Combined Efficacy of Acamprosate and Disulfiram in the Treatment of Alcoholism: A Controlled Study

Jacques Besson, François Aeby, Antoine Kaase, Philippe Lehert, and Adrian Potgeter

This study presents the results of a multiconter investigation of the afficacy of acompression in the treatment of pottents with chronic or aphodic alcohol dependence. One hundred aighteen patients were rendernly assigned to alther placebo or accomprosess, and both groups were strettled for concomitent voluntary use of discitingm. Treatment lasted for 350 days, with an additional 360-day follow-up period. The primary efficacy permineters evaluated were relepase rate and cumulative abetinence duration (CAD). Results were analyided according to Intention-To-Treat principles using χ^{α} , ξ , and muttiple regression analyses where appropriate. After 30 days on study medication, 40 of 65 (72%) acampropate-treated patients were abstiment, compared with 25 of 66 (43%) placety-treated partients ($\mu =$ 0.01%. The treatment advantage remained throughout the study medication period and was stadistically significant until day 270 (p. = 0.028, Twenty-even percent of patients on accomprosate and 5Th of patients on placebo had a Stat drink within the first 30 days of the study. The mean CAD was 137 days \$10% southent days for the polionia treated with acompropose and 75 days (21% abstraont days) for the placebo group $(\rho=0.013)$. No adverse inferection tectures. ecomprocate and disulfram occurred, and the subgroup who reserved both medications had a better autoons; on CAO lists the those on only one or no medication. Acomorpaste was well talerated. Diarrhea was the only significant treatment indused effect. It was concluded that acamprosets was a unable and safe pharmacofficiapy in the long-term treatment of alcoholism. Concomitant admiréstration of disulfram improved the affectiveness of ecomprosets.

Key Words: Release Prevention, Monhol Department, Acamprosets, Otsuffram.

LCORIOLISM IS one of the most commonly seen clinteral psychiatric syndromes in Western countries," and Switzerland is an exception." Despite its high prevalence, there is no generally recognized specific pharmacetherapy for alcoholism." A large constrained multicenter study" with disulfinam (antahuse), the most widely available pharmacetherapy used to promote abstinance from alcohol, failed to demonstrate its efficacy vessus either a placebo or no medication, as regards to the rate or duration of alignomes, employment, or social stability. Among those patients who death, however, the active medication was associated with a reduction in the number of days of thinking.

Other pharmscotherapentic agents have also been found to be of limited use in the treatment of alcoholism. Semmeninergic antidepressents seem to be helpful in climinishing the desire to driak (at least for short periods) and the serual consumption of alcohol in both animals and humans. Nultreache (recently marketed in the United States for this indication), is an opiate arragonist that showed moderate success in reducing relapses over 12 weeks. The effect was reinforced by the enteronitant use of enguitive skills therapy, but data on continuous long-term abstinence has not yet been published.

Asamprosate, a bonestaurine derivative, is a new syntheric compound whose electrical structure is related to that of taurine and y-uminobutyrse acid (GABA)," both of which are neuromediators. Research has demonstrated that acomprosure displaces GABA bound to GABA, and GABA_n recoprors in virro, and that is reduces corebellar oGMP concentrations in vivo." Acomprosite also uncreases the number of GABA receptor sites and modifies the affinity of the carrier proteins, as well as the entent of binding of GABA in different cerebral structures. 10 Recent studies indicate that summprome also are by reducing the offect of excitatory amino solds in the rat necessites.11 The results of these studies suggest that animprosite crosses the blood-brain barrier and acts on inhibitory, as well us excitatory, amino acids, producing a macked reduction in alcultof consumption in animals. 11

In animal pharmacological studies, accomprosed did not demonstrate any hypostic, anxiotyric, or mascle-relaxant properties. Which distinguishes it from both furnites and beneathing properties are indicated in the inactive instudies for detecting a tridepression artisity. Accompression does not influence several measures of alcohol training. 14

In an initial double blind, placeho-controlled study of 85 alcoholic patients in withdrawat. 33% of the accompressed patients reliapsed within 3 months against 66% of the placebo patients. Several subsequent studies in Pranct, 19 Belgium, 3 and Germany 2 coported a positive therapeutic effect with accompressed in maintaining abstituence in alcohol-dependent patients over periods up to 2 years.

The purpose of the present study was to evaluate the efficiety and safety of acamprosate in maintaining about nonce in weared alcoholics during a 360-day treatment period, with a 360-day fullow-up period. Due to the frequent use of disulfinant in Switzerland, concumitant pre-

Frace the Department of Frachistry, University of Lacrowse (F.B., F.A.), and the Bellelay Clinic (A.K.), Selicity, Switzerland; and the Cutholic Oniversity of Mora (F.L.), Brusseit, Belgiuw, Groupe LITMA Lyon, France (A.F.)

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Arnold M. Ludwig, Jerome Levine, Louis H. Stark

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