Statistical Analysis Plan: Title Page

Blood Loss and Visibility with Esmolol vs. Labetalol in Endoscopic Sinus Surgery: A Randomized Trial

Date: 09/04/2018

Study Summary and Aims

The purpose of this study is to compare esmolol and labetalol bleeding and visibility outcomes in FESS surgery. It is a double-blinded two-armed trial with no placebo control, conducted at a tertiary center. Participants include adults with history of CRS with or without nasal polyps, undergoing FESS for CRS. 38 patients were enrolled, with 32 receiving study drug (17 esmolol, 15 labetalol). Total study duration, including recruitment and analysis, was 1 year with no follow-up. Treatments involve giving intraoperative 20mg of Labetol (max dose = 300 mg for total operation) or infusing 0.1mg/kg/min esmolol (max dose after 30 minutes = 0.3mg/kg/min) when MAP rises above 80 mmHg. The primary aim is to evaluate the relative efficacy of these drugs in FESS surgery, specifically controlling bleeding and improving visibility.

Study Endpoints

March 2017 – March 2018 enrollment, drug administration only during surgery.

Sample Size Considerations

Futility analysis based on estimated blood loss data to see how many patients would be required to show significant differences in blood loss, and therefore mucosal visibility, between drug groups. Given the small differences in blood loss per minute during surgery between treatment groups (0.63 compared to 0.67), and given the relatively large standard deviations obtained (0.33 and 0.37), 1,245 patients would be required in each drug group (total N = 2,490), using a non-paired (two-sided) *t-test* for the comparison, to show a statistically significant difference between the 2 treatments with a power of 0.8 and type I error of 0.05.

These sample size calculations are based on the primary aims of determining a significant difference in FESS visibility between the two drugs.

The null hypothesis is that there will be no statistical difference between esmolol and labetalol in FESS visibility and bleeding parameters. The alternative hypothesis is that there will be a significant difference, in either drug, for improved FESS visibility and bleeding parameters.

The minimum difference that we judge to be statistically significant is a 1-point change on the visibility scores (Boezaart 5-point, Wormald 10-point).

Analysis Sets

N/A

Statistical Analysis and Description of Main Tables

All data for the study outcomes was analyzed with the Wilcoxon rank sum test, used to compare the confidence interval location shift differences between groups. P-value was based on asymptotic Wilcoxon two-sample test with continuity correction of 0.5. The 95% confidence interval for the location shift was based on Hodges-Lehmann estimation. Categorical data

(gender) analyzed with chi-square test. Results were analyzed using the statistical program IBM© SPSS© Statistics (Version 24). P-value < 0.05 was considered significant.

Table 1. Demographic Information and Baseline Characteristics of Study Patients

Characteristics	Group A (n=13)	Group B (n=15)	P-value
Age, years			
Mean (SD)			
Median (Q1, Q3)			
Male, No. (%)			
BMI, kg/m^2			
Mean (SD)			
Median (Q1, Q3)			
Lund-Mackay score†			
Mean (SD)			
Median (Q1, Q3)			
Septoplasty, No. (%)			

Figure 1. Trial profile

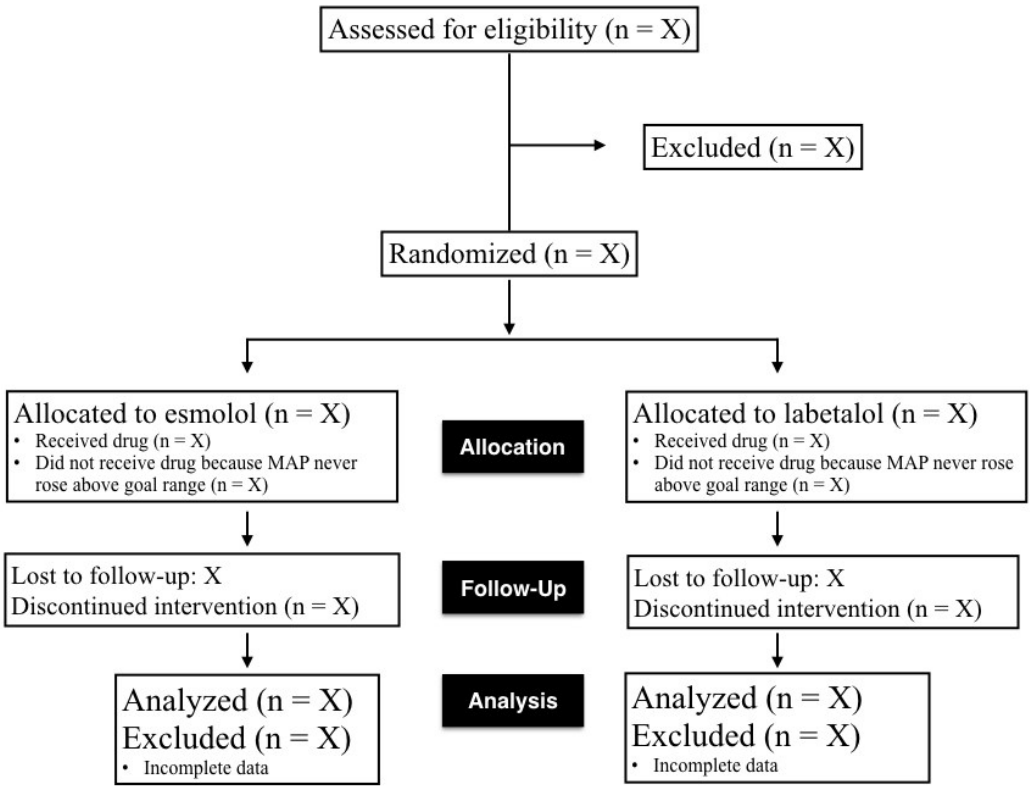

Table 2. Comparing Anesthesia and Surgical Parameters

Characteristics	**Group A (n=13)**	**Group B (n=15)**	**P-value Location shift† (95%CI)**
Duration, min			
Surgery			
Mean (SD)			
Median (Q1, Q3)			
Anesthesia			
Mean (SD)			
Median (Q1, Q3)			
PACU			
Mean (SD)			
Median (Q1, Q3)			
EBL, mL			
Mean (SD)			
Median (Q1, Q3)			
Rate of blood loss, mL/min			
Mean (SD)			
Median (Q1, Q3)			
Heart rate (bpm)			
Mean (SD)			
Median (Q1, Q3)			
Mean MAP			
Mean (SD)			
Median (Q1, Q3)			
Mean Boezaart score			
Mean (SD)			
Median (Q1, Q3)			
Mean Wormald score			
Mean (SD)			
Median (Q1, Q3)			

† Location shift = Group B – Group A