Statistical Analysis Plan

Official Title: Propofol EC50 for Inducing Loss of Consciousness in General Combined Epidural Anesthesia

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The sample size of 30 patients per group was determined based on the results of the previous simulation study that suggested that 20 to 40 subjects or six crossovers were sufficient to provide a stable estimate of the EC50 calculated by using the modified Dixon up–down method for most realistic scenarios (16). Continuous variables were tested for normality using the D'Agostino and Pearson tests. Variables with normal distribution were presented as the mean ± standard deviation (SD), and intergroup comparisons were performed using student's *t*-test. Variables with non-normal distribution were presented as the median and interquartile range (IQR), and intergroup comparisons were performed using the Mann–Whitney *U*-test. Categorical variables were presented as number (%) and were analyzed using the chi-square test.

The EC50 and EC95 values for EC50 of propofol were determined by calculating the mean of the midpoints of pairs of Ceprop administered in successive patients in which a positive response was followed by a negative response or a negative response was followed by a positive response (turning points) according to the modified up-and-down allocation method as described previously. At least six pairs of negative–positive responses were needed in each group for the final analysis (13, 17). The 95% confidence interval (CI) and SD for the EC50 values were calculated using the method suggested by Choi (17). Probit regression analysis was applied as a backup and sensitivity test by analyzing tallied numbers of positive patient and negative patients for each dose category for each group; estimates of the EC50 for propofol in each group were obtained and the difference between the two groups was quantified by calculating the relative mean potency with 95% CI. Emergence time was analyzed by using the Kaplan–Meier log-rank survival analysis to compare the cumulative probability of patients remaining unconscious after the discontinuation of propofol.

GraphPad Prism software version 5.0 (GraphPad Software Inc., San Diego, CA, United States), SPSS version 22.0 (SPSS, Inc., Chicago, IL, United States), and R package version 0.1.1 were used for statistical analysis. A p-value of <0.05 was considered to be statistically significant.