families with a high genetic loading for alcohol dependence have suggested that some may inherit an oversensitivity to this effect, and it has been suggested that this might contribute to the loss of control experienced by some drinkers [1]. Opiate antagonists such as naltrexone reduce ethanol-seeking in alcohol-dependent animals.

Two published double-blind randomised controlled studies in detoxified patients taking part in an out-patient treatment programme report that naltrexone 50 mg daily reduces the risk of self-reported relapse, at least for three months [2]. Objective markers of alcohol consumption have helped to support this result. Results of longer studies in larger samples are awaited.

Some patients who resume drinking while taking naltrexone report that they feel less of the ethanol 'high'. Perhaps they then experience less impulse to carry on drinking [2]. However, studies have found an increase in the numbers of patients who report achieving total abstinence as well as a reduction of drinking overall.

Naltrexone is not addictive in the sense that there is a withdrawal syndrome, it is well tolerated and it has a good safety record. Follow-up has not indicated rapid relapse on cessation of the drug.

More information is needed on which patients respond, which is the optimal timing and duration of use, and which psychological and social interventions are necessary compliments. As with other treatments psychological approaches enhancing compliance will be an important factor in determining the effectiveness of opiate antagonists in routine clinical practice.

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INCREASE IN NEURO-INHIBITORY AMINO-ACIDS DURING ALCOHOLIZATION AND IN NEURO-EXCITATORY AMINO-ACIDS DURING WITHDRAWAL

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During alcoholization, acute or chronic, an increase in the extracellular concentration of taurine, a major inhibitory amino-acid, was observed in the limbic system of male rats using the microdialysis technique. These studies were done on awake freely moving animals after implantation of micro probes into specific parts of the brain. The dialysates collected through these probes were then injected into HPLC coupled with electrodetection technique after derivatization with OPA. After chronic alcoholization using pulmonary alcoholization, amino-acids were also estimated during this withdrawal period. After 4 hours withdrawal a dramatic increase in glutamate, a major excitatory amino-acid, was observed and lasted for 32 hours. Both phenomena, i.e. increase in inhibitory amino acid taurine during alcoholization and increase in excitatory amino-acid glutamate during withdrawal, produce hyper-excitability in animals detected by tilting procedure.

New molecules were tested in order to decrease these combined amino-acids effects.

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DIFFERENT STRATEGIES OF RELAPSE PREVENTION: A META-ANALYSIS OF DRUG EFFICIENCY

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Newer approaches of pharmacological treatment of alcohol dependence/abuse try to reduce the craving for alcohol by manipulation of the endogenous "reward" circuit. A meta-analysis of placebo controlled clinical trials with anti-craving substances was performed in order to establish their overall efficacy and to examine the possible influence of study characteristics.

Eleven placebo controlled, randomised studies with a minimum length of three months were included. The following substances were taken into account: acamprosate, naltrexone, nalmefene, GHB, tiapride, atenolol and bromocriptine.

There was a significant overall efficacy of $r = 0.22$, corresponding to a verum-placebo responderrate difference of 22 percentage points. Naturally, the influence of drugs was confounded with design elements of the studies. Nevertheless, two variables, namely drinking status of the patients and the choice of the response criterion seemed to influence study results: Effect sizes of studies including non-detoxified patients were higher than effect sizes of studies with detoxified patients. Three of the anti-craving substances showed higher efficacy with controlled drinking than with abstinence as response criterion.

According to these results, the published studies show that anti-craving substances are superior to placebo in the treatment of alcohol dependence, and the effect size compares favorably to other Drug treatments in psychiatric disorders. Study design variables may have a large influence on the results.

LONG-TERM FOLLOW-UP OF ACAMPROSATE TREATMENT IN ALCOHOLIC PATIENTS

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In a total of 14 centres both the "old" Federal republic and the former East-Germany 272 patients took part in this II Phase study over a period of 2 years. In a randomised, double-blind design 136 patients received acamprosate treatment and 136 patients received placebo. 22.4% of the patients were female. In addition to the usual recording of patient's history and demographic details, extensive assessments of psychological status and social environment were performed.

134 (49.3%) patients completed the study after one year. The most sensitive indicator of efficacy proved to be cumulative duration of abstinence. The mean value in the acamprosate group was 178.5 days compared to 113.8 days in the placebo group. The difference between treatment groups is highly significant, with a p value of 0.0001. The differences were reflected in a similar way in the life-tables. A very marked difference between acamprosate and placebo treatment developed between 30 and 90 days after the start of therapy. The absolute value of this difference increased only slightly on further treatment. The Log Rank test, which is the usual method of statistical comparison on life-table data, yielded a similar result ($p = 0.0054$). At the end of the first year, the proportion of abstinent patients was twice as high in the acamprosate group. This is apparent from the course of the life-table curve, but can also be expressed using a direct comparison of patients at the end of the study. 42.8% of patients were abstinent in the acamprosate group and 20.7% in the placebo group.

The second year of the study was organized as a medication-free follow-up. At the end of this period 104 patients were still under observation, 66 on acamprosate and 38 on placebo. 5 to 6% of the patients in each group relapsed in the second year. At the end of the follow-up 40% of the remaining patients on acamprosate and 17% on placebo had never relapsed. This difference between the two groups was highly significant. There were no rebound phenomena at the termination of study medication.

The implications of the differences in drop-out rates and retention rates between the two groups during study medication and follow-up over 2 years are discussed.

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