

Pallidotomy: Effective and Safe in Relieving Parkinson's Disease Rigidity

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ABSTRACT

Introduction: Parkinson's Disease (PD) is a progressive neurological disorder caused by a loss of pigmented dopaminergic neurons of the substantia nigra pars compacta. The major manifestations of the disease consist of resting tremor, rigidity, bradykinesia and gait disturbances. Before the advent of Levodopa surgery was main stay of treatment of PD. Medical therapy is still the mainstay of treatment for Parkinson's disease but its prolonged use results in side effects like drug induced dyskinesia. In 1952 Dr. Lars Leksell introduced Pallidotomy that was successful in relieving many Parkinsonian symptoms in patients. Later on thalamotomy became widely accepted, replacing pallidotomy as the surgical treatment of choice for Parkinson's Disease. Thalamotomy had an excellent effect on the tremor, was not quite as effective at reducing rigidity rather bradykinesia was often aggravated by the procedure.

Objective: Effectiveness of Pallidotomy in rigidity in medically refractory Parkinson's disease and its complications.

Study Design: Descriptive prospective case series.

Setting of study: Department of Neurosurgery, Lahore General Hospital, Lahore.

Duration: June 2013 to April 2016.

Materials and Methods: Patients of Parkinson's disease with predominant component of muscular rigidity despite maximum medical therapy admitted through outdoor department. Detailed history and physical examination was done. Grading of muscular rigidity was done by applying UPDRS score Rigidity part 22. Secondary Parkinsonism was ruled out with the help of CT scan and MRI brain. Surgery was performed after informed consent.

Results: Twenty patients were included in the study with no lost to follow up. There were 14 (70%) male and 6 (30%) female patients. Mean age of the patients was 47.58 ± 8.69 years. There were 11 (55%) left sided procedures and 9 (45%) right sided Pallidotomy procedures performed. Mean pre-operative rigidity using UPDRS was 24.9 ± 1.47 , while post-operative score was 11.87 ± 1.53 . Pallidotomy procedure in our study had no mortality but 4 (20%) patients suffered from procedure related complications one patient (5%) had transient hemiparesis, 1 (5%) suffered from wound infection, 1 (5%) having dysarthria and 1 (5%) transient diplopia.

Conclusion: Pallidotomy is effective as well as safe surgical treatment option in reducing rigidity for medically refractory Parkinsonism's Disease.

Key words: Parkinson's disease, dyskinesia, rigidity, medically refractory.

Abbreviations: PD: Parkinson's Disease.

INTRODUCTION

Parkinson disease (PD) is one of the most common neurologic disorders, affecting approximately 1% of

individuals older than 60 years. It causes progressive disability that can be slowed, but not halted, by treatment. The classic motor features of Parkinson disease

typically start insidiously and emerge slowly over weeks or months. The 3 cardinal signs of Parkinson disease are resting tremor, rigidity, and bradykinesia. Postural instability is sometimes considered as the fourth cardinal feature.

The basal ganglia motor system modulates the cortical output necessary for normal body movements. Signals from the cerebral cortex are processed through the basal ganglia – thalamocortical motor pathway and return to cerebral cortex via a feedback pathway. The direct and indirect pathways exist within the basal ganglia circuit. In Parkinson disease, decreased striatal dopamine causes increased inhibitory output from the Globus Pallidus internus/substantianigra pars reticulata (GPi/SNr) via both the direct and indirect pathways. The increased inhibition of the thalamocortical pathway suppresses movement.¹

In the early 1900s, surgical treatment of Parkinson's Disease was common. A variety of operations targeted at destroying certain areas of the brain were tried in an attempt to relieve severe tremor and rigidity. In 1952 Dr. Lars Leksell introduced Pallidotomy for treating Parkinsonian symptoms. At the same time, thalamotomy became widely accepted, replacing pallidotomy as the surgical treatment of choice for PD. Thalamotomy had good control of tremor but was not effective at reducing rigidity; bradykinesia was often aggravated. In 1985, Dr. Lauri Laitinenre – introduced the pallidotomy, as a treatment for patients who had previously undergone thalamotomy but remained symptomatic. After 1992 encouraging experience of Lauri prompted other specialists to re-examine the role of pallidotomy in PD. Stereotactic pallidotomy being ablative procedure is not without certain surgical risks.

OBJECTIVES

Effectiveness of Pallidotomy in rigidity of medically refractory Parkinson's disease and its complications.

Operational Definitions

Effectiveness: Reduction in rigidity, grade 1 or more from base line, after pallidotomy measured by Unified Parkinson Disease Rating Score part 22 after 3 months.

Muscle Rigidity: resistance to passive movements of muscles measured with UPDRS part 22, grade 0 to 4.

Medical Refractory: PD patients getting maximum

dose of carbidopa (200 mg/day and levodopa 800 mg/day) for 6 months and have rigidity grade ≥ 2 .

MATERIAL AND METHODS

Study Design

Prospective Descriptive case series study.

Setting

Department of Neurosurgery, Postgraduate Medical Institute / Lahore General Hospital, Lahore.

Duration of Study

June 2013 to April 2016.

Sample Size

20 patients were included in this study.

Sampling Technique

It was Non probability consecutive sampling.

Inclusion Criteria

1. Adult population of both sexes having muscles rigidity grade 2 to grade 4 due to medical refractory Parkinson's disease.

Exclusion Criteria

1. Muscle rigidity due to stroke/ infarction, demyelination, trauma seen as hypodense area on CT or hyper intense on MRI.
2. Lesion in Basal ganglia on MRI

Data Analysis

All the collected data was entered and analyzed using IBM SPSS Statistics version 22. The qualitative data like demographics (Gender) was presented as percentage and frequency distribution tables. The Quantitative data like age was presented in Mean \pm S.D.

After fulfilling the parametric test assumptions, Paired sample t-test was used to determine the significance differences before and after treatment in UPDRS score. The complications were noted and presented as percentages. The p value of ≤ 0.05 was taken as significant.

Operative Technique

Antiparkinsonian medicine/s stopped 12 hours before procedure and kept patients nil by mouth for 6 hours. Under local anesthesia Leksell G stereotactic frame was applied followed by MRI brain plain and contrast. MRI brain images were transferred to Elekta Surgiplanto calculate anterior and posterior commissure, x, y, z coordinates and trajectory. After getting measurements of coordinates all frame attachments were adjusted on operation table. Surgical site was painted with povidine iodide solution and draping done. Draping is done in such a way that intraoperative assessment of the patients could be made i.e. patients eyes and face were not covered. Incision made at marked site under local anesthetic infiltration and 12mm burr hole made. The dura is coagulated and opened in cruciate fashion. Stereotactic frame adjusted and brought in positioned and the macroelectrode of 2.1 mm diameter with un-insulated tip was passed through burr hole. The electrode was placed at a point 4 mm above the target and macrostimulation was started by Cosman G Radiofrequency Lesion Generator. Macrostimulation was used to get optimal target location. On macrostimulation adverse effects like contractions of fingers, facial deviation, visual hallucination, and slurred speech were cautiously examined by Neurologist along with therapeutic effects like decreased in rigidity by pronation and supination, flexion and extension at elbow joint, bradykinesia by tapping of index finger and thumb. Problems in speech were also assessed during stimulation by asking the patient to repeat words or answer the simple question and observing any difficulties. Gradual increase in voltage from low to high stimulation was used to check proximity to optic nerve, internal capsule and any speech dysfunction. Same steps are repeated to go down each millimeter to find optimal target. Lesion made on target at 1.5 volt, temperature 60 to 90 degree °F for 60 seconds. After lesioning electrode withdrawn slowly and wound closed in layers. For bilateral Pallidotomy same procedure is repeated on other side. Patients were advised to continue with their preoperative anti-parkinsonian medications and analgesics and antibiotic. Assessment of the patient's rigidity, bradykinesia and dyskinesia were observed immediate post-operatively. On the first postoperative day the patients were assessed by the neurologist and the neurosurgeon and on satisfaction of both clinicians patients were discharged on first post-operative day.

Stitches were removed on fifth postoperative day. Follow-up visits were scheduled after 3 weeks and

then after 3 months to assess improvement in reduction in muscular rigidity.

RESULTS

In this study mean age of the patients was 47.58 ± 8.69 years. In this study 14 (70%) were male and 6 (30%) were female.

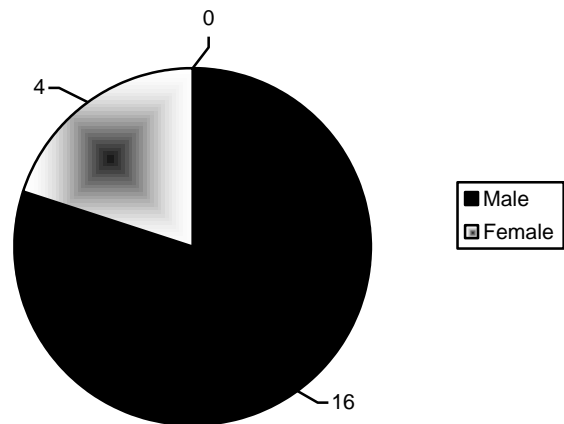


Fig. 1: Gender.

In this study 5 (25%) patients were below 40 years of age, 6 (30%) were between 40 to 50 years of age and 9 (45%) were aged more than 50 years of age.

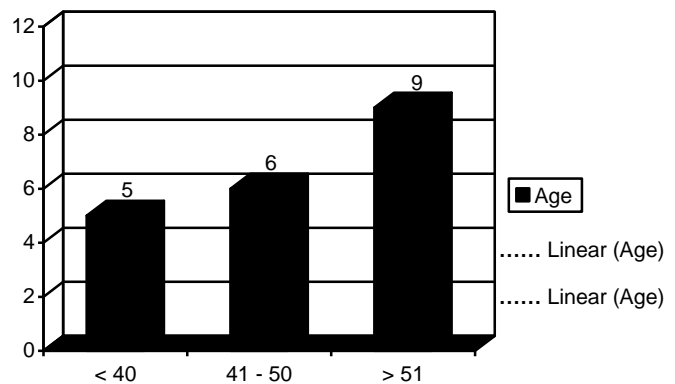


Fig. 2: Age Distribution.

There were 11 (55%) left sided procedures and 9 (45%) right sided Pallidotomy procedures were performed. Mean pre-operative rigidity using UPRDS was 24.9 ± 1.47 , while post-operative score was 11.87 ± 1.53 . Application of t-test (41.223) Pre and Post

Parkinsonian rigidity score was statistically significant ($p < 0.001$).

There was a statistically significant difference between Pre op and 3, 6 weeks and 3 months post op Parkinsonian rigidity using UPRDS (Table 2). There was also statistically significant difference between post op and 3, 6 and 3 months post op Parkinsonian rigidity using UPRDS (Table 3). There was numerically difference between 6 week and 3 months post operative UPRDS score but that not reached to statistical significance (Table 4).

Pallidotomy procedure in our study had no mortality but 4 (20%) patients suffered from procedure related complications one patient (5%) suffered from transient hemiparesis, 1 (5%) from wound infection, 1 (5%) having dysarthria and 1 (5%) transient diplopia.

DISCUSSION

Parkinson's Disease (PD) is a common neurodegenerative disorder. Symptoms of PD can be pharmacologically treated with drugs like levodopa. Surgery is option for patients who have advanced disease that is either refractory to pharmacotherapy or develop side effects like disabling dyskinesia.

Now more and more literature on neuromodulation therapy for PD is mushrooming using more advanced and sophisticated equipment and gadgets like DBS but in 1990s, publications on long term results of pallidotomy in treatment of PD rigidity and tremors actually reopened the door for functional neurosurgery.⁷ Moreover pallidotomy still holds its importance in developing countries where cost effectiveness of procedure does matter. The main argument against lesioning therapies for Parkinsonian rigidity and tremors like pallidotomy or thalamotomy is their irreversibility. There are certain situations like implant induced infection, non affordability favors more towards lesioning procedures. PD is a ongoing process and in certain cases people survive up to that advanced age that discussion arises about the cost effectiveness of revision of battery and social benefits

Table 1: Showing Disease Pattern Distribution.

| | Frequency |
|--------------------------------------------------------------------|-----------|
| Bilateral rigidity, Bradykinesia | 5 |
| Bilateral rigidity more on Right side | 4 |
| Bilateral Rigidity more on Left side | 3 |
| Bilateral rigidity, Bradykinesia, Ataxia | 4 |
| Difficulty Walking, Micrographia, Bradykinesia, Bilateral Rigidity | 4 |

Comparison of Pre and Post op. Parkinsonian rigidity using UPRDS.

| | Mean | Standard Deviation |
|---------|-------|--------------------|
| pre-op | 24.9 | 1.47 |
| post-op | 11.87 | 1.53 |

Table 2: Comparison of Pre and Follow up post op Parkinsonian rigidity score.

| | Mean | Std. Deviation | T test | p value |
|---------------------|-------|----------------|--------|---------|
| Pre Operative Score | 24.9 | 1.47 | | |
| 3 Weeks | 11.27 | 1.39 | 42.633 | < 0.001 |
| 6 Weeks | 10.67 | 1.03 | 46.542 | < 0.001 |
| 3 Months | 10.47 | .860 | 46.077 | < 0.001 |

Table 3: Comparison of post-operative and Follow up post op Parkinsonian rigidity score.

| | Mean | Std. Deviation | T test | p value |
|----------------------|-------|----------------|--------|---------|
| Post Operative Score | 11.87 | 1.53 | | |
| 3 Weeks | 11.27 | 1.39 | 4.539 | < 0.001 |
| 6 Weeks | 10.67 | 1.03 | 9.893 | < 0.001 |
| 3 Months | 10.47 | 0.860 | 5.279 | < 0.001 |

Table 4: Comparison of 6 weeks post op and 3 months post op Parkinsonian rigidity using UPRDS.

| | Mean | Std. Deviation | T test | p value |
|----------|-------|----------------|--------|---------|
| 6 Weeks | 10.67 | 1.03 | 1.00 | 0.326 |
| 3 Months | 10.47 | .860 | | |

of that particular person, as Parkinson's disease is not only decline in and degeneration of motor circuits but also in memory and cognition of patient. In these cases pallidotomy is still thought to be an effective augmentation in arsenal of different options of treatment of Parkinson's disease.

Parkinson's disease is well established disease of old and elderly age. 1% of population above 60 years of age are bound to have Parkinson's disease. The cause is not well known but genetic and environmental factors are postulated to be the cause of this disease. Some evidences have been identified favoring familial aggregation of genetic material. The genetic factors are thought to be contributing only 10% in causing this disease leaving main chunk of 90% as an etiological factor to environmental factors. These environmental factors include pesticide toxicity, heavy metal exposure, diet, working in high magnetic fields, smoking, water supply, exposure to urban lifestyle etc³. Pringsheim et al published meta-analysis of the worldwide data showed a rising prevalence of PD with age (all per 100,000): 41 in 40 to 49 years; 107 in 50 to 59 years; 173 in 55 to 64 years; 428 in 60 to 69 years; 425 in 65 to 74 years; 1087 in 70 to 79 years; and 1903 in older than age 80². Its onset before 40 years is rare according to the studies but in this study 5 (25%) patients were below age 40. Mean age of presentation in this study was 47.58 years. Younger onset of disease is associated with more motor complications and disease severity.⁴ This evidence provokes some serious questions about the environmental hazards and acquired factors in studied population.

Gender also cause a great difference in prevalence of PD as universally male are 1.5-2 times more effected than female. Also the disease manifests at a later age in women by a mean of 2.2 years. Women with PD may have better motor scores, but there is higher prevalence of dyskinesias. These gender differences are attributed to differences in life style and hormonal factors and also differences in exposure to risk factors for PD.⁵ In our study male to female ratio was 2.3:1.

Patients with different stages of Parkinson's disease and different UPDRS rigidity score were included in this study. Fourteen patients (70%) presented with UPDRS rigidity score 3 and 6 patients (30%) with rigidity score 4. After lesioning 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. Mean UPDRS score for rigidity at admission was 3.507 and on follow-up after three months mean UP-

DRS score for rigidity was 1.346. There was improvement in UPDRS score in term of reduction in rigidity was 2.161. In this study improvement in patients after pallidotomy in term of UPDRS was 47% on first post-operative day and these scores continued to improve in the follow up period. Improvement continued upto 3 months. But statistical improvement of UPDRS was upto 6 weeks. These findings are comparable with the previously published studies. de Bie RM et al reported in the "off" phase, the median UPDRS II score improved from 26.5 to 20.5 (23%) and the median UPDRS III score improved from 47.5 to 33.0 (31%).⁶ Laitinen et al did pallidotomies in 38 patients and described almost complete relief of rigidity in 92% of the patients.⁷ Dogali et al in 1995 described 60% improvement after pallidotomy.⁸ Schrag et al in 1999 described 44% improvement in UPDRS postoperatively after pallidotomy.⁹

Complications published in literature for pallidotomies are visual field deficits, weakness, fatigue, hypersomnia, drooling, dysphagia, speech disorders, hiccups, hemorrhage, seizures, apraxia, coma, infection, mental confusion, and impaired memory.¹⁰ Bilateral procedures have more complications than unilateral procedures. Pallidotomy procedure in our study had no mortality but 4 (20%) patients suffered from procedure related complications one patient (5%) suffered from transient hemiparesis, 1 (5%) from wound infection, 1 (5%) having dysarthria and 1 (5%) transient diplopia.

CONCLUSION

Pallidotomy is effective as well as safe surgical treatment option in reducing rigidity for medically refractory Parkinsonism's Disease where deep brain stimulation is not feasible, affordable or available.

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