Balanced Placebo Design With Varenicline: Pharmacological and Expectancy Effects on Medication Adherence

NCT03538808

12/05/17

Samantha Schiavon, M.A.

Study Protocol

All eligible participants completed baseline measures to determine tobacco history, medication expectancies, side effects, and smoking cessation outcomes (i.e., cravings, withdrawal, cessation fatigue, etc.). Following completion of the study questionnaires, participants were randomized into either: (1) told therapeutic dose (TD) medication + received varenicline; (2) told TD medication + received placebo; (3) told low dose (LD) medication + received varenicline; (4) told LD medication + received placebo. Randomization into one of the four conditions was balanced on race/ethnicity (African American or Caucasian) and baseline negative medication expectancies as measured on the Stanford Expectations of Treatment Scale (dichotomized as ≤ 3.7 or ≥ 3.8).

Once participants were randomized, they were provided with a two-week blister package of varenicline medication or matched placebo and given scripted instructions for either the low dose or therapeutic dose condition (see below). Additionally, all participants engaged in brief smoking cessation counseling (~15 minutes) and were provided a one-page tip sheet with cognitive and behavioral strategies to quit smoking.

Low Dose Instructions: "You will be receiving an extremely low dose of Chantix. You will experience some benefit from taking this dose, but should not experience side effects."

Therapeutic Dose Instructions: "You will be receiving a therapeutic standard dose of Chantix. You will experience maximum benefit from taking this dose, but may experience greater side effects."

All participants were instructed to take their first medication dose immediately following their baseline appointment and proceed with the standard titration schedule: Days 1 – 3 (0.5mg/daily), Days 4 – 7 (0.5mg/BID), Days 8+ (1 mg/BID). On days 1 – 13, participants completed ecological momentary assessments through a once-daily electronic "daily diary". This daily diary assessment was completed through a secure link on either their cellular phone or computer based on individual preferences. All participants were also given paper calendars as a backup method to collect data on daily medication adherence and cigarette use in the event they experience changes in cellular data coverage, internet accessibility, or technical issues with the data collection software.

On day 14 participants completed their final appointment and were instructed to bring their medication blister packages for adherence verification. Additionally, participants completed study questionnaires regarding side effects and smoking cessation outcomes. After all assessments were completed participants were engaged in a study manipulation check, in which they were told that deception was used on some of the participants and they would earn $1 if they could correctly guess whether or not they received a low or therapeutic dose of varenicline. The dollar compensation was meant to motivate a thoughtful guess, but was provided to the participants regardless of their answer. Following the manipulation check, all participants were provided with private debriefing information in an enclosed envelope to

ensure the study could remain double-blind. In addition to receiving $10 for completing the baseline appointment, study compensation was administered based on the percentage of daily diaries completed: at least 50% ($20), at least 80% ($40), and 90% or higher ($50).

Planned Analysis

A total of 76 participants completed at least 3 waves of data and were included in the Generalized Estimating Equations (GEE) model to evaluate Specific Aims 1 and 2. Time was structured daily for the 14-day medication regimen as assessed through the daily diaries. The outcome variable for medication adherence was dichotomized as *Yes* (coded 1) or *No* (coded 0). The GEE model was specified to predict medication adherence (i.e., "Yes" responses). All GEE models were conducted utilizing an exchangeable correlation matrix and binomial distribution with a logit link function. To evaluate the Exploratory Aim, a series of moderation analyses were conducted utilizing the PROCESS macro for SPSS.

Additionally, two statistical analyses were conducted to examine a possible association between the interaction effect of the study manipulations (medication received and instructional set) as it relates to experienced side effects and medication adherence. First, a repeated measures ANOVA was utilized to examine the interaction effect of medication received and instructional set on experienced side effects. Secondly, a moderated moderation analysis using a three-way interaction was conducted to examine if the interaction between medication received (varenicline v. placebo) and instructional set (therapeutic v. low dose) has a significant effect on the relationship between side effects and medication adherence.