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Infection related to deep brain stimulation in patients with Parkinson disease: Clinical characteristics and risk factors

Mi Sun Kim[a], Jae Sim Jeong[b,**], Ho-Sung Ryu[a], Sang-Ho Choi[c], Sun Ju Chung[a,*]

[a] Department of Neurology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea
[b] Department of Nursing, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea
[c] Department of Infectious Diseases, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea

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ABSTRACT

Objective: Risk factors of infection after deep brain stimulation (DBS) surgery in patients with Parkinson disease (PD) have been controversial. We aimed to investigate the clinical characteristics and risk factors of infection after DBS surgery in PD patients.

Methods: We retrospectively investigated 246 consecutive DBS surgeries in 169 advanced PD patients. Clinical data were collected and analyzed to clarify the clinical characteristics associated with infection after DBS surgery. Multivariate logistic regression analysis was used to assess risk factors for infection after DBS surgery.

Results: Infection occurred in 5% of all DBS surgeries and in 7% of all PD patients who received DBS surgery. Most infections (75%) occurred within 3 months after DBS surgery but it also occurred 21 months after DBS surgery. Gram-positive bacteria were the most common pathogens (75%). Infection after DBS surgery was associated with short period of prophylactic antibiotic therapy (OR = 0.62, 95% CI = 0.45–0.85, P = 0.002) and intensive care unit (ICU) management immediate after DBS surgery (OR = 5.43, 95% CI = 1.12–26.45, P = 0.036).

Conclusion: Our study suggests that short period of prophylactic antibiotic therapy and ICU management after surgery may increase the risk of infection in PD patients who received DBS surgery.

1. Introduction

Deep brain stimulation (DBS) of the subthalamic nucleus (STN) or globus pallidus interna (GPi) has been accepted as a well-established surgical treatment for advanced Parkinson disease (PD) when motor symptoms can no longer be treated adequately with medications. DBS has been reported to provide sustained and significant therapeutic benefit for motor functions and health-related quality of life in PD patients [1–3]. However, given the progressive nature of PD and the symptomatic benefit without neuroprotective efftect of DBS, the initial benefit for motor features wears off and non-motor symptoms take over the major contributor to the worsening of disease-related quality of life [4,5]. Furthermore, there are realistic problems of DBS surgery-related and DBS hardware-related adverse events [6].

Infection is one of the most worrisome adverse events associated with placement and maintenance of leads for DBS. In large studies, rates of infection requiring further surgery have ranged from 1.2 to 15.2% [6–8]. The management of infection related to DBS surgery may be dependent on therapeutic response to antibiotics. Infection may require a period of antibiotic treatment before consideration of surgery for DBS device replacement and if there is no therapeutic response to antibiotic treatment it most often requires device removal [9]. However, there are currently no well-established risk factors for infection related to DBS. The aim of the present study is to investigate the characteristics and risk factors of infection related to DBS surgery in PD patients.

2. Methods

2.1. Subject

We retrospectively studied consecutive 246 DBS surgeries in 169 advanced PD patients who received STN or GPi DBS between April 2001 and October 2014 in Departments of Neurology and Neurosurgery at Asan Medical Center, Seoul, Korea. The DBS surgery was performed by simultaneous implantation of DBS leads and impulse generators

* Correspondence to: S. J. Chung, Department of Neurology, Asan Medical Center, University of Ulsan College of Medicine, 88, Olympic-ro 43-gil, Songpa-gu, Seoul 05505, South Korea.
** Correspondence to: J. S. Jeong, Department of Nursing, University of Ulsan College of Medicine, Asan Medical Center, 88, Olympic-ro 43-gil, Songpa-gu, Seoul 05505, South Korea.
E-mail addresses: jsjeong@amc.seoul.kr (J.S. Jeong), sjchung@amc.seoul.kr (S.J. Chung).

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bilaterally in 77 PD patients (STN DBS in 75 patients and GPi DBS in 2 patients), while two DBS leads and impulse generators were placed by a staged approach separated by 3–4 months in 77 PD patients (bilateral STN DBS in 60 patients, bilateral GPi DBS in 14 patients, and unilateral STN and contralateral GPi in 3 patients). Unilateral STN DBS was performed in 12 patients and unilateral GPi DBS was performed in 3 patients. All PD patients underwent DBS surgery based on the institutional guideline for DBS surgery, including clinically diagnosed PD of > 5 years duration; severe levodopa-induced motor complications despite optimal adjustment of anti-parkinsonian medications; no evidence of Parkinson-plus syndrome or secondary parkinsonism; no surgical contraindications; and no severe dementia, depression, or psychosis. In pre-surgery assessment, all patients showed an improvement in the Unified Parkinson's Disease Rating Scale (UPDRS) part III motor score of > 30% in the levodopa challenge test by taking a suprathreshold dose of levodopa (150% of the usual first morning levodopa equivalent dose (LED) based on the pre-surgery usual first morning dose of anti-parkinsonian medication).

This study was approved by the Institutional Review Board of Asan Medical Center. The board waived the requirement for patient consent because of the retrospective and observational nature of the study.

2.2. Clinical assessment

All subjects underwent systemic institutional clinical assessment that is described in detail in previous reports [10–12]. Patients were evaluated postoperatively at 3 months, 6 months, and annually. All patients were assessed for clinical symptoms using UPDRS under four conditions: (1) off stimulation–off medication, after stimulation had been switched off for 1 h; (2) on stimulation–off medication, after stimulation had been switched on for 1 h; (3) off stimulation–on medication, after stimulation had been switched off for 1 h and after the administration of a suprathreshold dose of standard levodopa; and (4) on stimulation–on medication. The presence of infection was evaluated postoperatively in Neurology and Neurosurgery outpatient clinic. The following subjects were excluded: 1) subjects had similar infection before DBS surgery, 2) subjects died immediately after DBS surgery due to other causes, 3) subjects were lost to follow up > 6 months after DBS surgery.

Clinical data of all subjects were collected, including age at surgery, sex, occupation, disease duration, smoking, medical co-morbidities, steroid drug usage, obesity (body mass index > 30 kg/m^2), and the presence of malnutrition (body mass index < 20 kg/m^2). American Society of Anesthesiologists (ASA) physical score was used to assess the fitness of patients before surgery. Clinical features of PD were evaluated using UPDRS and modified Hoehn and Yahr stage. The LED was calculated according to the following conversion formula: standard levodopa dose × 1 + slow-release levodopa × 0.75 + ropinirole × 20 + pramipexole × 100 + [standard levodopa + (slow-release levodopa × 0.75)] × 0.33 if taking entacapone [13]. Cognitive function was assessed by Mini Mental State Examination (MMSE).

The comprehensive data related to DBS surgery and DBS hardware was also collected, including surgery target, surgery time (from skin incision to suture), DBS implanted pulse generator (IPG) (Soletra 7426®, Activa SC 37602®, 37,603®), pre-surgery prophylactic administration of antibiotics, hospitalization dates, body temperature, blood glucose and oxygen levels, first time of dressing after DBS surgery, and management of intensive care unit (ICU).

2.3. Infection assessment

Infection was defined by the surgical-site infection (SSI) criteria provided by the definition of the Centers for Disease Control and Prevention in the United States.

(https://www.cdc.gov/infectioncontrol/guidelines/ssi). According to the criteria, superficial incisional SSI involves only the skin and subcutaneous tissue of the incision. Deep incisional SSI involves the deep soft tissues of the incision (e.g., fascial and muscle layers) and organ/space SSI involves any part of the body deeper than the fascial/muscle layers, which is opened or manipulated during the operative procedure. To diagnose an infection, at least one of the following was required: (1) purulent drainage, (2) organisms isolated from an aseptically-obtained culture, (3) at least one of the following signs or symptoms of infection: pain or tenderness, localized swelling, erythema or heat, fever (> 38 °C), or spontaneous dehiscence, (4) an abscess or other evidence of infection that is detected on gross anatomical or histopathological exam or on an imaging test, (5) diagnosis of an SSI by a surgeon, attending physician, or other designee.

All infections were evaluated in detail by Infectious Disease specialist (S.H.C.) and Movement Disorders specialist (H.S.R. and S.J.C.). All SSIs were followed for 2 years, while risk factors for infection were evaluated using data of 6-months after DBS surgery. The nature and characteristics of infection was investigated in detail, including clinical signs and symptoms caused by infection, time to infection, infection site, degree of wound infection, microbial culture and diagnosis, and antibiotic treatment. The total expenses of the surgery and hospitalization charges were also evaluated. All antibiotic treatments were performed based on the consensus agreement among Infectious Disease specialists, Movement Disorders specialists, and surgeons.

Table 1
Clinical baseline characteristics of the patients with Parkinson disease who underwent deep brain stimulation surgery.

Characteristics	Patients (n = 169)
Female sex, n (%)	105 (62.1)
Age at surgery (year), mean ± SD	56.8 ± 8.9
Disease duration (year), mean ± SD	11.1 ± 4.7
Age at onset (year), mean ± SD	45.7 ± 9.5
UPDRS total, mean ± SD	79.5 ± 20.3
Hoehn and Yahr stage, mean ± SD	3.2 ± 0.8
LED (mg), mean ± SD	1337.6 ± 467.6
MMSE, mean ± SD (range)	27.1 ± 3.0 (12.0–30.0)

SD, standard deviation; UPDRS, Unified Parkinson's Disease Rating Scale; LED, levodopa equivalent doses; MMSE, mini-mental state examination.

2.4. DBS surgical procedures

The procedures of STN and GPi deep brain stimulation (DBS) surgery have been described in detail in previous reports [10,11]. The target sites (STN or GPi) of DBS were determined by a consensus decision made by physicians, patients, and their caregivers in clinical practice. There were two types procedures for the placement of extension line and IPG for DBS surgery (Supplementary Fig. 1). Procedure type A in this study indicated that a subcutaneous tunnel is placed in one side of the neck. The connector is divided into two extensions in the anterior chest and then connected to subpectorial IPG pockets in each side. Procedure type B in this study indicated that two subcutaneous tunnels are placed in both sides of the neck. Extension line is connected to the infraclavicular IPG pocket in each side.

2.5. Statistical analysis

Statistical analysis was performed using the SPSS 21.0 windows (IBM, U.S.) and the significance level was set at $P < 0.05$. Intergroup analysis was performed by either Student's t-test or a combination of chi-square test and Fisher exact test. The risk factors associated with infection were analyzed by multivariate logistic regression analysis using selected factors indicating a statistically significant difference ($P < 0.05$) in the univariate analysis.