Introduction

Practical Pharmacotherapeutic Management Strategies for Patients With Alcohol Dependence

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At the beginning of his novel *A Tale of Two Cities*, Charles Dickens observed, "It was the best of times, it was the worst of times. . . ." In some respects, a similar observation could apply to the current state of alcohol dependence and its treatment in this country.

First, the bad news: 17.6 million Americans (about 8.5% of the population) either abused or were dependent on alcohol in 2001–2002.[1] Worse yet, these numbers reflect an increase from a decade earlier (about 14 million).[1] The cost of alcohol abuse and dependence is enormous in medical, social, vocational, and purely human terms. Those who are "hazardous drinkers," drug abusers, or both have disproportionately high rates of injuries, hypertension, pneumonia, chronic obstructive pulmonary disease, and psychiatric disorders.[2] Recently, the Office of National Drug Control Policy estimated that total costs associated with drug abuse were over $180 billion in 2002, representing an increase of 5.34% annually since 1992. The largest proportion of costs was due to lost productivity.[3]

From the standpoint of care and treatment, there is further reason for concern. Data from the National Survey on Drug Use and Health suggest that only about 9% of the more than 22 million individuals with a drug or alcohol problem are actually receiving appropriate, specialized treatment.[4] In 2003, the estimated number of persons aged 12 years or older needing treatment for an alcohol or illicit drug problem was 22.2 million (9.3% of the total population). Yet only about 1.9 million of these people (8.5% of those who needed treatment) received treatment at a specialized facility. Thus, there is a significant demand gap—20.3 million persons (8.5% of the total population) needed but did not receive appropriate care.[4] There are many factors contributing to this sad reality, including unavailable services, fear of stigma, denial of illness, and inadequate ability to pay for treatment services. And, unfortunately, alcohol-dependent patients who do manage to get into treatment show disappointingly low rates of medication adherence—a theme we will explore in detail in this supplement. Psychosocial therapy, when used as the sole form of treatment, also has limitations, despite ambitious attempts to determine which therapy is best suited to various subtypes of alcohol-dependent patients.[5,6] Psychosocial therapy alone also does not address the biological aspects of alcoholism, particularly the specific neurotransmitter adaptations that occur with chronic alcohol use.

We also face challenges stemming from underutilization of effective treatments by clinicians. A case in point involves the opioid antagonist naltrexone. In a mail survey of alcohol treatment clinicians, our group found both clinical and nonclinical barriers to the use of this agent.[7] Thus, although 80% of physicians and 45% of nonphysicians reported prescribing or recommending naltrexone at least rarely, only 15% of physicians, including addiction specialists, prescribed naltrexone often. Among the strongest barriers to clinician recommendation of naltrexone were limited financing, inadequate knowledge about naltrexone, and a perceived lack of sufficient evidence regarding the drug's efficacy. We found that clinicians were most likely to recommend naltrexone if they were affiliated with treatment programs that supported its use. These findings suggest that new substance abuse medications require many factors to ensure acceptance and widespread use, including clinician and organizational support of the drug's efficacy and use, adequate financing, and education and communication about the drug to the entire alcohol treatment community and those who make public policy.[7]

AND NOW, THE GOOD NEWS

Despite increasing misuse of alcohol and difficulties with its treatment, these are very exciting times for the field of alcoholism research and treatment. First, we are beginning to understand the etiology of alcohol abuse and dependence at the most fundamental biochemical level. Advances in neurobiology have identified neurotransmit-

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ter systems that appear to initiate and sustain alcohol drinking. Reward-associated neurotransmitters, neuromodulators, and peptides, such as β-endorphin, serotonin, glutamate, γ-aminobutyric acid, and dopamine, as well as stress-related neurotransmitters such as corticotropin-releasing factor and neuropeptide-Y, are now targets for therapeutic research. Moreover, animal models utilizing chemical "probes" have identified putative pharmacologic agents that reduce alcohol consumption. These preclinical findings, in turn, are being translated into the development of similar agents that may reduce alcohol consumption in humans.[8,9]

Furthermore, recent advances in molecular and behavioral genetics are guiding the development of new medications for alcohol dependence and hold forth the promise of matching treatments to individuals, according to their genetic characteristics.[8] Indeed, pharmacogenomics—the study of how an individual's genetic makeup affects the body's response to drugs—is providing evidence supporting the classification of alcoholics into specific subtypes, for example, early and late onset.[9] Behavioral research is advancing to identify behavioral endophenotypes, such as craving and harm avoidance, that may be more proximal markers of behavioral genetic effects that lead to an increased risk for alcohol dependence. Of course, we still need much more research targeting pharmacologic responses within specific alcoholic subtypes and endophenotypes, such as those with and without comorbid depression, family history of alcohol dependence, etc.

THE WAY FORWARD

In this supplement, 5 leading clinicians and alcoholism researchers summarize the scope of the problem of alcohol dependence and provide practical information about its treatment using pharmacologic agents. In reviewing how far we have come, these clinicians also help point the way forward.

Michael J. Bohn, M.D., and I address the prevalence and impact of alcohol dependence, focusing on the considerable morbidity and mortality associated with misuse of alcohol. Ironically, as Dr. Bohn and I point out, alcohol-related disorders can be managed as effectively as chronic diseases like asthma and diabetes, yet alcohol dependence remains both underrecognized and undertreated. In discussing screening instruments, such as the CAGE, the Alcohol Use Disorders Identification Test (AUDIT), and the AUDIT Alcohol Consumption Questions, Dr. Bohn notes that early screening and brief intervention for alcohol misuse are feasible for clinicians, useful in establishing a diagnosis of alcoholism, and helpful in reducing alcohol-induced health risks and economic burden.

Jeffery N. Wilkins, M.D., discusses traditional pharmacotherapy of alcohol dependence, focusing on 3 of the 4 medications that have received U.S. Food and Drug Administration (FDA)–approved labeling in alcohol dependence: disulfiram, oral naltrexone, and acamprosate. Dr. Wilkins describes how these drugs work, their efficacy and safety, and how they are best used in practice, including the potential of combining medications in treatment. Dr. Wilkins also notes some of the barriers to use of medication that contribute to the glaring underutilization of pharmacotherapy for alcohol dependence.

Helen M. Pettinati, Ph.D., discusses the critical area of improving medication adherence among alcohol-dependent patients. Dr. Pettinati aptly observes that alcohol dependence is difficult to manage even in treatment-adherent patients; nonadherence creates even more formidable barriers to successful outcome. However, Dr. Pettinati reviews a number of promising strategies, ranging from manualized psychosocial interventions (such as BRENDA) to extended-release injectable agents that bypass daily pill taking.

James C. Garbutt, M.D., reviews new and emerging pharmacologic treatments for alcohol dependence. First, he reports on recent, placebo-controlled trials of 2 long-acting intramuscular formulations of naltrexone, 1 of which received FDA approval in 2006. Both formulations described in this supplement showed efficacy in reducing various measures of alcohol misuse. Dr. Garbutt then reviews the role of drugs traditionally used to treat other disorders but that have also been tried in the treatment of alcohol dependence, including selective serotonin reuptake inhibitors, ondansetron, and topiramate. He also discusses various investigative agents that may reduce alcohol dependence via a multitude of neurochemical mechanisms.

In short, clinicians who treat alcohol dependence have reason to be optimistic despite significant obstacles to successful treatment. As research on the fundamental mechanisms of alcoholism and its treatment continues, our understanding and ability to improve patients' lives grow in step. The material reviewed in this supplement gives one hope that we are, indeed, approaching the "best of times" in addressing the enormous problem of alcohol dependence.

Drug names: acamprosate (Campral), disulfiram (Antabuse), naltrexone (ReVia, Vivitrol, and others), ondansetron (Zofran), topiramate (Topamax).

Disclosure of off-label usage: The author has determined that, to the best of his knowledge, topiramate and ondansetron are not approved by the U.S. Food and Drug Administration for the treatment of alcohol dependence.

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