The Effect of Vibration on Pain during Intravenous Injection of Propofol: A Randomized, Controlled, Single-blinded Study

Registered United States Food and Drug Administration (FDA) Clinical Trial (**NCT #03509857**)

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Statistical Analysis Plan

All analyses will be computed using Stata v16.0 (College Station, TX: StataCorp LLC). Bivariate analyses will be performed using independent sample t-test, Mann-Whitney test, chi-square, Fischer's exact test, or Spearman correlation; multivariable analysis will be performed using log-binomial regression in order to evaluate the association between treatment group and pain outcome while adjusting for potential confounders. Variables with $p<0.20$ on bivariate analysis will be added to the model in backwards elimination fashion and will be kept in the model if they are found to alter the association between treatment group and pain outcome by more than 10%, or if they possess an independently significant association with pain outcome. All first order interactions will be assessed. Linearly weighted kappa will be used to evaluate inter-rater agreement. Statistical significance will be set at $\alpha<0.05$.

Results

Outcomes

A total of 100 participants were recruited between April 2019 and November 2019, 50 in each study arm (control versus treatment group) with no losses or exclusions after randomization; recruitment was stopped once the calculated sample size was obtained. The control group and treatment group were comparable with respect to demographic characteristics. The mean age of patients was 50.8 ± 13.9 years. 39% of patients were males. The mean patient BMI was 28.5. Agreement between the attending anesthesiologist and CRNA observers regarding pain scores (scale from 0 to 3 points) was excellent and statistically significant, with weight kappa (κ_w) = 0.82 ($p<0.001$).

A significantly lower incidence of pain was found in the treatment group as compared to the control group. Nine (18.0%) patients in the treatment group had pain during propofol injection as compared to nineteen (38.0%) patients in the control group (p=0.03), yielding a risk difference of 20.0%. Significantly lower severity of pain was found in the treatment group as compared to the control group. The median summative pain score (scale: 1-6) in the treatment group was 1 [IQR: 1-2] as compared to 2 [IQR: 2-4] in the control group (p <0.01).

A higher incidence of pain with propofol infusion was noted in patients with an intravenous catheter location in the hand as compared to other locations with a risk ratio of 2.7 (95% CI:1.07-6.97, p=0.04). A log-binomial regression analysis was performed adjusting for the intravenous catheter location. A significantly lower incidence of pain in the treatment group versus the control group was maintained in the regression analysis with a risk ratio of 0.44 (95% CI:0.22-0.86, p=0.02).

The propofol dose did not differ significantly between the treatment and control groups and did not differ significantly in patients with or without pain (p=0.95 and p=0.30, respectively).