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Clinical Study

Factors predicting incremental administration of antihypertensive boluses during deep brain stimulator placement for Parkinson's disease

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ABSTRACT

Hypertension is common in deep brain stimulator (DBS) placement predisposing to intracranial hemorrhage. This retrospective review evaluates factors predicting incremental antihypertensive use intraoperatively. Medical records of Parkinson's disease (PD) patients undergoing DBS procedure between 2008–2011 were reviewed after Institutional Review Board approval. Anesthesia medication, preoperative levodopa dose, age, preoperative use of antihypertensive medications, diabetes mellitus, anxiety, motor part of the Unified Parkinson's Disease Rating Scale score and PD duration were collected. Univariate and multivariate analysis was done between each patient characteristic and the number of antihypertensive boluses. From the 136 patients included 60 were hypertensive, of whom 32 were on angiotensin converting enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARB), told to hold on the morning of surgery. Antihypertensive medications were given to 130 patients intraoperatively. Age (relative risk [RR] 1.01; 95% confidence interval [CI] 1.00–1.02; $p = 0.005$), high Joint National Committee (JNC) class ($p < 0.0001$), diabetes mellitus (RR 1.4; 95%CI 1.2–17; $p < 0.0001$) and duration of PD >10 years (RR 1.2; 95%CI 1.1–1.3; $p = 0.001$) were independent predictors for antihypertensive use. No difference was noted in the mean dose of levodopa ($p = 0.1$) and levodopa equivalent dose ($p = 0.4$) between the low (I/II) and high severity (III/IV) JNC groups. Addition of dexmedetomidine to propofol did not influence antihypertensive boluses required ($p = 0.38$). Intraoperative hypertension during DBS surgery is associated with higher age group, hypertensive, diabetic patients and longer duration of PD. Withholding ACEI or ARB is an independent predictor of hypertension requiring more aggressive therapy. Levodopa withdrawal and choice of anesthetic agent is not associated with higher intraoperative antihypertensive medications.

1. Introduction

Deep brain stimulation (DBS) by implantation of electrodes has now become a clinical alternative in the treatment of advanced Parkinson's disease (PD) [1,2]. The procedure is performed in a staged manner, the first stage consisting of placement of the stimulating electrode in the subthalamic nucleus (STN) accompanied by microelectrode recording (MER), followed by a second stage to implant a programmable generator. The second stage may be done as a separate procedure or during the same setting as the first stage.

The initial part of the first stage involves providing moderate sedation accompanied by scalp infiltration with local anesthetic for the placement of the head frame (asleep phase). Subsequently, the sedation is discontinued and the DBS is placed followed by MER. A pre-requisite for adequate MER is an awake patient with a stable blood pressure (awake phase) [3]. Upon completion of mapping, sedation and analgesia may be restarted (asleep phase).

MER has been reported as the standard procedure in many leading centers [3,4], however it could be associated with an increased risk of brain hemorrhage due to either multiple passes of the microelectrode through the brain parenchyma or secondary to acute hypertension intraoperatively [4,5].

In this retrospective study we sought to evaluate the preoperative factors which could predict the incremental use of

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antihypertensive boluses during the testing period. Identifying patients who are most likely to need sustained management of their hypertension during the awake part of the DBS procedure can help us plan strategies to achieve more stable control of their intraoperative blood pressure.

2. Methods

Institutional Review Board approval was obtained to conduct this retrospective review of medical records. We retrospectively reviewed medical records of patients with PD who underwent MER placement between 2008 and 2011 and identified 136 patients. Preoperative data collection included age, sex, levodopa equivalent dose (LED), levodopa dose, comorbidities such as presence of preoperative hypertension according to Joint National Committee (JNC) 7 classification (Table 1) [6], baseline preoperative blood pressure collected during an office visit, type of medications used for hypertension, presence of diabetes mellitus (DM), a medical diagnosis of anxiety disorder documented on the medical records, the motor component of the Unified Parkinson's Disease Rating Scale (mUDPRS) score in off state (mUPDRS off) when the patient is off anti-parkinson medications and duration of PD in years. LED was calculated using standardized LED formulae based on dose intensities of different anti-parkinson medication described in the literature [7].

2.1. Surgical technique

The surgical technique in all these patients consisted of a stereotactic frame placement, MRI and CT scan acquisition, use of stereotactic navigation system for anatomic targeting and trajectory planning and MER for physiological targeting as previously described. The target of DBS placement was either STN or globus pallidus internus (GPi). The commercially available DBS electrode (either 3389 or 3387; Medtronic, Minneapolis, MN, USA) was placed at the final target. The second stage of the DBS procedure was implantation of the pulse generator which was performed under general anesthesia either on the same day as DBS placement or in a staged fashion on a different day.

2.2. Anesthetic management

All patients underwent a routine preoperative evaluation. Antiplatelets, anticoagulants and anti-parkinson medications were withheld prior to surgery. Anti-parkinson medications were withheld the night before the surgery to render the patients in an "off" drug state for intraoperative neurological testing. According to institutional policy all patients who were on beta blockers or calcium channel blockers for hypertension were told not to withhold medication on the morning of surgery. Those who were on angiotensin converting enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARB) were told to hold their medication on the morning of surgery. American Society of Anesthesiologists (ASA) monitors, non-invasive blood pressure or invasive blood pressure as deemed necessary and two peripheral intravenous catheters were placed in all patients upon arrival to the operating room. The anesthetic regimen during the asleep phase included infusion of propofol and/or dexmedetomidine. For statistical analysis however the four patients who received only dexmedetomidine were removed. Patients were breathing spontaneously with supplemental oxygen (2 to 8 L/minute) through a nasal cannula with the ability to monitor end tidal CO_2 and a nasal airway in most patients.

A forced-air warming device was used to maintain normothermia and axillary temperature was measured with a skin temperature probe. During the awake stage of the procedure, all sedation was stopped in order to be able to perform motor and cognitive assessment and MER. Based on published evidence of an association of intraoperative systolic blood pressure of >140 mmHg with cerebral hemorrhage, our institutional protocol mandates to maintain the systolic blood pressure at $\leqslant$130 mmHg during MER placement and during neurophysiologic monitoring [8].

Our primary outcome is the number of boluses of antihypertensive medication given during the period of testing. Systolic blood pressure during testing was not taken as an outcome in our study because the blood pressure was being aggressively managed whenever it was above 130 mmHg. The standard practice in our institute is to administer labetalol in increments of 5–10 mg, nitroglycerin 80–160 mcg, esmolol 20–30 mg, and hydralazine 5 mg, each of which is considered as one bolus in this study. Propofol and/or dexmedetomidine were restarted after completion of testing. Whether or not the programmable pulse generator was placed in the same setting, the antihypertensive boluses given during the testing period alone were taken into consideration for the purposes of the study.

Table 1
Reference card from the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure

Category	SBP, mmHg		DBP, mmHg
Normal	<120	and	<80
Pre-hypertension	120–139	or	80–89
Hypertension stage 1	140–159	or	90–99
Hypertension stage 2	$\geqslant$160	or	$\geqslant$100

DBP = diastolic blood pressure, SBP = systolic blood pressure.

2.3. Statistical analysis

Categorical variables are shown as number and proportions, continuous variables as mean ± standard deviation or median (interquartile range [IQR]). Differences in proportions between categorical variables were tested with the chi-squared test. Associations between patient characteristics and the number of intraoperative antihypertensive boluses were evaluated with Poisson regression models, and the associations were expressed as relative risks (RR) and their 95% confidence intervals (CI). The RR expressed the risk associated to the increase in one antihypertensive bolus. Univariate analysis was done between each patient characteristic and the number of antihypertensive boluses, and those characteristics with a $p < 0.2$ were chosen for multivariate analysis. In multivariate analysis, characteristics with a $p < 0.05$ were considered significant. SAS 9.2 (SAS Institute, Cary, NC, USA) was used for all statistical analysis. Multivariable analysis was adjusted for the duration of the total procedure.

3. Results

3.1. Demographic data

Retrospective analysis was carried out in 136 PD patients who underwent DBS placement using intraoperative MER. Collected data included baseline demographics, age, sex, weight and ASA class. There were 90 men and 46 women. Median age was 63 years with a range from 38 to 85 years. Average duration of PD was 10.5 years with a range from 3 to 25 years. Average off state mUPDRS score was 35.5 with a range of 11 to 67. Average levodopa dose was 950 mg/day with a range from 225 mg/day to 2350 mg/day. Average LED in this patient group was 1030 mg/day and maximum was 2600 mg/day. Total number of patients with a history of hypertension was 60 and the average JNC class was II. ACEI or ARB were used in 32 hypertensive patients, all of whom were