THE PHARMACOLOGICAL TREATMENT OF ALCOHOL DEPENDENCE: NEEDS AND POSSIBILITIES

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Abstract — Standard treatment for alcohol abuse may include pharmacotherapy to alleviate withdrawal symptoms followed by psychotherapy in inpatient and/or outpatient settings. Treatment goals include abstinence and reduced alcohol consumption. Standard treatment for alcoholism has a high rate of success in Germany; however, for various reasons, only a small percentage of alcoholic patients are admitted to alcoholism treatment programmes. A new drug, acamprosate, could benefit many more alcoholic patients. Several studies indicate that acamprosate reduces the craving for alcohol and enhances abstinence. Acamprosate's effect is dose-dependent and it has a few minor side-effects. In addition, the availability of acamprosate may enable family practitioners to play an increasingly important role in the treatment of alcoholic patients, thus allowing more patients to receive treatment.

THE STANDARD TREATMENT FOR ALCOHOL-DEPENDENT PATIENTS

The definition of standard treatment for alcoholic patients depends on the stage of the disease and the acute symptoms. Pharmacotherapy is indicated for patients with alcohol withdrawal symptoms. In many countries, this includes treatment with benzodiazepines, carbamazepine, or chlorpromazine. Once the patient has undergone detoxification, the goal is to maintain abstinence or reduce alcohol consumption. Although pharmacological treatments have been attempted (Fuller et al., 1986; Chick et al., 1992), most researchers agree that psychological treatment and counselling are essential components of therapy. Although the type of counselling and psychotherapy and the setting (inpatient versus outpatient) may vary, there are many similarities among countries in the psychological treatment of alcoholic patients.

In Germany, ~3 million people (5% of the adult male population and almost 2% of the female population) are alcohol-dependent. The traditional treatment, a 6-month inpatient period, has proved to be effective. In a large multicentre study, ~56% of the patients were abstinent 6 months after the conclusion of treatment, and 9% had reduced alcohol consumption. Twelve months later, reported abstinence rates were ~46%; while an additional 10% of the patients reported reduced alcohol consumption (Küfner and Feuerlein, 1989). Similar success rates were achieved in 6-week residential programmes that included a 1-year outpatient follow-up period. At the end of the 1-year period, ~64% of the patients were either abstinent (52%) or improved (12%). These results are based on self-reports, and on regular checks of biological markers such as the liver enzyme γ-glutamyltransferase and mean corpuscular volume (Mann and Batra, 1993).

Because of the preponderance of residential treatment programmes, outpatient counselling programmes for alcohol-dependent patients were begun only a few years ago in Germany. Empirical data are not yet available from these outpatient programmes.

The high success rates of German residential treatment programmes match the figures achieved in some American studies (Pettinati et al., 1982). Nevertheless, it must be emphasized that success is closely linked to selecting patients for therapy. In Germany, only 25 000 to 30 000 patients per year receive an inpatient treatment sequence (Wienberg, 1992). This represents 1% of all alcohol-dependent patients. Another 2.5% receive one or more inpatient detoxification treatments per year, without further counselling, therapy, or involvement in a self-help group.

Approximately 70% of all alcoholic patients are seen at least once a year by a family practitioner (Wienberg, 1992). An estimated 25% of all alcohol-dependent patients are admitted to inpatient programmes each year.
Alcoholic patients are admitted to general hospitals for medical or surgical complications caused by alcohol dependence. In many cases, however, neither the physician nor the patient recognizes the underlying disease.

Thus, although the existing treatment programmes are highly efficient, they reach few of the patients in need. The vast majority of patients either are not willing to get involved in a treatment plan or are not diagnosed and given proper advice. Alcoholism treatment programmes need to be expanded in Germany, as in other countries (Mann, 1994). The family practitioner may come to play an especially important role in future therapy programmes, provided that he/she has the tools necessary for diagnosing and treating alcohol-dependent patients. One such tool could be a drug that reduces the craving for alcohol and enhances abstinence.

ACAMPROSATE FOR REDUCING CONSUMPTION AND PREVENTING RELAPSE

Acamprosate (calcium acetylhomotaurinate) is a compound that has the potential to reduce alcohol intake. The first report on preclinical data showed a suppression of alcohol consumption in alcohol-preferring or alcohol-dependent rats (Boismare et al., 1984). Total fluid intake and food consumption were not altered. These findings were verified by other groups (Le Magnen et al., 1987; Littleton et al., 1988). Boismare et al. (1984) hypothesized a γ-aminobutyric acid (GABA)-ergic mode of action. However, the compound has been shown to reduce calcium flux into the neurons (Littleton et al., 1991) and inhibit excitatory amino acids (Zeise et al., 1994). Recently, De Witte (1996, this supplement) has pointed out an analogy with the inhibitory amino acid homotaurine.

Several clinical trials have been performed to assess the efficacy of acamprosate. The first positive results (Lhuintre et al., 1985) were followed by double-blind, randomized, placebo-controlled studies throughout Europe (Lhuintre et al., 1990; Pelc et al., 1992). Studies from Italy (Poldrugo et al., 1994) and Austria (Lesch et al., 1994) showed an increase in abstinence among acamprosate-treated patients. In France, Paille et al. (1995) studied 538 patients in three groups: 177 patients received placebo, 188 received acamprosate (1.3 g/day), and 173 received acamprosate (2 g/day) for 12 months. The treatment period was followed by a single-blind, 6-month period of placebo treatment. While the groups did not differ in sociodemographic variables or history of drinking, the outcomes were significantly different. The high-dose acamprosate group had higher abstinence figures than the low-dose group, which had higher abstinence rates than the placebo group. Continuous abstinence was reported by the high-dose group for an average of 153 days (± 197); for the low-dose group, 135 days (± 189); and for the placebo group, 102 days (± 165). A dose-dependent effect was also shown by a second group of researchers. Pelc et al. (1994) found that a patient group that received 2 g of acamprosate per day did significantly better than a second group that received 1.3 g per day who, in turn, did better than a placebo group.

In a multicentre study in Germany, 272 patients were randomized to receive either acamprosate or a placebo (Sass et al., 1996). Patients who weighed ≥60 kg received two tablets (333 mg each) three times daily; patients who weighed <60 kg received two tablets once daily and one tablet twice daily. There were no significant differences between the groups in demographic data, DSM-III-R diagnosis, or history of alcoholism. There were, however, differences in the educational status of the subjects, the number of days of abstinence prior to detoxification, the family history of alcoholism, and the baseline values of γ-glutamyltransferase. The medication phase of this study lasted for 12 months, followed by a 12-month observation period. One hundred and seventy-four patients (49.3%) completed the first year of the study. Significant differences were found between the three groups of subjects in time until first relapse and in total number of abstinent days during the treatment and observation periods. The cumulative duration of abstinence in the acamprosate-treated group was 178.5 days, whereas in the placebo group it was 113.8 days. Using multivariate statistical analysis, the investigators found that none of the previously mentioned unevenly distributed variables had a significant effect on outcome. At the end of the 12-month medication phase, 42.8% of patients in the acamprosate-treated group were abstinent, as compared with 20.7% in the placebo group.
Undesired effects, including headache and diarrhoea, were recorded in all clinical studies; no severe side-effects were reported (Paille et al., 1995). Some studies showed no difference between the acamprosate and the placebo groups with regard to these complaints. In other studies, there was a slight, but significant, increase in the number of side-effects reported in the acamprosate groups (Sass et al., 1995).

The combination of acamprosate with tetra-bamate, meprobamate, or oxazepam did not result in additional side-effects, which led Aubin et al. (1994) to conclude that acamprosate can safely be prescribed with these compounds, and that it can be given from the start of treatment.

Clinical studies of acamprosate in humans and preclinical studies in animals have given no indication of an abuse potential (Grant and Woolverton, 1989).

REFERENCES


Sass, H., Soyka, M., Mann, K. and Zieglgansberger, W.
