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Pharmacological treatment in the smoking cessation program in Brazil and the world

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Tratamento farmacológico no programa de cessação do tabagismo no Brasil e no mundo
Tratamiento farmacológico en el programa para dejar de fumar en Brasil y en el mundo

RESUMO

Objetivo: identificar como tem sido o tratamento farmacológico para pessoas inseridas no Programa Nacional de Cessação do Tabagismo (PNCT). Método: trata-se de uma revisão integrativa de literatura de artigos selecionados nas bases de dados: Biblioteca Virtual em Saúde e Pubmed, de 2015 a 2020, nos idiomas português, inglês e espanhol. Utilizou-se os descritores: Tabagismo e tratamento medicamentoso. A seleção foi feita através de uma adaptação do protocolo PRISMA, resultando em 7 artigos que compõem a revisão. Resultado: a associação de vareniclina com aconselhamento comportamental e redução gradual do número de cigarros antes de parar de fumar aumentam as taxas de cessação tabágica. Outras terapêuticas promissoras como Yoga, micronutrientes e a psilocibina ainda precisam de estudos posteriores. Conclusão: como tema de grande interesse para a saúde pública, espera-se que os achados possam melhorar o PNCT e instigar novas pesquisas brasileiras sobre a condução terapêutica nos grupos de cessação do tabagismo.
DESCRITORES: Saúde Pública; Tabagismo; Tratamento farmacológico.

ABSTRACT

Objective: to identify how the pharmacological treatment has been for people included in the National Tobacco Cessation Program (NTCP). Method: this is an integrative literature review of articles selected in the databases: Biblioteca Virtual em Saúde and Pubmed, from 2015 to 2020, in Portuguese, English and Spanish. The descriptors were used: Smoking and drug treatment. The selection was made through an adaptation of the PRISMA protocol, resulting in 7 articles that make up the review. Result: the association of varenicline with behavioral counseling and a gradual reduction in the number of cigarettes before smoking cessation increases smoking cessation rates. Other promising therapies such as Yoga, micronutrients and psilocybin still need further study. Conclusion: as a topic of great interest to public health, it is expected that the findings can improve the PNCT and instigate new Brazilian research on therapeutic management in smoking cessation groups.
DESCRIPTORS: Public Health; Tobacco Use; Pharmacological treatment.

RESUMEN

Objetivo: identificar cómo ha sido el tratamiento farmacológico de las personas incluidas en el Programa Nacional de Cesación del Tabaco (PNCT). Método: se trata de una revisión integrativa de la literatura de artículos seleccionados en las bases de datos: Biblioteca Virtual em Saúde y Pubmed, de 2015 a 2020, en portugués, inglés y español. Se utilizaron los descriptores: "tabaquismo" y "tratamiento farmacológico". La selección se realizó mediante una adaptación del protocolo PRISMA, resultando 7 artículos que componen la revisión. Resultado: la asociación de vareniclina con asesoramiento conductual y una reducción gradual del número de cigarrillos antes de dejar de fumar aumenta las tasas de abandono del hábito de fumar. Otras terapias prometedoras como el yoga, los micronutrientes y la psilocibina aún necesitan más estudio. Conclusión: como tema de gran interés para la salud pública, se espera que los hallazgos puedan mejorar el PNCT y suscitar nuevas investigaciones brasileñas sobre el manejo terapéutico en grupos de cesación del tabaquismo.
DESCRIPTORES: Salud Pública; Uso de tabaco; Tratamiento Farmacológico.

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INTRODUCTION

Smoking is a disease caused by nicotine dependence, and is related to the main reasons for morbidity and mortality from chronic non-communicable diseases (NCDs), such as cancer, lung and cardiovascular diseases. The World Health Organization (WHO) estimates that there are more than 1.1 billion smokers in the world and that more than 8 million people die annually from tobacco-related problems. [1]

In order to reduce damage, Primary Health Care (PHC), based on the guidelines of the National Tobacco Control Program (PNCT - Programa Nacional de Controle do Tabagismo), carries out actions in groups or individuals aimed at smoking cessation. The guideline is also linked to drug treatment, which helps users to minimize the symptoms of nicotine withdrawal syndrome. The Unified Health System (SUS) provides drug therapies such as nicotine replacement therapy (NRT) in the form of a transdermal patch/chewing gum and bupropion. [2] Already around the world, therapies include NRT in the forms of transdermal patch, chewing gum, oral inhaler, nasal spray, sublingual tablet and lozenge), bupropion and varenicline. [3]

It is already public knowledge that the problem of smoking cessation is the result of a social, psychological and political context that has historically favored individuals to start smoking and made it difficult for others to stop smoking. In view of this, during the treatment period, in addition to pharmacological measures, it became important to manage psychosocial interventions to also be able to assess situations of greater risk of relapse and possible obstacles. [4]

Brazil has shown a decreasing prevalence of tobacco use due to the actions adopted by the PNCT, despite this, this number is still high and there are projections of greater growth in the sale of other tobacco consumption devices for the coming years, such as electronic cigarettes. [5] Thus, it is essential to question how research has approached drug treatment and how new therapies are being used around the world to control tobacco use. The objective of the research is to identify in the scientific literature how drug treatment has been conducted for people who participate in the PNCT.

METHOD

This is an integrative literature review, developed respecting the following phases: 1) problem formulation; 2) data collection; 3) data evaluation; 4) data analysis; and 5) presentation and interpretation of results. The problem formulated (phase 1) is the need to acquire the knowledge available in the literature on the clinical practice of professionals to tobacco users participating in the smoking group in health units.

Data collection (phase 2) took place in the Virtual Health Library (VHL) and Pubmed database, using the Decs/Mesh descriptors: Tobacco use disorders (Tabagismo) and Drug therapy (tratamento medicamentoso) integrated by the Boolean connector "and", in all search strategies, according to the associations "tobacco use disorders and drug therapy" and "tabagismo and tratamento medicamentoso."

Inclusion criteria were: original article, published in full and available electronically, published between January 2015 and December 2020, in Portuguese, English or Spanish, regardless of the method used. Regarding exclusion: literature reviews/reflection, editorials, annals abstracts, theses, dissertations, course conclusion work, epidemiological bulletins,

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management reports, research developed with animals, official documents from national or international programs, books that do not meet the objective of this research and duplicates.

In the data collection phase, all the works were read, and in order to extract the information, an instrument was developed in order to obtain the results that showed how the treatment for smoking cessation has been conducted. To illustrate the process of selecting the works that were part of this review, an adaptation of the protocol for systematic reviews PRISMA Flow Diagram was used. [6]

After mapping the manuscripts in phase 3, the aid and operationalization of the data was carried out, using the MAXQDA Plus 2020 Student software, under license number 258245855, which consists of a free program that performs lexical analysis of words,

which allows different processing and analysis of the narratives produced. 7 For the construction of classes, words with $p<0.001$ (from the software) and convergence with the inference of the data were used. In the final stage of presentation and interpretation, the results were presented in a table, containing the characterization of the studies and in classes that emerged from the content.

RESULTS

The search in the databases resulted in 3,286 publications. After a thorough reading and application of the eligibility criteria, [7] articles remained, which include this integrative review (Figure 1).

All selected works are quantitative and international research, published in 2015, 2016 and 2017. Of these, most were carried out in the United States (n=3) and the others in the United Kingdom, Taiwan, Japan and Chile. No studies were found in Bra-

Figure 1. Flowchart of search and selection of studies.
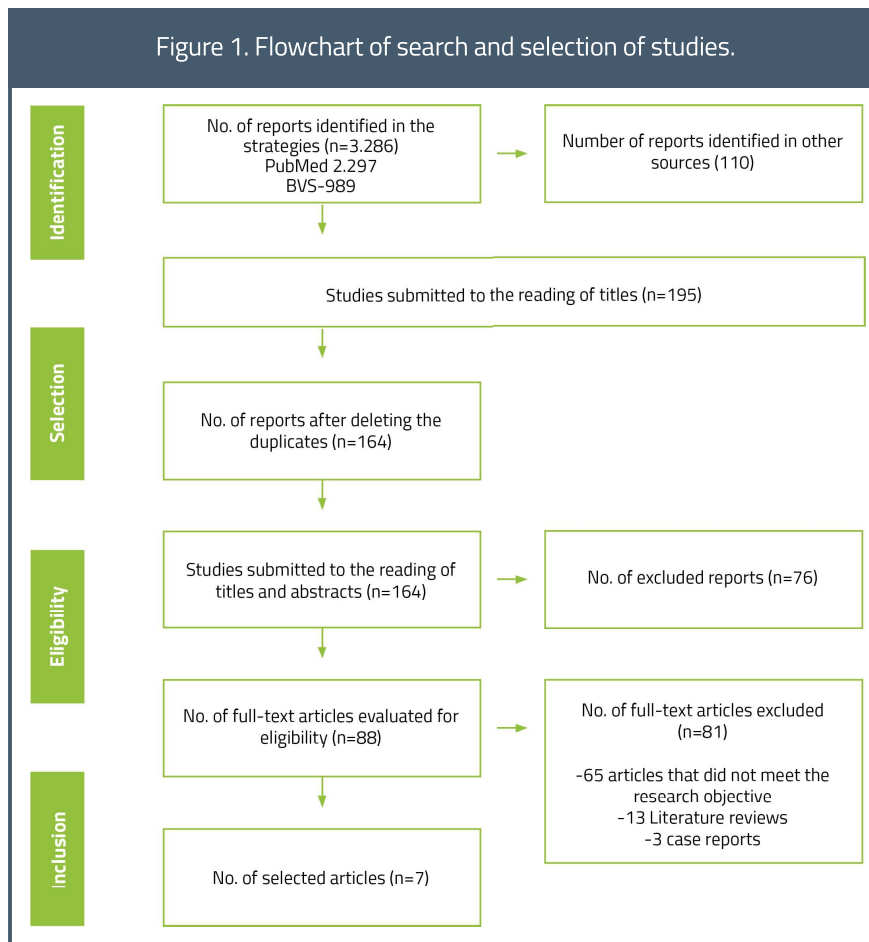
Source: Authors, 2021.

zil that addressed the criteria selected for this review.

Regarding the level of evidence, the studies were evaluated using the methodological approach based on the recommendations of the Agency for Healthcare Research and Quality (AHRQ). [8] According to their classification, the articles were categorized: level 1, controlled and randomized clinical trials (n=2); level 2, study with experimental design (n=4); level 3, quasi-experimental studies (n=1). The main results of the selected articles are listed in Table 1.

Figure 2 shows the word cloud, made from the organization of data in the MAXqda software, produced

from the main results of the studies that contemplate this review, highlighting the following words: varenicline, smoking, cessation, abstinence, smoking, stop and NRT, which will provide support to the categories listed from the analysis, identifying the emphasis of each study.

From the association of the results found in the analysis of the word cloud and the main results of the articles, the following classes were constructed: differentiating therapies used in the smoking cessation program around the world; and, identifying existing innovative therapies in this process.

In the first class, differentiating therapies used in the smoking cessa-

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ID	Main results	Year
	Table 1: Identification of the articles selected for the research.	
A01[19]	The highest rate of cessation was among participants who used prescription drugs (varenicline, bupropion, among others) and behavioral counseling, followed by those who used NRT along with behavioral counseling. While the lowest rate was among those who used only NRT. Another factor analyzed was the duration of medication use, the highest rates of cessation were among smokers who used the prescribed medication or NRT for more than 5 weeks. Higher socioeconomic status was also associated with a higher dropout rate and there was little evidence of the influence of sex.	2015
A02[10]	The study targeted smokers who used monotherapy for smoking cessation and were categorized into four: those who used patch-type NRT, chewing gum-type NRT, varenicline, or bupropion, in their first course of treatment. Participants who self-reported more abstinence were those using varenicline compared to patch users, regardless of gender or level of nicotine dependence. Differences in efficacy were not seen between users of bupropion, chewing gum and patch.	2016
A03[11]	The reduction in smoking in the Japanese subpopulation was consistent with the total reduce-to-quit (RTQ) study population, in which a higher rate of participants receiving varenicline compared to those receiving placebo reduced the number of cigarettes smoked by at least half in the fourth week. Therefore, treatment with varenicline and cigarette reduction before smoking cessation may provide an alternative approach to smoking cessation in smokers who wish to quit but are not ready or able to quit immediately.	2017
A04[12]	The study addresses people in a smoking cessation group with psychological support and varenicline use, who were followed up with telephone interviews for one year. The results presented leave the door open for future research aimed at intensifying therapy in subgroups at greater risk of failure, such as high dependence on the Fagerström test and those with low education. In them, it is possible to configure the hypothesis that more psychological sessions and prolonged pharmacological treatment could influence a better result.	2016
A05[13]	The Stop Smoking Service offered by the UK uses behavior change techniques in combination with personalized pharmacotherapy. It was found that men who participate in the smoking cessation service are more likely to be able to stop smoking, in addition to age and the type of counseling provided, which influence individual performance. Concomitantly, the use of varenicline in relation to NRT improves dropout rates in women when treatment occurs at 4 weeks. However, it is observed that women receive varenicline as an aid less frequently than men, which is an imbalance that can be corrected in the future.	2016
A06[14]	Studies show that the most effective smoking cessation medications generally demonstrate less than 31% abstinence at 12 months after treatment, while the present study found 60% abstinence more than a year after psilocybin administration. However, this may have been influenced by the small sample, open-label design, lack of a control condition, and the fact that the study only involved individuals who were motivated to quit smoking.	2017
A07[15]	Ninety-three participants were randomized. At the end of the study (6 months), the point prevalence of smoking abstinence rate was 40.0% in the varenicline group compared to 20.8% in the placebo group, and the prolonged smoking abstinence rate was 31 .1% and 8.3%, respectively. Nausea and sleep disturbance were more commonly reported in the varenicline group. But in the end, varenicline was both safe and effective in increasing smoking abstinence rates in a predominantly white smoking population. Varenicline's efficacy in this study was comparable to that seen in heavy smokers.	2016

Source: Authors, 2021.

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tion program around the world, most studies on the treatment of tobacco dependence have focused on interventions that use pharmacotherapy associated or not with behavioral therapy, since only the drug approach may be ineffective. Furthermore, it should be considered that such methods differ according to the protocols of each country, with cultural differences.

The second class, entitled identifying existing innovative therapies in the smoking cessation process, points out that the use of innovative therapies alone or associated with traditional treatment can be more effective in smoking cessation. New approaches are needed, as there is low adherence and high relapse rates among people undergoing conventional treatments. It should be noted that there are numerous factors that contribute to relapse, such as environmental, psychological and socioeconomic factors, which must be considered.

DISCUSSION

For smoking cessation to be successful, multiple factors must be taken into account. In Brazil, treatment for smoking cessation in the SUS, according to the PNCT, consists of counseling, mainly with a cognitive behavioral approach and pharmacological support. [16] Groups of smokers are also organized, in which weekly sessions lasting 90 minutes are held, which are recommended until the end of treatment, in order to increase patient maintenance rates. Pharmacotherapy, according to the PNCT, consists of NRT (transdermal patch, chewing gum, lozenges) and Bupropion. [17] In addition to these drugs used by the SUS, Varenicline is very effective, but less used than NRT, probably due to its high cost. [16]

To demonstrate which drug would be most effective in smoking cessation, a study of the smoking cessation

Figure 2. Word cloud organized using MAXqda software.
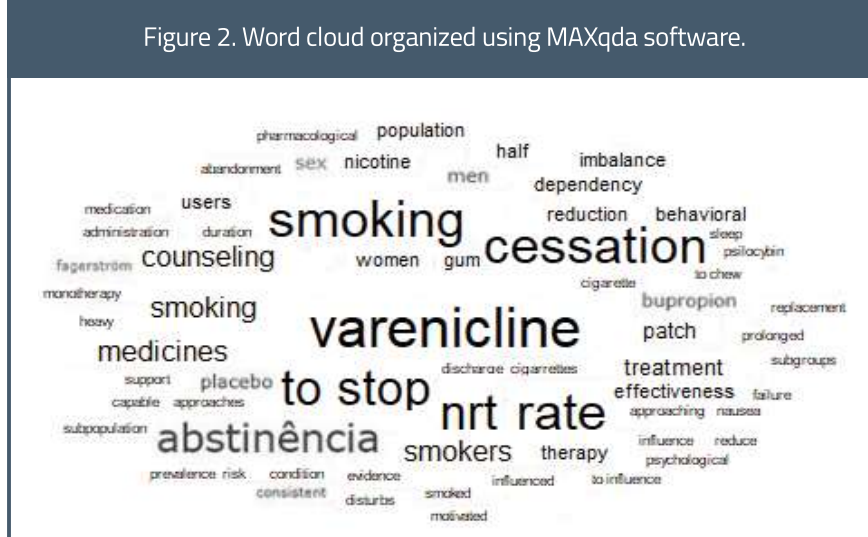
Source: Authors, 2021.

program in Taiwan targeted smokers who used monotherapy, being categorized into four: patch-type NRT, chewing gum-type NRT, varenicline or bupropion, in your first course of treatment. Participants who self-reported more abstinence were those using varenicline compared to patch users, regardless of gender or level of nicotine dependence. There was no difference in effectiveness between users of bupropion, chewing gum and patch. [10]

When combined, NRT proved to be more effective than using NRT alone. This was proven in a survey conducted in primary care clinics in Hong Kong, where participants were randomized to combined NRT (counseling, patch and nicotine chewing gum) or single NRT (counseling and nicotine patch). During the study period, participants in the combined NRT group were more likely to quit smoking than the other group, having the highest abstinence rate during an 8-week treatment. [18] However, using pharmacotherapy (varenicline, bupropion, or NRT) for more than 5 weeks is associated with a higher likelihood of quitting tobacco compared to using pharmacotherapy for shorter

periods, using only behavioral counseling, or trying to quit unaided. [9]

An Oxford study carried out in clinics among light smokers (up to 10 cig./day) also proved the effectiveness of varenicline in conjunction with an individualized behavioral counseling program. Participants received varenicline or placebo for 12 weeks and results were evaluated at 3 and 6 months, proving the drug's safety and efficacy in a predominantly white smoking population. [15] To analyze the differences in the quit rate between men and women, data from the Stop Smoking Service showed that men are more likely to be able to quit smoking. The use of varenicline in relation to NRT increases the dropout rate, especially in females. However, it is observed that women receive varenicline less frequently than men, which is an imbalance that can be corrected in the future. [13]

A randomized trial conducted in Australia aimed to assess the long-term (104 weeks) efficacy of varenicline plus Quitline counseling (telephone follow-up offering treatment for addictions) compared with Quitline counseling alone, in

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patients hospitalized for tobacco-related illnesses. It was found a greater efficiency, clinically and statistically, in favor of drug treatment together with counseling, when compared to counseling alone, and may become a standard for the treatment of hospitalized smokers, without increased risk of adverse effects. [19]

Data from a national sample of the general US population also demonstrated that combining pharmacotherapy with behavioral counseling increases smoking cessation success. Those participants who used either bupropion, varenicline, or NRT along with counseling had higher dropout rates compared with those who used NRT alone. [9]

According to a large-scale research, having individual counseling for at least 6 months, regardless of pharmacotherapy, can increase the chance of quitting smoking by between 40% and 80%, compared to minimal support (brief advice, usual care, or provision of self-help materials). [20] However, behavioral counseling alone was more effective than using Varenicline or Bupropion alone for less than 4 weeks. [9]

A survey carried out in Chile also evaluated the association of Varenicline with personalized CBT, which focuses on the processes of motivation, strengthening of the will and prevention of relapses. Of the patients who were treated with Varenicline who completed one year of follow-up, the majority achieved complete abstinence within one year, demonstrating the benefit of associated psychological and pharmacological therapy. Failure rates may be related to higher risk subgroups, such as those with high dependence on the Fagerström test and those with low education. [12]

In addition to the therapies commonly used for smoking cessation, other methods have been studied to increase smoking cessation rates.

One of these would be Psilocybin, a pharmacotherapy that demonstrated a 60% abstinence rate after one year, compared to 31% abstinence using other drugs or CBT alone. However, this may have been influenced by the small sample, lack of a control condition or by the study involving only individuals motivated to quit smoking. Because of this, more research on this treatment is needed. [14]

Another alternative approach was developed in Japan, using the "reduce to quit" (RTQ) method, which gradually reduced the number of cigarettes smoked before quitting. In it, a higher rate of participants receiving Varenicline compared to those receiving placebo managed to reduce the number of cigarettes smoked by at least half in the fourth week, providing an option for smoking cessation in smokers who want to quit but are not ready or unable to quit immediately. [11]

In addition to these researches, a clinical trial investigated the impact of micronutrients in reducing smoking, particularly in the first 4 weeks of abstinence. In it, it was found that the ingestion of capsules containing minerals, vitamins, amino acids and antioxidants, moderated the stress of withdrawal and promoted a reduction in the number of cigarettes smoked, whose results were evaluated by measuring carbon monoxide levels. However, further studies are needed. [21]

The association of CBT with Yoga proved to be effective for smoking cessation, as Yoga reduces stress, negative mood and can help with weight control, factors that are barriers to quitting smoking. The results showed that in addition to light smokers, heavy smokers had a significant reduction in daily cigarette consumption, being more likely to quit smoking. [22]

CONCLUSION

The results of this review showed that the main strategies used in the world for smoking cessation include CBT associated with drug therapy (varenicline, bupropion and NRT). However, no studies were found in Brazil that addressed the criteria selected for this review, demonstrating the need for further research on therapeutic management in smoking cessation groups in the country.

Drug therapy associated with CBT, recommended by the Ministry of Health, helps in the addiction cessation process, but international studies have shown that using varenicline, despite its high cost, is more effective than bupropion or NRT.

An alternative to increase the smoking cessation rate would be the use of pharmacotherapy for at least 5 weeks, being more effective than trying to quit smoking alone. Another successful option would be to gradually reduce the number of cigarettes before quitting associated with varenicline, an alternative for smokers who are not ready or unable to quit promptly. In addition, behavioral counseling proved to be more effective when performed for a longer period and with more intense individual follow-up.

In addition, different types of innovative therapeutic approaches were found, such as the use of micronutrients, Psilocybin and Yoga, which proved to be effective, however, they require further studies. As the topic of smoking is of great interest to Public Health, it is expected that the findings of this project can in the future complement and improve the PNCT offered by PHC, in order to increasingly reduce the number of smokers as well as the comorbidities associated with tobacco in the country and that this study can stimulate new Brazilian research on this topic.

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