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Tobacco use during a clinical trial of mecamylamine for alcohol dependence: Medication effects on smoking and associations with reductions in drinking

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Abstract

Mecamylamine is a nicotinic acetylcholine receptor (nAChR) antagonist that was recently used in a clinical trial to treat alcohol use disorder (AUD) in both smokers and non-smokers. The current manuscript reports a reanalysis of data from this clinical trial in which we examine changes in smoking that occurred over the course of the trial. We focused on examining the effects of mecamylamine on smoking and the association between reductions in alcohol use and smoking. Participants were the subgroup of smokers who participated in the clinical trial of mecamylamine (10 mg/day) to treat their AUD ($n = 76$). Smoking was assessed prior to randomization and tracked throughout the course of the 12-week medication treatment phase. Participants were categorized as treatment responders or non-responders based on their changes in drinking over the course of the clinical trial. Participants showed a reduction in smoking over the course of the clinical trial, but there were no significant differences in smoking outcomes between the mecamylamine and placebo groups. Among moderate/high dependence smokers, those who successfully reduced drinking showed a significant reduction in cigarettes smoked per day over the clinical trial. Mecamylamine had no detectable effect on smoking outcomes. Reductions in alcohol use predicted more favorable smoking outcomes among moderate/high tobacco dependence smokers irrespective of medication condition. The reduction in smoking among patients who decreased their alcohol use responders highlights an opportunity for patients being treated for AUD to reduce their smoking.

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Declaration of Interests

Sherry A. McKee has consulted to Cerecor and Embera, has received research support for investigator-initiated studies from Pfizer, Inc. and Cerecor, and has ownership in Lumme, Inc. Ismene L. Petrakis has served as a consultant to Alkermes. All other authors declare no conflict of interest.

Keywords

cigarette smoking; mecamylamine; antagonist medication; alcohol use; smoking reduction

1. Introduction

People receiving treatment for AUD smoke at rates higher than the general population (Baca & Yahne, 2009). There is a well-documented relationship between alcohol and tobacco: overlap in the neurobiological mechanisms of action of alcohol and nicotine (Dani & Harris, 2005; Tizabi, Copeland, Louis, & Taylor, 2002) may promote co-use of these drugs. Specifically, nicotinic acetylcholine receptors (nAChR) are involved in pleasurable reinforcing effects of both tobacco and alcohol (Soderpalm, Ericson, Olausson, Blomqvist, & Engel, 2000). This association between smoking and problem alcohol use is further supported by epidemiological evidence showing that smokers are at higher risk for heavy drinking compared to nonsmokers (McKee, Falba, O'Malley, Sindelar, & O'Connor, 2007). The high degree of overlap between these two commonly abused drugs has led to interest in the interaction of smoking and alcohol drinking during treatment for either condition. There are several recent examples of medications indicated for smoking cessation showing efficacy for drinking reduction and *vice versa* (Litten et al., 2013; O'Malley et al., 2006; O'Malley et al., 2018). Given the close relationship between drinking and smoking, it is important to understand how treatment-related changes in the primary substance-of-abuse can alter patterns of use of the co-abused drug. For example, researchers have examined how reductions in smoking related to treatment outcomes in a clinical trial of varenicline for AUD, showing that reductions in smoking predict more favorable drinking outcomes among those receiving varenicline (Falk, Castle, Ryan, Fertig, & Litten, 2015; O'Malley et al., 2018).

Mecamylamine is a nAChR antagonist that has been investigated as a smoking cessation medication. By blocking the pharmacologic effects of nicotine, mecamylamine is hypothesized to reduce rates of cigarette use via an extinction learning mechanism (Rose, Westman, & Behm, 1996). In a pair of randomized clinical trials, Rose et al. (1994; 1996) found that mecamylamine combined with nicotine replacement therapy (NRT) improved abstinence rates among smokers attempting to quit. These results were later replicated in a Phase 3 clinical trial (Rose, 2006). However, a subsequent large, multi-center, randomized controlled trial found no effect of mecamylamine on smoking cessation rates in a sample of 540 smokers (Glover et al., 2007). No prior research has reported on the effects of mecamylamine on smoking behavior in heavy drinking smokers. Considering the role of nAChRs in both tobacco and alcohol use (Tizabi et al., 2002), mecamylamine may be more effective at reducing tobacco use among smokers who also engage in heavy alcohol use. Further, given the close association between tobacco and alcohol use, reductions in alcohol use may lead to changes in tobacco use. Because many heavy drinkers also smoke tobacco (Grant et al., 2015), there is interest in understanding whether treatment-related reductions in drinking are associated with changes in smoking. Reductions in drinking during treatment for AUD may be associated with reductions or increases in smoking. Laboratory research indicates that alcohol cue exposure (Gulliver et al., 1995) and alcohol administration can

prime smoking behavior (Kahler et al., 2014), suggesting that reduced tobacco use will naturally follow reductions in drinking. On the other hand, participants may increase their smoking to help cope with the demands of reduced drinking.

Our group recently conducted a randomized, placebo-controlled clinical trial testing mecamylamine as a treatment for alcohol use among smokers and non-smokers with alcohol dependence (Petrakis et al., 2017). Participants were randomized to receive placebo or 10 mg/day mecamylamine for a 12-week treatment period. The goal of this reanalysis was to examine changes in smoking that occurred over the course of this clinical trial. The primary outcome variable for this reanalysis was cigarettes per day, and secondary smoking outcomes included tobacco craving and withdrawal symptoms. Consistent with the primary endpoint from the clinical trial (i.e., alcohol use during the final month of treatment), we examined smoking outcomes during the final month of treatment. We also examined changes in smoking that occurred early in the medication treatment period since prior research has found that mecamylamine causes an increase in smoking immediately following medication initiation (Rose et al., 1996). As such, we examined changes in smoking that occurred during the first week of the medication phase. We hypothesized that participants receiving active medication would show an increase in smoking from baseline.

Participants were further classified based on selected pre- and post-medication treatment characteristics. First, participants were classified according to their level of tobacco dependence. The parent project included participants with variable smoking habits, ranging from infrequent nondaily smokers to daily smokers. Tobacco dependence severity is a robust predictor of smoking cessation treatment outcome (Bolt et al., 2009; Fagerstrom, Russ, Yu, Yunis, & Foulds, 2012; Transdisciplinary Tobacco Use Research Center Tobacco et al., 2007) and it moderated treatment outcomes in previous smoking cessation trials (Fucito et al., 2011; Fucito, Latimer, Salovey, & Toll, 2010; McGeary et al., 2012). As such, it is important to account for pretreatment smoking habits when examining changes that occur over the course of treatment. Second, to examine whether reductions in drinking were associated with changes in smoking, we classified participants as treatment responders or non-responders according to their alcohol use treatment outcomes. A recent clinical trial of varenicline for AUD in smokers identified a group of patients receiving active medication who showed a reduction in cigarette use as they stopped drinking (O'Malley et al., 2018). This finding suggests a link between reductions in alcohol and tobacco use that may occur in the context of medication treatment targeting the cholinergic system.

2. Method

2.1. Participants

Participants in this study were recruited from the community through advertisements. After signing informed consent, volunteers were evaluated and included in the clinical trial if they were between the ages of 18–70 years, met *DSM-IV* criteria for current alcohol dependence, determined by the structured clinical interview for *DSM-IV* (First, Spitzer, Gibbon, & Williams, 1995) and reported on average at least 21/14 drinks per week for men/women and at least two heavy drinking days per week (defined as 5/4 for men/women) during a consecutive 30-day period within the 90 days prior to baseline evaluation. Participants were

screened for medical problems by interview and physical examination, including EKG. Females were not pregnant and were using adequate birth control. Exclusion criteria included dependence on illicit drugs (aside from marijuana), unstable psychotic symptoms or current serious psychiatric symptoms, such as suicidal or homicidal ideation, or medical problems that would contraindicate use of mecamlamine. Volunteers who were currently taking psychiatric medication, including those thought to influence alcohol consumption (e.g., naltrexone), did not participate. Randomization to medication condition was stratified by smoking status: participants who endorsed any cigarette use over 90 days preceding intake were classified as smokers. The current reanalysis of these data focused on cigarette use, so only data from participants who endorsed smoking were included ($n = 76$). This sample included three participants who were randomized as nonsmokers in the parent clinical trial but later endorsed some cigarette use.

2.2. Medication Conditions

Participants completed a baseline assessment during intake. Eligible volunteers were randomized to one of two groups for a 13-week medication treatment period, including 12 weeks of treatment and 1 week of taper. Participants were randomly assigned to receive mecamlamine (10 mg/day; $n = 41$) or placebo ($n = 35$), and both participants and clinical staff were blind to participants' medication condition. During the first two weeks, mecamlamine was titrated upward, starting at 2.5 mg/day and then increased over two weeks to 10 mg per day in a divided dose (5 mg twice daily). Recognizing the high rate of adverse side effects (e.g., constipation) associated with the 10 mg mecamlamine dose, participants were allowed dose reductions as needed. All medications were dispensed in blister packs. During week 13, medication was tapered down over 7 days. All participants ($n = 76$) also received medical management therapy (Carroll, Nich, Ball, McCance, & Rounsavile, 1998; O'Malley et al., 2018) conducted by trained research personnel. Medical management therapy benefits patients by providing them with nonspecific common factors of a psychotherapeutic relationship (e.g., support, positive regard, empathy) and ongoing assessment and management of their substance use. Participants were motivated to reduce or stop drinking alcohol, but smoking cessation was not a goal of the study. Medication compliance was assessed at each visit.

2.3. Measures

2.3.1. Tobacco use outcomes.—Daily cigarette use was assessed using the Substance Abuse Calendar, which is based on the timeline follow-back interview. The Substance Abuse Calendar was administered by highly trained research personnel at each weekly visit throughout the 12-week treatment period. Self-reported smoking was biologically verified by measuring breath carbon monoxide and urine cotinine levels. Baseline (past 90-day) substance use was assessed at intake. Those who smoked every day over the past 90 days were classified as daily smokers ($n = 40$), and those who reported any days without cigarette use were categorized as nondaily smokers ($n = 32$). Tobacco use was biologically confirmed by urine cotinine levels during each clinic visit. Craving was assessed using the Questionnaire of Smoking Urges QSU; Visual Analog Scale (VAS) 1–100 (Tiffany & Drobes, 1991). Tobacco craving was assessed during the baseline assessment and again at 1, 3, 6, and 12 weeks following randomization and medication initiation. Dependence severity

was assessed using the Fagerström Test of Nicotine Dependence (FTND; Heatherton, Kozlowski, Frecker, & Fagerström, 1991) administered at baseline. According to their baseline FTND scores (range 1–10), participants were classified as having low dependence (1–4) or moderate/high dependence (5–10). Tobacco withdrawal symptoms were measured using the Minnesota Nicotine Withdrawal Scale (MNWS; Hughes & Hatsukami, 1986). A subset of participants did not complete the MNWS ($n = 14$), because it was added to the protocol after data collection began.

2.3.2. Alcohol use treatment response status.—Alcohol use was monitored using the Substance Abuse Calendar. For the current reanalysis, drinking outcomes were only considered to examine how treatment changes in drinking related to smoking outcomes. Treatment response/non-response was operationalized as percentage reduction in drinking days that occurred during the treatment phase relative to their baseline drinking habits. Only participants with at least 1 month post-baseline alcohol use data were categorized as responders or nonresponders ($n = 72$). Drinking days, rather than heavy drinking days, was selected to operationalize treatment response status based on data that even low doses of alcohol can prompt smoking behavior (Kahler et al., 2014). Those who showed a 40% or greater reduction in drinking days from baseline were classified as responders and those with a reduction of less than 40% were classified as non-responders. This classification strategy was primarily based on a median split but is similar to one classification cut score recommended by the European Medicines Agency (i.e., 50% reduction in alcohol consumption; Agency, 2010).

2.4. Data Analysis

Outcome data were analyzed using a modified intent to treat approach. Participants were included in analyses for which they had a full set of observations. Baseline smoking (mean cigarettes per day over the 90 days before starting medication) was compared to smoking during the final month of the treatment phase (treatment days 61–90). Cigarettes per day were analyzed using a 2 (medication condition: placebo vs. mecamylamine) X 2 (time: baseline vs. treatment month 3) X 2 (FTND group: low vs. moderate/high dependence) X 2 (responder status: nonresponder vs. responder) mixed-design analyses of variance (ANOVAs). Only effects that include time as a factor are reported. Significant interactions were probed using *a priori* *t* tests. Only participants with month 3 smoking outcome data were included in these analyses ($n = 62$).

A similar mixed-design 2 (medication condition) X 2 (time) X 2 (FTND group) mixed-design ANOVA was used to examine changes in cigarettes per day from the last week of the baseline assessment to the first week of medication treatment. Because this analysis focused on smoking behavior early during medication treatment, treatment response status (i.e., responder vs. nonresponder) was not included as a variable in this analysis. Medication effects on MNWS scores during the first week of medication treatment were analyzed using a similar 2 (medication condition) X 2 (FTND group) between-participant analysis of covariance (ANCOVA) that controlled for baseline MNWS scores. Only participants with week 1 tobacco use data ($n = 75$) and MNWS data ($n = 61$) were included in each respective analysis.

All subscales of the QSU were analyzed using a 2 (time) X 2 (FTND group) X 2 (medication condition) X 2 (treatment responder status) mixed design multivariate analysis of variance (MANOVA). Baseline scores were compared to scores at the end of medication treatment, and only participants with data from both observations available were included ($n = 59$).

3. Results

3.1. Demographics and Baseline Smoking Variables

Participant demographic and baseline substance use data are presented separately by medication condition and presented in Table 1. As seen in this table, there were no significant differences between groups on demographics or baseline smoking or alcohol use. FTND group (low vs. moderate/high dependence) was not associated with medication condition, $\chi^2(1, N = 76) = 0.70, p = 0.403$.

3.2. Medication Compliance

Most participants receiving active medication tolerated titration up to the 10 mg/day dose ($n = 37, 90.2\%$). The mean maximum dose received among participants receiving active medication was 9.56 mg/day ($SD = 1.69$). Compliance rates (i.e., medication compliant 10 weeks) were similar between the placebo (65.7%) and mecamylamine (73.1%) groups. The difference in rates of medication compliance between these groups was not significant, $\chi^2(1, N = 76) = 0.50, p = 0.481$. Data on treatment emergent adverse events are reported in the parent manuscript.

3.3. Drinking Outcomes in Smokers

Primary alcohol use outcomes are reported in the parent publication. Briefly, participants (both smokers and nonsmokers) showed a significant reduction in alcohol use that did not differ by medication condition. Eighteen (58.1%) and 18 (43.9%) of participants receiving placebo and mecamylamine, respectively, were classified as treatment responders. A chi-square test of independence found that responder classification was independent of medication condition, $\chi^2(1, N = 72) = 1.42, p = 0.234$. On average, treatment responders showed a 69.42% ($SD = 20.56\%$) reduction in number of drinking days, whereas non-responders showed a 10.65% ($SD = 20.19\%$) reduction in drinking days. Descriptive data by responder status is presented in a supplemental table.

3.4. Smoking Outcomes during Treatment Month 3

3.4.1. Cigarettes per day.—The mixed-design ANOVA found a significant main effect of time on cigarettes per day, $F(1, 54) = 12.23, p < 0.001$, confirming a reduction in smoking over the course of treatment. There was no time X medication condition interaction, $F(1, 54) = 0.15, p = 0.702$, suggesting that there was no effect of medication on smoking outcomes. Figure 1 illustrates smoking over the course of treatment in each medication group. There was no evidence that FTND group or treatment responder status had a significant effect on medication efficacy, as evidenced by the nonsignificant time X medication condition X treatment responder status, $F(1, 54) = 0.86, p = 0.358$, and time X medication condition X FTND group, $F(1, 54) = 1.29, p = 0.262$, interactions. There was,

however, a significant time X FTND group X treatment responder status interaction, $F(1, 54) = 4.62$, $p = 0.036$. The pattern of effects described by this interaction is graphed visually in Figure 2. Subgroups showing significant reduction from baseline in cigarettes per day are identified in this figure. As seen in this figure, treatment responders in the moderate/high FTND score group showed a substantial reduction in cigarettes per day from baseline ($M = -7.95$, $SD = 8.00$, $d = -0.99$) over the treatment period. A smaller but significant reduction was also observed among non-responders in the low FTND score group, $M = -2.41$, $SD = 3.60$, $d = -0.67$.

3.4.2. Craving.—Medication effects on QSU scores are reported in a supplemental table. There was a significant main effect of time on the anticipation of positive outcomes and relief from withdrawal/negative affect subscales (results presented in a supplemental table), confirming that these facets of craving decreased over the course of treatment. There was no significant time X medication condition interaction, suggesting that the reduction over time was similar in both the medication and placebo groups. No interaction effect involving FTND group or treatment responder status was significant ($ps = 0.414$).

3.5. Smoking Outcomes during Treatment Week 1

3.5.1. Cigarettes per day.—In the placebo group, participants smoked 14.62 ($SD = 8.96$) and 12.23 ($SD = 6.75$) cigarettes per day the week before and after starting medication, respectively. In the mecamylamine group, participants smoked 11.20 ($SD = 8.96$) and 8.98 ($SD = 7.45$) cigarettes per day before and after starting medication, respectively. The mixed-design ANOVA found a significant main effect of time, $F(1, 71) = 7.39$, $p = 0.008$, confirming that participants reduced smoking during the first week of the treatment phase. There was no significant medication condition X time interaction, $F(1, 71) = 0.01$, $p = 0.919$. No interaction effect involving FTND group was significant ($ps = 0.169$).

3.5.2. Tobacco withdrawal symptoms.—At week 1, mean MNWS scores adjusted for baseline levels were 6.03 ($SD = 5.81$) and 3.89 ($SD = 4.80$) in the placebo and mecamylamine groups, respectively. The ANCOVA found a significant main effect of medication condition, $F(1, 56) = 4.87$, $p = 0.031$. Participants receiving mecamylamine rated their withdrawal symptoms as significantly less severe compared to those receiving placebo. Neither the main effect of FTND group ($p = 0.094$) nor the FTND group X medication interaction ($p = 0.643$) was significant.

4. Discussion

The primary purpose of this study was to report tobacco use outcomes from a clinical trial of mecamylamine for alcohol dependence. There was no effect of mecamylamine on cigarette use or any facet of cigarette craving. Mecamylamine failed to decrease smoking behavior in both low and moderate/high nicotine dependent smokers. These results support null findings of a recent large scale clinical trial (Glover et al., 2007) against prior published (Rose et al., 1994; Rose et al., 1996) and unpublished (see Rose et al., 1996 for a description of this clinical trial) research showing mecamylamine reduced smoking rates. Contrary to previous evidence that mecamylamine increases smoking immediately following initiation (Rose et

al., 1996), smoking did not change during the first week of medication maintenance. We also found no evidence that mecamylamine precipitated nicotine withdrawal, even when the analysis was limited to the first week following medication induction. In fact, participants receiving mecamylamine reported less severe withdrawal symptoms compared to those on placebo, although symptoms were not clinically significant in either group. This finding is consistent with prior research that mecamylamine attenuates withdrawal symptoms following a quit attempt in dependent smokers (Rose, Behm, & Westman, 1998). We found that, independent of medication condition, participants who showed a reduction in drinking days also showed a significant reduction in number of cigarettes smoked per day. This finding is noteworthy because participants in the study were not necessarily interested in quitting smoking. This clinically important reduction in cigarettes per day highlights a favorable change in cigarette use among highly dependent smokers who successfully reduce their drinking over the course of treatment.

There are several possible reasons why mecamylamine failed to reduce tobacco use. One possibility is that the dose used (10 mg/day) was not sufficient to provide sustained blockade of nAChR at a level required to block the central effects of nicotine. Mecamylamine attenuates the positive effects of tobacco by blocking nicotine from binding with central and peripheral nAChR, reducing nicotine-induced release of dopamine in the nucleus accumbens (Marshall, Redfern, & Wonnacott, 1997). A higher dose may have been necessary to generate sustained changes in smoking over the course of a treatment program. However, similar doses of mecamylamine have produced effects on smoking (McKee, Weinberger, Harrison, Coppola, & George, 2009; Rose, Behm, & Westman, 2001) and blocked central nervous system effects of nicotine (Pickworth, Herning, & Henningfield, 1988). Further, higher doses of mecamylamine (> 10 mg/day) are associated with a treatment limiting side effects (Tennant Jr, Tarver, & Rawson, 1984). A prior clinical trial found that combining mecamylamine with nicotine replacement therapy (NRT) improved smoking outcomes beyond either drug alone (Rose et al., 1998). Indeed, varenicline, a mixed agonist/antagonist medication, is a highly effective smoking cessation drug (Gonzales et al., 2006). A more likely possibility is that the mixed agonist-antagonist approach is intrinsically more effective for smoking reduction; mecamylamine may have been more effective in the current study if participants had received nicotine replacement therapy in combination with mecamylamine.

This reanalysis also examined the association between reductions in alcohol use and smoking. Participants who successfully reduced their alcohol use over the course of treatment also showed an incidental reduction in cigarettes smoked per day, specifically among participants who endorsed moderate/high nicotine dependence at baseline. This reduction in smoking among treatment-responders is important because individuals being treated for alcohol dependence often smoke. The current study documents a naturally occurring reduction in smoking among patients who reduced their drinking. Co-use of alcohol and tobacco is common, particularly in people with AUD (Harrison, Desai, & McKee, 2008). Many smokers report high rates of smoking while drinking (Witkiewitz et al., 2012), perhaps because combined nicotine/alcohol administration produces additive dopamine release in the nucleus accumbens (Tizabi et al., 2002). Thus, reductions in drinking may promote reductions in smoking. Results from other clinical trials of varenicline for AUD highlight a potential association between reductions in alcohol use and

smoking, although these associations appear to be specific to patients receiving active medication (Falk et al., 2015; O'Malley et al., 2018). The current reanalysis adds additional evidence for a link between tobacco use and drinking outcomes and suggests a link between these outcomes that may occur independently of pharmacotherapy.

Among those who successfully reduced their alcohol use, the reduction in smoking among only occurred in smokers with moderate/high tobacco dependence. There are several possible explanations for this finding. Cigarette and alcohol use may be more closely linked in patients with more severe nicotine dependence. In more dependent smokers, there may be a stronger history of associative pairing of tobacco and alcohol. Alcohol use may act as a stronger cue for smoking in these participants compared to less frequent smokers (Cooney, Cooney, Pilkey, Kranzler, & Oncken, 2003). Another possible explanation is that participants with low levels of dependence smoked relatively fewer cigarettes at baseline; this restricted range may have limited our ability to observe a significant reduction in smoking over the course of treatment.

The current study provides important information regarding the effects of mecamylamine on smoking behavior and the association between reductions in alcohol use and smoking during a clinical trial for alcohol dependence; however, findings should be interpreted cautiously given some limitations. Participants in the current study were not in treatment for smoking and were not necessarily interested in smoking cessation. Medication effects may have been seen in patients who are motivated to quit smoking. However, this sample was ideal for examining reductions in smoking that occur during treatment for alcohol dependence. Relatedly, we did not measure motivation to quit smoking at baseline. Future clinical trials including tobacco users should incorporate standardized measurement of motivation to quit, because motivation to quit is a key determinant of smoking outcomes (Curry, Wagner, & Grothaus, 1990). The clinical trial included an upper dose of 10 mg/day of mecamylamine; it is possible that a higher dose of mecamylamine is more effective in reducing rates of smoking by achieving a more complete blockade of nAChR. Higher doses may be difficult to achieve, however, due to the side effects of the medication.

5. Conclusions

Results of the current re-analysis did not support an effect of mecamylamine on smoking outcomes in a group of smokers in treatment for alcohol dependence. Among participants with moderate/high tobacco dependence, reductions in drinking were associated with reductions in smoking during the treatment period. This reduction in cigarette use highlights an opportunity for smoking intervention among highly dependent smokers in treatment for alcohol use disorder. Results do not support the clinical utility of mecamylamine for smoking cessation but provide additional evidence for the association between drinking outcomes and smoking behavior in patients being treated for their alcohol use (Falk et al., 2015; O'Malley et al., 2018).

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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- Tobacco use was examined during a clinical trial of mecamlamine for alcohol use
- Mecamlamine had no detectable effect on smoking
- Patient who reduced their drinking also reduced tobacco use
- Successful alcohol dependence treatment may improve smoking outcomes

Figure 1.
Effects of mecamylamine on self-reported cigarettes per day across the medication treatment period. Capped bars are SEM.

Figure 2.

Changes in number of cigarettes per day in treatment responders and nonresponders. Top panel (2a) reports on patients with low baseline nicotine dependence (FTND < 5). Bottom panel (2b) reports on patients with moderate/high tobacco dependence (FTND ≥ 5). Capped bars are SEM. Asterisks indicate significant reduction in cigarettes per day during treatment month 3 compared to baseline within indicated subgroup. * $p < 0.05$, ** $p < 0.001$.

Table 1.Demographic and baseline smoking information (mean [SD] or *n* [%])

	Medication Condition	
	Placebo (<i>n</i> = 35)	Mecamylamine (<i>n</i> = 41)
Age (years)	48.54 (8.61)	45.46 (8.58)
Sex		
Male	31 (89%)	35 (85%)
Female	4 (11%)	6 (15%)
Ethnicity		
African		
American	19 (54%)	24 (59%)
European		
American	13 (37%)	12 (29%)
Other	3 (9%)	5 (12%)
Veteran Status		
Veteran	16 (46%)	15 (37%)
Non-veteran	19 (54%)	26 (63%)
Marital Status		
Married	2 (6%)	9 (22%)
Non-married	33 (94%)	32 (78%)
FTND	4.80 (2.25)	4.80 (2.64)
Low Dependence	17 (49%)	16 (39%)
Mod/High		
Dependence	19 (54%)	25 (61%)
Smoking Group		
Nondaily	18 (51%)	18 (44%)
Daily	17 (49%)	23 (56%)

Note. FTND is Fagerström Test of Nicotine Dependence. Low dependence and Mod/High dependence report number of participants with baseline FTND scores 1–4 and 5–10, respectively.