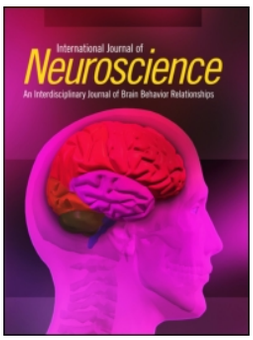

International Journal of Neuroscience

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/ines20

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To cite this article: Sabiha T. Aydemir , Müge Kuzu Kumcu , Çağrı Ulukan , Batuhan Bakirarar & M. Cenk Akbostancı (2021): Patient preference of device-based treatment of Parkinson's disease, International Journal of Neuroscience, DOI: 10.1080/00207454.2020.1853723

To link to this article: https://doi.org/10.1080/00207454.2020.1853723

Published online: 05 Jan 2021.

INTERNATIONAL JOURNAL OF NEUROSCIENCE
https://doi.org/10.1080/00207454.2020.1853723

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ORIGINAL ARTICLE

Patient preference of device-based treatment of Parkinson's disease

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ABSTRACT

Introduction: Subthalamic nucleus deep brain stimulation (STN-DBS), continuous subcutaneous apomorphine infusion (APO), and levodopa–carbidopa intestinal gel infusion (LCIG) are treatments used to treat severe motor fluctuations and dyskinesia in patients with advanced levodopa responsive Parkinson's disease (PD), who can no longer be managed with available combinations of oral medications. This study aims to evaluate patient choice of one of three device-based treatment methods.

Methods: A total of 58 patients clinically diagnosed with PD were included in the study. Eligibility for device-based treatment of PD patients with motor symptoms despite optimal medical treatment was assessed based on Hoehn & Yahr Stages, and Unified Parkinson's Disease Rating Scale-Part III. All three device-based treatment methods were thoroughly explained with on-hand demonstrations. Preferences and reasons for choice were recorded.

Results: Nineteen patients were ineligible for STN-DBS due to neurological causes. A total of 23 patients preferred STN-DBS, 23 preferred APO, and only one patient preferred LCIG. Thirteen patients preferred to continue oral medical treatment, while two patients positively approached both STN-DBS and APO.

Conclusion: The most common reason patients declined STN-DBS and LCIG was concerned about the surgical operation, while the most common reason APO was declined was its frequent administration of the injection. While STN-DBS was preferred by younger, less severe patients, APO was preferred by older patients who had a longer duration of disease.

ARTICLE HISTORY
Received 14 December 2019
Revised 30 October 2020
Accepted 5 November 2020

KEYWORDS
Deep brain stimulation; apomorphine infusion; levodopa–carbidopa intestinal gel infusion; device-based treatment; Parkinson's disease

Introduction

Currently, motor complications such as 'peak dose dyskinesia' frequently occur at high concentrations of levodopa causing involuntary movements, and 'wearing off', when the effective duration of the drug is shortened and effect wears off before the next dose may develop in the treatment of Parkinson's disease (PD) due to progressive neurodegeneration and long-term use of oral levodopa [1]. When these symptoms do not improve with optimal oral treatment, alternative treatment options include deep brain stimulation, apomorphine (APO) infusion, or levodopa–carbidopa intestinal gel infusion (LCIG) [2,3]. APO is a potent dopamine agonist and can be administered as subcutaneous infusion or intermittent injections. Subthalamic nucleus deep brain stimulation (STN-DBS) inhibits the hyperactivity of this nucleus by stimulating it at high frequency [4]. As for LCIG, the drug is continuously infused into the jejunum *via* a gastrojejunostomy to achieve constant levodopa levels in the blood [5,6]. There is no randomized, controlled study comparing these three device-based treatment options. Therefore, the selection of device-based treatment is often based on studies supplying less strong evidence, the clinician's judgment and the patient's preference [7]. So far, there is no study in the literature that investigates three device-assisted treatment choices, along with reasons of patients with PD who are eligible for these treatments. This study aims to evaluate the perspectives of PD patients who are suitable for device-based treatment.

Material and methods

Participants

Study participants were volunteers who gave consent, clinically diagnosed with PD, eligible for device-based

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treatment, and included among patients who applied to the department of neurology.

In our study, PD patients included the study who has motor complications despite the best medical therapy. Following a pilot study conducted with 16 patients to determine the sample size, our study was conducted with a total of 58 patients (26 females, 32 males) between September 2016 and June 2017.

Patient and methods

We used Hoehn & Yahr (H&Y) staging to evaluate the stage of PD [8]. The patients' daily living activities were evaluated with United Parkinson's Disease Rating Scale-II (UPDRS-Part II), and motor problems with UPDRS-III [9,10]. In addition, to identify patients with contraindications for STN-DBS, Mini-Mental State Examination (MMSE) [11] was used to assess the presence of dementia, and Beck Depression Inventory (BDI) [12] for the presence of depression. Positive and negative aspects of all three treatment methods were explained to patients who were eligible for device-based PD treatment, according to a standardized text for about 30–40 min. During the explanation, STN-DBS battery, APO and LCIG pumps, and connection cables were demonstrated, and the explanation was also supported by printed visual material. After the explanation, patients were encouraged to ask questions and an attempt was made to make sure all methods were completely understood. Afterwards, patients' preferences were questioned and reasons why a method was preferred or refused were recorded for each three procedures.

Statistical analysis

A pilot study of 16 patients was conducted for sampling. After this study, when sampling was assessed with nine degree of freedom Chi-square test of 80% power and 5% significance. When patients did not prefer any treatment, the percentages were 27.3%, 36.4%, 18.2%, 18.2%; for DBS 40%, 10%, 10%, 40%; for APO 16.7%, 50%, 16.7%, 16.7%; for LCIG 20%, 40%, 20%, 20%; therefore, a 58 patient sample group was found sufficient for this study.

All statistical analyses were performed using SPSS for the Windows 11.5 software program (SPSS Inc., Chicago, IL). For the quantitative variables, mean ± standard deviation and median (min–max), for the categorical (qualitative) variables' percentage (frequency), were used as descriptors in the study. When to look whether there was a statistically significant difference between the categories of a qualitative variable with two categories in terms of a quantitative variable, Student *T*-test was used if the normal distribution assumptions were met; if not, Mann–Whitney *U* test was used. Shapiro–Wilk test and skewness and kurtosis values were used to determine normality. When to look whether there was a statistically significant difference between the categories of a qualitative variable with three or more categories in terms of a quantitative variable, one-way ANOVA was used if the normal distribution assumptions were met; if not, Kruskal–Wallis test was used. The relationship between nominal variables was evaluated with Chi-Square or Fisher Exact tests. Significance level was set at $p = 0.05$.

Results

Descriptive characteristics of the patients are summarized in Table 1. Of the 58 patients with PD who participated in the study, 23 (39.7%; 15 male, 8 female) preferred STN-DBS, 23 (39.7%; 11 male, 12 female) preferred APO, and one patient (1.7%; one female) preferred LCIG. Two patients indicated that they would choose either APO or STN DBS. Thirteen patients refused all treatments and wished to continue oral treatment. Thus, a total of 60 selections were made.

The mean MMSE score was 25.5 ± 4.2 and the mean BDI score was 15.8 ± 9.6.

Nineteen of the patients were ineligible for STN-DBS treatment due to reasons such as potential dementia, major depression, advanced age, and multiple ischemic gliotic lesions on MRI. Although STN-DBS was explained to these patients as a treatment option, they were recommended not to choose this option, and recorded as 'ineligible for treatment' for this method. Of the patients ineligible for DBS treatment, 10 patients preferred APO, one patient preferred LCIG, while 8 patients declined device-based treatment and wished to continue oral treatment. Also, 3 patients were ineligible for APO because of psychosis and atrial fibrillation. Although this method was explained to them, they were recommended not to choose this option. All three patients wanted to continue oral treatment.

Of the 35 patients who did not prefer STN-DBS; 19 (54.3%) already had contraindications for STN-DBS, 12 (34.3%) had concerns about the surgical procedure, and 4 (11.4%) stated financial concerns as the reason for not preferring this treatment. Of the 35 patients who did not prefer APO; 14 (40.0%) had fear of injection, 10 (28.6%) did not want to carry a pump, 6

Table 1. Descriptive data of the series.

Age	Sex (F/M) (%)	Duration of disease	Age of onset	Duration of motor complications	Hoehn Yahr stage	UPDRS-II	UPDRS-III OFF state
63.1 ± 11.0 (28.0–91.0)	26/32 (44.8/55.2%)	10.4 ± 6.9 (2.0–34.0)	52.6 ± 11.8 (23.0–73.0)	3.3 ± 3.3 (0.5–15.0)	2.4 ± 0.5 (1.0–3.0)	13.3 ± 7.5 (0.0–32.0)	33.1 ± 18.2 (1.0–79.0)

All values are either average ± standard deviation (range) or percentages.
SOFAS: Social and Occupational Functioning Assessment Scale; UPDRS-II: Unified Parkinson's disease Rating Scale-II; UPDRS-III: Unified Parkinson's disease Rating Scale-3.

(17,1%) lacked confidence in using it, 3 (% 8,6) already had contraindications for APO and 2 (5.7%) had concern of adverse effects as reason for not preferring this treatment. Of the 57 patients who did not prefer LCIG; 35 (61.4%) had concerns about the surgical procedure, 20 (35%) did not wish to carry a pump, 2 (3.5%) lacked confidence in using it as reason for not preferring this treatment.

Age, duration of disease, H&Y and UPDRS-II scores were compared between 23 patients who preferred STN-DBS and 35 who refused it. STN-DBS group was significantly younger and had lower H&Y and UPDRS-II scores. There was no significant difference in duration of disease and UPDRS-III scores between groups. Comparison of patients who preferred and refused deep brain stimulation treatment is given in Table 2.

Age, disease duration, H&Y and UPDRS-II scores were compared between 23 patients who preferred APO and 35 who did not. APO group was significantly older, and had longer duration of disease. There was no significant difference in terms of UPDRS-II or UPDRS-III scores and H&Y stages between the groups. Comparison of patients who preferred and refused apomorphine infusion treatment is given in Table 3.

Twenty-three patients who preferred APO and the 23 patients who preferred STN-DBS were compared in terms of age, disease duration, H&Y and UPDRS-II and -III scores. STN-DBS group was significantly younger. There was no significant difference in terms of UPDRS-II or UPDRS-III scores and H&Y stage between the groups. Comparison of patients who preferred STN-DBS and preferred apomorphine infusion treatment is given in Table 4.

Discussion

In our study, a total of 58 patients planned for transition to device-based treatment were evaluated on their preference between STN-DBS, APO, and LCIG treatment methods after a detailed explanation. To the best of our knowledge, this is the first study in the literature to evaluate device-based treatment of PD in detail based on patient preference. After a detailed explanation of all three options, 45 (77.5%) patients accepted the transition to device-based treatment. We believe that the inclusion of the patient to the decision-making process is compatible with the contemporary patient–physician relationship.

In this study, LCIG treatment was much less frequently preferred than other treatments. The likely causes of this include the concerns of surgical intervention and its potential complications, the presence of a

Table 2. Comparison of patients who preferred and refused deep brain stimulation (DBS) treatment.

	Patients who preferred STN-DBS (23)		Patients who refused STN-DBS (35)		*p* value
	Mean ± SD	Median (min.–max.)	Mean ± SD	Median (min. –max.)	
Age	58.8 ± 10.9	60.0 (28.0–76.0)	65.8 ± 10.3	65.0 (35.0–91.0)	***0.014***
Disease Duration	9.8 ± 5.6	8.0 (2.0–25)	10.8 ± 7.7	10.0 (2.0–34.0)	0.930
H&Y	2.1 ± 0.6	2.0 (1.0–3.0)	2.5 ± 0.5	2.5 (1.5–3.0)	***0.009***
UPDRS-II	14.5 ± 7.0	17.0 (1.0–26.0)	20.3 ± 8.2	21.0 (3.0–36.0)	***0.006***
UPDRS-III **(OFF state)**	30.1 ± 18.0	27.0 (3.0–78.0)	35.0 ± 18.47	33 (7.0–79.0)	0.325

DBS: deep brain stimulation, UPDRS-II: Unified Parkinson's Disease Rating Scale-II, UPDRS-III: Unified Parkinson's Disease Rating Scale-3.
Bold values are statistically significant at $p < 0.05$.

Table 3. Comparison of patients who preferred and refused apomorphine infusion (APO) treatment.

	Patients who preferred APO (23)		Patients who refused APO (35)		*p* value
	Mean ± SD	Median (min.–max.)	Mean ± SD	Median (min.–max.)	
Age	67.3 ± 8.9	68.0 (50.0–91.0)	60.2 ± 11.4	61.0 (28.0–78.0)	***0.026***
Disease Duration	13.4 ± 8.4	11.0 (2.0–34.0)	8.5 ± 4.9	7.0 (2.0–25.0)	***0.024***
H&Y	2.4 ± 0.5	2.5 (1.5–3.0)	2.3 ± 0.6	2.5 (1.0–3.0)	0.843
UPDRS-II	19.2 ± 9.5	21.0 (1.0–36.0)	17.3 ± 7.4	18 (3.0–35.0)	0.414
UPDRS-III (OFF state)	31.5 ± 17.9	33 (3–79)	34.1 ± 18.7	34 (7–78)	0.606

APO: apomorphin infusion; UPDRS-II: Unified Parkinson's Disease Rating Scale Part-II; UPDRS-III: Unified Parkinson's Disease Rating Scale Part-III.
Bold values are statistically significant at $p < 0.05$.

Table 4. Comparison of patients who preferred apomorphine infusion (APO) and deep brain stimulation (DBS).

	Patients who preferred STN-DBS (23)		Patients who preferred APO (23)		*p* value
	Mean ± SD	Median (min.–max.)	Mean ± SD	Median (min.–max.)	
Age	58.8 ± 10.9	60.0 (28.0–76.0)	67.3 ± 8.9	68.0 (50.0–91.0)	***0.010***
Disease Duration	9.8 ± 5.6	8.0 (2.0–25.0)	13.4 ± 8.4	11.0 (2.0–34.0)	0.100
H&Y	2.1 ± 0.6	2.0 (1.0–3.0)	2.4 ± 0.5	2.5 (1.5–3.0)	0.098
UPDRS-II	14.5 ± 7.0	17.0 (1.0–26.0)	19.2 ± 9.5	21.0 (1.0–36.0)	0.064
UPDRS-III (OFF state)	30.1 ± 18	27 (3–78)	31.5 ± 17.9	33 (3–79)	0.794

APO: apomorphine infusion; DBS: deep brain stimulation; UPDRS-II: Unified Parkinson's Disease Rating Scale Part-II; UPDRS-III: Unified Parkinson's Disease Rating Scale Part-III.
Bold values are statistically significant at $p < 0.05$.

permanent gastrojejunostomy catheter, and the requirement to carry a large drug pump. When this method is explained to patients, it seems relatively complicated, since it not only requires surgical intervention, but also learning new information on catheter care, and administration of the drug *via* a pump. All of these seem to be factors that sway patients and their relatives from choosing LCIG as their initial treatment method.

When comparing patients who preferred and refused DBS treatment, the patients that preferred the treatment were younger and had relatively less severe disease according to UPDRS-Part II scores and H&Y staging (Table 2). The fact that younger patients with a probable active work life preferred STN-DBS, which does not involve additional responsibilities or burden such as carrying a pump or a catheter was no surprise.

In the comparison of patients who preferred and refused APO, the patients who chose APO were relatively older and had longer disease duration (Table 3). We think it is reasonable that patients who have lived with PD for many years would prefer a treatment which does not require aggressive surgical intervention and easy to give up if unsatisfied about the outcome.

Equal number of patients chose APO and STN-DBS. However, when the ineligible patients for STN-DBS and APO were considered for each treatment option, preference rates were 74.3% (23/39, STN-DBS) and 41.8% (23/55, APO), respectively. Patients who preferred STN-DBS made their choice mostly due to lack of requirement to carry a device and to learn the additional procedure. When patients who chose these two treatments were compared, younger patients tended to prefer DBS (Table 4). Patients who preferred APO because it does not require surgery or permanent catheter and works only with a small pump.

In light of all of this information, quality of life of PD patients who experience motor complications may be improved with new developments in the device-based treatment field. Taking into account the needs and preferences of the patient and detailed explanation of all device-based treatments builds trust in doctor–patient relationship and this cooperation improves patients' compliance to the treatment. There is a need for further studies on this subject.

We think one of the superior aspects of our study is having a face-to-face interview to explain the positive and negative aspects of all three treatment

methods with actual devices. Also asking open-ended questions about the treatment options is less restrictive to get the actual opinion of the patient instead of web-based surveys which was the method chosen in previous studies [7].

Several pitfalls of this study are a small number of patients, and ineligibility of some patients for some of the device-based treatments, and the UPDRS data were recorded only when patients were in 'off' state. To our knowledge, this is the first study in English literature to quantify patients' preferences for all three device-based PD treatments. This study demonstrated the tendency of younger PD patients to prefer STN-DBS and older patients with long-term disease duration to choose APO. LCIG treatment is the least preferred choice because it requires both a surgical procedure and carrying a large pump.

Disclosure statement

No potential conflict of interest was reported by the authors.

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