Incorporating Alcohol Pharmacotherapies Into Medical Practice: A Review of the Literature*

Update

Reviews Literature From November 1, 2009, through June 10, 2010

Treatment Improvement Protocol (TIP) Series

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Updated Findings From the Literature, June 2010

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Updated Findings From the Literature, June 2010

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Findings on Disulfiram

Two studies added to the literature on disulfiram. A Danish study randomized 39 subjects to disulfiram and cognitive-behavioral therapy (CBT) or to a placebo and CBT (Ulrichsen, Nielsen, & Ulrichsen, 2010). After 6 months of supervised treatment, researchers found no significant differences between the two groups in abstinence from alcohol intake during the study period, time to first drink, number of alcohol-free days, or completion of CBT.

Diehl and colleagues (2010) retrospectively compared the long-term effectiveness of disulfiram and acamprosate in 353 subjects, who had been alcohol dependent an average of 13.5 years. Thirty-eight percent had a co-occurring psychiatric disorder, such as depression or anxiety. The 108 subjects in the disulfiram group tended to be younger, less educated, and employed less than subjects in the acamprosate group (n=245). In addition, subjects in the disulfiram group had had an alcohol use disorder (AUD) for more years, consumed higher amounts of alcohol daily, and had been in detoxification programs more often than those in the acamprosate group. Another significant difference was that 20.4 percent of patients in the disulfiram group had other substance use disorders (SUDs) in addition to alcohol dependence, compared with 9.8 percent in the acamprosate group.

Nevertheless, compared with the acamprosate group, subjects in the disulfiram group had significantly longer times until relapse (1 month versus 3.5 months, respectively). Subjects in the disulfiram group also attended outpatient treatment significantly longer than subjects in the acamprosate group (14.9 months, compared with 2.7 months). The disulfiram group was abstinent an average of 9.75 months, compared with 2 months for the acamprosate group. The authors attribute part of the success seen in the disulfiram group to the high frequency of contact required to treat subjects with disulfiram.

Findings on Oral Naltrexone

One new trail on oral naltrexone compared treatments for subjects with alcohol dependence and co-occurring depression (Pettinati et al., 2010). Subjects (N=170) were randomized into one of four groups to receive 14 weeks of naltrexone plus an antidepressant (sertraline), sertraline plus a placebo, naltrexone plus a placebo, or a double placebo. All subjects received weekly CBT. Subjects excluded from the trial included those with other SUDs (besides tobacco), as well as those with bipolar affective disorder, schizophrenia, or other psychiatric diseases. The study compared depression scores (using the Hamilton Depression Rating Scale [HAM-D]), days abstinent, and time to relapse among the groups.

Subjects were largely white and male and had an average of 14 years of education. The average length of AUD was 21 years. At the beginning of the study, the average number of drinks on any drinking day was 12, and the HAM-D score averaged 23.

Across the 14 weeks, adherence rates averaged 87 percent and did not differ significantly among groups. Subjects in the naltrexone plus antidepressant group had significantly better drinking outcomes than subjects in the other three groups. More subjects (53.7 percent) in the naltrexone plus antidepressant group were abstinent for the 14 weeks than subjects in the other groups combined. Subjects in the naltrexone plus antidepressant group also drank less heavily and had longer time to relapse relative to subjects in other groups. The percentage of subjects who were not depressed at the end of treatment was significantly greater in the naltrexone plus antidepressant group when compared with all other groups combined, although there was no statistical difference when comparing depression scores across all groups (Pettinati et al., 2010).

Ray and Oslin (2009) looked at COMBINE data to assess the effectiveness of naltrexone in African Americans. Of the 1,383 participants enrolled in the COMBINE study, 100 were African American. Of these, 51 received naltrexone (with or without acamprosate) and 49 received a placebo. Participants were largely male (70 percent), and the average age was 44. Data analysis showed no significant difference in percentage of days abstinent or time to first heavy drinking day for African-American subjects treated with

naltrexone. These findings cannot be generalized to imply that no African Americans will benefit from naltrexone; more studies are needed.

Findings on Extended-Release Injectable Naltrexone

Lee and colleagues (2010) studied the feasibility of using extended-release injectable naltrexone (XR-NTX) coupled with medical management (MM) in a primary care setting. The open-label study was conducted at two primary care clinics in lower Manhattan. The average age of subjects was 46, most were white and male, and 93 percent were binge drinkers. MM was provided at the time of the subjects' monthly XR-NTX injection. Physicians were trained on MM concepts and recorded progress on a standardized form, but MM delivery itself was not standardized in this study. No incentives were offered to patient for their participation; however, those who returned for the final data collection visit (month 4) received $20. Sixty-five subjects started the trial and received the first injection, 49 received the second injection, and 40 received all three injections. Subjects who received all three injections decreased drinks consumed per day from a median of 4.1 to 0.5. The authors conclude that retention rates and success rates suggest that primary care settings may be a feasible venue for XR-NTX treatment.

Findings on Acamprosate

A small (N=56) study in Sweden contributed to the debate on whether acamprosate reduces craving for alcohol (as opposed to alcohol consumption) in people with AUDs (Hammarberg et al., 2009). Subjects were randomized to 21 days of treatment with acamprosate or a placebo. Craving was measured through a self-report tool (Obsessive Compulsive Drinking Scale) at baseline and at day 21, and results were compared. At day 21, both groups reported a significant reduction in craving, but the difference was greater for subjects treated with acamprosate.

Kennedy and colleagues (2010) published a review of acamprosate trials from 1995 through 2009. Their key conclusions are as follows:

- Acamprosate is a safe and effective medication to help subjects maintain abstinence from alcohol; most side effects are mild.

- U.S. studies failed to show the benefit of acamprosate over a placebo. Unlike European trials that showed efficacy, U.S. trials (including the COMBINE study) enrolled subjects who used substances in addition to alcohol and who were not required to be abstinent or to have withdrawn from alcohol dependence before participating in the studies.

- In meta-analyses, acamprosate has been shown to be more beneficial than a placebo.

- The combination of naltrexone and acamprosate is not more effective than treatment with acamprosate alone.

- Acamprosate may be more beneficial if prescribed in combination with psychosocial treatments.

Findings on Combined Medication Therapy

Gueorguieva and colleagues (2010) reassessed COMBINE data using a trajectory model to better understand the effects of naltrexone, acamprosate, and combined behavioral intervention (CBI) on drinking trajectories. For subjects who reported any drinking, the data were organized into six trajectories: (T1) abstainers, (T2) infrequent drinkers, (T3) frequent to infrequent drinkers, (T4) increasing to frequent, (T5) increasing to nearly daily, and (T6) nearly daily drinkers. The trajectory for abstainers did not mean that subjects did not drink at all during the study period; rather it meant that the odds of drinking on any given day approached zero. Results of the analysis supported findings from the original COMBINE study. There was no significant association with acamprosate (alone or in combination with other therapies) on the likelihood of being in a positive trajectory (T1–T3). Nevertheless, naltrexone decreased the possibility of being in the (T4) increasing to frequent and (T6) nearly daily drinkers trajectories. CBI decreased the probability of being in the (T5) increasing to nearly daily trajectory. Naltrexone and CBI in combination increased the chances of being in the (T1) abstainer trajectory and in the (T3) frequent to infrequent category.

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