

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

Jacques Besson, François Aubry, Antoine Kasse, Philippe Leheret, and Adriaen Potgieter

This study presents the results of a multicenter investigation of the efficacy of acamprosate in the treatment of patients with chronic or episodic alcohol dependence. One hundred eighteen patients were randomly assigned to either placebo or acamprosate, and both groups were stratified for concomitant voluntary use of disulfiram. Treatment lasted for 360 days, with an additional 360-day follow-up period. The primary efficacy parameters evaluated were: relapse rate and cumulative abstinence duration (CAD). Results were analyzed according to Intention-To-Treat principles using  $\chi^2$ , t, and multiple regression analyses where appropriate. After 36 days on study medication, 40 of 55 (73%) acamprosate-treated patients were abstinent, compared with 26 of 55 (47%) placebo-treated patients ( $p = 0.019$ ). The treatment advantage remained throughout the study medication period and was statistically significant until day 270 ( $p = 0.028$ ). Twenty-seven percent of patients on acamprosate and 34% of patients on placebo had a first drink within the first 30 days of the study. The mean CAD was 137 days (90% abstinent days) for the patients treated with acamprosate and 75 days (21% abstinent days) for the placebo group ( $p = 0.013$ ). No adverse interaction between acamprosate and disulfiram occurred, and the subgroup who received both medications had a better outcome on CAD than the those on only one or no medication. Acamprosate was well tolerated. Diarrhea was the only significant treatment-induced effect. It was concluded that acamprosate was a useful and safe pharmacotherapy in the long-term treatment of alcoholism. Concomitant administration of disulfiram improved the effectiveness of acamprosate.

**Key Words:** Relapse Prevention, Alcohol Dependence, Acamprosate, Disulfiram.

**A**LCOHOLISM IS one of the most commonly seen clinical psychiatric syndromes in Western countries,<sup>1</sup> and Switzerland is no exception.<sup>2</sup> Despite its high prevalence, there is no generally recognized specific pharmacotherapy for alcoholism.<sup>3</sup> A large controlled multicenter study<sup>4</sup> with disulfiram (antabuse), the most widely available pharmacotherapy used to promote abstinence from alcohol, failed to demonstrate its efficacy versus either a placebo or an medication, as regards in the rate or duration of abstinence, employment, or social stability. Among those patients who drank, however, the active medication was associated with a reduction in the number of days of drinking.

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Other pharmacotherapeutic agents have also been found to be of limited use in the treatment of alcoholism. Serotonergic antidepressants seem to be helpful in diminishing the desire to drink (at least for short periods) and the actual consumption of alcohol in both animals and humans.<sup>5</sup> Naltrexone (recently marketed in the United States for this indication), is an opiate antagonist that showed moderate success in reducing relapses over 12 weeks.<sup>6</sup> The effect was reinforced by the concomitant use of cognitive skills therapy,<sup>7</sup> but data on continuous long-term abstinence has not yet been published.

Acamprosate, a homotaurine derivative, is a new synthetic compound whose chemical structure is related to that of taurine and  $\gamma$ -aminobutyric acid (GABA),<sup>8</sup> both of which are neurotransmitters. Research has demonstrated that acamprosate displaces GABA bound to GABA<sub>A</sub> and GABA<sub>B</sub> receptors *in vitro*, and that it reduces cerebellar cGMP concentrations *in vivo*.<sup>9</sup> Acamprosate also increases the number of GABA receptor sites and modifies the affinity of the carrier proteins, as well as the extent of binding of GABA in different cerebellar structures.<sup>10</sup> Recent studies indicate that acamprosate also acts as an inhibitory effect of excitatory amino acids in the rat neocortex.<sup>11</sup> The results of these studies suggest that acamprosate crosses the blood-brain barrier and acts on inhibitory, as well as excitatory, amino acids, producing a marked reduction in alcohol consumption in animals.<sup>12</sup>

In animal pharmacological studies, acamprosate did not demonstrate any hypnotic, anxiolytic, or muscle-relaxant properties,<sup>13</sup> which distinguishes it from barbiturates and benzodiazepines. Acamprosate also proved to be inactive in studies for detecting an antidepressant activity. Acamprosate does not influence several measures of alcohol toxicity.<sup>14</sup>

In an initial double blind, placebo-controlled study of 85 alcoholic patients in withdrawal, 53% of the acamprosate patients relapsed within 3 months against 66% of the placebo patients.<sup>15</sup> Several subsequent studies in France,<sup>16</sup> Belgium,<sup>17</sup> and Germany<sup>18</sup> reported a positive therapeutic effect with acamprosate in maintaining abstinence in alcohol-dependent patients over periods up to 2 years.

The purpose of the present study was to evaluate the efficacy and safety of acamprosate in maintaining abstinence in treated alcoholics during a 360-day treatment period, with a 360-day follow-up period. Due to the frequent use of disulfiram in Switzerland, concomitant pre-

# Lsd And Alcoholism A Clinical Study Of Treatment Efficacy

**Jessica J Manson**



## **Lsd And Alcoholism A Clinical Study Of Treatment Efficacy:**

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