Validity of Bispectral index monitoring during deep sedation for botulinum toxin injection in children with cerebral palsy

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Study Protocol

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This prospective observational study was approved by the institutional review board of Yeungnam medical center and was registered with ClinicalTrials.gov on the March 28, 2014 (NCT02096549). Written informed consent from parents and verbal assent from child, when appropriate, were obtained before enrollment of study. Twenty-two ASA physical status 1 and 2 children, aged between 3 and 18, with cerebral palsy (CP) scheduled for botulinum toxin injection under deep sedation were enrolled. Children were excluded from the study when either they had an anticipated difficult airway, unstable cardiac disease, craniofacial defect, allergy to drugs used

in this study and recent (< 8 week) history of pneumonia, bronchitis, asthma attack or upper respiratory infection.

No participant received premedication. A 22-guage intravenous catheter was inserted at a superficial vein in arm or hand by an expert nurse 1 hour before estimated induction of sedation. On arrival of child with one of parents in the operating room, he/she was placed in supine position with a soft roll under his/her shoulder to slightly extend the neck. They were continuously monitored by electrocardiography, noninvasive blood pressure (NIBP) and pulse oximetry. An age and head size-appropriate bispectral index (BIS) sensor was applied to unilateral forehead and connected to a BIS monitoring system (VISTA^{TM}; Aspect Medical system, Newton, MA, USA) in accordance with the manufacturer's instruction. The BIS monitor screen was covered during the procedure to ensure that the anesthesiologist, who was responsible for induction and maintenance of sedation and analgesia, was blinded to the BIS value. All baseline data were collected before administration of remifentanil. Supplemental oxygen was administered by a simple face mask at a flow rate 5 L/min throughout procedure. Ventilation was monitored by respiratory rates per minute and continuous waveform of expired CO_2 using a sampling line, located around a nostril inside the face mask, connected to a side-stream capnography during sedation.

Before administration of propofol, remifentanilinfusion at a rate of 0.05 μg/kg/min was started. Five minutes after start of remifentanil infusion, an attending anesthesiologist administered propofol (1 mg/kg) mixed with lidocaine (1 mg/kg) over 1 minute followed by continuous infusion of propofol on the basis of clinical signs of arousability, movement, blood pressure, heart rate and respiratory rate in a spontaneous breathing child. Two independent investigators assessed the level of sedation using the clinical sedation scale such as UMSS and the modified Observer's Assessment of Alertness/Sedation (MOAAS) every minute during induction and maintenanceof sedation (Table 1).MOAASincludes only the responsiveness component of the original OAA/S (5).These twoobservers performing the clinical sedation score assessmentswere blinded to the BIS monitor throughout study period. Another third investigator recorded the BIS and EMG values, oxygen saturation, respiratory rate, blood pressure and heart rate immediately before eachassessment of clinical sedation score.The BIS and EMG values with a signal quality index (SQI) ≥ 50 were accepted for analysis. Deep sedation was defined based on clinical sedation scale categories: a UMSS score of 3-4 or a MOAAS score of 0-1.

Statistical analysis plan

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The sample size was calculated with α error of 0.05 and a power of 80% to determine the validity of BIS values to detect deep sedation in children with cerebral palsy. A minimum 19 participants was required to detect a correlation coefficient of 0.6 for repeated measures. We enrolled 22 patients, taking into consideration of 15% drop-out rate.

Statistical analysis was performed with SPSS version 22.0 (SPSS Inc, Chicago, IL, USA) for Windows. Continuous variables were presented as mean ± standard deviation for normal distributed data or the median and interquartile range for non-normal distributed data after the Kolmogorov-Smirnov test with Lilliefors correction. Categorical variables were presented as number of patients (%).The BIS values at each UMSS and MOAAS score were compared using one-way ANOVA followed multiple pairwise comparisons with Bonferroni correction. BIS values were categorized into ranges of <50, 50-59, 60-69, 70-79, 80-89 and 90 or higher. The Kappa was calculated to determine the agreement between the BIS value categories and clinical sedation score between 2 independent observers. A kappa ≥ 0.7 was considered good agreement.The correlation between the paired BIS value categories and clinical sedation scores was determined by Spearman rank correlation test. Receiver operating characteristic (ROC) curve analysis was performed to determinethe sensitivity and specificity of BIS for predicting deep sedation based on clinical sedation scores. A cut-off BIS value for detecting deep sedation in children with CP was also calculated. A p value of 0.05 was considered to be statistically significant.