

Opioid consumption and prescription in Brazil: integrative review

Uso e prescrição de opioides no Brasil: revisão integrativa

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ABSTRACT

BACKGROUND AND OBJECTIVES: In the past twenty years, the number of deaths caused by opioid overdose has tripled in the United States. There is, in literature, a scarcity of up-to-date evidence regarding opioids consumption in the Brazilian scenario. The objectives of this study was to know, through a literary review, the pattern of opioid analgesics consumption in Brazil.

METHODS: An integrative review of the literature, performed in the PubMed, BVS and Scielo databases from August 30 to October 22, 2020. The search strategy included the following terms, “Opioid-related disorders” or “Opioid epidemic” or “Opioid analgesics” and “Brazil”. Inclusion criteria: published in the last five years; studies on humans. Exclusion criteria: studies not related to the objective of this review; letters, editorials, commentaries and secondary studies.

RESULTS: The results showed patients’ dissatisfaction with pain management when compared to patients from developed countries, the lack of knowledge and adequate public policies on the use of opioids among health professionals make them view opioids as the last treatment alternative. The practice of analgesic self-medication is frequent in patients with chronic diseases, which may be the cause of the low prescription of opioid analgesics by health professionals.

CONCLUSION: It is noteworthy that there is a lack of data related to the prescription and use of opioids in Brazil. Further studies should be conducted to assess the use of opioids in general medical practice.

Keywords: Analgesics, Drug prescriptions, Opioids.

RESUMO

JUSTIFICATIVA E OBJETIVOS: Nos últimos 20 anos, o número de mortes causadas por overdose de opioides triplicou nos Estados Unidos. São escassas na literatura evidências atualizadas sobre o consumo de opioides no cenário brasileiro. O objetivo deste estudo foi conhecer, por meio de revisão literária, o padrão de consumo de analgésicos opioides no Brasil.

MÉTODOS: Revisão integrativa da literatura, realizada nas bases de dados Pubmed, BVS e Scielo, no período de 30 de agosto a 22 de outubro de 2020. A estratégia de busca incluiu os termos “Transtornos relacionados ao uso de opioides” ou “Epidemia de opioides” ou “Analgésicos opioides” e “Brasil”. Critérios de inclusão: publicação nos últimos cinco anos; estudos em humanos. Critérios de exclusão: estudos não relacionados ao objetivo desta revisão; cartas, editoriais, comentários e estudos secundários.

RESULTADOS: Os resultados mostraram a insatisfação dos pacientes com o manejo da dor quando comparados a pacientes de países desenvolvidos, a falta de conhecimento e de políticas públicas adequadas sobre o uso de opioides entre os profissionais de saúde faz com que estes vejam os opioides como a última alternativa de tratamento. A prática da automedicação analgésica é frequente em pacientes com doenças crônicas, o que pode ser a causa da baixa prescrição de analgésicos opioides pelos profissionais de saúde.

CONCLUSÃO: Faltam dados relacionados à prescrição e uso de opioides no Brasil. Novos estudos devem ser realizados para avaliar o uso de opioides na prática médica geral.

Descritores: Analgésico, Opioides, Prescrições de fármacos.

INTRODUCTION

Statistical data from the United States shows that in the last 20 years the number of deaths from opioid overdose has tripled due to increased prescription and an imbalance in the regulation and access to these drugs by the population¹. Particularly in developed countries, over-prescription of opioids results in misuse, and is highly related to abuse, addiction, and recreational use of these drugs².

In addition, the increase in life expectancy and better treatments that permit survival in previously lethal diseases in-

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HIGHLIGHTS

- Lack of public policies directed to the management of chronic pain;
- Lack of knowledge on analgesia by professionals;
- Prejudice against opioid analgesics.

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crease the demand for analgesia, alerting to the possibility of reverberation of the phenomenon in Brazil. In this context, data shows that there was an expressive increase in the average of Brazilian patients with chronic pain significantly higher than the world average, affecting 41% of the population². It is known, however, that the use of opioid analgesics in the Brazilian reality predominates basically in the fields of acute pain and chronic oncologic pain, with no data for chronic non-oncologic pain².

In the medical literature, little updated information and data overall is available on the use of opioids in the Brazilian scenario and possible developments, such as dependence and deviation of function. Considering the palpable possibility of a reflection of the North American opioid epidemic, this study is justified and aimed to comprehend, through a literature review, the pattern of opioid analgesic use in Brazil and disorders related to its use.

Understanding the need for more studies about the Brazilian reality, this study is based on the question: "What are the scenarios of opioid analgesic prescription for patients in general in the Brazilian reality in relation to rational use?"

METHODS

An integrative literature review, with systematized search, performed by five reviewers, the method consists of gathering and synthesizing the results of a literature search on a specific topic, in an orderly and systematic way, in order to contribute to the scientific knowledge previously elaborated on the subject³.

A literature review was carried out, in which qualitative and quantitative articles were included, according to the Preferred Reporting Items for Systematic Review and Meta-analyses (PRISMA) methodology⁴.

The PICO⁵ strategy allows, through the elaboration of a research question, an evidence-based bibliographic search. The construction of the research question must be based on the acronym PICO: Patient/problem (description of the problem or population), Intervention (proposed intervention), Control/comparison (description of the intervention), Outcome (intervention effect). Through the strategy, the following question was formulated: "What are the outcomes of opioid analgesics prescription for patients in general in the Brazilian reality in relation to rational use?", in order to search for papers that presented as characteristic the cross-sectional study follow-up extension.

For the search, the NCBI/Pubmed (National Center for Biotechnology Information), BVS (*Biblioteca Virtual em Saúde* - Virtual Health Library) and Scielo (Scientific Electronic Library Online) databases were used, whose accesses occurred between August and October 2020, with the date of the last search being October 22, 2020. The search strategy used was:

- search made in Scielo ("Advanced Search" was selected) - Used keywords: (tw:(Opioid-related disorders)) OR (tw:(Opioid epidemic)) OR (tw:(Opioid analgesics)) AND (tw:(Brazil)). Nine results were found and then additional filters were added: Portuguese or English (9 results) language, last 5 years (3 results). 3 results were obtained, 2 of which were used;

- search made in BVS ("Advanced Search" was selected) - descriptors used: (tw:(Opioid-related disorders)) OR (tw:(Opioid epidemic)) OR (tw:(Opioid analgesics)) AND (tw:(Brazil)). 109 articles were found. Then, the additional filters were added: publication year range in the last 5 years (2015 - 2020) + language: English (23), Portuguese (7) + full text (29). 29 results were obtained, 4 of which were used;

- search made in Pubmed - Keywords: Opioid-related disorders; Opioid epidemic; opioid analgesics; Brazil; Search strategy: ("Opioid-related disorders" OR "Opioid epidemic" OR "Opioid analgesics") AND Brazil. A total of 455 results were found. Next, the following filters were added: full text available; publication date in the last 5 years; English or Portuguese language. At the end of the search, 156 results were found, and 8 were used.

For the selection, the inclusion criteria used in the studies found were composed by the publication date of studies between 2015 and 2020, available in full in English or Portuguese, admitting publication bias, in addition to the content that addressed epidemiological, preventive, and social aspects of opioids in Brazil. In general, information on title, author, date of publication, number of participants, and results about prescription and use of opioids in Brazil were collected. Exclusion criteria were: studies not related to the objective of the present review; letters, editorials, commentaries, and secondary studies.

RESULTS

Figure 1 illustrates the path followed for the selection of studies. The number of articles found in Scielo, BVS, and Pubmed databases were 9, 109, and 455, respectively, totaling 573. After exclusion of duplicates, 546 articles remained. Next, 532 articles were excluded because they were not related to the PICO ques-

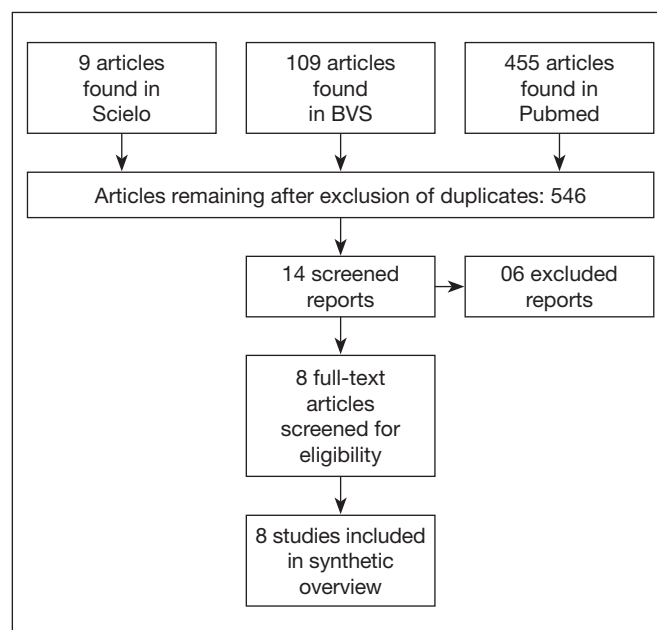


Figure 1. Study selection

Source: Prepared by the authors

tion of this systematic review. Subsequently, 6 articles were excluded due to the eligibility criteria. Finally, 8 articles remained and were included in the integrative review.

The characteristics of the studies used to assist in data extraction were presented, and are shown in table 1. The studies were listed as A1, A2, A3, consecutively, until the last article.

To combine the results of the different studies, each one was read individually and, through descriptive methods, the results presented reveal that there is a scarcity of data related to the prescription and use of opioids in Brazil.

Although the number of prescriptions of these drugs has grown, especially due to the increased use of codeine, there is still

Table 1. Description of selected studies

Authors	Studied sample	Main outcomes
Santos Garcia et al. ¹⁰	74 articles selected with the objective of discussing the main indications, pharmacological characteristics, safety, tolerability, availability, and impact on pain control provided by tramadol.	Tramadol is used to treat a broad spectrum of non-oncologic pain conditions (such as post-surgical, musculoskeletal, post-traumatic, neuropathic, fibromyalgia) as well as oncologic pain. Its relevance when treating special patient groups (e.g. the seniors) is recognized. Main reasons for tramadol's high importance as a treatment option are: its broad efficacy, a discrete safety profile, and its availability, considering that access to strong analgesics - mainly controlled drugs (classical opioids) - is highly restricted in some countries.
García et al. ¹¹	34 articles, found by searching Medline, LILACS, Scielo and EM-BASE databases, with the key words "Latin America" and "pain", and by manual search following recommendations of experts on the subject.	In Latin America, undertreatment of pain seems to be frequent, and a substantial number of patients feel that their pain is not adequately controlled. There is a scarcity of data related to pain management and opioid use in Latin America. Many chronic pain patients do not have access to effective opioid treatment. A variety of reasons lead to undertreatment of pain, including opioid-ignorance and opiophobia, use of nonsteroidal anti-inflammatory drugs (NSAIDs) and other non-opioid analgesics in patients with moderate to severe pain, limited access to health care, and regulatory barriers.
Krawczyk et al. ¹	Data from registered pharmacies throughout Brazil on the legal sale of opioids between 2009 and 2015, collected in ANVISA's Sistema Nacional de Gerenciamento de Produtos Controlados (National Controlled Products Management System).	Opioid sales increased nationwide from 1,601,043 prescriptions in 2009 to 9,045,945 prescriptions in 2015, corresponding to a 465% increase in 6 years. The largest absolute increase was for codeine products, accounting for over 98% of prescriptions in both years. Oxycodone had the largest relative increase, and fentanyl products had the smallest absolute and relative increase.
Silva et al. ⁹	41,433 people of all ages in Brazilian urban regions. The majority of the population was represented by women between 20 and 59 years old, with 1 to 8 years of schooling.	The majority of individuals were female (52.8%), aged between 20 and 59 years (57.2%), with 1 to 8 years of education (45.6%). The overall prevalence of analgesic use was 22.8%. The use of analgesics was significantly higher among women, adults and seniors (20 years or more), individuals with high schooling and respondents who reported: diagnosis of one or more chronic diseases, use of three or more drugs, with health insurance and with one or more admissions for emergency care or hospitalizations in the last year. Non-opioid analgesics were the most commonly used agents (18.5% of the sample), followed by NSAIDs (6.9%) and opioid analgesics (0.5%). The most commonly used drugs were metamizole (37.8% of all analgesics), paracetamol (25.3%), and diclofenac (10.7%).
Lino et al. ⁷	141,161 opioid prescriptions by 36,929 dentists.	A total of 141,161 opioid analgesics prescriptions were made by 36,929 dentists. The frequency of opioid type prescriptions was codeine associated with paracetamol n=117,493 (83.2%), tramadol n=13,562 (9.6%), codeine and other non-opioid analgesics n=4,308 (3.1%).
Avelar et al. ⁶	15,250 questionnaires were sent to Brazilian dentists about the prescriptions of psychotropics. 969 were answered.	257 professionals prescribe psychotropic drugs and 223 know the legislation. A worrying percentage of professionals prescribing these drugs do not know the content of the Administrative Rule 344/1998. Opioid analgesics are the most prescribed drugs. The specialists are the ones who prescribe the most psychotropic drugs, and those who prescribe anxiolytics know the legislation more often. Oral and maxillofacial surgeons and temporomandibular joint disorder specialists are the most familiar with the legislation and prescribe psychotropic drugs. Intense pain and fear are the two main reasons for prescription.
Krawczyk et al. ⁸	16,273 residents in Brazil, with data extracted from the 2015 Brazilian Household Survey on Substance Use (BHSU-3).	The prevalence in Brazil of non-medical use of opioid analgesics throughout life, in the last year, and in the last month was 2.9, 1.4, and 0.6, respectively. Considering those who responded having used the drug in the last year, the prevalence was lower among males, individuals between 12 and 24 years old, people with monthly family income above \$286.00, and unemployed.
Barros et al. ²	416 participants from an urban Brazilian population. 190 had chronic pain, with the majority being women. Of those with chronic pain, 149 were self-medicating with analgesics. 145 participants used non-steroidal anti-inflammatory drugs and only 4 used weak opioids.	Self-medication with analgesics is practiced by 78.4% of chronic pain patients. The most common analgesic treatment currently consists of nonsteroidal anti-inflammatory drugs (dipyrone and paracetamol). Weak opioids are rarely used and only 2.6% of individuals with chronic pain were taking these analgesics. None of the individuals were taking potent opioids.

Source: Prepared by the authors

an “opioid-ignorance” and “opiophobia” (coming from both the physician and the patient)¹¹, preference for the use of nonsteroidal anti-inflammatory drugs (NSAIDs) and other non-opioid analgesics, the limited access and high cost of opioids⁸.

The great problem on this issue is that patients show dissatisfaction with pain management, especially when compared to patients in developed countries, where the prescription of opioid analgesics is higher. In a way, the lack of knowledge and training on the use of opioids among health professionals⁶, associated with inadequate and restrictive public policies, make these professionals see opioids as a “last case” alternative.

Furthermore, the practice of self-medication with analgesics is frequent among individuals with chronic diseases, which can cause professionals to fear prescribing more potent analgesics. Self-medication with analgesics is practiced by 78.4% of patients with chronic pain². The most common analgesic treatment today consists of nonsteroidal anti-inflammatory drugs (dipyrone and paracetamol). Weak opioids are rarely used and only 2.6% of individuals with chronic pain were taking these analgesics.

However, even without access to these drugs, many Brazilians of all ages use analgesics to treat their pain, especially women, adults, and the seniors, opting for non-opioid analgesics, followed by NSAIDs, knowing that they may not be effective. When one looks at countries where opioids are more prescribed, such as the United States, where there are already programs for monitoring the prescription of opioid analgesics, it's possible to notice that Brazil has a very low number of prescriptions, which are more restricted to codeine dental prescriptions and prescriptions issued by oncology services, although many professionals do not know about the current legislation^{1,7,9}.

In Brazil, it's noticeable that, by the use of opioids in the treatment of moderate, intense, and chronic pain, the population may associate the use of opioids with cancer and end-of-life situations, which makes it difficult to prescribe them. Besides, these drugs also have a higher cost when compared to other analgesics, therefore, they end up not being an option for patients^{10,11}. Analyzing the risk of bias among studies, it was stated that there is the risk of publication bias, since publications in Portuguese and English were selected. However, the studies brought information that allows the conclusion that Brazil does not have recreational opioid use. No additional analyses were done in the present study.

DISCUSSION

From the results obtained, four justifications for the deficiency in opioid consumption in Brazil were elaborated: the Brazilian legislation, lack of knowledge of health professionals, public misunderstanding, and low priority of chronic pain as a public policy.

Brazilian legislation

The right of pain patients to receive adequate treatment is a basic premise of medicine, however, when assessing the Latin American scenario, one perceives that this right is not as well protected as it should be. Pain management is still inadequate due, mainly,

to the presence of an exacerbated regulation, resulting in unnecessary suffering for many patients¹⁰.

A survey conducted in the state of Minas Gerais with dentist-surgeons showed that those who know, even if superficially, the legislation, have 2.97 more chances of prescribing the appropriate drugs for the intensity of the patient's pain than those who do not know it. However, it is evident that 68.8% of the participants know about the existence of the legislation, but do not have a deep knowledge of the subject proposed by it¹.

In another analysis, among the factors that lead to the precariousness of opioid drug prescription in low-income countries, the fear of potential addiction, limited financial resources, bureaucracy of supply, and the low availability of opioid analgesics for application stand out. Still in this context, it is noteworthy that the restricted resources and infrastructure, associated with the costs of regulation, taxation and importation in low-income countries act as impediments to the correct analgesia of patients by inflating the prices of these drugs. Thus, one can relate the insufficient profit of manufacturers and importers when trading with such countries to the shortage of supply of these drugs and, consequently, to the apprehension regarding their use¹².

Lack of knowledge among professionals

Studies show that 41% of Brazilians have chronic pain, and opioids are the most important analgesics in the treatment of moderate to severe pain². Therefore, the Ministry of Health, in 2002, understanding the magnitude of the issue, created the National Program of Education and Assistance to Pain and Palliative Care¹³.

In Brazil, opioids are used mainly in the treatment of severe acute pain and chronic pain in oncologic patients, but they have been underused by health professionals in clinical practice in general. There is few data in the literature on the pattern of analgesic use in Latin America. However, there still is a belief that the medical community is afraid of stimulating the opioid crisis due to recreational use, as it already occurs in other countries².

In Latin America, tramadol is unanimously accepted in the treatment of patients with severe acute pain, such as postoperative, post-traumatic pain and low back pain, moderate to severe chronic pain in neuropathic conditions, osteoarthritis, moderate pain in senior patients unable to be treated with nonsteroidal analgesics, in patients with cancer pain, and fibromyalgia.

However, unlike what is recommended, in these countries the opioid is used almost as a solo drug and not as a member of a therapeutic arsenal for adequate analgesia in patients. There are some factors that explain its acceptability unlike other opioids, such as lower incidence of respiratory depression, lower risk of dependence and addiction, and lower immunosuppressive effect when compared to the others. In addition, it is easy to titrate and is available in various formulations, which facilitates access to the drug¹⁰.

This aversion to opioids is understood as opioid-phobia, that is, aversity to the prescription of opioids resulting from misinformation, fear of generating dependence, lack of knowledge, and inadequate training of health professionals regarding the use of

these drugs¹⁴. Therefore, the guidelines are not followed by the professionals, and the treatment is influenced by prejudices and previous personal experiences.

A study carried out with health professionals¹³ showed that doctors, pharmacists, and nurses are unaware of and have prejudices about these drugs. In one of the interviews, a pharmacist said that “the use of opioids should only be done in hospitals and under medical supervision and control”. In the interview with nursing professionals, the authors report that there was also a lack of knowledge of these professionals in some aspects, inferring that the little knowledge tends to underestimate the experiences of intense pain of their patients. In addition, two occurrences were observed in which, even though morphine was prescribed “if necessary”, the nurses would confirm with the medical team about the administration of the drug, which shows insecurity and fear on the part of the nursing team. When it came to the physicians, half of the interviewees did not reveal knowledge about the pain scales¹³.

It is important to emphasize that, in addition to the reasons already mentioned above, this topic is generally neglected in the training curricula of health professionals. Other difficulties encountered involve bureaucracy and the lack of multidisciplinary action of health professionals focused on pain management¹³. In the country, also, it is noticeable that analgesia is not provided in a totally adequate manner even in the oncologic scenario, depending on the health service where the patient is inserted⁹.

Prejudice from the population

Due to its use practically limited to oncology in the country, the population makes a simplistic association of the use of opioids exclusively in life-terminating situations⁹. Thus, in many situations where there is a suggestion of analgesic opioid treatment, patients are reluctant to accept it because they do not understand the clinical applications of the drug. In addition, due to the significant adverse effects of this class of drugs, many patients are limited to seeing the possible harm of its use instead of considering the cost-benefit relation of its use. In general, an “opioid-phobia” scenario occurs in the popular imagination, in which the use of opioids is limited to situations of contraindication for paracetamol or NSAIDs⁷.

Low priority of chronic pain as a health policy

The Brazilian population culturally uses analgesic drugs for pain control, especially non-opioids, having an increased prevalence of its use in women, seniors, individuals with higher education, individuals with chronic diseases, and polydrug users. The use of opioid analgesics in Brazil has a low incidence due to the low level of prescription of these drugs by health areas other than dentistry and oncology, services in which there is a large prescription of codeine, especially associated with paracetamol. This fact may infer the scarcity of adequate palliative care services in the country¹⁰.

In opposition to what happens in the United States of America, the consumption of opioids in Brazil is historically limited mainly due to the structural bottleneck and low budget of most public health services, the lack of integration between health care

and the uneven incorporation of palliative care in the various health services.

Nevertheless, an increase in the sale of opioids in pharmacies has been noticed during the period from 2009 to 2015, with a growth of 465%, stimulated mainly by the prescription of codeine, considered an analgesic for mild or moderate pain. When evaluating the absolute values, oxycodone, a drug sold under prescription retention regime with the objective of controlling its use in the country, showed the highest increase in consumption during this period, reflecting the growing use of opioids with more potent analgesic action and traditionally diverted for recreational use⁷.

Before presuming dependence and deviation of the drugs' function for their increasing prescription, it is prudent to point out that, especially in the case of Brazil, a better pain treatment may be taking place.

Despite this, there is a need for further investigation in order to improve the regulation and monitoring of prescription standards in the country, considering the importance of a clear direction in the education of professionals in order to enable access to adequate treatment by the patient without increasing the risk of misuse of opioids and the consequences that result from this¹. Another important aspect to be evaluated is the influence of socioeconomic factors related to health and to the Brazilian states, reflecting the existence of differences in access to these drugs according to geographical distribution. A survey with dentists noticed that Brazilian states with greater access to dentists have greater sales of opioid analgesics⁶.

Albeit contradictory, the 2015 Brazilian National Household Survey on Substance Use showed an opioid analgesic use higher in older age individuals and lower among people from higher income groups, which may be related to distinct socioeconomic conditions¹. Although heroin consumption seems to be insignificant, other opioids seem to be on the rise in Brazil either through legal or illegal means.

It is important to discern whether the current numbers reflect an important emerging public health problem and to ensure appropriate policies. Finally, although it is plausible to assume a deficiency of health policy regarding chronic pain control, it is not possible to infer an association with economic conditions.

CONCLUSION

Lack of medical training, insufficient education, and low priority of chronic pain as a health policy are growing concerns and result in unequal access to opioids and therefore inadequate treatment of patients. However, the authors highlight the shortage of data on opioid prescribing and consumption in Brazil. Further studies are needed in order to evaluate opioid use in general clinical practice.

AUTHORS' CONTRIBUTIONS

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Supervision

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