Deep Brain Stimulation in Parkinsons Disease in Nepal

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ABSTRACT

Background

Parkinsons disease is a central nervous system degenerative disorder affecting motor system and characterized by progressive tremor, rigidity, gait abnormalities. Surgical treatment of Parkinsons disease is based on the changes in the basal ganglio-thalamocortical circuits which is altered in Parkinsons disease. Currently pallidotomy and Deep Brain Stimulation are available modes of surgical treatment of Parkinsons disease.

Objective

To know efficacy of deep brain stimulation in Parkinsons Disease in Nepal.

Method

All patients of idiopathic Parkinsons disease who underwent Deep Brain Stimulation in Annapurna Neurological Institute and Allied sciences since 2014 were included. The standard functional coordinates for Subthalamic nucleus and Globus pallidus internus was used. We used Zamarano-Dujovny (ZD) Fisher Frame with its software. Patients' Unified Parkinsons disease rating score, Modified Hoehn and Yahr Staging and Schwab and England Activities of daily living Scale were evaluated preoperatively as well as postoperatively.

Result

Ten patients underwent Deep Brain Stimulation. The male is to female ratio was 2:1. The mean age was 55.4±8.9 years and duration of illness was 5.5±2 years. There was a significant improvement in the scores for the main motor manifestations of the disease between the preoperative off-dopa and postoperative off-dopa/on-stim conditions. There was a significant improvement in Schwab and England Activities of daily living scale scores in the off-dopa condition between the preoperative score and the postoperative M6 score.

Conclusion

Our result of Deep Brain Stimulation is quite promising. However, it is very expensive and requires frequent follow-up for neuromodulation.

KEY WORDS

Deep brain stimulation, Parkinsons disease, Unified parkinsons disease rating score

INTRODUCTION

Parkinsons disease (PD) is a neurodegenerative disease which involves the degeneration of dopaminergic neurons in substantia nigra of the brain. It was first described by James Parkinson in 1817.[1] The characteristic motor symptoms of PD are resting tremor, slow movement, muscular rigidity and postural instability like freezing gait. The most commonly used drug in Parkinsons disease is Levodopa (1960) but, despite its positive effects, its prolonged use can lead to motor fluctuations and dyskinesias.[2] In this context, surgical intervention like Deep Brain Stimulation (DBS) is one of the most important innovation in treatment of PD and it is already an established science. Many studies have shown that DBS has significantly improved the motor conditions of PD with reduction of dyskinesia.[3-5] DBS was pioneered and popularised by Benabid and colleagues in Grenoble in the late 1980s.[6] The study is done to know efficacy of deep brain stimulation in Parkinsons Disease in Nepal.

METHODS

All patients of idiopathic PD who underwent DBS in Annapurna Neurological Institute and Allied sciences since 2014 were included in this study. This research has been approved by the Institutional Review Committee of the institute. The patients undergoing pallidotomy for same disease were excluded. The inclusion criteria for DBS were patients with Idiopathic Parkinsons disease, dopamine responders, medically and psychologically stable patients, with drug related adverse effects like dyskinesia and affordability of the patients. Patients' Unified Parkinsons disease rating score (UPDRS) was evaluated preoperatively seven days before surgery, then postoperatively within 10 days of surgery. It was also calculated at three months and 6 months postoperatively. Similarly Modified Hoehn and Yahr Staging (H&E) and Schwab and England Activities of daily living (S&E) Scale was also evaluated at the same duration of time.

Statistical analysis was performed using SPSS 13 (version 13.0; SPSS Inc., Chicago, IL, USA) Data was presented as means ± standard deviation (SD). The scores of the different scales rated before surgery, 3 months and 6 months afterward were compared using nonparametric repeated-measures analysis of variance. Paired comparison was performed between the different times of evaluation using the Wilcoxon rank sum test. For all analyses, a p value of < 0.05 was considered significant.

Surgical techniques

All patients underwent Brain MRI (1.5-3 T, Philips) with no spacing and 3D Volume reconstruction imaging and it was obtained in a DICOM CD. Then Stereotactic frame (Z-D Fisher) frame was applied and CT scan head was done (1 slice Siemens with 2 mm thickness) with no tilt. These images were again retrieved in a DICOM CD. Then these two images were fused in the workstation and standard Globus palidus internus or Subthalamic Nucleus were visualized anatomically. The standard functional targets for GPi and STN were used. The targets were also reverified by the inbuilt Schaltenbrand Atlas. Then the patients were taken to the operating room and the frame was fixed in the Mayfield. Two burr holes were created 4 cm lateral to midline and 1 cm in front of coronal suture under local anesthesia and dura was coagulated and cut. Then the DBS electrodes were inserted in GPi/STN. It was confirmed with the c-arm as well. Microelectrode recording (MER) was also used for STN nucleus. Continuous monitoring of the motor symptoms, speech and visual symptoms of the patients was done. Brio rechargeable IPG (Implantable Pulse Generator) was inserted subcutaneously in infraclavicular region and connected to the leads in the same setting or the next day under General Anesthesia. The stimulation was carried out slowly. All the patients were followed up and their UPDRS (Unified Parkinson's Disease Rating Score), Modified Hoehn and Yahr (H&Y) Staging and Schwab and England (s7E) Activities of Daily Living Scale was compared. Their IPG Parameters were also noted. The changes in the medications specially if there is any decrease in the dose of dopamine was also noted.

RESULTS

There were ten patients who underwent DBS. Two patients had GPi DBS and remaining eight had STN DBS. The male is to female ratio was 3:1 and mean age was 55.4±8.9 years. The mean duration of illness was (5.5±2) years as shown in Table 1. Out of ten cases two cases had GPi DBS where as remaining eight had STN DBS. Seventy percent of our patients were from the capital city (Kathmandu) and 30% were from outside Kathmandu. All of our patients were dopamine responder with minimum 20% improvement in UPDRS between on and off stage. All patients had bilateral lead placement except the first one who had unilateral lead placement.

Table 1. Showing the demographics

Total number of Patients	10
Male:Female	3:1
Mean age(years)	55.4±8.9 years
Duration of illness(years)	5.5±2 2 in Gpi and 8 in
Site	STN
Complication	1 hemorrhage

There was an improvement in the scores for the main motor manifestations of the disease between the preoperative off-dopa and postoperative off-dopa/on-stim conditions. The effect was significant for the UPDRS III between the preoperative and both the postoperative M3 and M6

Table 2. Showing the Motor scores of UPDRS and S & E and H & Y scores

		Off Dopa			On Dopa	
	Baseline	DBS(M+3)	DBS(M+6)	Baseline	DBS(M+3)	DBS(M+6)
Rating scale	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD
UPDRSII (/52)	22.56±7.41	9.78±5.51	10.77±9.01	10.12±5.8	7.77±7.03	8.11±6.95
UPDRSIII (/108)	51.22±14.02	23.22±12.77	24.22±19.54	24.33±13.25	16.9±17	18.2±17
Schwab and England (S&E) (/100)	50±22	72±17	70±10	61±20	74±17	70±15
Hoehn and Yahr (H &Y) (/5)	3±1	2.27±0.83	2.2±0.8	2.5±0.84	2.1±0.6	2±0.1
		p value		Baseline vs M+3	p value	
UPDRS II	Baseline vs M+3	0.004		Baseline vs M+6	0.031	
	Baseline vs M+6	0.004		M+3 vs M+6	0.125	
	M+3 vs M+6	0.688		Baseline vs M+3	0.688	
UPDRS III	Baseline vs M+3	0.004		Baseline vs M+6	0.039	
	Baseline vs M+6	0.004		M+3 vs M+6	0.039	
	M+3 vs M+6	0.526		Baseline vs M+3	0.688	
Schwab and England	Baseline vs M+3	0.953		Baseline vs M+6	0.889	
	Baseline vs M+6	0.02		M+3 vs M+6	0.075	
	M+3 vs M+6	0.016		Baseline vs M+3	0.033	
Hoehn and Yahr	Baseline vs M+3	0.289		Baseline vs M+6	0.219	
	Baseline vs M+6	0.219		M+3 vs M+6	0.039	
	M+3 vs M+6	0.004			0.063	

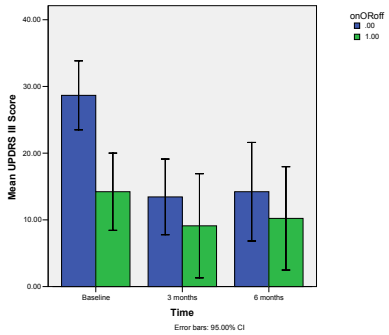

Figure 1. Showing UPDRS III score in on and off stage of dopamine during stimulation

scores in the off-dopa condition. There was a significant improvement in S&E scores in the off-dopa condition between the preoperative score and the postoperative M6 score (Table 2 and Fig. 1). There was the same tendency for H&Y score in the off-dopa. (Table 2)

All of our patient had high frequency stimulation ranging from 130 Hz to 150 Hz except one who had low frequency stimulation 50 Hz and bilateral freezing was her main complaint. Most of our patients had bipolar leads activated and few had monopolar leads. The pulse width ranged from 62 us to 75 us and the current parameter ranged from 2 to 3 mv. The average follow up visit is once in three months to once in six month time. There is decrease in the dose of medications in STN DBS cases (about 30%) after six months follow up period. We had one complication of postoperative intracerebral hematoma which had to be evacuated and luckily this patient has one of the best response of DBS.

DISCUSSION

The improvement in the motor condition of PD after DBS is already an established science. Both GPi and STN DBS is effective in reducing all the cardinal motor signs of PD by reducing dyskinesia, increasing on time and improving the fluctuations in the motor signs.[7]

We had more number of male patients than female patients who underwent surgery. This result was similar with twice the number of male patients on the literature.[8,9] Our mean age of the patients was 55.4±8.9 years and the mean age of the patients according various literature review was 59.25±3.76 years.[10] Two of our patients (20%) were in their late 40s and we believe that they were young onset parkinsons disease.

The mean duration of illness was 5.5±2 years and with the range of 5-9 years. We have not operated on the patients who have less than three years duration of illness. It was to rule out parkinsons plus disease who deteriorate rapidly. The majority of patients have retired from professional life and are dependent on help in their activities of daily living. The low morbidity and impact of STN-DBS may justify operating on patients at an earlier stage to prevent the inevitable decline in quality of life and social participation. In one of the studies it was shown that quality of life was significantly better in early surgical group (6.8±1 year) rather than best medical treatment.[11] DBS may be considered in suitable patients at the end of the drug honeymoon period, when the first motor complications start to emerge but it

still has to be proved.[12] Hariz et al. has also explained that patients with surgical therapy will definitely experience less severe symptoms than the best medical therapy regardless of disease state at baseline.[13,14]

Many studies have shown improvement in Off UPDRS score ranging from 31% to 50%.[15-18] Similarly change in ADL score also ranged from 32% to 50%.[15,17,18] Our improvement in motor score of UPDRS in three and six months follow up period was also comparable. Similarly the on stimulation and off stage dopamine improvement in terms of H&E score and S&E ADL was also comparable.

However the result of DBS varied in long term follow up with little to no benefit after 1 to 2 years.[17] Some studies have shown maintained benefit up to 4 years.[19,20] However this variability may be due to poor patient selection, improper lead placement or variation in parameter adjustment.

Both of our patients with GPi have no change in medication but there is 30% decrease in the dose of dopamine in STN DBS patients. As described in the literature there is significant reduction in dopaminergic medications in case of STN DBS and hence also reduces the medications related adverse effect.[21,22] In one of the meta-analysis of the outcome of the STN DBS, the average reduction in L-dopa equivalents following surgery was 55.9%.[23] One of our patients developed intracranial hemorrhage which had to be evacuated and we believe that it is because of the multiple trajectories of MER recording in this case. Fortunately she is one of the best responders among our cases. We have now started using single MER trajectories only. A meta-analysis by Zrinzo et al. of all DBS publications with more than 40 patients has shown that MER results in far more haemorrhage than image-guided DBS.[24]

Another patient had superficial skin infection which got cured with medications. The infections or skin erosion rates are relatively common (1-15%) and the literature has reported the complications like hemorrhage (0.7-3.1%) and even death (1-2%).[25]

Typical stimulation parameters for chronic DBS are monopolar stimulation, voltage 2.5-3.5 V, impulse duration 60-90 ms and frequency 130-180 Hz.[5] All our cases had similar parameters except for the bipolar mode in all cases as shown in the table. One patient benefitted from low frequency stimulation whose main complaint was rigidity and gait disturbances and some studies have shown therapeutic effect of low frequency stimulation.[26,27]

Limitation of this study include small sample size and lack of long term follow up.

CONCLUSION

Our result of DBS is quite promising. However, it is very expensive. We need to adjust various parameters of the IPG and it varies in different cases which may need frequent follow up visits.

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