Acetyl-L-Carnitine for Alcohol Craving and Relapse Prevention in Anhedonic Alcoholics: A Randomized, Double-Blind, Placebo-Controlled Pilot Trial

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Abstract — Aim: The study aimed to evaluate the efficacy of acetyl-L-carnitine (ALC), at different doses, in relapse prevention and craving in anhedonic detoxified alcohol-dependent subjects. Method: Randomized, double-blind, placebo-controlled, pilot study in 64 alcohol-dependent anhedonic patients: 23 received ALC at a dose of 3 g/day, 21 received ALC at a dosage of 1 g/day and 20 were given placebo. Intensity of alcohol craving was evaluated by Visual Analogue Scale. Subjects were evaluated at the beginning of treatment and after 10, 30, 60 and 90 days. Results: Survival analysis showed that patients treated with ALC remained completely abstinent for longer than those treated with placebo (Z=-2.27; P<0.05). From the 10th day onwards, a greater reduction of craving was observed in the ALC 1 g group than with placebo (P=0.035). The two groups did not differ in the percentage of subjects remaining abstinent for the entire study period or the number of subjects who relapsed (defined as five or more standard drinks (four for women) on a single occasion or drinking on five or more days in 1 week). Conclusions: The results of this study suggest that ALC can reduce craving and the time to first drink. ALC use was safe. Further studies are needed to clarify to extent, over longer periods, these short-term outcome benefits.

INTRODUCTION

Craving, usually defined as the conscious and unbearable desire to use alcohol, is an important heuristic construct with treatment implications. Because high levels of craving have been associated with increased probability of relapse, especially in the early post-treatment period, intervention that reduce craving may have therapeutic benefits (Flannery et al., 2001; Anton et al., 2006).

Avoiding relapse and decreasing craving are major challenges for people who have weathered detoxification from substances of abuse, and various pharmacological strategies have been investigated with partial but not universal consensus (Leggio, 2009). In the last few years, the mechanism of craving for alcohol has been of interest in alcoholism treatment studies (Addolorato et al., 2005) but, due to the complexities of the concept of craving, researchers have yet to reach a consensus definition of this phenomenon.

Acetyl-L-carnitine (ALC) is an endogenous compound representing a small amount of the physiological pool of carnitines (Juliet et al., 2003). The main physiological role of ALC is to contribute to the homeostasis of coenzyme A, exporting acetyl-CoA groups from the mitochondria (Bremer, 1983). ALC crosses the blood-brain barrier using a low affinity, carrier-mediated, sodium-dependent active transport system (Burlina et al., 1989; Kido et al., 2001). Pharmacologically, it acts as a precursor of acetylcholine (White and Scates, 1990) and stimulates intermediate energy production (Aureli et al., 1990) and cytochrome oxidase activity in mitochondria (Villa and Gorini, 1991).

From a pharmacokinetic viewpoint, there are a number of features that distinguish ALC from conventional drugs. First and foremost, it is an endogenous compound that is present not only in humans but also in most, if not all, animal species. The pharmacokinetics of ALC are non-linear, due to the particular filtration/active re-absorption process that it undergoes in the kidneys (Parnetti et al., 1992; Mancinelli et al., 1995). It has an absolute bioavailability ranging between 2.1 and 2.4 and does not bind plasma proteins (Cardace and Marzo, 1993). ALC has a high bioavailability through IV infusion, while lower plasma levels are usually obtained from oral administration (Marzo et al., 1989; Parnetti et al., 1992).

As regards the role of ALC in neurotransmission, it may facilitate cholinergic neurotransmission either directly or by shuttling acetyl groups that can be used for acetycholine synthesis (Gibson and Shimada, 1980; Janiri and Tempesta, 1983; Burlina et al., 1989; White and Scates, 1990). Indeed, ALC has an excitatory activity on cortical cholinergic neurons (Nakamura et al., 1998) and moderate synthesis of acetycholine from ALC has been observed (Falchetto et al., 1971). Janiri et al. (1991) showed that ALC exerted a mild excitatory effect on cortical cholinergic receptors in vivo, providing further evidence of the influence of ALC on the cholinergic system.

With regard to the effect of ALC on dopamine outflow, commonly implicated in alcohol and substance use disorders (see for review, Castorina and Ferraris, 1994), carnitine supplementation has been shown to increase levels of dopamine in the cortex, hippocampus and striatum of rat brain (Juliet et al., 2003), while other animal studies have shown that ALC administration persistently increases dopamine outflow in the nucleus accumbens (Scheggi et al., 2004). Recent studies in animals and humans suggest that dopaminergic agents may be an important class of pharmacotherapies for alcohol dependence (Kenna et al., 2004a,b; Martinotti et al., 2009).

Another system believed to relate to alcohol dependence is N-methyl-D-aspartate (NMDA) neurotransmission. ALC is believed to modulate, either directly or indirectly, through activation of cholinergic receptors, the NMDA subtype of glutamate receptors (Calvani and Carta, 1992). Furthermore, studies have shown that glutamate receptor ligands alter the reinforcing effects of ethanol: infusion of NMDA receptor antagonists attenuates oral ethanol consumption in rats (Lin and...
while several different compounds each believed to influence the NMDA receptor, such as acamprosate, N-acetylcysteine, modafinil, topiramate, lamotrigine, gabapentin, pregabalin and memantine, have promise for the treatment of alcohol withdrawal, craving and relapse prevention although much of the data are in animal rather than human studies (see for review, Gass and Olive, 2008).

In addition, the acute administration of ALC increases β-endorphin levels in healthy subjects and normalizes them in patients with dementia, Alzheimer’s disease and depression.

Clinical trials with ALC have been performed in Europe since the late 1970s and in the USA since 1990. ALC has been extensively studied in Alzheimer’s disease, and exploratory work has been conducted in other patient populations (Pettegrew et al., 2002; Zanardi and Smeraldi, 2006; Rossini et al., 2007; Chiechio et al., 2009). In all these studies, ALC appeared to be efficacious and safe.

The aim of this pilot study was to evaluate the efficacy of ALC in relapse prevention and craving in anhedonic detoxified alcohol-dependent subjects. Secondary study outcomes were the number of abstinent and heavy drinking days during the study period and the effect of ALC on withdrawal symptoms. This pilot study was designed as a randomized, double-blind, dose-determining, placebo-controlled trial, stratified by sex and age (≤ or >35).

MATERIALS AND METHODS

Patients and treatment

Between December 2004 and September 2008, 205 alcohol-dependent subjects, referred to the alcohol outpatient treatment unit of the Psychiatry and Drug Dependence Day-Hospital of the Agostino Gemelli University General Hospital in Rome, were consecutively screened for the study. Random allocation was conducted using a dedicated website, the investigator entering the programme and inserting sex and age after which a specific randomization code was generated allowing assignment stratified by sex and age (≤ or >35). In this way, 64 subjects were randomized to receive:

ALC at a dosage of 3 g/day by slow IV infusion (500 ml of solution infused in 3–4 h) for 10 days and then 3 g three times a day orally for the remainder of the study (80 days) (n=23), or ALC 1 g/day by slow IV infusion for 10 days and then 3 g three times a day orally for the remainder of the study (80 days) (n=21), or placebo (n=20) (all treatments supplied in sachets).

The treatment sequence was identical for placebo and ALC groups. The sequence of IV and oral treatment was based on previous studies showing a faster increase of plasma level ALC when IV infusion preceded oral administration (Marzo et al., 1989; Parnetti et al., 1992). We used a proprietary form of ALC.

All the patients were evaluated by attending psychiatrists using the Structured Clinical Interviews for Diagnostic and Statistic Manual for Mental Disorders, 4th edition (DSM-IV) SCID I and II (First et al., 1990, 1995) and the European Addiction Severity Index (Blanken et al., 1994). Axis II diagnosis was divided into Cluster A (paranoid, schizoid, schizotypal), B (antisocial, borderline, histrionic, narcissistic) and C (avoidant, dependent, obsessive–compulsive), according to DSM-IV. Inclusion criteria were age between 18 and 65 years; diagnosis of alcohol dependence according to DSM-IV-TR criteria, with a history of alcohol use disorders for at least 3 years and a daily alcohol intake of at least six drinks (one drink containing 12 g ethanol) in the month before the screening; and presence of anhedonic symptoms, with SHAPS (Snaith–Hamilton Pleasure Scale) (Snaith et al., 1995) dychotomic score ≥3. Exclusion criteria were the presence of delirium tremens or hallucinosis; a score of over 5 on the Clinical Institute Withdrawal Assessment for Alcohol (CIWA-Ar) (Sullivan et al., 1989); blood alcohol concentration higher than 0.1 g/L; substance abuse; Axis I diagnosis other than alcohol dependence; evidence of a mental disorder severely interfering with cognitive capacity; epilepsy; severe cardiac failure; diabetes mellitus; severe liver impairment; liver encephalopathy; kidney failure; neoplastic disease; lack of cooperating relatives; intake of psychotropic medications such as anticonvulsants, antidepressants or antipsychotics; pregnancy or lactation; and a history of severe adverse reaction or well-known hypersensitivity to ALC.

Study procedures

The study was designed to last for 142 days, with a screening phase (7 days), a treatment phase (90 days) and a follow-up phase (45 days). Subjects were assessed at the following times: at the beginning of treatment (T0) and after 10 (T1), 30 (T2), 60 (T3) and 90 (T4) days of therapy. A follow-up assessment (T5) was carried out 45 days after the last therapy intake.

During the treatment phase (90 days) patients received the treatments described above, according to the allocated group. Compliance was verified by counting the sachets returned for each treatment period at the corresponding assessment. Subject flow by treatment group is shown in Fig. 1.

During the study period, patients were only given diazepam (20 mg/day or equivalent as required) for insomnia according to established and validated protocols (Lejoyeux et al., 1998). In cases in which withdrawal symptoms severely interfered with the clinical condition, the patients were adequately treated and considered as dropouts.

For the entire study period, all the patients attended a self-help group based on a psychosocial programme twice per week.

Abstinence from alcohol was evaluated on the basis of the participant’s self-evaluation and a family member interview. Abstinence was confirmed by determining blood alcohol concentration at each outpatient control, measuring alcohol abuse hepatic indices [aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma glutamyl-transpeptidase (GGT)] and measuring mean cellular volume (MCV). Toxicological urinalysis was performed at baseline and at each outpatient control in order to identify poly-drug abuse and benzodiazepines.

The intensity of alcohol craving was evaluated by a 10-cm Visual Analogue Scale (VAS) (Mottola, 1993) at the beginning of treatment (T0) and after 10 (T1), 30 (T2), 60 (T3) and 90 (T4) days of therapy.

Effectiveness measures included the Clinical Global Impressions scale (CGI) (Guy, 1976). Safety parameters were...
monitored throughout all the study and are described in a separate paper, which also reports the effect of ALC on anhedonic, melancholic and negative symptoms (Martinotti et al., unpublished data).

The study protocol was approved by the Ethical Committee of the Catholic University of Rome and by the Institutional Review Boards in accordance with local requirements. It was conducted according to the Declaration of Helsinki Guidelines (1964). After receiving information about the drug, any possible side effects and the dosing rate, as well as the possibility of dropping out of the study at any time, all patients (or their legal representatives) provided their written informed consent prior to randomization. Each patient was informed that an alcohol relapse, non-compliance or the onset of side effects would lead to their exclusion from the trial. In any case, patients were free to leave the study at any time. No reimbursement was contemplated for the subjects included in the study.

Statistical analysis
The primary study outcomes were maintenance of abstinence and the reduction of alcohol craving as measured by VAS. A return to drinking any alcohol, regardless of the quantity, marked the end of the abstinence. Differently from ‘end of abstinence’, relapse to drinking was defined as either drinking five (four for women) or more standard drinks on a single occasion or drinking on five or more days in 1 week. This definition is currently reported for research purposes in different studies (Volpicelli et al., 2002; Gastfriend et al., 2007). Secondary study outcomes were the number of abstinent days (which includes both the days before the end of abstinence and, eventually, those abstinent days following the first alcohol use), of heavy drinking days (characterized by ≥4 drinks per day for women and ≥5 per day for men) during the study period, and the effect of ALC on withdrawal symptoms. In Italy a ‘drink’ is considered to contain 12 g of ethanol.

Student’s t and chi-square tests were employed in order to compare socio-demographic and clinical data.

Primary and secondary efficacy analyses were performed on the per-protocol population, which included all randomly assigned patients assessed during the entire treatment phase (T1–T4). All the drop-out subjects were eliminated from the analysis on application of this method. Time to first drink (survival remaining abstinent) was compared across groups using Kaplan–Meier survival curves and the log rank test.

Safety analysis was performed on the intent-to-treat population, which included all randomly assigned patients who took at least one dose of study medication.

Craving data were analysed at baseline and at different times by analysis of variance for repeated measures, with time...
as ‘within’ factor and treatment, age and sex as ‘between’ factors. Where appropriate, a Bonferroni correction was applied to control for the number of comparisons. We defined P values of 0.05 or below as statistically significant.

RESULTS

Patients and disposition

A total of 205 patients were screened, of whom 141 were excluded. In 78% of patients excluded, the reason was the absence of anhedonia (a SHAPS dichotomic score lower than 3). There were no significant differences between the other baseline characteristics of patients who did not pass the screening compared with those who were included. The three groups of randomized patients did not vary in terms of socio-demographical and clinical characteristics, level of craving (VAsc) and average alcohol consumption in the month before the assessment (Table 1). (Despite screening out the patients who at screening had a CIWA-Ar score over 5, some patients presumably had resumed drinking because several had scores over 5 at their baseline interview some days later.)

During the study period two subjects used diazepam, at a dosage of 20 mg/day, for 2 and 4 days of treatment, respectively. For both cases the reason was insomnia, as permitted by protocol.

Table 1. Socio-demographic characteristics, alcohol history and clinical data of the sample. Percentages are given in brackets

<table>
<thead>
<tr>
<th>Parameters</th>
<th>ALC 3 g + 3 g n=23</th>
<th>ALC 1 g + 3 g n=21</th>
<th>Placebo n=20</th>
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<tbody>
<tr>
<td><strong>Socio-demography</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Age (M, SD)</td>
<td>44.9, 13.8</td>
<td>38.6, 8.47</td>
<td>42.7, 12.3</td>
</tr>
<tr>
<td>Males</td>
<td>12 (52)</td>
<td>12 (57)</td>
<td>12 (60)</td>
</tr>
<tr>
<td>Females</td>
<td>11 (48)</td>
<td>9 (43)</td>
<td>8 (40)</td>
</tr>
<tr>
<td><strong>Marital status</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>6 (26.1)</td>
<td>2 (9.5)</td>
<td>3 (15)</td>
</tr>
<tr>
<td>Married</td>
<td>12 (52.2)</td>
<td>14 (66.7)</td>
<td>12 (60)</td>
</tr>
<tr>
<td>Separated/divorced</td>
<td>5 (21.7)</td>
<td>4 (19)</td>
<td>3 (15)</td>
</tr>
<tr>
<td>Widowed</td>
<td>0</td>
<td>1 (4.8)</td>
<td>2 (10)</td>
</tr>
<tr>
<td><strong>Level of education</strong></td>
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<td></td>
<td></td>
</tr>
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<td>Elementary school</td>
<td>1 (4.3)</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Lower secondary school</td>
<td>4 (17.4)</td>
<td>4 (19)</td>
<td>5 (25)</td>
</tr>
<tr>
<td>High school education</td>
<td>14 (60.9)</td>
<td>14 (66.7)</td>
<td>12 (60)</td>
</tr>
<tr>
<td>Degree</td>
<td>4 (17.4)</td>
<td>3 (14.3)</td>
<td>3 (15)</td>
</tr>
<tr>
<td><strong>Employment condition</strong></td>
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<tr>
<td>Retired</td>
<td>4 (17.4)</td>
<td>2 (9.5)</td>
<td>4 (20)</td>
</tr>
<tr>
<td>Employed</td>
<td>14 (60.9)</td>
<td>13 (61.9)</td>
<td>12 (60)</td>
</tr>
<tr>
<td>Unemployed</td>
<td>5 (21.7)</td>
<td>6 (28.6)</td>
<td>4 (20)</td>
</tr>
<tr>
<td><strong>Alcohol-related history</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of alcohol dependence (years: M, SD)</td>
<td>9.1, 5.2</td>
<td>8.7, 4.8</td>
<td>9.9, 4.5</td>
</tr>
<tr>
<td>Daily drinksa (M, SD)</td>
<td>7.9, 3.9</td>
<td>8.3, 2.5</td>
<td>8.8, 4.9</td>
</tr>
<tr>
<td><strong>Values at the baseline</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VAsc score (M, SD)</td>
<td>4.2, 2.9</td>
<td>1.98, 1.3</td>
<td>4.98, 2.26</td>
</tr>
<tr>
<td>SHAPS score (M, SD)</td>
<td>4.96, 1.77</td>
<td>5.1, 2.1</td>
<td>5.75, 2.12</td>
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<tr>
<td>CIWA-Ar (M, SD)</td>
<td>9.56, 4.45</td>
<td>10.9, 9.08</td>
<td>8.87, 5.52</td>
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<td><strong>Dual diagnosis (Axis II)</strong></td>
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<td></td>
<td></td>
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<tr>
<td>Cluster A</td>
<td>2 (8.7)</td>
<td>1 (4.8)</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Cluster B</td>
<td>4 (17)</td>
<td>4 (19)</td>
<td>3 (15)</td>
</tr>
<tr>
<td>Cluster C</td>
<td>2 (8.7)</td>
<td>3 (14.3)</td>
<td>2 (10)</td>
</tr>
<tr>
<td>NAS</td>
<td>1 (4.3)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Weight (M, SD)</strong></td>
<td>68.4, 14.6</td>
<td>66.4, 12.1</td>
<td>69.8, 14.2</td>
</tr>
<tr>
<td><strong>Height (cm: M, SD)</strong></td>
<td>168.8, 8.74</td>
<td>168.7, 9.26</td>
<td>169.6, 11.7</td>
</tr>
<tr>
<td><strong>Body mass index (BMI) (M, SD)</strong></td>
<td>24.1, 5.29</td>
<td>23.3, 3.43</td>
<td>24.4, 5.05</td>
</tr>
</tbody>
</table>

*a1 drink=12 g or 0.5 oz.

VAsc, Visual Analogue Scale for Craving; SHAPS, Snaith–Hamilton Pleasure Scale; CIWA-Ar, Clinical Institute Withdrawal Assessment for Alcohol.

Efficacy

The survival curve for time to first drink (duration of abstinence) is shown in Fig. 2. The survival function showed that patients treated with ALC remained abstinent from any amount of alcohol for a longer time than those treated with placebo (Z=−2.27; P < 0.05).

In relation to craving, a significant reduction as measured by VAsc was found between times in all groups (P=0.039). The global effect of ALC treatment during times was stronger than treatment with placebo (P=0.035). Greater reduction in anhedonia in the ALC 1 g group than the placebo group was found at T1, T2 and T3 (respectively Δ=−3; 95% Confidence interval (CI): −5.1, −0.8; P=0.005; Δ=−2.5; 95% CI: −4.8, −0.1; P=0.038; Δ=−2.4; 95% CI: −4.6, −0.1; P=0.045). In relation to craving, no differences between patients with and without a psychiatric Axis II diagnosis were found.

The percentage of subjects remaining abstinent for the entire study period (ALC 1 g=26%; ALC 3 g=28.5%; Placebo=20%) and the number of subjects who relapsed (ALC 1 g=19%; ALC 3 g=17%; Placebo=40%) were not significantly different (X²=1.16; X²=3.4) between groups, although a trend towards better outcome in the treated groups was observed. The percentage of subjects excluded from the study due to lack of compliance (ALC 1 g=24%; ALC 3 g=39%; Placebo=25%) was not significantly different between groups.

The mean number of abstinent days (ALC 1 g: 72.6 ± 43.7 days; ALC 3 g: 76.1 ± 21.2 days; Placebo: 63.1 ± 46.4 days) by on July 2, 2010 http://alcalc.oxfordjournals.org Downloaded from
To our knowledge, this is the first trial evaluating the efficacy and safety of ALC in alcohol use disorders. Multiple substance abuse and Axis I diagnoses other than alcohol dependence were exclusion criteria, and our sample was therefore composed solely of heavy drinking alcoholics, with an average intake of eight drinks per day and a history of abuse/dependence for over 7 years. A comparison of the data observed in this study with those of other published reports on ALC is difficult because of the diverse typologies of patients included, the response criteria used and the absence of a placebo group in some studies (Pettegrew et al., 2002; Zanardi and Smeraldi, 2006).

The daily dosage of ALC (1 g or 3 g) was defined on the basis of previous clinical studies in other psychopathological conditions (Villardita et al., 1984; Tempesta et al., 1987; De Simone et al., 1988; Nasca et al., 1989; Bella et al., 1990; Fulgenti et al., 1990; Garzera et al., 1990; Gecele et al., 1991; Pettegrew et al., 2002; Hudson and Tabet, 2003; Zanardi and Smeraldi, 2006). The use of diazepam for insomnia was allowed for reasons of safety. Despite few days of treatment being characterized by its use in two patients for 2 and 4 days, it represents a possible limitation.

In this study, ALC was associated with prolonging abstinence compared to placebo. The efficacy of ALC in reducing craving may be responsible for these results. This magnitude of the effect seemed greatest during the first week of the study and gradually waned over time. With regard to relapse to heavy drinking, only a tendency in favour of ALC was seen. The mean number of abstinent days and heavy drinking days did not differ significantly between groups.

The better outcome of the ALC 1 g group merits further investigations. However, the fact that this did not emerge from the ALC 3 g group deserves explanation, because one would have hoped to see a dose–response effect. However, the higher number of subjects excluded from the study due to lack of compliance in the ALC 3 g groups would have reduced the statistical power for this group.

Indeed, the high drop-out rate is a limiting factor in interpreting this study. We hypothesized that it might be due to the severity of a sample composed by anhedonic alcoholics, who might be expected to lack the drive to remain involved in treatment, as described in other trials with anhedonic subjects (Liraud and Verdoux, 2001).

The anti-craving effect of ALC could be mediated by its influence on the dopamine outflow (Juliet et al., 2003) and its modulation on the NMDA glutamate receptors (Calvani and Carta, 1992).

![Fig. 2. Survival remaining abstinent. *P < 0.05 (Z=-2.27) between Placebo and the ALC groups.](http://alcalc.oxfordjournals.org)
The positive effects of ALC on anhedonic symptoms are another possible explanation for the efficacy of ALC in alcoholics. Treating anhedonia in detoxified alcohol-dependent subjects could be critical in terms of relapse prevention strategies, given its strong relationship with craving (the higher the craving scores, the higher the level of anhedonia) (Janiri et al., 2005). As to this, the effect of ALC on anhedonia, melancholia and negative symptoms has been described in a separate paper, which reports a significant reduction of anhedonia in patients receiving ALC at 1 g and 3 g per day (Martinotti et al., unpublished data). Therefore, the mechanism involved in the efficacy of ALC in relapse prevention could be potentiated by the treatment of these dimensions. These data are supported by the results of other studies showing ALC’s effect in the treatment of dysthymia and depression (Pettegrew et al., 2002; Zanardi and Smeraldi, 2006). Nevertheless, we do consider that the presence of anhedonia could be better explained by a chronic alcohol misuse rather than by a previous personality trait.

In this randomized, double-blind, placebo-controlled study, both dosage groups of ALC appear to prolong duration of abstinence (Fig 2), and therefore a dosage of 1 g day could be considered the dosage of choice, in particular given that it appeared to reduce craving.

Finally, liver function tests in all the treated subjects showed significantly improved results, with no differences between groups at any of the times. These data, together with the haematological and ECG results, corroborate what has been previously reported regarding ALC in other psychopathological and medical conditions (e.g. De Grandis, 2007; Sima, 2007; Evans et al., 2008; Ruggenenti et al., 2009), confirming its favourable safety profile in alcoholics. In addition, a protective role of carnitines, as scavengers, has been postulated in relation to brain injuries observed after drug abuse and methamphetamine administration (Virmanni et al., 2002). These data represent a further aspect that prompts the use of ALC in toxic conditions induced by alcohol and other substances.

We recognize that the small sample size and the high percentage of dropouts limit the interpretation of our results. Also, anhedonic alcoholics represent a specific subpopulation of subjects, and therefore general conclusions cannot be drawn from our data.

Nevertheless, we believe further study is merited to clarify the role of ALC in reducing craving, and to test over a longer period, the short-term effects that we observed. In the meantime, for a selected patient population, the results of our pilot study indicate a possible role of ALC in the treatment of anhedonic alcoholics.

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