A randomized trial of concurrent smoking-cessation and substance use disorder treatment in stimulant-dependent smokers

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Background:

- Prevalence of smoking is 75-80% in cocaine abusers and 87% in methamphetamine abusers, as compared to 19.8% of the general population.
- Smoking cessation treatment can significantly increase smoking abstinence.
- Intensive smoking cessation treatment may enhance abstinence of non-nicotine substance use.

Objective:

- This study looked at the potential effects of a concomitant smoking cessation program in patients currently addicted to cocaine and/or methamphetamine.
- Hypothesis: Concurrent treatments for substance use disorder and smoking cessation will improve stimulant-use outcomes.

Methods:

- Randomized, two group study, not blinded
- In a 1:1 ratio patients were either selected to a smoking cessation treatment program in addition to their substance abuse disorder treatment, or receive substance abuse disorder treatment alone ("treatment as usual")
- Duration: 10 weeks, with follow-ups at 3 and 6 months
- Inclusion Criteria:
    - Enrolled in outpatient substance use disorder treatment
    - Interested in quitting smoking.
    - Meet DSM-IV-TR criteria for current cocaine or methamphetamine dependence
    - Smoke at least 7 cigarettes per day
    - Carbon monoxide (CO) level ≥ 8 ppm
    - Must have smoked cigarettes for at least 3 months
- Exclusion Criteria:
    - Medical or psychiatric condition potentially making participation unsafe
    - Current treatment for nicotine dependence
    - Pregnancy, breastfeeding, or unwillingness to use adequate birth control
    - Use of tobacco products other than cigarettes in the past week
    - Had all stimulant-positive urine drug screen results during screening/baseline
    - Seeking or receiving opioid-agonist treatment
- 538 participants; 267 received smoking cessation, 271 received treatment as usual
- 52% male; 60% white, 32% African American; Mean age= 36
- 56% of patients were cocaine dependent; 39% were methamphetamine dependent; 5% were dependent on both.

- During the 10 week treatment phase, all attended two research visits per week assessments
- All participants received treatment for substance use disorder -at least 1 treatment session per week during the treatment phase.
- Participants also assigned to smoking-cessation treatment received:
    - Bupropion HCL XL 300mg daily for treatment; 150mg used for dose escalation and taper.
    - The NICOTROL inhaler was also used for the trial. Starting with the target quit date (study day 20) through week ten, 6–16 nicotine cartridges per day as desired; 3-week taper following week 10.
    - Weekly 10-minute smoking-cessation counseling sessions during study weeks 1–10.
    - Prize-based contingency management (drawing reward chips from a bowel) was used to reinforce negative CO (i.e. CO < 4 ppm) results during the post-quit phase. The number of draws earned escalated with each consecutive week of abstinence and reset if the patient smoked.
- Outcomes Measures:
    - Primary- Weekly proportion of stimulant-abstinent participants during the treatment phase
        - Assessed by stimulant-negative urine drug screen and self-report of no stimulant use.
    - Secondary
        - Proportion of stimulant-abstinent participants at follow-up
        - Proportion of drug-abstinent participants during active treatment and follow-up
        - Stimulant-free and drug-free days during the active treatment phase and follow-up
        - Smoking point-prevalence abstinence at the end of treatment and follow-up
        - Substance use disorder treatment attendance during the active treatment phase
- Data Handling- Intent to treat (All 538 patients included in safety and efficacy analysis)

<u>Results</u>:

- 89% (n=479) of participants completed the 10-week active treatment period; 85% completed the 3-month follow-up; 79.6% (n=428) completed the 6-month follow-up
- Approximately 93% of the bupropion pills were taken (92% self-report; 94% pill count)
- Only approximately 6% of patients used the NICOTROL inhaler as directed (at least 6 times daily)
    - Most patients (56%/62%) used it less than once daily
- On average, patients attended 8.6/10 smoking cessation counseling sessions
- Primary outcome Results: Weekly proportion of stimulant-abstinent participants
    - No statistically significant difference between the two treatment groups (p=.42)
    - 77.2% stimulant-abstinent weeks in smoking cessation group
    - 78.1% stimulant-abstinent weeks in treatment as usual group
- No difference in stimulant-abstinence at 3 months and 6 months
- No difference in stimulant-free days either by weekly proportion during the study or at the 3 and 6-month follow-ups

- Smoking point-prevalence rates were significantly higher in the group receiving smoking cessation treatment during treatment and at follow-ups
    - 25.2% vs 2.2% at week 10; 19.1% vs 3.0% at 3-months; 13.1 % vs. 3.7 % at 6 months.
    - No statistically significant findings looking at drug-abstinence, treatment attendance, or drug-free days.
    - Patients receiving smoking cessation treatment tended to have better drug-free days outcomes.
- Safety outcomes
    - 73% of patients receiving the smoking cessation regimen reported at least 1 adverse event compared to 58% in the treatment as usual group.
    - 48% of patients in the smoking cessation group reported an AE due to a study medication.
    - 13 patients (5%) discontinued the study due to bupropion complications; 7 patients (2.6%) discontinued due to Nicotrol-related AE's
    - Insomnia, anxiety, nausea, dry mouth, headache, and throat irritation were all AE's that were reported in over 5% of smoking cessation patients and were statistically significant when compared to the treatment as usual group.
    - There was no difference in groups in terms of serious AE's.
- Author's Conclusions:
    - Hypothesis of providing smoking cessation treatment in addition to substance use disorder treatment would improve stimulant-use outcomes was rejected.
    - There was no significant treatment effects for drug abstinence but that participants receiving smoking-cessation treatment may experience better outcomes for drug-free days.
    - Substance use disorder treatment attendance did not differ between the participants receiving smoking-cessation treatment and those only receiving substance use disorder.
        - This differs from a previous student suggesting a decrease in attendance with smoking cessation treatment
    - Results suggest that smoking-cessation treatment significantly improved smoking-abstinence outcomes for stimulant-dependent
        - Indicated by the odds ratio of 18.23 for smoking-cessation treatment, compared to treatment as usual, for end-of-treatment point-prevalence abstinence rate

<u>Strengths</u>:

- 12 sites and large sample makes the results more generalizable
- Study was conducted with individuals seeking treatment at substance use disorder treatment programs - results are most likely generalizable to individuals in treatment for stimulant-dependence disorders
- High retention rate
- Strong adherence to smoking cessation regimen

<u>Limitations</u>:

- No blinding; No placebo
- Monetary rewards for smoking abstinence limit the applicability of the study
- Intensive smoking-cessation intervention may be better/more intense than what's generally available to the public
- High rate of stimulant abstinence- hard to find a difference in stimulant abstinence in the smoking cessation group.
- Lack of a biomarker for medication adherence- adherence rates were likely upper limit estimates.
- Nicotrol inhaler not a commonly used, widely accepted means of tobacco replacement
    - Its side effect profile limits its use and adherence.
- CO levels, rather than urine cotinine tests used for screening smoking abstinence.
- Handling of the missing data
    - Patients missing a bi-weekly screening, but reporting no substance use we recorded as not having used the substance.

Conclusions:

- Providing concurrent smoking cessation programs to these patients' substance use disorder treatment improves smoking outcomes, in particular, smoking abstinence
- Numerous non-serious adverse effects are associated with smoking cessation treatment discontinuation and limit the usefulness of the program in stimulant-dependent patients.
- Monetary rewards, as well as drug and tobacco use screening regimens/techniques, limit the generalizability of the study's results.
    - I would have liked to have seen urine cotinine testing rather than CO monitoring
    - Patients are likely more willing to report not smoking, given the chance of a reward
- I would have liked to have seen different tobacco cassation regimens used (e.g. bupropion alone, nicotine patch, nicotine gum)
    - Other regimens may be associated with less adverse effects, leading to a higher adherence rate, and easier statistical analysis.

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