Clinical Advances in Pharmacological and Integrated Treatment Approaches for Alcohol and Drug Use Disorders

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Abstract: In this review, we highlight recent developments in the pharmacological treatment of alcohol and other substance use disorders and in programs designed for those with dual diagnosis disorders. The depot formulation of naltrexone, which recently received U.S. Food and Drug Administration approval, presents a more effective alternative to oral administration for alcohol dependence. Inconsistent support for the efficacy of acamprosate, however, underscores the need for more research concerning its optimal use. Recent testing of a depot naltrexone preparation for opioid-dependent patients shows promise for its clinical use. Buprenorphine represents a viable treatment option for opioid-dependent patients when combined with psychosocial modalities such as network therapy or contingency management. There has been an increase in the number of integrated programs for patients with a dual diagnosis, incorporating evidence-based psychosocial treatments combined with mutual self-help approaches, including 12-step-based and more global peer-led approaches.

In this review, we highlight recent developments in the treatment of alcohol and drug use disorders that should be of particular value to the general psychiatrist. We address both pharmacological options in the management of alcohol, opioid, cocaine, and marijuana-related disorders and treatment programs designed for individuals with dual diagnosis disorders.

Treatment for Alcohol Disorders

Oral Naltrexone

Naltrexone was approved by the U.S. Food and Drug Administration (FDA) in 1994 for the treatment of alcohol dependence. The use of naltrexone in the treatment of alcohol dependence is based on the assumption that alcohol exerts its effects, at least in part, by its impact on opioid receptors. By administering naltrexone, an opioid antagonist, the rewarding effects of alcohol use may be diminished (1, 2). Numerous controlled clinical trials assessing the impact of naltrexone versus placebo on one or more drinking outcomes including rate of relapse, number of drinking days, number of drinks per drinking day, and rate of time to first relapse have been conducted, and subsequent meta-analyses of these data have been published. In a meta-analysis of nine clinical trials conducted in the United States, Kranzler and Van Kirk (3) found that, across similar alcohol use measures, outcomes among naltrexone-treated subjects were 12%–19% better than for those treated with placebo, with the greatest difference being in percent drinking days. In the clinical trials, there was no effect of naltrexone on retention. Srisurapanont and Jarusuraisin (4) ana-

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lyzed data from 24 randomized clinical trials, in which most subjects received intensive psychosocial treatment (e.g., cognitive behavior therapy). Naltrexone significantly reduced the risk of relapse (relative risk = 0.64) but was unrelated to short-term discontinuation of treatment. Roozen et al. (5) analyzed data from 13 controlled clinical trials and reported a 13% difference in relapse rates in favor of naltrexone. However, there was insufficient evidence to support any long-term effect of naltrexone use in terms of percent drinking days and time to first relapse. Overall, statistically significant findings were obtained for the short-term efficacy of naltrexone, although the magnitude of the effects was small, and the long-term benefit is uncertain. This leaves open the issue of whether a medication's pharmacological effect may be less important than its role in medicalizing the issue of alcoholism for certain patients who would be influenced by a medical connotation to the illness.

DEPOT NALTREXONE

A number of concerns have been expressed about poor adherence to oral naltrexone in the treatment of alcohol dependence (6, 7). To address the problem of poor adherence, a long-acting injectable formulation of naltrexone was tested. In a multisite, 12-week, double-blind clinical trial of an injectable naltrexone depot preparation, 315 alcohol-dependent subjects were assigned to receive the active agent or a placebo every 4 weeks, accompanied by motivational enhancement-based psychosocial support (8). The naltrexone group was found to have a greater mean number of cumulative abstinent days compared with the placebo group (52.8 versus 45.6), and a greater median time to first drinking day compared with the placebo group (5 days versus 3 days). Garbutt et al. (9) conducted a 6-month, randomized, double-blind, placebo-controlled trial at 24 public facilities with 624 alcohol-dependent individuals receiving at least one injection of the naltrexone depot preparation or placebo. All patients received a 12-week, low-intensity, psychosocial intervention (BRENDA model) (10). In this case, the BRENDA intervention was administered by different types of health care professionals, including nurses, psychologists, and physicians. In contrast with the majority of clinical trials of oral naltrexone, which required patients to be abstinent before starting the medication, most patients in this study of depot naltrexone were actively drinking at the time they enrolled in the study. The depot product (380 mg) resulted in a significant reduction in the event rate of heavy drinking days (hazard ratio = 0.75; i.e., there was a 25% reduction of heavy drinking relative to that for the placebo group). The positive effect of naltrexone was greater for those patients who were abstinent during the 7-day lead-in period than for those patients who were drinking at the time that they received their first injection. In April 2006, the FDA approved a naltrexone extended-release injection for once-monthly administration in the treatment of alcohol dependence for use in combination with psychosocial support. The long-term benefit of its use in the typical clinical setting remains to be ascertained.

ACAMPROSATE

Acamprosate was approved by the FDA in 2004 for the treatment of alcohol dependence. The exact mechanism underlying its action is unknown, although it may exert a therapeutic effect in the treatment of alcohol dependence through the inhibition of glutamatergic transmission and subsequent reduction in withdrawal excitability, particularly via *N*-methyl-D-aspartate receptor sites (11). By acting on the glutamatergic mechanism for withdrawal excitability, negative reinforcement for drinking during withdrawal would be reduced. Kranzler and Van Kirk (3) conducted a meta-analysis on data from 11 randomized, placebo-controlled trials comparing acamprosate and placebo. The composite total sample size in the acamprosate analyses varied from 3,077 to 3,204. Treatment outcomes for subjects treated with acamprosate were 7%–13% better than for those treated with placebo, and the positive effect of acamprosate on treatment outcomes was similar to that of naltrexone. They also compared the effect sizes for percentage of subjects abstinent and study retention but found no differences between naltrexone and acamprosate. In a more recent meta-analysis of 17 randomized, controlled trials with sample sizes varying from 1,670 to 4,087, Mann et al. (12) reported that patients taking acamprosate had higher continuous abstinence rates at 3 months (46% versus 34%), 6 months (36% versus 23%), and 12 months (27% versus 13%) than did those treated with placebo and had a modestly greater rate of retention.

Two clinical trials were conducted to assess the impact of the combination of naltrexone and acamprosate in the treatment of alcohol dependence. Kiefer et al. (13) assessed the effects of naltrexone and acamprosate alone and in combination in a randomized, double blind, placebo-controlled clinical trial of 160 German patients with alcohol dependence. Patients in the combined medication group had a significantly lower relapse rate than did those receiving acamprosate or placebo, but the rate was comparable to that for patients receiving naltrexone alone.

To assess the effects of combined pharmacotherapies and behavioral interventions, the National In-

stitute on Alcohol Abuse and Alcoholism (NIAAA) sponsored a randomized, controlled 16-week trial among 1,383 individuals with alcohol dependence from 11 U.S. academic sites (14, 15). Patients were assigned to either naltrexone, acamprosate, a naltrexone-acamprosate combination, or a placebo-pill condition with or without an intensive counseling behavioral intervention (CBI), making a total of eight study conditions. A ninth condition comprised patients assigned to CBI-no pill. With the exception of the CBI-no pill condition, all conditions tested included a series of nine medication management sessions. The CBI intervention administered by an alcohol treatment specialist included components of cognitive behavior therapy and a focus on attendance at Alcoholics Anonymous (AA) meetings. Primary treatment outcomes included percent days abstinent from alcohol and time to first heavy drinking day. Among patients receiving medical management, the naltrexone-no CBI, placebo + CBI, and naltrexone + CBI groups had higher percentages of days abstinent during treatment than did the placebo-no CBI group (81%, 79%, and 77% versus 75%).

Acamprosate, whether alone or combined with CBI or naltrexone, had no significant effect on treatment outcomes relative to those with placebo. The authors suggested that the lack of a positive effect for acamprosate in this study may be attributable to methodological differences involving the required length of prestudy enrollment abstinence, the prestudy treatment setting (outpatient versus inpatient), and standardization of the psychosocial intervention. Patients in the CBI-no pill, no medication management condition had a lower percentage of days abstinent (67%) than did patients receiving medical management in the placebo-no CBI group (74%) and placebo + CBI (80%) group, indicating a significant placebo effect.

In view of these findings, the effectiveness of acamprosate has yet to be definitively established. On the other hand, the risk of heavy drinking was significantly reduced by naltrexone. Of importance, though, statistical significance was not maintained for any of the group differences at the 12-month follow-up in the NIAAA study.

TREATMENT FOR OPIOID DISORDERS

ORAL NALTREXONE

Naltrexone was approved by the FDA in 1984 for the maintenance of heroin dependence. As an opioid antagonist medication, naltrexone binds tightly to opioid receptors, thereby blocking the effects of drugs such as heroin, which act via opioid receptors (16). Unlike opioid agonists such as methadone, naltrexone is nonaddicting and can be prescribed without concerns about diversion. However, clinical studies conducted on outpatients indicated a high dropout rate and poor medication adherence with the oral product (17, 18). In reviewing the results of clinical trials, Kirchmayer et al. (19) and Roozen et al. (5) concluded that there was a lack of evidence to support the effectiveness of oral naltrexone in the maintenance treatment of opioid dependence.

Certain select groups who are highly motivated and receive treatment within a specialized program may, however, benefit from naltrexone. Cornish et al. (20) reported lower rates of opioid-positive urine samples and reincarceration among individuals randomly assigned to a 6-month program of probation plus naltrexone combined with brief counseling than for those assigned to probation plus counseling alone. In a comprehensive outpatient aftercare program in which naltrexone was prescribed to a sample of opiate-dependent business executives and physicians, Washton et al. (21) reported that most patients were opiate-free during 6 months of treatment and remained opiate-free at 12–18 months of follow-up.

Psychosocial modalities involving contingency management (CM) and family supports in combination with oral naltrexone have been shown to improve treatment outcomes. Preston et al. (22) randomly assigned subjects either to an experimental condition, i.e., voucher incentives contingent on naltrexone ingestion or to one of two control conditions, i.e., noncontingent vouchers or no voucher as part of a 12-week naltrexone maintenance study. Subjects in the control conditions had access to weekly counseling conditions. The contingent group remained in treatment longer than the no voucher group did (7.4 versus 2.3 weeks) and had a greater adherence to the thrice weekly naltrexone administration schedule. Carroll et al. (23) compared level of adherence, retention, and drug use when naltrexone was administered thrice weekly for 12 weeks among opioid-dependent patients randomly assigned to either standard naltrexone treatment that included weekly cognitive behavior coping skills group sessions, to naltrexone with CM, or to naltrexone with CM and support from significant others. Patients receiving CM remained in treatment longer (7.4 weeks versus 5.6 weeks) and had a greater number of opioid-free urine samples than did those not receiving it. Support from significant others resulted in improvement in retention, medication adherence, and drug use outcomes, exceeding that for CM only among partici-

pants who attended at least one family counseling session. A subsequent study of low-value and high-value CM found that both were comparable with regard to increased reduction in opioid use relative to standard naltrexone treatment (24). Fals-Stewart and O'Farrell (25) obtained similar positive outcomes for a behavioral intervention involving family supports relative to individual therapy. It appears that the patient population and the choice of psychosocial intervention are important factors in determining whether patients will derive benefit from this pharmacological treatment.

DEPOT NALTREXONE

An injectable sustained release form of naltrexone was developed as one possible option for improving medication adherence. In a study of 12 heroin-dependent individuals, Comer et al. (26) found that the depot formulation of naltrexone was associated with lower heroin-induced subjective ratings at 3 and 5 weeks after injection at doses of 192 and 384 mg and had no adverse side effects. In a subsequent randomized, double-blind, 8-week trial, participants received either a placebo or one of two doses of the study medication given 1 month apart. All patients received concurrent manualized relapse prevention therapy. The higher dose of naltrexone resulted in a greater retention in treatment: 68% of those receiving 384 mg remained in treatment at the end of the 2-month study period compared with 60% of those receiving 192 mg and only 39% of those given the placebo (27). Although not yet approved by the FDA for opioid dependence treatment, depot naltrexone holds considerable promise for use, particularly for specialized populations under monitoring such as parolees or impaired physicians.

BUPRENORPHINE IN THE TREATMENT OF OPIOID DEPENDENCE

Buprenorphine has received considerable attention recently as an alternative pharmacotherapy in the treatment of opioid dependence. A μ-opioid partial agonist, buprenorphine has many of the advantages of agonist treatments such as methadone with few of its disadvantages (28). As a maintenance treatment, buprenorphine, like methadone, has a long duration of action and is acceptable to opioid-dependent patients (29). Abrupt discontinuation of buprenorphine is associated with a milder withdrawal syndrome than is methadone withdrawal (30). Furthermore, a buprenorphine overdose does not result in the significant respiratory depression reported with a methadone overdose (31). As is the case for naltrexone, buprenorphine can act as a blocking agent, thereby reducing opiate self-administration. Both liquid and tablet formulations of buprenorphine have been used in clinical trials. A sublingual tablet is now widely used, with one form containing buprenorphine only and the other containing a combination in a 4:1 ratio of buprenorphine and naloxone. The latter was developed to reduce the risk of diversion, because, if a tablet is crushed and injected by an opioid-dependent individual, this combination formulation will precipitate severe withdrawal.

The Drug Addiction Treatment Act passed in 2000 permits qualified physicians to prescribe FDA-approved drugs for opioid dependency. In 2002, the FDA approved buprenorphine sublingual tablets with a schedule III designation for the maintenance treatment of opioid dependence. Qualified physicians must have completed approximately 8 hours of formal training or be certified in either addiction psychiatry or addiction medicine and be able to refer patients for appropriate counseling and other ancillary services. This qualification is important as there is concern about the possibility of overprescribing and possible illicit diversion.

The federal regulations enable physicians to treat patients for opioid dependence with buprenorphine in their offices rather than having to refer them to specialized opiate treatment programs, as previously required under federal law. In December 2006, the maximum number of patients that a qualified physician can treat with buprenorphine was increased from 30 to 100 (32). It is estimated that only about 14% of the 810,000 chronic heroin users in the United States have received methadone treatment as of this writing (33). Buprenorphine is an alternative option that provides the potential to expand opioid maintenance treatment services. It may attract individuals in need of treatment who are unable or unwilling to access services in current methadone maintenance programs either because of lack of openings or limited geographical access (34) or negative attitudes toward methadone maintenance treatment (35).

The efficacy of buprenorphine in the maintenance treatment of opioid dependence has been assessed in a number of clinical trials. Fudala et al. (36) conducted a multisite, placebo-controlled trial with 326 opiate-dependent individuals randomly assigned to office-based treatment with either the buprenorphine-naloxone combination tablet (16 mg), the buprenorphine tablet monoproduct (16 mg), or a placebo administered daily for 4 weeks with concomitant HIV and weekly individualized counseling. The study was terminated early because both pure buprenorphine and the combination for-

mulation were found to have greater efficacy than did the placebo in terms of percentage of opiate-free urine samples (18 and 21 versus 6, respectively).

In a meta-analysis of data collected from 11 controlled clinical trials, buprenorphine and methadone were compared with respect to their impact on retention as well as on heroin and cocaine use (37). The pattern of results differed depending on whether the agents were administered according to a flexible, fixed-low, or fixed-high dosing schedule. With flexible dosing, buprenorphine was comparable to methadone with regard to the number of morphine-positive and cocaine-positive urine samples but resulted in a lower rate of retention. When a fixed dose was used in the low range (i.e., 2–4 mg of buprenorphine versus 20–35 mg of methadone) buprenorphine and methadone had comparable effects. However, when a fixed dose was used in the higher range (i.e., 6–12 mg of buprenorphine 60–80 mg of versus methadone), methadone resulted in a greater reduction in heroin use, as shown by the number of morphine-positive urine samples, but no differences were found between buprenorphine and methadone in retention rates or the number of cocaine-positive urine samples.

Recently, a number of psychosocial interventions administered in combination with buprenorphine maintenance have been assessed in relation to treatment outcomes. Galanter et al. (38) evaluated the impact of network therapy (NT), a modality in which family members and/or friends are used to support adherence to treatment relative to a control condition [medical management (MM)] among 66 patients who were inducted onto buprenorphine for 16 weeks and then tapered to zero dose. NT resulted in a greater percentage of opioid-free urine samples than did MM (65% versus 45%). By the end of treatment, patients receiving NT were more likely to experience a positive outcome relative to secondary heroin use (50% versus 23%). The use of NT in office practice may enhance the effectiveness of eliminating secondary heroin use during buprenorphine maintenance.

Montoya et al. (39) assessed the relationship of weekly interpersonal cognitive therapy attendance to treatment outcome in terms of urine morphine levels among 90 outpatients with cocaine and heroin dependence who completed a 70-day buprenorphine maintenance trial. More frequent therapy attendance was associated with lower morphine levels among patients receiving 16 mg of buprenorphine, a relationship that became stronger as the study progressed, indicating a significant time by therapy interaction. Grob et al. (40) assessed the impact of two CM conditions relative to a control condition (i.e., counseling only) among 90 patients dependent upon heroin and cocaine during 12 weeks of buprenorphine maintenance treatment. One contingency condition entailed a voucher being awarded for every drug-free urine sample, with a graded schedule. The second condition entailed a medication contingency wherein the buprenorphine dose was split in half, with one half being administered on submission of an opiate- and/or cocaine-free urine sample and the other half for clinic attendance. All participants received standard counseling on a weekly basis. There was no difference between the three study groups with regard to retention. The medication contingency group had a greater average of weeks with continuous abstinence from opiates and cocaine than did the voucher contingency group (5.9 versus 2.9). These findings indicate that treatment outcomes related to reduction in illicit drug use may be improved with concomitant psychosocial interventions. Fiellin et al. (41) assessed the impact of different intensities of counseling and frequency of medication dispensing upon retention and percentage of opioid-free urine samples. There were no differences among the treatment conditions with respect to retention or opioid use in the medical setting they used, suggesting that no additional benefit to buprenorphine treatment was afforded by extended counseling sessions.

Despite intensive efforts by the National Institute of Drug Abuse, the Center for Substance Abuse Treatment and other institutions to disseminate information about buprenorphine practice guidelines and to sponsor various training venues, the extent of adoption of buprenorphine treatment by service providers is unknown. Whether a sizable new cohort of individuals with opioid dependence are presenting for treatment, as was anticipated, has also not been established. However, two recent publications address these issues. To explore the adoption of buprenorphine, Knudsen et al. (42) analyzed data from 576 substance abuse treatment centers drawn from the National Treatment Center Study. They used baseline data collected between 2002 and 2004 and at 1-year follow-up. At the 1-year follow-up, 14% of centers reported using buprenorphine. Buprenorphine was more likely to be used in private centers than in public centers (21% versus 7%). This difference in adoption of buprenorphine may be accounted for by certain treatment center characteristics: Private centers were significantly more likely to be accredited, to operate on a for-profit basis, and to offer detoxification and naltrexone treatment than were public centers.

Sullivan et al. (43) assessed whether patients

with no history of methadone treatment enrolled in a 26-week trial of buprenorphine maintenance provided in a primary care clinic (PCC, N=96) differed with respect to clinical characteristics from patients who enrolled in an opioid treatment program (OTP, N=94) and were maintained on methadone. Compared with OTP patients, PCC patients were more likely to be male, employed full-time, younger, and white and were less likely to have a history of injection drug use and hepatitis. These findings suggest that a new cohort of opioid-dependent patients may be accessing treatment and that buprenorphine may facilitate earlier access to treatment. Changes may occur in the utilization of buprenorphine treatment services in the future if the injection depot formulation of buprenorphine currently being tested is approved for use (44).

TREATMENT FOR COCAINE DEPENDENCE

MODAFINIL

At present, there are no medications approved for the treatment of cocaine dependence. Modafinil is a schedule IV controlled substance approved for the use of narcolepsy and has been shown to have little potential for abuse among individuals with cocaine dependence (45). The rationale for the use of modafinil as a treatment for cocaine dependence is based on recent findings suggesting that the medication can enhance glutamatergic system functioning. This in turn can benefit individuals with cocaine dependence, as repeated exposure to cocaine has been associated with altered glutamate release (46). In a recent 8-week, randomized, placebo-controlled clinical trial with 62 cocaine-dependent patients who all received twice-weekly cognitive behavior therapy, patients receiving modafinil had lower cocaine use in terms of more benzoylecgonine-negative urine samples and were more likely to achieve 3 or more weeks of cocaine abstinence than were patients in the placebo condition (47).

TREATMENT FOR MARIJUANA DEPENDENCE

RIMONABANT

There is at present no pharmacologic agent that has been shown in controlled clinical trials to be effective in the treatment of marijuana dependence. One medication currently being considered is the cannabinoid CB1 receptor antagonist, rimonabant, originally developed for the treatment of obesity (48). Huestis et al. (49) conducted a randomized, placebo-controlled, double-blind study in which 63 men with a history of marijuana use received this agent or a placebo pill and then 2 hours later smoked a cigarette containing tetrahydrocannabinol or placebo. The medication was found to block both the subjective and physiological effects of the marijuana. Phase III clinical trials are currently underway to assess the effectiveness of rimonabant in smoking cessation (48, 50). The exact mechanism of its action has yet to be established. Additional research is needed to determine the specific nature of the neurotransmitter systems involved in the effects of cannabinoid CB1 receptor blockade on addictive behaviors (51).

TREATMENT PROGRAMS FOR PATIENTS WITH SUBSTANCE USE AND CO-OCCURRING DISORDERS

A number of different approaches have been developed for treating combined mental illness and substance abuse disorders. In the sequential model, first one and then the other condition is treated. In the parallel approach, both conditions are addressed simultaneously but in different programs, each with its own staff. In the integrated model, the two types of disorders are treated simultaneously by providers with expertise in managing both conditions who combine and modify traditional substance abuse and psychiatric treatments. In a review of 26 controlled studies of psychosocial interventions, Drake et al. (52) concluded that the findings supported the effectiveness of integrated treatment. The consensus of experts in the field supports the integrated approach as the standard of care for use with patients with co-occurring disorders (53–56).

Treatment approaches incorporating formal psychosocial/behavioral modalities from the mental health and addiction fields have been proposed for specific co-occurring mental health disorders such as mood disorders (57) and posttraumatic stress disorder (58, 59), some of which have specified motivational, cognitive behavior, and/or CM evidence-based treatments. In addition, peer-led self-help approaches constitute a core component of integrated programs in the care of individuals with dual diagnosis disorders.

A number of studies conducted on large patient samples treated in U.S. Department of Veterans Affairs (VA) substance abuse treatment programs provide empirical support for the utility of 12-step-based self-help approaches. In a study of 981 male

patients with dual diagnosis disorders, Moggi et al. (60) found that 12-step group participation was associated with increased adaptive coping and abstinence at 1-year follow-up. Moos and colleagues (61) analyzed data on 3,018 patients from VA inpatient programs to assess treatment outcomes associated with 12-step approaches relative to cognitive behavior and eclectic program approaches. More than one third (35%) of these patients had a concomitant psychiatric diagnosis. Patients treated in 12-step-oriented programs were more likely to be abstinent and free of substance abuse problems at 1-year follow-up than were patients treated in programs that were either cognitive behavior or eclectic in nature (61). Using the same sample of 3,018 patients, Ouimette et al. (62) compared the treatment outcomes of patients self-selected into one of four aftercare conditions (i.e., outpatient plus 12-step, outpatient only, 12-step participation only, or no aftercare). The findings indicated that patients in the outpatient-12-step aftercare condition were more likely to be abstinent than were patients in any of the other aftercare groups. Humphreys et al. (63) assessed the relationship of VA treatment program focus and patient outcomes relating to substance use and psychological functioning and reported that as the 12-step orientation of the inpatient treatment programs increased, the degree of involvement in and benefit from the 12-step approach increased as well.

To determine whether the relationship between involvement in AA and improved treatment outcomes may be causal in nature, McKellar et al. (64) analyzed data from a subset of the VA sample (N=2,319) using structural equation modeling and reported that 1-year posttreatment levels of AA affiliation predicted fewer alcohol-related problems at 2-year follow-up, both for patients with and without psychiatric comorbidity.

Although traditional 12-step-oriented approaches have been applied in the treatment of patients with substance use disorders and co-occurring psychiatric disorders, patients may be reluctant to participate because of perceptions they have regarding how others will relate to them in terms of their use of medication, their involvement with the mental health system, and their potential for recovery. In an effort to better address the needs of individuals with dual diagnosis disorders, the orientation of 12-step self-help groups (65) and 12-step facilitation techniques have been modified (66). Such dual-focus 12-step-based approaches have been evaluated in a number of studies. Laudet et al. (67) reported that individuals with greater participation in dual-focus 12-step groups reported less substance use and emotional distress. Magura et al. found that dual-focus 12-step program involvement was correlated with adherence to medication (68) and with positive outcomes at 1-year follow-up (69). Brooks and Penn (70) compared treatment outcomes of 112 patients with dual diagnosis disorders alternately assigned to either a 12-step treatment program adapted for dual diagnosis or to a self-management and recovery training (SMART) intervention based on the Rational Emotive Behavior Theory Model developed by Albert Ellis. There was a greater decrease in alcohol use and increasing social interaction in the 12-step condition, whereas the SMART intervention was associated with positive treatment outcomes relating to change in health status and employment. Bogenschutz (66) conducted a pilot study to assess the feasibility of a manualized 12-step facilitation intervention based on Project MATCH (71) and modified for use with individuals with dual diagnosis disorders. Although the sample size was small (N=10), the results are promising: Over the course of the 12-week treatment, there was an increase in 12-step group attendance that was associated with a decrease in substance use.

A treatment program incorporating a broad peer-led self-help approach combined with professional treatment that can be applied to bring about systems-level change in a variety of settings where persons with dual diagnosis disorders are treated was developed at Bellevue Hospital Center. The program consists of three different clinical units: an inpatient dual diagnosis ward, a halfway house, and an ambulatory day program (72). These three programs were designed to provide the needed multiple levels of care in which the peer-led approach could be combined with conventional psychiatric and pharmacological management for patients at different functional capacities. A peer-led, token economy was implemented on the inpatient ward to address problems with patient adherence and regressed behavior. The token economy allowed for a gradual initiation of patients into 12-step groups and provided the means for operant reinforcement of continued participation. The peer-led format in the halfway house and the ambulatory day program was adapted from the model of the therapeutic community (73) and allowed for active participation of patients in the operation of these units in terms of both on-site groups and in serving as liaison with clinical units that refer patients to the program.

A number of studies were conducted on this patient population and the treatment system. On the inpatient unit, equivalent remission in psychiatric symptomatology over the course of hospitalization was demonstrated among persons with schizophre-

nia who varied with respect to severity of antecedent drug use (74). In the halfway house, only 12% of patients were found to have positive urine toxicology results during their treatment, despite the fact that patients have limited access to entry and departure (75). Psychiatric symptoms were found to decline during the first 3 months and over the remaining course of patients' treatment (76), even with a rigorous interactional program. A history of fewer psychiatric admissions and greater job experience were associated with lower dropout rates (77). Significantly, there was no difference in length of stay or improvement in social adjustment on the unit among patients with a record of criminal convictions (78). When the ambulatory day program was evaluated, 69% of patients were found to have had three consecutive negative urine toxicology results immediately before discharge, reflecting a criterion set for a positive outcome (79). Patients with dual diagnosis disorders demonstrated equivalent or better outcomes in terms of retention, visit rates, and negative urine toxicology results compared with patients without a co-occurring axis I mental health disorder (80). All of the above studies assessed only in-treatment outcomes. To assess whether the program might be related to postdischarge outcome, patients with dual diagnosis disorders treated in the inpatient peer-led self-help treatment unit were compared with patients with dual diagnosis disorders treated in standard psychiatric inpatient wards (81). The peer-led self-help program was associated with a higher rate of aftercare attendance only among patients with no prior psychiatric hospitalizations. Patients who presented with a history of hospitalizations for substance use and/or mental illness were more difficult to retain in aftercare than were patients without such an extensive history. Different integrated treatment approaches may have to be developed to promote engagement in aftercare treatment for patients with chronic illness.

Summary

The depot formulation of naltrexone may benefit patients with alcohol dependence who are likely to have problems adhering to an oral medication regimen and can be administered to patients who are either actively drinking or abstinent. The optimal conditions under which acamprosate is likely to be effective in the treatment of alcohol dependence require further study because it has not been shown to be consistently superior to placebo in large-scale clinical trials. With regard to the treatment of opioid dependence, oral naltrexone is of limited utility among patients who are not highly motivated. Depot naltrexone was found to be effective in promoting retention in treatment and therefore will probably prove to be a better option than oral naltrexone, although long-term results have yet to be determined.

Buprenorphine, the newest pharmacological agent to become available for the treatment of opioid dependence, has an effectiveness comparable to that of methadone except among patients requiring high doses of methadone and can be used in primary care and private office settings. The adoption of buprenorphine appears to be proceeding slowly, but its use may become more widespread with the recent increase in the number of patients who can be treated by certified physicians. There is as yet no widely established pharmacotherapy for cocaine and marijuana dependence. As more information becomes available on its effects, rimonabant, a cannabinoid receptor antagonist, may prove to be beneficial in the treatment of a broad spectrum of addictive disorders. Finally, there has been an increase in integrated programs for individuals with the dual diagnosis disorders, combining evidence-based treatments drawn from the mental health and addiction fields. A core component of integrated programs involves peer-led self-help, which, when applied within the professional treatment system, can address the needs of patients requiring different levels of care.

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