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

Update

Reviews Literature From June 2010 through December 2010

Treatment Improvement Protocol (TIP) Series

49

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UPDATED FINDINGS FROM THE LITERATURE, DECEMBER 2010

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Updated Findings from the Literature, December 2010

This Treatment Improvement Protocol (TIP) Literature Review update includes findings published between June 11, 2010, and December 31, 2010.

General Findings

During the period covered in this literature review update, the American Society for Addiction Medicine (ASAM) published *ASAM Patient Placement Criteria: Supplement on Pharmacotherapies for Alcohol Use Disorders* (Fishman, Shulman, Kolodner, Mee-Lee, & Wilford, 2010). This book provides guidance on treatment placement for patients with alcohol use disorders (AUDs), and reviews the use of medications used to treat AUD. The journal, *Current Pharmaceutical Design*, published a special issue in 2010 that focused on pharmacotherapy for AUDs.

Zahm (2010) summarized articles about physiological, pharmacological, biochemical, and molecular biological bases of substance use disorders (SUDs), in general, as well as some of the medications used to treat AUDs. Some medications show a slight to moderate level of effectiveness. Medications that change the activity of the part, or parts, of the brain involved in substance abuse and craving complement, but do not replace, long-term behavior modification or other psychosocial approaches. The author concluded that, with instances of severe addictions to substances, the most effective long-term approaches are long-term behavior modification, cognitive behavioral therapy, and, particularly, mutual help groups. The advances made in understanding the pathophysiology involved in SUDs may help in the development of medications that specifically target the areas of the brain that have been changed by substance abuse. The author stated that relapse and relapse prevention remain the most persistent challenges in substance abuse treatment.

Findings on Disulfiram

Krampe and Ehrenreich (2010) summarized the literature on disulfiram published between 1937 and 2000, and reviewed 13 clinical trials published between 2000 and 2008. The authors stated that the 13 clinical trials found that, when taking disulfiram under supervised conditions (referred to supervised disulfiram), and when combined with psychotherapy, the medication was effective in treating AUDs. The authors also found that, in the majority of studies that compared supervised disulfiram, acamprosate, topirimate, gamma-hydroxy butyrate, supervised disulfiram was as or more effective than the other medications. According to the authors, psychotherapy to accompany supervised disulfiram should include psychoeducation regarding how disulfiram works, the importance of continuing to take it, and its role in treatment. The authors also emphasized the need for a medical professional to administer the medication. The authors noted that patient adherence is a major problem with disulfiram. Two studies cited in the review included some of the reasons why patients discontinued taking disulfiram: to resume drinking, and the belief that the individual could remain abstinent without it. The authors surmised that psychotherapy could improve medication adherence by addressing these two issues, and helping the client work through them.

Rieckmann and colleagues (2010) reported on a nationwide longitudinal survey of Single State Authorities (SSAs), or their representatives, from all States and the District of Columbia (DC). The survey was designed to determine SSAs' perceptions of the use of medication-assisted treatment (MAT) in SUD treatment in their States. This survey used quantitative and qualitative methods and used data obtained through recorded telephone interviews. Of the medications approved by the U.S. Food and Drug Administration (FDA) to treat AUDs, disulfiram was the only medication included in the survey.

Results of the survey found that disulfiram was used in 36 States and DC. Reported barriers to use of MAT in general included:

- Public, provider, and client resistance to MAT.
- Limited infrastructure for providing medications, including funding, required shifts in organizational procedures, and staff development.
- Legislation, policies, and regulations preventing implementation.
- Prevailing public attitudes that medications should not be used to treat addiction, based on a perception that a drug should not be treated by using another drug.

The researchers concluded that access to medication is a priority for SSAs, but that such access is slow to be implemented.

Findings on Oral Naltrexone

Garbutt (2010) reviewed the effectiveness and tolerability of naltrexone in the treatment of AUDs. This review revealed that naltrexone is effective in reducing relapse to *heavy* drinking, but only modestly effective in enhancing complete abstinence. In the studies cited by Garbutt, the medication's effect ranged from small to moderate, but still showed a statistically significant effect on patients' drinking. The author expressed concern that naltrexone's lack of effectiveness in certain studies may discourage clinicians from using it, even though the medication could be an important component of a treatment program. The article included information about two tolerability issues: risk of liver damage, and side effects. At the usual dose of 50 mg, naltrexone was found to have no adverse effect on the liver. The medication produced few serious side effects. The most common side effects reports were nausea, headache, dizziness, fatigue, insomnia, and nervousness. The author identified two areas in which further research is needed: to determine the effects that naltrexone may have on long-term outcomes, and to learn which patients are most likely to benefit from naltrexone treatment.

Findings on Extended-Release Injectable Naltrexone

A study of extended-release injectable naltrexone (XR-NTX) attempted to determine if it could be successfully used in a primary-care setting (Lee et al., 2010). The researchers assessed the use of XR-NTX in conjunction with medical management. The 3-month observational cohort study evaluated treatment retention, patient satisfaction, and alcohol use among individuals in need of treatment for AUDs at two medical clinics at urban public hospitals. The treatment offered consisted of medical management (MM) and three monthly XR-NTX injections. Physician-

delivered MM stressed alcohol abstinence, medication effects, attendance at mutual-help groups, and counseling. The physicians helped patients who wanted additional support locate mutual-help groups or outpatient treatment programs. Of the 72 patients who enrolled in the study, 90 percent (65 of 72) received the first XR-NTX injection; 75 percent (49 of 65) received the second XR-NTX injection; 62 percent (40 of 65), received the third XR-NTX injection.

The researchers noted that few participants remained abstinent for the 3-month duration of the study. The 40 participants who completed the program reported fewer drinks per day, fewer drinking days per month, and fewer heavy drinking days per month. This improvement was correlated with retention, which was, in turn, correlated with participation in Alcoholics Anonymous (AA, a mutual-help group), outpatient treatment, or a combination of the two. The researchers concluded that XR-NTX and MM, delivered in a primary care setting, appeared feasible and acceptable to patients.

Findings on Acamprosate

Koeter and colleagues (2010) performed a meta-analysis of 11 clinical trials to determine the influence of early and late adherence to acamprosate on treatment attendance and duration of abstinence in the treatment of AUD. The authors examined data from 11 randomized controlled trials comparing acamprosate (n = 1,128) with placebo (n = 1,177) in studies published between 1985 and 2006. The meta-analysis confirms that nonadherence remains a serious problem; the early discontinuation of acamprosate may compromise the medication's effectiveness, because of its delayed onset of action. Conversely, treatment with disulfiram or oral naltrexone yields immediate pharmacological actions. The study confirmed that a person's motivation to become abstinent significantly affects treatment adherence and improves medication efficacy. Therefore, providing motivational interventions early in treatment can improve the likelihood of a person's adherence in taking medication, and thus the prospect of long-term abstinence.

Findings on Combined Medication Therapy

No articles were published on this topic that met the selection criteria.

Methodology

The methodology used in the development of TIP 49 was used in the preparation of this update (see http://www.kap.samhsa.gov/products/manuals/tips/pdf/TIP49_LitRev.pdf).

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