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Comparing Acamprosate and Naltrexone Treatment in Patients with Alcohol Use Disorder (AUD) for Relapse Preventing

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1. Abstract

Alcohol Use Disorder (AUD) is a disorder widely spread in the modern world. The interventions and treatments for AUD has not changed since 2010, and it is using psychosocial interventions and drugs like Acamprosate and Naltrexone. The Comparison between Acamprosate and Naltrexone effectiveness was done to provide the best option for relapse prevention and maintaining abstinence. The findings were that some studies found that Naltrexone was twice as effective in preventing relapse during a one-year timeline than Acamprosate. Others showed that Acamprosate had better results in increasing abstinence rate [OR: 1.88 (1.57, 2.25), P < 0.001], and Naltrexone on the other hand had significantly reduced relapse rate [OR: 0.62 (0.52, 0.75), P < 0.001] but without any noticeable difference in abstinence rate [OR: 1.26 (0.97,1.64), P = 0.08]. As well as combining both Acamprosate and Naltrexone was incomparably better in relapse prevention. In conclusion Naltrexone was proved to show better results in general in relapse prevention and increasing abstinence rate.

2. Introduction

Alcohol use disorder (AUD) is "a term used to refer to the misuse of alcohol. Several specifically defined conditions better categorize patterns of alcohol misuse." [1]. Alcoholism is another more common name for (AUD). Alcohol is a drug that is widely spread in the world, which is accessible to many people, and this opens the door for many more issues to come with it. As it is easy to get, it can be misused and mistreated, which allows for many complications and health issues to happen. According to a survey done in America around 14.1 million adults aged eighteen and older had AUD in 2019 [2]. AUD is caused by many factors; some are controllable, and some are not. For example, genetics and family history of alcoholism are uncontrollable risk factors for alcoholism that increase the chance of alcoholism greatly. On the other hand, controllable factors can be like, being exposed at a young age to stress and trauma, and consuming alcohol early in life [3]. Misusing alcohol results in a massive impact on health. It can affect most if not all the major organs causing diseases like alcoholic hepatitis, gastritis, hypoglycemia, nystagmus, osteoporosis and many more. Moreover, it can affect other areas of life other than health. It can ruin relationships, impact performance at work, have an increased chance of committing violent crimes, and even worse leading to problems with other riskier substance use. There are a couple of

drugs approved by the FDA for treatment of alcohol use disorder, they are (from first to last approved) Disulfiram, Acamprosate, and Naltrexone. Naltrexone was the last drug to be approved by FDA in 1994. From that time till now there have been some drugs that were made but not approved by FDA that are used in some countries like, Baclofen [3]. The drugs approved by FDA are used till now, but each drug has its benefit in its own way, and they show variability in the treatment response [4]. According to BMJ Best Practice [1] the treatment algorithm for moderate to severe alcohol dependence as the first line is using psychosocial interventions and in addition to that is using drugs like naltrexone, or acamprosate. This way of prescribing acamprosate and naltrexone has been used since 2010 and it is still followed till now, and therefore this research is important because at the end of it, it will be clear which drug is most effective for treating alcohol use disorder, so drugs that are more effective to be used and not waste resources and prevent further complication of the already dangerous addiction that they suffer with.

3. Methods

During my research I used PUBMED by using MESH terms Alcoholism, AND Acamprosate, AND Naltrexone, this gave me 225 results. After that I narrowed my search to clinical trials, randomized clinical trials, English, Human species and full text and got 52 results, I used 4 of them. Finally, I limited my search to systemic review which gave me 3 results and I used 1 of them.

4. Results

The first source shows that combining both acamprosate and naltrexone was incomparably more effective in preventing alcohol dependent patients from relapsing. This meant that they lowered the relapse rates [5]. The second source mentions that naltrexone was more effective in relapse prevention of alcohol dependent patients, and it was a better treatment on the time to first relapse to have no depression. As well as acamprosate had low effect on the patients [6]. The third source was a long term of 1 year to compare the effect of naltrexone and acamprosate in their ability to keep alcohol dependent patients abstinent from alcohol and reduce their relapses. It has shown that patients that have been treated with naltrexone had twice the amount patients abstaining from alcohol than patients that were treated with acamprosate. Another statistic is that 41% of the naltrexone group had not relapsed and 54% were abstained from alcohol in comparison with 17% (not relapsing) and 27% (abstained) with treatment of acamprosate. Another major finding is that if a patient had drunk some alcohol relapse would happen on average 12 days later for the patients being treated with naltrexone in comparison with acamprosate it happened after only 6 days [7]. The fourth study. This study tested the blood concentration of naltrexone in alcohol use disorder patients. It has been found that the concentration of naltrexone in the blood is highly correlated with reduction of alcohol craving and reducing their obsessive-compulsive drinking scale (OCDS). This indicates that lowering alcohol craving can relate to reduced relapse in alcohol use disorder patients when using naltrexone [8]. The fifth study. In this study the aim was to compare disulfiram, naltrexone, and acamprosate in their ability to reduce the first time to heavy drinking day (HDD), days of abstinence from drinking, and severity of alcohol dependence data (SADD). It has shown that between naltrexone and acamprosate there was no difference in (HDD) or increasing the time for first drink. However, SADD scores were much higher in naltrexone group than acamprosate group. This indicates that naltrexone is much better for heavy alcohol dependent patients [9]. The sixth study. This study tested the findings of other literature that naltrexone benefit is for only severe alcohol dependence and to reduce heavy drinking rather than abstinence. What was found from this study is that patients with higher severity alcohol-dependence when receiving XR-NTX 380 mg (n = 50) compared with placebo (n = 47) had much less heavy drinking days (hazard ratio=0.583; p = 0.0049). as well as showing an average of 37.3% reduction in heavy drinking days compared with placebo 27.4% (p = 0.039). patients with lead-in abstinence had experienced a high level of maintenance of initial and six-month abstinence. This shows us that naltrexone has a high ability in reducing heavy drinking as well as maintaining abstinence [10]. The seventh study. This study tested the efficacy of acamprosate in maintaining complete abstinence in alcohol dependent patients. The results of this study were that the group treating with acamprosate showed higher number of complete abstinence of 47.2% (77/163 subjects) compared to placebo 36% (59/164 subjects) (P = .039) The difference in complete abstinence between the two groups was 11.3% (95% CI, 0.6%-21.9%) [11]. The eighth study. This systemic review and meta-analysis have compared efficacy of naltrexone and acamprosate in treatment of alcohol dependence. Measuring relapse, abstinence rates, and treatment compliance. Acamprosate was associated with a significant improvement in abstinence rate [odds ratio (OR): 1.88 (1.57, 2.25), P < 0.001] and days of cumulative abstinence [WMD: 26.55 (17.56, 36.54]. Administration of naltrexone reduced the relapse rate significantly [OR: 0.62 (0.52, 0.75), P < 0.001], but was not associated with a significant modification in the abstinence rate [OR: 1.26 (0.97,1.64), P = 0.08], It shows that acamprosate is better for achieving abstinence, but naltrexone was shown to be more effective for controlled consumption [12].

5. Discussion

The different treatments like naltrexone and acamprosate have shown different effectiveness in treatment of alcohol dependence. For the first study the limitations of it were the limited duration of treatment, as 12 weeks were not enough to get the full results

of the study [5]. The third source, the limitations were that the study did not remain blinded. Another point is that naltrexone's advantage could have been from the participants being patients with moderate alcohol dependence. Furthermore, the testing of the level of compliance to the treatment was by doing questionnaires to the family, this could have been not very accurate, and another accurate method was to use riboflavin as a urinary marker. Another one is the use of GGT (which is a helpful, but not perfect, marker of drinking) appeared to corroborate a better reported outcome in the naltrexone group, but the advantage failed to reach statistical significance. Lastly, in this study there was a major level of family support to the patients if this was not available the results could have differed [7]. The fourth study limitation was that because no blood was obtained after the occurrence, the predictive validity of plasma levels for relapse could not be determined. As a result, the decrease of craving was chosen as the primary outcome measure. Although craving reduced as plasma concentrations of naltrexone and 6-naltrexol increased, no upper threshold, which is typically determined by adverse events, was established since side effects were not known at this time [8]. The fifth study had some limitations. The first being the comparison between the study groups is not adequately justified and restricts the results because the precise average daily/weekly pill count is unknown because the count was calculated only from the patient diary. Except in the DIS group, where the average weekly alcohol consumption was doubled but still far below the baseline, the average weekly alcohol consumption remained at the level of the continuous medication period. The research medicine was not under strict control or monitoring, which is the second limitation. Patients were asked to name a follow-up person, which was not regulated by the research doctors. As a result, the findings cannot be compared to trials including a strict drug regimen or monitoring control [9].

6. Conclusion

To conclude, the findings from this review are that Naltrexone has shown better results than Acamprosate in maintaining abstinence and preventing relapse, as well as keeping alcohol dependent patients abstained from alcohol and preventing them from relapsing.

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