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Case Report

Anticraving Efficacy of Nalmefene in a Treatment Program to Alcoholism Oriented to Abstinence

David Cáceres Anillo[1], Carlos Morillo-Velarde Quintero[2], Esther Ontanilla Reyes[3] and Vanesa Canton[4]

[1]*Medical Director of Hogar Renacer Foundation , University of Córdoba, Spain*
[2]*Psychiatrist Hogar Renacer Foundation , University of Cordoba, Spain*
[3]*Psychologist Hogar Renacer Foundation , Universidad de Sevilla , Spain*
[4]*Degree in Nursing, University of Cordoba, Spain*

***Corresponding author**
David Cáceres Anillo, Medical Director of Hogar Renacer Foundation, University of Córdoba, C / Juan Felipe de Vilela No. 22, Cordoba, Spain. Tel: 34 -957 237388; Fax: 34-957454188; Email: david.caceres@hogar-renacer-cordoba.com

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Abstract

In the case presented, Nalmefene is administered daily as part of a comprehensive treatment program aimed at achieving and maintaining abstinence. Nalmefene is effective in achieving a significant maintained reduction in patient's level of craving during eight months, helping to increase significantly the abstinence time and to reduce patient's difficulties to prevent the relapse.

ABBREVIATIONS

HRCL: High Risk Consumption Level; **DSM - V:** Diagnostic and Statistical Manual of Mental Disorders 5th edition; **HDD:** Heavy Drinking Days: > or = 60 g alcohol / day in men or > or = 40 g / day in women; **TAC:** Total alcohol consumption (grams of alcohol/day)

INTRODUCTION

Nalmefene is the latest specific pharmacological contribution to treat alcohol use disorders [1]. Its efficacy has not been studied in comparison with other opioid antagonists and the available information of this drug currently remains scarce [2].

It acts differently on the opioid receptors, and this fact explains its modulating effect on this system, unlike naltrexone with which it only shares the antagonistic effect on Mu-opioid receptors:

- Exerting an antagonistic effect on the Mu - opioid receptor, like Naltrexone, it generates a craving decrease (desire or craving of alcohol in abstinent patient that leads him to start drinking) [3]. Its antagonism on Delta- opioid receptor also contributes to this effect.
- Its effect on priming reduction (loss of consumption control after the first alcohol drink), as some clinical trials has showed [4, 5] can be explained by the activity of this molecule on kappa opioid receptors: partial agonist effect.

Currently, this drug is indicated to reduce alcohol consumption in patients with alcohol use disorder (dependents and abusers) which submit an HRCL, as a part of psychosocial support program and it is used when patients perceive risk of consuming alcohol or intends to do so [6].

The present case is not strictly limited to this indication: It shows the benefits that it can produce as a part of an abstinence program for its ability to reduce craving levels, helping to prevent relapses and the abstinence maintenance.

CASE PRESENTATION

Background

We report the case of a man who is 44 years old, active worker as a lawyer, requesting assistance for alcohol use disorder in the outpatient consultation of Clínica Hogar Renacer.

In his clinical history many families's background of alcoholism are recorded (his father and three of his brothers). However, it does not collect any other psychiatric or medical history of interest.

He has not got any noteworthy medical background, however his psychiatric medical history included the presence of a diagnosis of Mixed anxiety-depressive disorder twelve years before the first contact. He had received antidepressant treatment on several occasions, with a partial response conditioned by their inability to maintain alcohol abstinence, which resulted in

a therapeutic incompletion. No other toxic consumption except alcohol.

The first treatment attempt to wipe out his alcohol use disorder was done in a non specialized center, with poor results. Then he went to specialized centers and initially he achieved abstinence periods up to 6 months, in programs that included the use of disulfiram depots and supportive psychotherapy. However, during the two previous years the periods of abstinence were dramatically reduced and the severity of relapses increased as they became more frequent and prolonged.

Initial assessment (Current Disease)

In the initial evaluation at our hospital the patient was diagnosed by Grave Alcohol Use Disorder 303.90 (Figure-1), meeting 9 of the 11 DSM - V criteria for this diagnosis (all except the criteria 8 and 11) [7].

The patient reports that his alcohol consumption started when he was 14 years old, although he did not begin to worry about his problem until he was 30 when he had a significant loss of consumption control.

During some years an intermittent consumption pattern connected to social contact was the predominant. However, in the last six years it worsened and it became in an alone pattern oriented to self-treatment of anxious- depressive symptoms or to reduce the presence of intense craving states.

During the previous year the patient reported adherence to the treatment program which consisted in disulfiram depot administration every 45 days and supportive psychotherapy. Information about the craving level during this period of time was collected. To measure the perceived craving the patient should indicate a value between zero (no desire to drink) and ten (uncontrollable desire to drink) in every situation. The patient reported that after administration of disulfiram depot and during the first 20-30 days of coverage craving level was low (3-4 / 10), and then it was gradually increasing moving from 5/10 at the 35 days to 9-10 / 10 between the 45 and the 60 days. The high craving level brings the patient to avoid the next disulfiram depot administration and it hastens the patient to start drinking again.

At the initial assessment, the patient has cyclic episodes of alcohol abuse every two months according to the pattern described, with an average duration of 4-6 days (2-3 days of excessive consumption –DEC- and with 150-200mg of alcohol per day – TAC-). During these episodes, the patient loses the control of the situation, abandoning completely his social, work and family obligations, and he presents inappropriate behavior and black- outs behavior with intense feelings of guilt and shame after the consumption.

During the last year he was the following pharmacological treatment:

Fluoxetine 20mg 1-0-0, Acamprosate 333mg 2-0-2, perphenazine 8 mg 0-0-1, Amitriptyline 12.5 mg / 5 mg medazepam 0-0-1 and depots Disulfiram every 45 days.

Starting blood test:

Intervention

The patient is incorporated into an outpatient treatment program aimed at maintaining abstinence which includes:

- Individual consultations for medical follow-up (two consultations / month), psychological (2-3 consultations / month) and psychiatric (a monthly consultation).
- Weekly attendance to Group Therapy in Relapse Prevention Program.

During the first month the coverage is done with oral disulfiram and disulfiram depots are administered every 45 days.

Acamprosate is suspended and Nalmefene treatment is initiated with 18 mg in 1-0-0 pattern taken daily. However, we indicate the patient that if he decides to abandon the abstinence goal and choose to drink alcohol he can keep taking Nalmefene to benefit from its antipriming effect.

We proceed to the first psychiatric evaluation and he is diagnosed of Induced Depressive Disorder in remission and we indicate a removal pattern of Perphenazine. The rest of the treatment is remained.

Evolution

The patient comes regularly to medical, psychological and a psychiatric monitoring review, as well as he attends weekly to the Relapse Prevention Group Therapy, showing adherence to pharmacological scheduled treatment.

In medical consultations the craving level that he felt in each period was evaluated every 15 days or so. It underwent a significant decrease maintained over time (Figure 1), keeping a 0-1/10 level since the second month of the treatment. It allowed prolonging the abstinence time up to 8 months and it facilitated a better adherence to the therapy program, without avoiding the disulfiram depot administration. From the first month of treatment no anxious or depressive symptoms appeared while he remained abstinent, showing an improvement in his quality of life.

After 8 months using Nalmefene, we proceed to removal it. It caused a later increase of the craving level. He abandoned the disulfiram depot treatment and he relapsed in alcohol consumption, following his previous alcohol pattern (100-150gr/ day of TAC during 3 days).

In connection with the Nalmefene tolerability we should note that during the first 4-5 days of the treatment the patient referred nonspecific complaints, as “mental dullness” and “generalized sense of skin hypersensitivity” with “feeling of metallic taste in the mouth”. The discomfort had a low intensity and it was self-limited, it disappeared spontaneously after the first few days of treatment.

DISCUSSION

We believe that this case reflects the efficacy of Nalmefene to reduce craving level in patients with Grave Alcohol Use Disorder, as it might be expected for their action on the mu opioid receptors, similar to naltrexone [8].

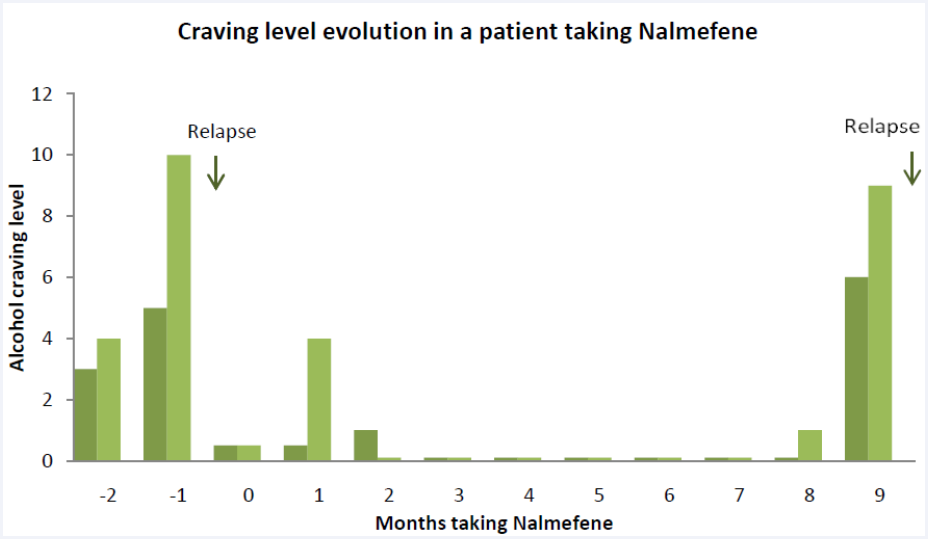

Figure 1 Craving level evolution in a patient taking Nalmefene.

It demonstrates its usefulness in everyday regimen to prevent alcohol consumption relapses as a part of a comprehensive treatment program aimed at abstinence, allowing his combination with other measures: combined used with aversive drugs, psychopharmacological treatments for dual diagnosis and individual and group psychotherapy.

In turn, that use is compatible with the indication as antipriming in case the patient suffers a consumption relapse. We should indicate the patient to continue taking the drug if he starts to drink alcohol in order to reduce the control loss as well as the relapse's negative consequences.

However, we must be cautious with this drug's indication, because of the limited studies published and the short clinical experience.

At the moment there is no evidence of the efficacy of Nalmefene as anticraving drug. Although in clinical practice we find it effective in specific cases, controlled studies are needed to confirm this and to support this indication.

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Conflict of Interest

We declare that it does not exist any financial interest or conflict of interest.

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