Effectiveness of Deep Brain Stimulation in Iraqi Patients with Parkinson Disease

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Abstract

Background: Surgical treatment for advanced Parkinson disease (PD) is considered when medical therapy fails to control the symptoms.

Objective: Assessment of effectiveness of deep brain stimulation (DBS) in controlling motor manifestations of advanced PD.

Patients and Method: Twenty patients (14 male and 6 female) whom fulfill the requirements for DBS surgery, were included in this study. All patients were on Levodopa (L-dopa), procyclidine, pramipexol, and amantadine medications. The study conducted between March 2017 and March 2018 in the neurosurgical teaching hospital and neuroscience hospitalin Baghdad/Iraq. Unified Parkinson's Disease Rating Scale(UPDRS) was used before and after surgery.

Results: There was a statistically significant improvement in the tremor, rigidity, and bradykinesia.

Conclusion: Most disabling axial symptoms of gait and postural instability, that failed to respond to medical therapy, will show effective response to the bilateral STN stimulation in advanced PD cases.

Keywords: *Parkinson disease, deep brain stimulation, subthalamic nucleus.*

Introduction

PD is a chronic degenerative disease of the basal ganglia, it includes both motor function and non-motor clinical manifestations, treated symptomatically by dopamine replacement .Every year, an average of nine-thousand DBS procedures are done for patients with PD around the world.(1) Ninety percent of PD are sporadic, while the monogenic forms of the disease account for approximately 3–5%.(2)

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Perhaps not since neurosurgery introduced to thecommunity,by Harvey Cushing, has there been a surgical treatmentthat has got the intention of the neurosurgeons and the thoughts of the patientsto the extent that DBS did. Since its introduction in its current form 30 years ago, DBS remains innovative in the mind of many and is acknowledged as underutilized.(3)

Benabid's clinic first reported DBS for the management of PD in 1993. After FDA authorizationfor essential tremor on 1997, DBS was widespread used. It was first admitted to Iraq in 2007, and all the implantations were carried out in the neurosciences hospital in Baghdad/Iraq. (4)

DBS provides for the PDpatients a remarkable therapeutic effect. It generates measurable electrical stimulation pulses at the goal target in the brain which

leads to intrusion with neural activity and creating areversible lesion in the implanted target nucleus whichresults, eventually, in improvement of motor characteristics of PD (bradykinesia, rigidity, and tremor).(5)

However,risingdataimplies that "DBS is more than just a neuromodulatory switch to control debilitating motor symptoms". Chronic DBS has been revealed to stimulatecontinuingreformation of neuronal circuits throughout enhanced synaptic plasticity and neurogenesis. Thus DBS can cause slowing of disease progression and increase survival in some PD cases.(6)

Symptomatic treatment using dopamine replacement remedycontinued to be the most useful management of PD since L-dopa was initially brought to use since the 1960s. In the end, they were coupled with motor fluctuations and L-dopa-induced dyskinesia. In a community-based study, the mean times of onset of dyskinesia were 6.6 years.(7)

In the lack of disease-modifying therapies, the presentmanagement of PD is principallyconcentrated on minimizing motor symptoms by drugs that augment intracerebral dopamine level (e.g. L-dopa, MAO-B inhibitor) or excite dopamine receptors (e.g. Dopamine agonist). On the continuing, side effects of dopaminergic treatment, counting on/off motor fluctuations and dyskinesias, commonly occur. (8) DBS of subcortical nuclei such as the subthalamic nucleus (STN),globus pallidus internus(GPI), and infrequently ventralis intermedius nucleus (VIM), can be presented as a conventional treatment for properly selected patients with L-dopa-responsive motor symptoms who suffer from disabling drug-associated side effects.(9)

The progress in DBS for movement disorders can be grouped in terms of the steps of the DBS workflow, which consist of selection of patients, selection of target and imaging, selection of hardware, surgical technique, and postoperative programming and maintenance.

Advances in every of the exceeding domains are continuing and to improve the excellence and effectiveness of DBS for movement disorders. (3,5,10,11).

Aim of the study: Assessment of effectiveness of DBS in controlling motor manifestations of advanced PD.

Patients and Method

Patients Selection: This is a prospective clinical study that incorporated 20 patients (14 male and 6 female) for whom DBS was implanted at the neurosurgical and the neurosciences teaching hospitals in Baghdad/Iraq, from March 2017 to March 2018 for bilateral stimulation of the STN. The patients were fulfilling the Movement Disorder Society Clinical Diagnostic Criteria for PD. (12)

The DBS were implanted using a fusion system of the CT and MRI images (Stealth Station- Medtronic®) to identify the site of the STN in relation to the mid-commissural point.

All the patient were right handed, and all of them were on L-dopa, procyclidine, pramipexol, and amantadine medications. In addition, intraoperative neuronal electrical activity recording was made.

All of the patients were followed for 2 months after staring of stimulation.

The inclusion criteria were:

1. Diagnosis of idiopathic PD and duration > 5 years.
2. Intolerable L-dopa related motor complications despite of optimal adjustment of antiparkinsonian drugs.
3. Improvement of motor symptoms > 50 % during L-dopa test
4. Age below 70 years.
5. No surgical contraindications.
6. No cognitive abnormality or significant continuing psychiatric illness.
7. No medical co-morbidity
8. Normal brain MRI

The severity of the disease is assessed before and after DBS implantation using UPDRS, which is a 50 question assessment of both motor and non-motor symptoms of PD.

Any patient who did not fulfill the above criteria was not a candidate for DBS implantation (e.g. severe brain atrophy, brain lesions, coagulopathy, anticoagulation therapy, immunosuppression, active psychosis, major depression with suicidal thoughts, personality disorder impairing compliance, drug abuse impairing compliance,

and poor general health conditions like severe ischemic heart disease, hypertension, and diabetes).

As a routine of the workup, the general preoperative list of diagnostic tests including hematology, biochemistry, serology, ECG, CXR and standard brain MRI were done for each patient.

The severity of the disorder was assessed, and the motor fluctuation were evaluated after the diagnosis of idiopathic PD. Also drug related dyskinesia were evaluated according to the UPDRS.[13]

Every patient should have new set of MRI studies. Closed MRI(3 Tessla) were used in our study.

The patientsresumed their preoperativedrugs regimenstraight away postoperatively to keep away from dopaminergic withdrawal symptoms.

CT scans and/or MRI were done for all the patients postoperativelyto review the electrode position and the intracranial condition. Additionally, plain X-rays were obtained to review the position and geometry of the leads and hardware. Modification of the drugs may be needed according to the patients' clinical condition. If stable, patients were allowed to return home as early as 24 hours following the surgery.

The process of programming of the patient susually started 7 days after the implantation so as to bypass the phase of lesioning result of the surgery.

Statistical Analysis: Descriptive analysis in the form of percentage was calculated using Microsoft Office Excel Worksheet and presented in the relevant tables shown below. Chi-Square test was used for statistical analysis by utilizing the Statistical Package for Social Sciences (SPSS) version 17(p value< 0.05 was considered significant).

Results

The explanatory data of the patients incorporated in this study are demonstrated in table 1.

Table 1: Descriptive data of the patients before DBS

Patient number	Gender	Age (years)	Tremor UPDRS score	Rigidity UPDRS score	Bradykinesia UPDRS score
1	Female	60	4	3	3
2	Female	33	3	3	4
3	Female	55	3	3	2
4	Male	57	3	3	4
5	Male	60	3	2	2
6	Female	56	2	2	3
7	Male	55	3	3	3
8	Male	45	2	3	3
9	Male	67	4	4	4
10	Male	50	3	2	5
11	Male	54	2	2	2
12	Male	50	2	3	3
13	Male	56	4	2	4
14	Male	67	3	2	2
15	Female	42	2	2	3
16	Male	47	3	3	3
17	Male	69	3	2	2
18	Male	53	3	3	2
19	Male	43	2	2	3
20	Female	50	2	2	4

We analyzed the demographic data, rigidity, tremor, and bradykinesia before and after the DBS, and the relation of the patient's age to the improvement in rigidity, all measured according to the UPDRS.

1. **Tremor:** The improvement in the tremor grade post-operatively was statistically significant ($p< 0.05$) [table 2].

Table 2: Tremor grade pre-operative and post-operative.

Patient number	Tremor UPDRS score Pre-operative	Tremor UPDRS score Post-operative
1	4	0
2	3	0
3	3	0
4	3	0
5	3	0
6	2	0
7	3	1
8	2	1
9	4	0
10	3	0
11	2	0
12	2	1
13	4	1
14	3	0
15	2	0
16	3	0
17	3	1
18	3	0
19	2	1
20	2	0

$p < 0.05$

2. **Rigidity:** The improvement in the rigidity of our patients post-operatively was statistically significant [$p < 0.05$] (table 3).

Table 3: Rigidity grade pre-operative and post-operative.

Patient number	Rigidity UPDRS score Pre-operative	Rigidity UPDRS score Post-operative
1	3	0
2	3	0
3	3	0
4	3	0
5	2	0
6	2	0
7	3	1
8	3	0
9	4	1
10	2	0
11	2	1
12	3	0
13	2	1
14	2	0
15	2	0
16	3	1
17	2	0
18	3	1
19	2	0
20	2	0

$p < 0.05$

3. **Bradykinesia:** There improvement in the bradykinesia of our patients post-operatively was statistically significant [$p= 0.01$] (table 4).

Table 4: Bradykinesia grade pre-operative and post-operative.

Patient number	Bradykinesia UPDRS score Pre-operative	Bradykinesia UPDRS score Post-operative
1	4	0
2	3	0
3	3	0
4	3	0
5	3	0
6	2	0
7	3	1
8	2	0
9	4	1
10	3	1
11	2	0
12	2	0
13	4	1
14	3	1

Patient number	Bradykinesia UPDRS score Pre-operative	Bradykinesia UPDRS score Post-operative
15	2	0
16	3	0
17	3	0
18	3	1
19	2	0
20	2	0

$p < 0.05$

Complications: We had only 2 cases of surgical wound infection who responded well to conservative treatment by antibiotics and meticulous dressing.

Discussion

DBS has become an already established surgical option for medically intractable PD.[14] After the implantation, the motor symptoms improves comparatively to the pre-implantation response to L-dopa. The reduction of the disabling motor symptoms eventually leads to a significant reduce in the dopaminergic drugs doses with subsequent drop of drug – related dyskinesia.[15,16]

GPI and STN stimulation showed similar efficacy rates. However other studies claimed that STN stimulation is possibly superior in controlling the symptoms of PD. Choosing STN stimulation over the GPI is frequently based according to the foundational, surgeon, and programming practices and preferences. There is a more reliabletendency for major reduction in dopaminergic drugs consumption andl esser current requirement with consequential longer battery time, with the STN stimulation.[17,18,19]

In our study we followed 20 patients(14 males and 6 female), with age range from 33 to 69 years.

Lopiano et al reported improvement in tremor, bradykinesia, rigidity, dyskinesia, and motor fluctuations symptoms after DBS for PD, while hypophonic speech, dysphagia, micrographia, freezing of gait (especially if occurring in the “on” state), cognitive dysfunction, and dysautonomia did not show improvement.[13]

In our study there was a significant improvement in rigidity, tremor, and bradykinesia.

Paul Krack et al reported that in the first few days after DBS implantation, the complications related to the device were rare (less than 1%). One patient had an infection that was managed bytransitorytaking away of the subcutaneous extension lead and IPG, three deaths, one patient developed an intra-operative intracerebral hemorrhage and remained bedridden and died three years after surgery, one patient died 11 months after surgery due to myocardial infarction, and one patient had severe depression and suicidal thoughts three months before the implantation and eventually committed suicide six months after surgery.[20] This is not comparable to our results because of the bigger number of cases and extended period of follow up by Paul Krack et al.

Paul Krack et al, in five years follow up on patients with PD who had bilateral DBS-STN, found a significant decrease in the requirement for L-dopa (or equivalent drug) postoperatively (11of 42 patients did not took L-dopa anymore, and 3 patients did not took any dopaminergic drugs).[20]

Conclusions

The advantages of DBS in advanced PD is symptomatic control rather than therapeutic effects. The fate or progress of the illness will not be changed. DBS is completely reversible in comparison with the other ablative procedures. Most disabling hypokinetic manifestations, that failed to respond to medical therapy, will show effective response to the bilateral STN stimulation in advanced PD cases.

Ethical clearance- Taken from the scientific unit and medical ethics committee of Alkindy college of medicine/University of Baghdad**.**

Source of funding: Self

Conflict of Interest: Nil

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