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ABUSIVE USE CONTROL OF ALCOHOL WITH PSYCHOPHARMACOLOGY CONTROLE DO USO ABUSIVO DO ÁLCOOL COM PSICOFÁRMACOS CONTROL DEL USO ABUSIVO DE ALCOHOL CON PSICOFÁRACOS

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Objective: to identify the main positive effects of treatment with psychoactive drugs in the control of alcohol abuse. Method: this is an integrative review, without temporal delimitation, in MEDLINE, CINAHL and LILACS databases. Incorporation of evidence was used. The procedures adopted for the critical analysis of the studies in three crossings identified 77 potentially eligible publications. In the end, five of them were selected by two independent researchers, using an instrument adapted to verify the level of evidence. Results: three psychoactive drugs were identified: acamprosate presented better tolerance and did not prevent late recurrence; naltrexone does not reduce the frequency of drinking, but reduces the intensity of consumption when used alone; the disulfiram effective in abstinence, with varied reactions. Conclusion: it is concluded that the results of the treatment of alcohol abuse with psychoactive drugs present high level of evidence, conditions, and recommendations for primary and secondary outcomes. Descriptors: Alcoholism; Substance-Related Disorders; Pharmacology; Psychiatric Nursing; Alcoholic Intoxication; Binge Drinking.

RESUMO

Objetivo: identificar os principais efeitos positivos do tratamento com psicofármaco no controle do uso abusivo do álcool. Método: revisão integrativa, sem a delimitação temporal, nas bases de dados MEDLINE, CINAHL e LILACS. Utilizou-se incorporação de evidências. Os procedimentos adotados para a análise crítica dos estudos, em três cruzamentos, foram 77 publicações potencialmente elegíveis, selecionando-se, ao final, cinco por dois pesquisadores independentes, usando-se instrumento adaptado para verificar o nível de evidência. Resultados: identificou-se três psicofármacos: o acamprosato apresentou melhor tolerância e não evita a recorrência tardia; a naltrexona não reduz a frequência de beber, porém reduz a intensidade do consumo quando usada isoladamente; o disulfiram eficaz na abstinência, com reações variadas. Conclusão: conclui-se que os resultados sobre o tratamento do uso abusivo do álcool com psicofármacos apresenta elevado nível de evidência, condições e recomendações para os resultados primários e secundários. Descritores: Alcoolismo; Transtornos Relacionados ao Uso de Substâncias; Farmacologia; Enfermagem Psiquiátrica, Intoxicação Alcoólica; Bebedeira.

Objetivo: identificar los principales efectos positivos del tratamiento con psicofármaco en el control del uso abusivo de alcohol. *Método*: revisión integradora, sin la delimitación temporal, en las bases de datos MEDLINE, CINAHL y LILACS. Se utilizó la incorporación de evidencias. Los procedimientos adoptados para el análisis crítico de los estudios, en tres cruzamientos, fueron identificadas 77 publicaciones potencialmente elegibles. Al final se seleccionaron cinco por dos investigadores independientes, usando instrumento adaptado para verificar el nivel de evidencia. Resultados: Se identificaron tres psicofármacos: el acamprosato presentó mejor tolerancia y no evita la recurrencia tardía; la naltrexona no reduce la frecuencia de beber, sin embargo reduce la intensidad del consumo cuando usada aisladamente; el disulfiram eficaz en la abstinencia, con reacciones variadas. Conclusión: se concluye que los resultados sobre el tratamiento del uso abusivo del alcohol con psicofármacos presentan elevado nivel de evidencia, condiciones y recomendaciones para los resultados primarios y secundarios. *Descriptores*: Alcoholismo; Trastornos Relacionados al Uso de Substancias; Farmacología; Enfermería Psiquiátrica; Intoxicación Alcohólica; Borrachera.

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INTRODUCTION

Drug use that changes mental status follows the history of the human being for religious, cultural and recreational reasons as a way of coping with personal and social problems. As a mental disorder, the diagnosis is multifactorial, including compulsion until the abandonment of social activities. 1 Thus, currently, the abuse of alcohol and other drugs becomes relevant to explore the theme. mainly because it is a global public health problem. Epidemiological studies, in view of the National Survey of Alcohol and Drugs (LENAD), show that 17% of Brazilians use alcohol or are dependent on alcohol, with 9% showing a detrimental effect on the family nucleus.2

Alcohol is responsible for 1.8 million deaths a year worldwide. Within this overwhelming perspective of deaths, young people between 15 and 29 years old are the most affected. Thus, approximately 60 pathologies are related to the harmful use of alcohol.³

The abusive use of alcohol can lead the user to risk behaviors, family complications, social and health problems. Studies show that 48.7% of a university population does not have safe sex when they are under chemical effects, 27.3% have headaches and 3% have alcoholic coma.⁴

In a nationwide analysis, the largest outbreaks of chemical consumption were detected in 149 municipalities, with a percentile of 52 million people. Of them, 15.6% became chemical dependents.⁵

A survey that generated the I National Survey on the Use of Alcohol and Other Drugs among University Students and conducted in 27 Brazilian capitals, determined that the prevalence of binge drinking for men is 43.7% and 29% for women.⁶ Another study showed that 72.8% of respondents felt ill due to alcohol use.⁴ Thus, there is an imminent need for an educational project on drug use, also encompassing public policies of control of alcohol use.

The psychological and social implications of the treatment of alcoholism are traditionally psychosocial focused on interventions, incorporating recently pharmacological components.⁷ With pharmacology plausible care option, there are interventions such as tracking related problems to the use, promotion of debates, conversations circles and alert about abusive use.4

In view of the satisfactory family life, which is desirable, although the different forms of organization in Western societies are recognized, it is important to highlight the

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importance of evaluating family factors in the treatment, providing information relevant to the development of comprehensive care to the users and their families.⁸

Given the above, as motivation and justification, this study intends, through an integrative review, to answer the following guiding question: What are the main positive effects of treatment with psychoactive drugs in the control of alcohol abuse?

OBJECTIVE

 To identify the main positive effects of treatment with psychoactive drugs in the control of alcohol abuse.

METHOD

This is an integrative review⁹ in which the six steps were adopted: the guiding question of the research was defined, the criteria of inclusion and exclusion, the databases and the search of the scientific productions were carried out, the data was analyzed, the data was discussed and the synthesis of the review was presented.¹⁰

The databases and library used were Scientific Electronic Library Online, Medical Literature Analysis and Retrieve System Online (PUBMED/MEDLINE), Cumulative Index to Nursing and Allied Health Literature (CINAHL), and Latin American and Caribbean Literature in Health (LILACS). Both virtual scenarios were accessed by two researchers, concurrently, in different computers, in order to guarantee reliability in the selection of articles eligible for the research. It was opted for the lack of time cut, to capture all publications available in each database, with the intention of providing a broad selection of studies.

Complete articles available free of charge in the selected databases, which addressed the results on the main positive effects of treatment with psychoactive drugs in the control of abusive use of alcohol, published in Portuguese, Spanish or English were the defined inclusion criteria, with the exception of studies in editorial format, letter to the editor, dissertations and theses, experience report.

From the point of view of methodological rigor, it is emphasized that an integrative review serves different purposes and directions for elucidation of concepts, revision of theories or methodological analysis of the included studies of a particular topic, allowing, in the end, a general picture against the evidence found.⁹

The descriptors indexed in Descriptors in Health Sciences (DeCS) and Medical Subject Headings (Mesh): Alcohol Abuse, Psychotropic,

Drug Therapy and Drug Interactions were adopted in the survey of the articles. Subsequently, the crossing of the descriptors was performed as follows: Alcohol Abuse AND Psychotropic; Alcohol Abuse AND Psychotropic AND Drug Therapy; Alcohol Abuse AND Psychotropic AND Drug Interactions, characterized as a controlled search: Alcohol Abuse AND Psychotropic - MEDLINE / PUBMED = 1.372, CINAHL = 659, LILACS = 04; Alcohol Abuse AND Psychotropic AND Drug Therapy - MEDLINE / PUBMED = 81, CINAHL = 214,

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LILACS, 00; and subsequent level of evidence (LE) and referral forces (RF) of the scientific publications included in this study classified according to the scale Oxford Center for Evidence-based Medicine - Levels of Evidence. 9,11-2

After completing the initial data collection stage and applying the inclusion and exclusion criteria, by reading each article, there were the following the steps: title and abstract; and in its entirety, the sample consisted of four articles.

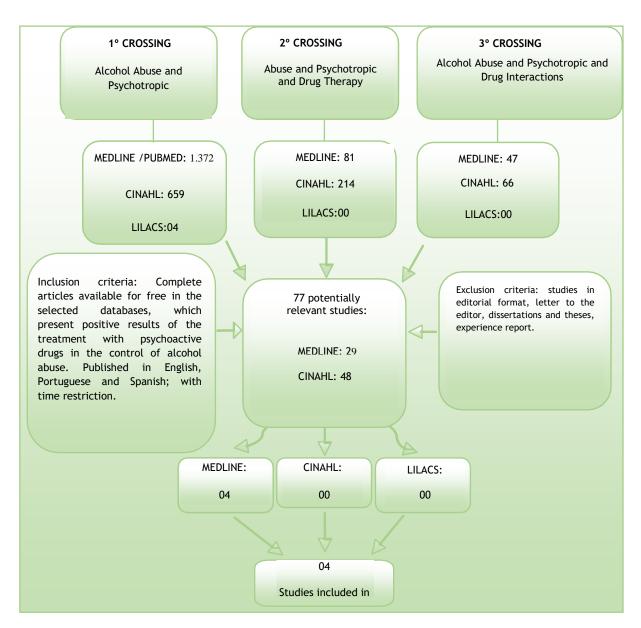


Figure 1. Search strategy and selection of articles in the databases of CINAHL, PUBMED/MEDLINE and LILACS Natal (RN), Brazil, 2018.

To meet the objective and the research question, the analysis of the data was based on the following routing: identification of the article; year of publication; place of research development; authorship; goals; study design; level of evidence, drug used for treatment with psychoactive drugs in the control of alcohol abuse; positive result of drug treatment for alcohol abuse.¹³

RESULTS

Regarding the years of publication of the articles, timeliness was chosen, but results were obtained for the period from 2011 to 2015. All the journals analyzed are of origin and foreign language, more specifically, in English. Most of the research was done in the United States of America, totaling four articles and only one of them in Canada. Of them, the three drugs found in the studies as categories objectively highlighting the respective therapeutic classes and the main positive effects during the treatment of

people who abuse alcoholic beverages. Three psychotropic drugs were identified: Acamprosate; Disulfiram (DSF), Naltrexone (NTX).

It should be noted that the three drugs are used in the treatment of alcohol dependence in adults, approved in Brazil and the US, respectively, by the National Agency of

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Sanitary Surveillance (ANVISA) and Food and Drug Administration (FDA), while Naltrexone is approved for alcohol dependence in Europe. The results were classified according to the level of evidence. The caption was adopted: P: Population; ** LE: Level of Evidence; *** UD: Used drug; **** TC: Therapeutic Class (Figure 1).

	Plac				Methodol					Positive
Ar tic le	e Cou ntry Year	Authorsh ip	Objective s	P*	ogical rigor	Method	LE **	UD* **	TC* ***	Results
Reducti on of Alcohol Drinkin g in Young Adults by Naltrex one: A Double- Blind, Placebo - Control led, Rando mized Clinical Trial of Efficacy and Safety. 16	Estados Unidos 2015	O'Malley SS, Corbin WR, Leeman RF, DeMarti ni KS, Fucito LM, Ikomi J, Romano DM, Wu R, Toll BA, Sher KJ, Gueorgu ieva R, Kranzler HR.	To compare the efficacy and safety of naltrexo ne administ ered daily with a placebo-controll ed dosage to reduce alcohol intake in young adults engaging in excessiv e consump tion of alco hol.	140	A study with two parallel groups, taking One hundred and forty patients for a period of eight weeks.	A double- blind, placebo - controll ed study of naltrex one.	1A	Naltrexone	Opioid antagonist	Reduced secondar y measures of drinking intensity by reducing and the amount of alcohol ingested.
Acampr osate Produce s Its Anti- Relapse Effects Via Calcium . 20	United States- 2014	Rainer Spanag el; Valenti na Vengeli ene; Bernd Jandel eit Wolf- Nicolas Fischer , Kent Grindst aff; et al.	To elucidat e the molecul ar mode of action of acampr osate in calcium channel relapse.	1,5 mil hão	Six types of studies containin g an extensive screening panel, data in vitro and preclini cal studies	Functi onal flow tests.	1A	Acamprosate	nes	Patients treated with acampro sate with elevated calcium levels (active portion) showed improve ments in the primary efficacy paramet ers, such as time to relapse and abstinen ce cumulat ive.

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	Lo		_	Methodolo					Positiv
Artigo	ca Autor l a Pa ís Ano	ri Objectives	P *	gical rigor	Method	L N* *	UD* **	TC* ***	e Results
Pharmacog enetics of alcohol, nicotine, and drug addiction treatments . 23	Jessi ca ES, Tony PG, Jame s LK, Andr eas H, Danie I JM	drug addiction, pharmacot herapy,	141 + 60 4 / G+ 40 /A A + 31g = 816	Articles published between the year 2000 and 2010, where they evaluate the pharmaco genetic effects and their results in the treatment of dependen cy.	Bibliogr aphic researc h	1A	Naltrexone	Opioid antagonist	Alcoholdependentindividuals with a Gallelehavebetterclinicalresponses, includinglowerrates of relapse.
Gabapenti n Combined With Naltrexon e for the Treatment of Alcohol Dependen ce. 17	Raymond F. Anto n, M.D., Hugh Myric k, M.D., Tara M. Wrig ht, Patri cia K. Lath am, Ph.D. Ph.D. et al.	persistenc e of the effects of naltrexone and its placebo during the early withdrawal phase of the drink (first six weeks).	1 5 0	Um total de 150 indivíduos dependen tes do álcool foram alocados aleatoria mente para um curso de 16 semanas com naltrexon a sozinho e naltrexon a com Gabapenti na até as primeiras 6 semanas.	Ensa io clíni co	1B	Gabapentina + Naltrexona	iista Opiáceo	A interação medicam entosa de naltrexo na / gabapen tina teve mais tempo para a recaída.

Figure 2. Summarization of the selected articles regarding the variables of interest. Natal (RN), Brazil, 2018.

DISCUSSION

Previously, when discussing psychotropic drugs in abusive alcohol control, it is noteworthy that the treatment of alcohol and other drugs are part of the network of psychosocial care for people with alcohol and other problems related to drugs, which emphasizes the authors' familiarity with the

psychosocial care processes focused on alcohol and other drugs.

It concerns the clarification that psychopharmacological treatment refers to the hospital-centered context, which differs from the primary health care network, general hospitals, emergency and specialized services and the psychosocial area.¹⁴

The network of care in all these spaces alone does not guarantee the transformation of the modus operandi, insofar as the abusive use of alcohol associated with other drugs, alcohol becomes a causal factor for the development of more than 60 types of diseases.¹⁵

The most commonly used drugs were Naltrexone and Acamprosate. 11-4 Disulfiram was mentioned as aversive in treatment. Thus, it is necessary to discuss with the users about the options available for the treatment to sensitize them regarding their co-

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responsibility in choosing the best drug according to the medical indication, as well as best adherence practices. The conviction and motivation for total abstinence from alcohol to use Disulfiram is fundamental since serious adverse effects can lead to death. 16-7

One of the main strategies for the treatment of these dependents is pharmacological therapy (Figure 2), even though it still presents low success rates. 18-9

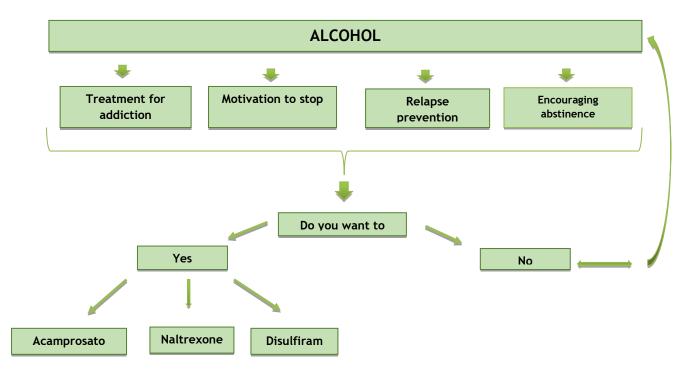


Figure 3. Proposed psychopharmacological intervention for the abusive use of alcohol from the articles in the libraries and databases PUBMED/MEDLINE, CINAHL, and LILACS. Natal (RN), 2018.

♦ ACAMPROSATO

Patients with elevated plasma calcium levels from the Acamprosate treatment had better primary efficacy parameters, such as time to relapse and abstinence.²⁰

Acamprosate has a similar effect to gamma-aminobutyric acid (GABA), acting in the decrease of the excitatory activity of the Central Nervous System. Therefore, it is considered a partial agonist of N-methyl-D-aspartate (NMDA) receptors, in this way it acts in neurotransmitters, gabaergic, taurinergic and glutamatergic, acting as benzodiazepines.²⁰

It is worth highlighting the effects of Acamprosate that are described in more than 450 initial investigations and published clinical trials and 1.5 million treated patients, possibly attributed to calcium.²¹

A research developed by the Program of the Interdisciplinary Group of Alcohol and Drug Studies/GREA of the University of São Paulo showed that Acamprosate was efficient in a group of people surveyed, where 25% of the patients who were receiving Acamprosate and 20% of the patients receiving treatment, that is, 75% of the population studied evolved to a positive prognosis.²²

Acamprosate has been a drug that presented better tolerance in the individuals surveyed, so the substance does not prevent late recurrence.²⁰

The most common adverse effects are diarrhea, headache, nausea, vomiting and heartburn. Acamprosate has no alcohol interaction and can continue to be used even if the patient has relapsed. It should not be used in patients with severe liver or kidney problems.²⁰

♦ DISULFIRAM (DSF)

Disulfiram is specifically classified as a drug for the treatment of drug dependence. DSF is an enzymatic inhibitor, where it acts in the dopaminergic system, inhibiting the conversion of dopamine to norepinephrine in the reaction catalyzed by dopamine betahydroxylase.²¹

It is the first drug approved for the treatment of alcohol dependence and it

remains one of the most used agents. It produces an opposite reaction with alcohol, interfering in the metabolization of alcohol. alcohol is initially converted acetaldehyde, which is then metabolized by enzyme aldehyde dehydrogenase. the inhibits this latter reaction, Disulfiram leading to an accumulation of acetaldehyde, which triggers unpleasant effects such as nausea, vomiting, palpitations and headaches when the individual uses alcoholic beverages. 18-22

Patients should always be informed about the reactions caused by the drug Disulfiram. The reactions are the most varied, for example: facial flushing, sweating, nausea, palpitations, shortness of breath, hypotension, dizziness and convulsions, and may present more serious reactions such as myocardial infarction, loss of consciousness, heart failure and respiratory and death.²²

♦ NALTREXONE (NTX)

An opioid antagonist, that is, it is inserted in the class of opioids, where it has demonstrated effectiveness in the reduction of relapses.¹⁶

In a study on the effects of NTX, a randomized, double-blind, placebo-controlled type with the following criteria: age between 18-25 years old, reporting \geq 4 days of heavy consumption in the previous 4 weeks. Interventions included Naltrexone 25 mg per day and 25 mg targeted (maximum per day) in anticipation of consumption (n = 61) or placebo per day (n = 67).¹⁷

Every participant every two weeks received a personalized feedback session and brief counseling. The main results were for one hundred days of heavy consumption and abstinence during the treatment period for eight weeks. Secondary outcomes included a number of probable doses per day and percentage of days with estimated blood alcohol levels (BAC) $\geq 0.08 \, \text{g/dL.}^{17}$

Studies confirm possible genetic predisposition to consumption and problems related to drinking. The NTX did not reduce the frequency of drinking or days of heavy consumption, but reduced the intensity of drinking, although the effects are modest, it has a risk-benefit ratio, to help young adult drinkers in reducing the amount of alcohol they drink.²³⁻¹⁷

Three placebo-controlled clinical trials have found that alcohol-dependent individuals with a G allele have better clinical responses, including lower relapse rates, in NTX than those with the A allele. In another with alcohol-dependent patients, found that individuals with a G allele had lower relapse rates with NTX, while those receiving placebo

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did not differ from other genotypes in terms of relapse.²³

In the last of the three trials conducted with individuals of European ancestry, the presence of a G allele was found to be associated with the reduced drink and increased abstinence in NTX, while subjects with an AA genotype showed no difference in response. A study with heavy drinkers showed that the ability of NTX to block alcohol-induced stimulation, positive mood, desire, and appreciation was greater in patients with the G allele.²³

In a study of 150 alcohol-dependent individuals, they randomly received sixteen weeks of Naltrexone (50 mg / day [N = 50]) with Gabapentin (up to 1200 mg / day [N = 50] for the first six weeks), or placebo twice (N = 50) while receiving medical treatment. In the first phase, the Naltrexone/Gabapentin group had more time to relapse than the Naltrexone alone group - (p = 0.04), which in turn was not different from the placebo group. However, during the remainder of the trial, there were no differences between the treatment groups (Naltrexone/Gabapentin Naltrexone/placebo). 17

Naltrexone is an approved drug for the treatment of heavy alcohol consumption, that is, addiction related to the consumption of alcoholic beverage. The results of the tests in patients alcoholic showed that combined with psychosocial interventions, Naltrexone decreased the chance of relapse by 50%, reduced the desire to drink and the number of drinking days presenting a better result than that associated with another drug. Common side effects are nausea, headache, anxiety, and drowsiness. Naltrexone is used at a dose of 50 mg once daily.²²

The numerous early deaths, medical complications and socioeconomic implications drugs and alcoholism improvements in treatment strategies with the contributions of pharmacogenetics as a means to predict response to medication. Side effects and appropriate dosages are relatively new conditions and situations in the field of drug addiction. In the literature on pharmacogenetics advances are observed in the field of drug dependence, particularly for alcohol and tobacco, to provide a summary of implicated efficacy genes in the pharmacotherapy for dependence.

Studies have pointed to the prediction of clinical response to Naltrexone in alcoholism and nicotine replacement therapy in smokers with genetic factors. Opinions differ on pharmacogenetic tests, in particular on cost-

effectiveness, requiring further investigation.¹⁶⁻²³

For many years pharmacotherapeutic interventions for alcoholism were restricted to the period of detoxification and to the treatment of signs and symptoms of alcohol withdrawal syndrome, in an often emergent character. In general, substance use disorders are prevalent in sectors of general and psychiatric emergencies, reaching rates of 28% of occurrences in general emergency rooms. However, professionals in the emergency sector identify less than 50% of cases of alcohol-related problems.²⁴

The limitation of scientific knowledge resulting from the present study and from personal experience is recognized beforehand, but the critical analyzes found in the articles allow us to conclude that of the four studies, three studies presented levels of evidence 1A and 1B. 16-23

Regarding the degree of recommendation, the level studies, on the one hand, present as a strong representation in the choice. excellent levels of evidence to recommend the conduct with Naltrexone, Acamprosate, and Disulfiram whose benefits have a weight greater than the gain, therefore they present conditions and recommendations for use. On the other hand, studies with level of recommendation B of level 1 refer to the generalization of the findings that can recommend the action in function of the important outcomes in relation to the risks of damage, can be supported the recommended its use. 11-2

From a pharmacokinetic point of view, the opioid antagonist has a satisfactory effect with a higher degree of recommendation. Therefore, Naltrexone is the most evident psychotropic drug in publications for the control of alcohol either alone or associated with benzodiazepines, enzyme inhibitor dopaminergic and anticonvulsant drugs. 16-17

In this sense, this study highlights the main effects on the control of alcohol abuse, independent of the primary and secondary effects, besides the uncertain benefit that some of the psychotropic drugs may present, as well as the genetic effects:

Reduction of the intensity of drinking, and the amount of alcohol ingested; improvements in relapse time and cumulative abstinence; in the chronic use of alcohol relieves the psychological and physiological discomfort and reduction in craving for alcohol.

Regarding the countries of origin of the studies, the USA and Canada predominated,

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which can be said that Brazil as well as Latin America and the Caribbean do not have studies on the positive effects on the control of alcohol abuse with psychoactive drugs, on the basis of data, during the period studied, and, according to the inclusion and exclusion criteria. Therefore, it indicates a gap in the knowledge that requires future investigations. The statistics show that millions of Brazilians have alcohol dependence, which makes clear the need to improve the treatment of alcoholism.¹⁸

The prevalence of alcohol use is very high worldwide. Because of its legal drug status, there is no legal control as for substances such as opium, cocaine, cannabis, among others. However, there are similarities in both as dependence. On the one hand, the importance of the treatment of alcohol was equated with that of opioids, with laws uniformly throughout the world for its control, as a public health policy.²⁵

On the other hand, the adoption of an effective and efficient educational strategy starts in the school context, because the preadolescents' initiation into the use and abuse of alcohol and other drugs is occurring more and more prematurely. Interdisciplinary and intergenerational dialogue should be added in the centrality of the educational process, even recognizing the precariousness of affective relationships and social and cultural conditions as critical ones, stirring up the fragility of the family and school, but potentially capable of exercising their protective roles and prevention in the fight against alcohol and drugs.²⁶

CONCLUSION

Acamprosate has better tolerance and does not prevent late recurrence, indicating continued use. Naltrexone whose modest effects do not reduce the frequency of drinking nor days of consumption, but reduces the intensity. Disulfiram shows efficacy in abstinence whose reactions are as varied as possible.

Scientific publications related to drugs for the treatment of alcohol dependents are scarce, representing a scientific gap. Thus, it is necessary to develop new studies due to the importance and relevance of the theme.

Finally, the limitations of the study are recognized, which does not make it less relevant, but it encourages the deepening in relation to psycho-drugs and alcohol abuse that has not yet been explored.

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