Is there a drug interaction between varenicline (Chantix®) and buprenorphine/naloxone (Suboxone®)?

Varenicline (Chantix®) is approved by the Food and Drug Administration (FDA) as an aid to smoking cessation.[1] It acts as a partial agonist on the neuronal alpha-4-beta-2 nicotinic acetylcholine receptor. This agent is not metabolized hepatically and does not inhibit or induce cytochrome P450 (CYP) isoenzymes. The United States Preventive Services Task Force (USPSTF) and the Department of Health and Human Services (DHHS) recommend use of varenicline as a first-line treatment option for tobacco dependence.[2,3]

Buprenorphine/naloxone (Suboxone®) is approved by the FDA for treatment of opioid dependence.[4] Buprenorphine is a partial agonist at the mu-opioid receptor and is available alone or in combination with naloxone, an opioid antagonist. This product is metabolized by CYP3A4 and may have drug interactions with CYP3A4 inducers or inhibitors. The American Society of Addiction Medicine (ASAM) and the Substance Abuse and Mental Health Services Administration (SAMHSA) recommend use of buprenorphine/naloxone to treat opioid addiction.[5-7]

Regarding a potential drug-drug interaction between varenicline and buprenorphine/naloxone, several drug information databases were consulted and none identified an interaction.[8-10] Additionally, the prescribing information for these products does not identify a drug interaction.[1,4]

The aforementioned guidelines on treatment of tobacco dependence and treatment of opioid dependence were also consulted to determine whether there are concerns for concurrent use of varenicline and buprenorphine/naloxone. With regard to guidelines on treatment of tobacco dependence, the USPSTF does not address an interaction between varenicline and buprenorphine/naloxone, nor does it address concurrent use of varenicline with agents to treat opioid dependence.[2] Similarly, the DHHS does not address use of buprenorphine/naloxone nor address an interaction between varenicline and buprenorphine/naloxone.[3]

In contrast, the ASAM recommends assessment for tobacco use and recommends smoking cessation in patients with an opioid use disorder.[5] They assert that use of nicotine should not be a reason to discontinue addiction treatment for opioids and that patients may be treated for both opioid addiction and other substance use disorders concurrently. The ASAM notes significant interactions when using buprenorphine with alcohol and sedatives, hypnotics, or anxiolytics (enhancing the central nervous system depressant effects of buprenorphine). However, no interaction was noted between buprenorphine and varenicline.

In their guideline for use of buprenorphine for opioid addiction (Treatment Improvement Protocol [TIP] 40), SAMHSA recommends smoking cessation and treatment in patients with tobacco dependence.[6] In TIP 43, SAMHSA recommends that opioid treatment programs routinely address nicotine dependence and states that patient treatment plans should include tobacco cessation.[7] They note that research has demonstrated that smoking cessation interventions do not affect addiction recovery. Patients with opioid use disorders have the same risk of nicotine relapse as patients who are not addicted to opioids. SAMHSA does not address use of varenicline or a potential interaction between varenicline and buprenorphine/naloxone in either of these guidelines.

From a search of the literature, no studies were identified evaluating potential interactions between varenicline and buprenorphine/naloxone. However, 2 studies were found that describe use of varenicline among patients receiving buprenorphine/naloxone.[11,12] Shah et al conducted a cross-sectional study in

which they characterized use of smoking cessation methods among patients receiving office-based buprenorphine/naloxone maintenance treatment.[11] They interviewed patients with opioid use disorder who were receiving treatment at a Bronx, New York community health center. Investigators collected data on demographic characteristics, substance use, buprenorphine/naloxone doses and duration of therapy, nicotine dependence, and past smoking cessation attempts. A total of 68 patients completed the study. The mean age was 48.6 years. Most of these patients were male (69.1%) and Hispanic (67.6%). The median length of buprenorphine/naloxone therapy was 36.5 months and median dose was 24/6 mg. Approximately 87.7% of patients (n=57) were currently smoking cigarettes; 54.3% (n=31) were deemed to have high nicotine dependence. Among lifetime smokers (n=65), 83.1% (n=54) reported at least 1 prior quit attempt, and 78.5% (n=51) reported using a medication for tobacco dependence. Approximately 75.4% (n=49) used 1 or more forms of nicotine replacement therapy (NRT), 29.2% (n=19) used varenicline, and 9.2% (n=6) used bupropion. More frequent smoking was significantly associated with higher buprenorphine/naloxone doses and longer duration of therapy – daily smokers, compared to non-daily smokers, had median buprenorphine/naloxone doses of 24/6 mg vs. 16/4 mg, respectively, and median duration of therapy of 32.9 months vs. 26.5 months, respectively. Shah et al concluded that patients receiving buprenorphine/naloxone have a high prevalence of cigarette smoking, and that many have prior experience with medications for smoking cessation.

Hall et al conducted a clinical trial in which they sought to evaluate the effects of 2 different interventions on cigarette abstinence rates in patients receiving buprenorphine/naloxone for opioid use disorders.[12] Patients who were receiving buprenorphine/naloxone treatment through a service operated under the San Francisco Department of Public Health were randomized to an extended innovative system intervention (E-ISI) or standard treatment control (STC). E-ISI was defined as a combination of 1) motivational interventions and 2) extended pharmacotherapy added to cognitive behavioral therapy. Pharmacotherapy involved NRT (patches in combination with gum or lozenges), administered for 6 months, or varenicline. Varenicline was offered to patients who failed to achieve abstinence with NRT, defined as inability to stop smoking for 24 hours. STC involved written information about quit-lines, medication, and resources. The primary outcome was 7-day biochemically verified point-prevalence cigarette abstinence, and patients were monitored at 0, 3, 6, 12, and 18 months. A total of 175 patients were included in the trial, 95 (54%) of whom received E-ISI. Differences in cigarette abstinence were observed at 3 months but not at months 6, 12, and 18. However, patients in the E-ISI group were more likely to have a goal of complete abstinence and be in a more advanced stage of change than patients in the STC group. Notably, only 3 of the patients in this study requested varenicline, and all 3 were medically ineligible, due to presence of medical or psychiatric conditions precluding use of varenicline. Therefore, the effects of varenicline in patients receiving buprenorphine/naloxone were not formally observed.

Though these studies were not designed to evaluate a potential interaction between varenicline and buprenorphine/naloxone, they provide documentation of concurrent use of varenicline and buprenorphine/naloxone.[11,12] Though Hall et al were not able to formally evaluate the effects of varenicline in their study population, it is important to note that their interventions were planned a priori and received approval by their Institutional Review Board (University of California at San Francisco), suggesting that their protocol was deemed ethical and appropriate.[12] Also, the methodology and clinical practices described in both studies appear to be in line with the recommendations of the ASAM and SAMHSA, which stress the importance of assessment and management of tobacco dependence in patients with opioid use disorders.[5-7,11,12]

In summary, varenicline and buprenorphine/naloxone are FDA-approved medications indicated to treat tobacco dependence and opioid dependence, respectively.[1,4] Based on the available literature, it appears

that there is a lack of evidence to suggest that there is an interaction between varenicline and buprenorphine/naloxone. Interactions resulting from concurrent use of these agents were not identified in the product labels or several drug information databases.[1,4,8-10] Furthermore, studies have been published that describe intentional, concurrent use of varenicline and buprenorphine/naloxone with no mention of drug-drug interactions.[11,12] The ASAM and SAMHSA both recommend assessment and management of tobacco dependence in patients with opioid use disorders.[5-7] Based on the recommendations of the USPSTF and DHHS, the clinician may be advised to consider varenicline in patients concurrently using buprenorphine/naloxone, provided that the patients are without contraindications or intolerance to the medications.[2,3]

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