with neural loss in enteric plexus resulted in constipation and sleep disorders. In stage 3 motor symptoms like rigidity and tremors appeared and took many years to develop. It is associated with 50% neuronal loss in the substantia nigra. In stage 4, neuronal loss reached up to mesocortex and in stage 5 and 6 this loss reached to cortical areas which are responsible to control cognition and emotions of the patients resulted in confusion and dementia.

Parkinson's disease is a disease of different age groups, but usually occurred in middle to old age groups. Stephen et al (2011), studied the incidence of Parkinson's disease which rises with age<sup>14</sup> and rapidly increased after the age of 60. Its onset before 40 years is rare. It was seen in the study that only 1 patient (1.3%) was presented at the age of 30 while 2 patients (2.7%) presented at the age of 40. The difference in onset of disease could be due to environmental, host response or genetics and hereditary.<sup>15</sup> As the study shows that the maximum incidence lies between fifth and sixth decades. Seven patients (9.3%) were presented in 65 years of age. Mean age of presentation was 54.30 years shown in Table 1.

Regarding the incidence of PD, it was more common in male than female. Wooten (2004)<sup>16</sup> described that Parkinson disease seems to occur more commonly in men than woman. He concluded his hypothesis on the basis of an increased death rate and prevalence of Parkinson's disease in men. The risk of developing Parkinson's disease is 1.5 in men as compared to women. The reason for this increase number of men's involvement is that men are more prone to trauma, exposure to environmental toxicant, neuroprotection of women by sex hormone like estrogen, mitochondrial dysfunction, genetics risk factors related to X linkage.<sup>17</sup> Estrogen works as neuroprotective in nature. It activates the mitogen activated protein kinase pathways and it also helps in free radicals scavenging by glutathione.<sup>18</sup>

Anthony et al 2007, hypothesized that when the disease reached up to substantia nigra other processes triggered like oxidative stress, resulted in increased turnover of dopamine, reduced level of glutathione, increased iron and excitotoxicity. Specific disease

modifying therapies should require which address not only the basic mechanisms of the neurodegeneration and the additional biologic processes specific to the dopamine producing structure like subthalamic nucleus.<sup>19</sup>

Patients suffering from Parkinson disease require long term treatment which resulted in abnormal drug induced movements. This study shows 4 patients (n = 75, 5.3%) required treatment for 1 year, 5 patients (n = 75, 6.7%) for 2 years, 6 patients (n=75, 8%) for 3 years, 15 patients (20%) for 4 years, 16 patients (21.3%) for 5 years, 12 patients (16%) for 6 years, 6 patients (8%) for 7 and 8 years each and 5 patients (6.5%) for 9 years. Annet et al (2000),<sup>20</sup> estimated that 10% of patients taking Antiparkinson medicines developed motor fluctuation per year<sup>21</sup> and 50% of these patients suffered drug induced complications after 5 years.<sup>22</sup> Motor complication prone to occur in younger onset of disease and with greater disease severity.<sup>23</sup>

The current study included different stages of Parkinson's disease and different UPDRS score. 37 patients (n = 75, 49.3%) presented with the UPDRS rigidity score 3 and 38 patients (50.9%) with rigidity score 4. After Pallidotomy assessment of patients were done by UPDRS rigidity score on first post-operative day and after three months. There was marked reduction in rigidity subjectively and objectively. The mean UPDRS score for rigidity at admission was 3.507 and on follow-up after three months mean UPDRS score for rigidity was 1.346. There was improvement in UPDRS score in term of reduction in rigidity was 2.161 (chi-square test 14.427, p = 0.0001). M. Dalai et al (1995) published his experience of 18 patients with Parkinson, refractory to medical therapy and developed drug induced dyskinesia. He found that following Pallidotomy, patients improved in their symptoms like rigidity, bradykinesia, tremors with resolution of drug induced dyskinesia. He compared pre-operative and post-operative UPDRS score and found significant improvement (65%) in rigidity score.<sup>24</sup>

## CONCLUSION

This study infers Pallidotomy for Parkinsonian muscular rigidity developed drug induced dyskinesia is better surgical procedure which keep improving in reduction with time. It is associated with less number of complications, more effective than previous and

especially in improving the quality of life of Parkinsonian patients.

## ROLE OF AUTHORS

Dr. Imran Ali: Paper Writing.

Dr. Hassaan Zahid: Results Writing.

Dr. Adeeb-ul-Hassan: Paper Editing and Results Writing.

Dr. Khalid Mahmood: Study Design.

## Additional Information

### Disclosures and Conflict of Interests:

Authors report no conflict of interest.

**Human Subjects:** Consent was obtained by all patients/participants in this study.

In compliance with the ICMJE uniform disclosure form, all authors declare the following:

**Financial Relationships:** All authors have declared that they have no financial relationships at present with any organizations that might have an interest in the submitted work.

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