Study: "Association Between Burst Suppression During Anesthetic Induction With Postoperative Delirium in Cardiac Surgery"

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STUDY PROTOCOL

After local ethics committee evaluation, patients over 65 years of age scheduled for elective cardiac surgery requiring extracorporeal circulation will be invited to participate. Those who are interested will be interviewed by a member of the research team who, in case of meeting the inclusion and exclusion criteria, will obtain the informed consent signature. After this, routine pre-anesthetic evaluation will be carried out plus preoperative cognition test (MiniCog), delirium screening (CAM) and assessment of frailty using the Clinical Frailty Scale (CFS).

Once in the intraoperative period, standard monitoring (EEG, NIBP, SatO2) will be stablished, plus installation of an arterial line with local anesthesia and a peripheral venous line for drug administration. A basal blood sample will be taken to study baseline inflammatory status (CRP). Subsequently, a SedLine® frontal electroencephalography (EEG) electrode (Root, Masimo) will be installed, and the patient will be asked to close his/her eyes to obtain a baseline recording for 5 minutes. Then, after pre-oxygenation (100% oxygen), the induction of general anesthesia will be initiated in a protocolized way: Fentanyl 5-10 ucg / Kg intravenous (i.v)., Propofol 0.5 mg / kg i.v. (plus rescue of 0.5 mg / kg i.v. after 1 minute if necessary), Vecuronium 0.1 mg / Kg i.v. and vasoactive drugs (ephedrine, phenylephrine or norepinephrine) to maintain mean arterial pressure (MAP) between ± 20% of baseline. Orotracheal intubation will be carried out on a regular basis and will be connected to standard mechanical ventilation (Tidal volume: 6-8 ml / Kg, Respiratory Rate: for exhaled CO2 between 32-35 mmHg, PEEP 5). The SedLine® monitor screen will remain hidden from the anesthesiologist in charge during baseline recording and induction (up to approximately 10 minutes after endotracheal intubation). After that, this phase of the study will end, and anesthesia and surgery will continue. Intraoperative variables such as duration of surgery and anesthesia, time in extracorporeal circulation, total drug use, temperature, among others, will be recorded. The anesthesiologist in charge can use the SedLine monitor to guide the administration of anesthetics once the initial phase (induction) has been completed according to usual practice. Upon completion of the case, the EEG data will be retrieved for further analysis.

At the end of the surgery, in post-cardiac anesthetic recovery unit (Cardiac PACU), POD evaluation will be performed using CAM / CAM-ICU twice a day (AM and PM) for the first 72 postoperative hours. In addition, a structured chart review will be carried out in order to identify records that describe POD. Patients will be considered to have POD if they present a positive evaluation with CAM / CAM-ICU or if the structured chart review is positive within the first 3 postoperative days.

EEG ANALYSIS

We will record the EEG data using Sedtrace (SedLine®) electrodes on the forehead located approximately at Fp1, Fp2, F7 and F8, the ground electrode at approximately Fpz and the reference electrode approximately 1 centimeter above Fpz. The data will be recorded with a preamplifier bandwidth of 0.5 to 92 Hz, a sample rate of 89 Hz, with a resolution of 16 bits and 29 nanovolts. Electrode impedance will be kept less than 5 kΩ on each channel.

For each patient, we will select 2-minute EEG segments that will represent the baseline period, the response to the propofol bolus (burst suppression, yes or no) and the phase of maintenance of general anesthesia prior to cardiopulmonary bypass. We will visually inspect the selected segments in both time and spectral domains to ensure data quality. We will calculate the multitaper spectral estimates using Matlab's Chronux toolbox with the following parameters: window length T = 2 seconds without overlap, product of time bandwidth TW = 3, number of tapers K = 5. We will equally weight the signals from Fp1, Fp2, F7 and F8 channels. Patients will be considered to present burst suppression if they present alternating episodes of spontaneous high amplitude electrical activity (bursts) followed by suppression periods longer than 1 second (electrical variability <10 μV). These analyzes will be performed in time domain as well as spectral domain.

STATISTICAL ANALYSIS

Initially, we will study the association between burst suppression (yes or no) with POD (yes or no) using univariate logistic regression. In addition, we will perform a univariate analysis for known risk factors for PDO (preoperative cognition, frailty, temperature in CPB, etc). Subsequently, we will perform a multivariate analysis with logistic regression to study the association between burst suppression with POD, after confounding variables adjustment. We will then use our data to generate a ROC curve and determine the area under the curve, sensitivity, specificity, positive predictive value, and negative predictive value of burst suppression to predict POD. Finally, we will use our variables to create a predictive model of POD that includes the burst suppression and other known risk factors for POD.
For descriptive statistics, continuous data will be presented using the mean ± standard deviation or the median and its interquartile range, as appropriate. In addition, the groups will be compared by Student's t test for independent samples or the Mann-Whitney U test according to their distribution. In the case of categorical data, they will be presented as absolute counts and their corresponding percentage. Differences will be studied using Fisher's test or Chi square. For the association study, univariate and multivariate linear or logistic regressions will be performed, as appropriate. A significance level of 0.05 with its respective 95% confidence interval will be considered. All calculations will be performed in R statistical language.

Sample size calculation: With a sample of 72 subjects, we will have 80% power to detect a difference if the proportion of patients that present POD and burst suppression is 0.66 and the proportion patients that present POD and that do not present burst suppression is 0.33 with a significance level of 0.05 using a chi-square test. Considering 10% data loss, we will recruit a total of 80 patients.