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Alan Fisch, MD National Library of Addictions

ALCOHOLISM MEDICINE for the 21ST CENTURY

Disulfiram or Antabuse (trade name) was discovered by accident as a treatment for alcoholism in 1948. Over the following fifty years, no further discoveries were made until recently. Over the past decade, we now have available a portfolio of four drugs with proven efficacy in alcohol treatment planning. Since there is still no single "cure" or a "silver bullet", what we are left with is clinical assessment and judgment and sensitivity to the level of the client's motivation for sobriety. The four adjunct medications are:[1] Disulfiram, Acamprosate, Naltrexone, and Topiramate. Some of these drugs help the patient achieve abstinence, while others assist in maintaining sobriety.

The three major pillars for alcohol dependence treatment are: 1. Medication; 2. Psychotherapies; 3. Self-help or 12-step groups. This article will focus on the medication for the treatment of alcoholism.

Each of the medications has different pharmacology and therefore different ways of helping with the goal of sobriety: some are better for early abstinence; others may be more effective for blunting the urges to drink or get intoxicated.

What are the DSM-IV-TR criteria for the diagnosis of alcohol dependence? Three or more of the following symptoms:

1. Tolerance
2. Withdrawal
3. Persistent desire for alcohol or unsuccessful at cutting down or controlling alcohol use
4. Drinking larger amounts than planned or intended
5. Much time spent in obtaining and using alcohol, or recovering from its effects
6. Forgoing or reducing important social, occupational or recreational activities because of alcohol
7. Continuing to consume alcohol despite adverse physical, psychological, social, or legal consequences.[2]

Alcoholism or alcohol dependence is defined as a maladaptive pattern of behaviors that result from the overwhelming urge to obtain and consume beverage alcohol despite obvious negative consequences, external and internal.

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How does Disulfiram or Antabuse work? This medication helps to maintain an enforced sobriety by negative reinforcement. In the metabolism of ethanol (alcohol), acetaldehyde, a potent toxic material, is an intermediary metabolite. Ordinarily, and with a normal liver, acetaldehyde is metabolized quickly; Disulfiram inhibits the enzyme required to accomplish this task and leads to accumulation. A build-up of acetaldehyde produces severe sweating, flushing, nausea, vomiting, headache, low blood pressure and tachycardia. Even days after the last Disulfiram dose, a small amount of alcohol can induce these powerful, uncomfortable symptoms.

The dose of Disulfiram is 125 to 500 mg once daily. This drug is FDA-approved for alcohol dependence. The contraindications are severe cardiac disease, psychosis, pregnancy and current alcohol consumption. Potential side effects may be: drowsiness (which is self-limited), seizures, arrhythmia, liver toxicity, peripheral neuropathy, and psychosis. Patients can start on Disulfiram after a zero serum alcohol concentration and 12 hour abstention from alcohol. Tablets come splittable at 250 mg. LFT's should be obtained at baseline, then 2 weeks, 6 weeks, and every 3 to 6 months.

Naltrexone: This drug is FDA-approved for alcohol dependence. The dose is usually 50 mg once daily but may go up to 100 mg twice daily or 380 mg IM once every four weeks. This medication decreases the frequency and severity of relapse. It also reduces the number of drinking days. Since naltrexone can cause liver toxicity, it can't be used where patients have acute hepatitis or end-stage liver disease. LFT's should be checked monthly for the first three months and then every three months thereafter. Other common side effects are nausea, headache, and muscle aching. Since naltrexone antagonizes the opioid receptors, do not administer it to active opioid abusers or chronic pain patients who require opioids. Naltrexone will precipitate acute withdrawal reactions in those cases.

Acamprosate: This medication is indicated for relapse prevention in patients who have already stopped drinking. It is used to maintain abstinence but appears to have little effect on initiation of abstinence. It is structurally similar to GABA and appears to inhibit the glutamatergic system. This is the activating system responsible for the hyperarousal and hyperactivity seen in alcohol withdrawal. GABA is the chief inhibitory neurotransmitter in the human brain. It generally has relaxing, anti-anxiety and anti-convulsive effects.

Acamprosate comes in a 333-mg tablet. Recommended dosage is two tablets TID. Side effects tend to be transient and mild, especially diarrhea and other GI side effects. There also appeared to be some increases in suicidal ideation and attempts compared with placebo. This drug should not be given to patients with severe renal disease.

Topiramate: Topiramate exerts a strong effect by decreasing the desire to drink and decreasing craving (compared to placebo). Similar to naltrexone, it has shown benefit early in treatment and has a beneficial effect on relapse prevention. However, it has not yet achieved FDA approval for alcohol dependence. Topiramate potentiates the neurotransmitter GABA and inhibits excitatory glutamate transmission. The dose is given as 300 mg in divided doses. Start at 25mg/day and increase over several weeks. Some of the bothersome side effects are: dizziness, decreased concentration, tingling, and lethargy. It also may reduce the effectiveness of oral contraceptives.

Medication clearly has a role in treating alcohol dependence, but comprehensive substance abuse treatment still requires behavioral therapy and support, such as in self-help groups.[3]

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