Original Research Paper

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Pharmacology

"SAFETY AND EFFICACY OF ACAMPROSATE FOR THE TREATMENT OF ALCOHOL DEPENDENCE SYNDROME"

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KEYWORDS :

Introduction:

According to WHO at least 4% of all the deaths in the world is due to abuse of alcohol[1]. Alcoholism is a complex disorder which is characterised by excessive and compulsive drinking, chronic relapse, presence of withdrawal symptoms and impaired social functioning[2,3]. The treatment strategies for substance use disorders include medical management, self help support groups and cognitive behavioural therapy .The three currently FDA approved drugs for the treatment of alcohol dependence syndrome are Disulfiram, Naltrexone and Acamprosate[4].

One of the first drugs to be approved for the treatment Alcohol dependence syndrome (ADS) is Disulfiram. It has been the mainstay for treatment of ADS for over 6 decades[5].Disulfiram inhibits Acetaldehyde dehydrogenase thus resulting in an accumulation of acetaldehyde which leads to an aversive reaction which is characterised by nausea, vomiting, breathing difficulties, hypotension, dizziness and tachycardia[6].Thus disulfiram is a deterrent and is effective because of the patients avoidance due to these side effects.In addition Disulfiram is also known to produce unintentional side effects like fulminant hepatitis, neuritis, confusion, psychosis, myocardial infacrtion, CHF and respiratory depression[7].

Naltrexone was approved for prevention of relapse in Alcohol dependent patients in 1994.Studies have revealed that Naltrexone is considered to have a safer and a tolerable profile over Disulfiram. Naltrexone has been reported to cause hepatocellular toxicity and is generally contraindicated in those individuals who have hepatic insufficiency[8].

Acamprosate is a $GABA_a$ receptor agonist[9] .It is available as 333mg enteric coated tablet which is given orally three times daily. The most common side effect observed with the use of Acamprosate is mild diarrhoea which limits by the first four weeks of treatment. Since acamprosate is not metabolised in the liver it is relatively safe in individuals with varying degrees of hepatic insufficiency. Acamprosate is considered to have an excellent safety and tolerability profile[10]

Various studies have evaluated efficacy of acamprosate with psychosocial interventions and Acamprosate was considered to be statistically superior to placebo in maintaining abstinence.It was noticed that the use of Acamprosate was associated with a large improvement in days of cumulative abstinence as well as the rate of abstinence.The efficacy measures were divided as primary and secondary outcomes. The primary outcome included 1)return to drinking 2)cumulative duration of abstinence during the study.The secondary outcomes were 1)return to heavy drinking(5 or more drinks per occasion) 2)elevated GGT levels[11,12].in view of the above said we reviewed that the safety and efficacy of acamprosate in treating alcohol dependence syndrome.

Materials and methods

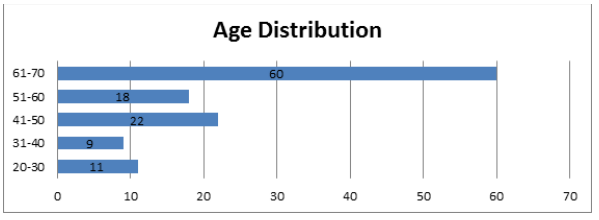
A total of 60 patients having ADS admitted to the deaddiction ward with history of Alcoholism and met a predefined criteria are chosen for the study. Inclusion criteria: Patients who are newly diagnosed with ADS with normal renal parameters. AGE:18-60 Exclusion criteria: Patients with renal failure, Hepatic failure,history of other drug abuse. Relapsed cases of ADS

A detailed history of patients was recorded. Informed consent was taken from all patients during the study. Data collected was entered in a specially designed proforma for the study. No lab tests. Safety will be assessed by a questionnaire on adverse effects of Acamprosate.the patients were reviewed at the beginning(day 1)and at the end of 1 month and 2 months.

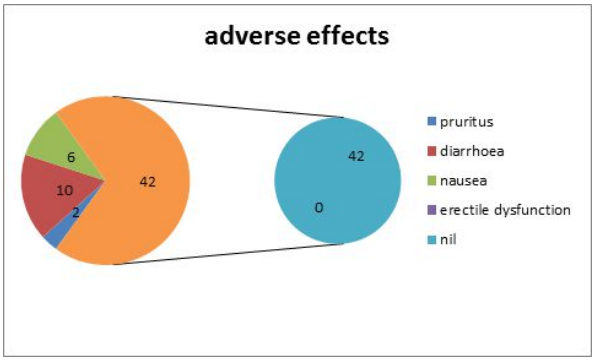
Results and Analysis

In our study all cases admitted with ADS admitted for deaddiction were males. The most common age was 40-50 years (25 cases). The mean duration of alcoholism was 10.45 years it ranged from 4 to 25 years. We found significant reduction in the use of liquor

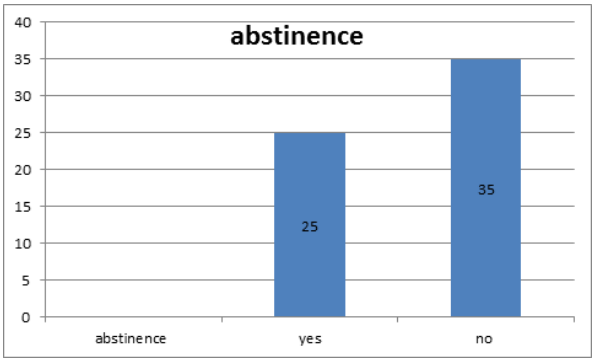
In our study the total treatment period was six months, in the first three months patients received medication and in the following three months patients remained in the treatment without medication.Complete abstinence in the acamprosate group was 42.% (25/60 subjects), in our study pruritus was noted in 2 cases and diarrhoea in 10 cases



Graph 1 : age distribution



graph 2 ; side effects



Graph 3 :abstinence

Discussion

Acamprosate is an amino modulator that has shown adequacy in some

clinical trials in diminishing liquor intake patients following deaddiction. While acamprosate is sheltered and for the most part all around endured, not all examinations have shown clinical adequacy that is better than fake treatment

Acamprosate was originally synthesized in the laboratories of the French pharmaceutical company Meram and was first approved for clinical use in France in 1987. .

Higuchi S enrolled 327 patients with ICD-10-defined alcohol dependence demonstrated significantly superior efficacy on the primary endpoint the proportion maintaining complete abstinence in the acamprosate group was 47.2% (77/163 subjects), [13]

Danilo Antonio Baltieri et.al did a double-blind randomized study showed that in the last week of the study 17 patients from the acamprosate group (42,5%) and seven from the placebo group (20%) were abstinent since the first consultation,[14]

Sass et al[15] (1996) performed a 48-week study with 272 alcohol-dependent patients who received acamprosate or placebo. At the end of the treatment, 39% of patients treated with acamprosate were abstinent,

Lhuintre et al [16] found some side-effects, as follows: nausea, erectile dysfunction and pruritus Whitworth et al[17] reported that among some of the side-effects reported by patients diarrhea was the most frequent one in patients of the acamprosate group, (p=.021).

CONCLUSIONS:

Acamprosate is superior in maintaining abstinence in patients with alcohol dependence. Acamprosate was a safe and well-tolerated medication.

A limitation of our study was the small number of patients when compared to similar studies

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