Risk of opioid abuse in non-oncologic chronic pain outpatient clinic

Risco de abuso de opioides em ambulatório de dor crônica não oncológica

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ABSTRACT

BACKGROUND AND OBJECTIVES: Chronic pain has become an extremely prevalent disease and an ever more recurrent reason for seeking medical attention. It has been treated with opioids, opening the possibility for abuse. This study's objective was to analyze the risk profile for opioid abuse in chronic pain outpatients.

METHODS: Cross-sectional study with 72 patients seen in an outpatient clinic of a public hospital in the period of July and August 2019. The variables analyzed were age, gender, comorbidities, drugs in use, and aspects related to pain such as intensity, anatomical location, etiology, and need to be absent from work. In addition, a questionnaire was applied to assess the risk of opioid abuse.

RESULTS: The study analyzed 72 patients with chronic pain, most of whom were women (84.7%). The mean age was 52.8 years. Patients were classified into three groups according to the risk of opioid abuse: high (21%), moderate (29%) and low (50%). There was an association of increased risk with opioid use (p=0.004) and presence of depression (p=0.003).

CONCLUSION: Half of the patients presented low risk for opioid abuse. Increased risk for opioid abuse is related to the presence of depression or depressive symptoms. No relationship was observed between benzodiazepines use and increased risk for opioid abuse. Patients considered at high risk for opioid abuse are more likely to develop aberrant behaviors. Knowing the patient's risk profile is necessary to increase the safety and effectiveness of chronic pain treatment.

Keywords: Analgesics opioids, Chronic pain, Prescription drug misuse, Risk management.

RESUMO

JUSTIFICATIVA E OBJETIVOS: A dor crônica tem se tornado uma doença extremamente prevalente e um motivo cada vez mais recorrente para procura de atendimento médico. Tem sido tratada com opioides possibilitando o abuso de seu uso. Este estudo teve como objetivo analisar o perfil de risco para abuso de opioides em pacientes ambulatoriais com dor crônica.

MÉTODOS: Estudo transversal com 72 pacientes atendidos em ambulatório de um hospital público no período de julho e agosto de 2019. As variáveis analisadas foram idade, sexo, comorbidades, fármacos em uso e aspectos relacionados à dor como intensidade, localização anatômica, etiologia e necessidade de se afastar do trabalho. Além disso, foi aplicado um questionário para avaliar o risco de abuso de opioides.

RESULTADOS: Foram analisados 72 pacientes com dor crônica, sendo a maioria mulheres (84,7%). A média de idade foi de 52,8 anos. Os pacientes foram classificados em três grupos conforme o risco de abuso de opioides: alto (21%), moderado (29%) e baixo (50%). Houve associação do aumento do risco com o uso de opioides (p=0,004) e com a presença de depressão (p=0,003).

CONCLUSÃO: Metade dos pacientes apresentou baixo risco para abuso de opioides. O aumento do risco de abuso de opioides está relacionado à presença de depressão ou sintomas depressivos. Não foi observada relação entre o uso de benzodiazepínico e o aumento no risco de abuso para opioides. Pacientes considerados de alto risco para abuso de opioides têm mais chances de desenvolverem comportamentos aberrantes. É preciso conhecer o perfil de risco do paciente para aumentar a segurança e eficácia do tratamento da dor crônica.

Descritores: Analgésicos opioides, Dor crônica, Gestão de riscos, Uso indevido de medicamentos sob prescrição.

INTRODUCTION

Chronic pain (CP) is a multidimensional health condition defined as pain that persists or recurs for more than three months, not considered a symptom, but a disease, directly impacting quality of life[1]. It's estimated that CP affects 34.5% of the population in general, that is, approximately three out of 10 individuals[2]. In Brazil, these numbers are not very different, since about 37% of the Brazilian population refer to this type of pain[3]. It's more associated with women, the elderly, smokers, people with less than 4 years of formal education, and people with anxiety or depression[4].

It's one of the most common reasons for seeking medical care because of its interference in several aspects of the patient's life, such as social, work, sexual, emotional balance and sleep[5]. Thus, its treatment becomes crucial for the improvement of quality of life.

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In that sense, opioid use constitutes one of the treatment options since there is proven efficacy regarding their short-term use in neuropathic and musculoskeletal pain. However, there are still controversies about their efficiency and safety in long-term use[6]. Adverse effects related to the use of opioids are also an issue, including constipation, urinary retention, cardiovascular effects, and some effects on the immune system[7].

Opioids predominantly exert their analgesic effects by binding to μ-receptors, which are densely concentrated in brain regions where they regulate pain perception, including emotional responses induced by pain, and in brain reward regions, providing feelings of pleasure and well-being, analgesia, and euphoria, which can lead to inappropriate drug use, characterizing abuse, a major concern in treatment[8]. The term abuse can be defined as misuse with consequences and with intent to modify or control behavior or mental state in a way that is illegal or harmful to oneself[7].

Recent years have seen a large increase in the prescription of opioid painkillers, especially in the United States. One study shows were 47 million prescriptions for this drug per quarter and by the end of 2013 that number reached 60 million. Between 1997 and 2005, there was a 933% increase in the number of methadone prescriptions. In addition, the number of unintentional deaths from opioid overdose shows a significant increase: rising 129% between 1999 and 2002. Moreover, individuals in chronic opioid use tend to have more psychiatric problems, such as depression and anxiety, as well as aberrant behaviors[9,10].

In Brazil, the number of opioid prescriptions also had a significant increase, especially with codeine and oxycodone, but there is still a low prescription of opioids for patients with CP resulting from the lack of training in pain management in Brazilian medical curricula[11,12].

Therefore, it's necessary to separate patients in risk groups regarding the abuse of these drugs. The Opioid Risk Tool (ORT) is one of the options to perform this screening, classifying the patient for low, moderate, or high risk, in an attempt to determine which patients, have a higher risk of developing opioid abuse, allowing to stratify and identify high-risk patients before the beginning and during opioid treatment with the purpose of establishing appropriate levels of monitoring, allowing options for other types of treatment, or treating possible substance abuse disorders[9,13].

The present study's objective was to perform risk stratification regarding opioid abuse in non-oncologic CP outpatients and associate biopsychosocial factors with this risk.

METHODS

Cross-sectional study conducted with 72 patients seen at the Pain Outpatient Clinic of Teaching Hospital of the Federal University of Sergipe (HU-UFS), between July and August 2019. It's not considered a pilot study due to its sample size being larger than that expected for a pilot study.

The data collected from the medical record and in an interview with the patient provided information regarding age, gender, comorbidities, drugs in use, aspects related to pain such as intensity, which was measured with the visual analog scale (VAS), anatomical location, etiology, need for time off work, and the translated ORT (Table 1).

Table 1. Translated Opioid Risk Tool

Questions		Score	
		Woman	Man
Family history of substance abuse	Alcohol	1	3
	Illicit drugs	2	3
	Prescribed drugs	3	4
Personal history of substance abuse	Alcohol	3	3
	Illicit drugs	4	4
	Prescribed drugs	5	5
Age	Between 16 and 45 years old	1	1
Preadolescence history of sexual abuse		3	0
Psychological diseases	Attention deficit hyperactivity disorder, OCD, Bipolar disorder or Schizophrenia	2	2
	Depression	1	1

OCD = obsessive-compulsive disorder

The tool evaluates personal and family history of alcoholism, smoking, abuse of illicit drugs and pharmaceuticals, age, history of sexual abuse, mental disorders and depression, establishing the score in relation to gender and classifying the risk of opioid abuse in high for zero to three points, moderate for four to seven and low for higher than seven points.

Depression diagnosis was based on the Hospital Anxiety and Depression Scale (HADS)[14]. The ORT has not yet been validated and cross-culturally adapted to the Portuguese language, which characterizes a limitation of the present study. Furthermore, it's also important to highlight that the small sample of an isolated service cannot be extrapolated to the reality of a continental country like Brazil, thus more detailed research and new more comprehensive studies are very important.

The study used a convenience sample. The inclusion criteria were patients over 18 years old, in treatment for non-cancer pain for at least six months, who were able to comprehend and answer the questionnaire, and who agreed to participate by signing the Free and Inform Consent Term (FICT). The exclusion criteria were: patients under 18 years old, having non-cancer pain lasting less than six months, who were not able to comprehend and answer the questionnaire, and who refused to participate.

The study was approved on 06/28/2019 by the Research Ethics Committee of the Federal University of Sergipe under CAAE number: 14385019.4.0000.5546.

Statistical analysis

Pearson's chi-squared test was used. The significance level adopted for rejection of the null hypothesis was 5% ($p \leq 0.05$).

RESULTS

A total of 72 patients diagnosed with CP who were undergoing specific outpatient follow-up at the HU were interviewed. The mean age of the patients was 52.8 years, with the minimum and maximum being 26 and 87 years, respectively. Of the 72 patients, 84.7% were women.

The most frequent sites of pain reported were lower back, generalized pain, head, face or neck, lower limbs, abdomen, upper limbs, thoracic region and pelvic region (Table 2).

Table 2. Distribution of patients according to site of pain

	n (%)
Lumbar region	27 (37.5)
Generalized pain	16 (22.2)
Head, face, or neck	10 (13.9)
Lower limbs	6 (8.3)
Abdomen	4 (5.6)
Upper limbs	3 (4.2)
Thoracic region	3 (4.2)
Pelvic region	3 (4.2)

The most frequent CP etiologies were miofascial syndrome, fibromyalgia, post-operative CP and post-traumatic CP (Table 3).

Table 3. Distribution of patients according to chronic pain etiology

Pain etiology	n (%)
Miofascial syndrome	27 (37.5)
Fibromyalgia	16 (22.2)
Post-operative	14 (19.9)
Post-traumatic	5 (6.9)
Herniated disk	3 (4.2)
Postherpetic neuralgia	2 (2.8)
Others	5 (6.9)

According to the ORT, 50.0% of patients were classified at low risk, 29.2% at moderate risk, and 20.8% at high risk for opioid abuse (Table 4).

Table 4. Distribution of patients according to risk for opioid abuse

Risk	n (%)
High	36 (50.0)
Moderate	21 (29.2)
Low	15 (20.8)

Daily use of benzodiazepines was quite common, being observed in 37.5% of interviewed patients, while the use of some type of opioids was seen in 13.9%.

An association between opioid use and increased risk for abuse of this drug was noted (p=0.004). In addition, there was a strong association between the patient having depression and the increased risk profile in the ORT (p=0.003) (Table 5).

Table 5. Distribution of patients according to opioid use, presence of depression and Opioid Risk Tool risk profile

Risk of abuse	Depression		Opioid use	
	Yes (%)	No (%)	Yes (%)	No (%)
High	13 (86.7)	2 (13.3)	6 (40)	9 (60)
Moderate	16 (76)	5 (24)	2 (9.5)	19 (90.5)
Low	15 (41.7)	21 (58.3)	2 (5.5)	34 (94.5)
Total	44	28	10	62
	p=0.003		p=0.004	

No association between benzodiazepines use and increased risk of opioid abuse was observed (p=0.464). However, there was an association between the use of this type of drug and the presence of depression (p=0.06).

DISCUSSION

Patients and doctors have different concerns about the adverse effects of opioid treatment. Doctors fear overdose, while patients fear addiction. Thus, a shared understanding of the risks and benefits that this treatment may bring is necessary[15].

CP has been widely associated to the female gender. The present study's sample revealed that the great majority of patients were women. In another Brazilian study with a sample of 27.000 patients, this same pattern was observed. Of the total number of patients with CP, 84.6% were women[16]. Similar results can be found in a study conducted in São Paulo[4]. More recent studies indicate that gonadal hormones, especially estrogen, act in the modulation of pain, and therefore can explain a factor related to this predominance in women[17].

The mean age of patients in the present study was 52.8 years, similar to the mean age obtained in other studies[18,19]. A study concluded that the prevalence of CP in individuals between 18 and 25 years old is 14.3%, while in the age group over 75 years it's 62%, revealing that the disease is more associated with aging[19].

The present study indicated the lumbar region as the most common site of CP. In this study, 37.5% of the patients had had pain for more than six months in this location. Similarly, the authors[13] presented that 35% of their patients reported pain in this region, which was also the site with the most complaints. Low back pain is one of the main causes of work-related disability and days missed from work[20]. Moreover, 54.2% of the patients in the present study claimed that they had to leave their jobs for at least seven days due to pain. This social impact is confirmed by another study[2], which showed that 61% of patients were less able or unfit to work outside their homes, 19% lost their job, and 13% had to change their activity because of the pain. Moreover, a study[21] showed that patients with CP associated with depression were more likely to be unable to work due to health problems.

The present study's sample classification by risk group for opioid abuse according to the ORT had results similar to those found in a work done with 114 cancer patients, which were classified as 57% for low risk, 22% for moderate, and 21% for high risk[10].

In the present study, it was observed that 13.8% of the patients were already using opioids, similarly to other results[22], in which 20% of the patients had been prescribed opioids. Moreover, it was also noted that the use of opioid analgesics was related to an increased risk profile for opioid abuse (p=0.004). Among the patients at moderate risk, 9.5% were using opioids and among those at low risk only 4.5% were using them. However, the high-risk group had 40% of patients using this type of drug, which is extremely alarming. Similarly, there are papers that have shown this same association. That is, patients at low risk tended not to have used opioids in the first six months of treatment, while those at high or moderate risk tended much more to have received this type of drug for treating CP[18].

The use of opioids is safe and has good results in the treatment of CP. Patients with no history of substance abuse such as alcohol, pharmaceuticals and drugs have a low likelihood of developing abuse if they are prescribed opioids. Nevertheless, the results obtained in this study are of great concern, as they show that half of the patients are at high or moderate risk for abuse of some drug of this class.

The most common behaviors of abuse described in the literature are soliciting opioids from other sources, increasing dosage without medical authorization, using opioids other than those prescribed, and skipping or canceling scheduled medical appointments. These behaviors are exhibited with greater frequency according to the increase in risk for abuse. In a study of 185 patients seen in a pain clinic, 94.4% of patients at low risk did not show aberrant behaviors, while among the patients classified at high risk, these behaviors were identified in 90.9%[9].

Also considering the association between biopsychosocial factors and the risk found, another aspect to be addressed in CP is the coexistence of depression or depressive symptoms in patients. In this study, 61.1% of the interviewed patients had depression associated with CP. The literature presents similar numbers: a study[21] with 1204 people diagnosed with CP showed that 60.8% of them met criteria for depression and that the costs to the health care system of these patients were higher compared to those without depression.

Several imaging studies have shown that brain regions activated by nociceptive stimuli can also be affected by various emotional and behavioral states. Moreover, nociceptive stimuli, consciously perceived, can be modulated by the emotional context. Thus, the relationship between these two diseases can be explained[23].

The association between the presence of depression and increased risk for opioid abuse (p=0.003) was also notable in this study. A study[24] observed that depression is related to long-term opioid use.

The number of patients with CP that use benzodiazepines is high. In the present work, 37,5% of the interviewees used benzodiazepines. Even though such use was not associated with increased risk for opioid abuse (p=0.464), there is evidence showing that patients on benzodiazepines need more opioids than those who do not use them[25]. Also, a study[25] showed that 29% of CP patients used some benzodiazepine, among whom 62% also used opioids, and that the group of patients using benzodiazepines was significantly more associated with opioid use, higher levels of depression, pain catastrophizing, and greater pain intensity than those not using benzodiazepines.

The study has limitations regarding the ORT, since it has not yet been validated for Portuguese, and to the small sample size (n). Moreover, it's also important to highlight that the small sample of an isolated service cannot be extrapolated to the reality of a continental country such as Brazil, since the research was carried out in a single center. Therefore, more detailed investigations and more comprehensive new studies are of utmost importance.

CONCLUSION

The study showed a higher prevalence of CP among women and adults, with the lumbar region being the most affected, and the most common etiology being myofascial syndrome. Furthermore, half of the evaluated patients presented low risk for opioid abuse. The increased risk of opioid abuse is associated with the presence of depression or depressive symptoms. No relationship was observed between benzodiazepines use and increased risk of opioid abuse. Patients considered at high risk for opioid abuse are more likely to develop aberrant behaviors. Knowing the patient's risk profile is necessary to increase the safety and efficacy of the CP treatment.

AUTHORS' CONTRIBUTIONS

Allan Guilherme Santana da Costa
Statistical analysis, Data collection, Research, Writing - preparation of the original, Writing - Review and Editing
Maria Luíza Souza Rates
Writing - Review and Editing
Vera Maria Silveira de Azevedo
Resource Management, Project Management, Supervision

REFERENCES

1. Treede RD, Rief W, Barke A, Aziz Q, Bennett MI, Benoliel R, et al. Chronic pain as a symptom or a disease: the IASP Classification of Chronic Pain for the International Classification of Diseases (ICD-11). Pain. 2019;160(1):19-27.
2. Breivik H, Collett B, Ventafridda V, Cohen R, Gallacher D. Survey of chronic pain in Europe: prevalence, impact on daily life, and treatment. Eur J Pain. 2006;10(4):287-333.
3. Giacomello CM, Paula TA, Ferreira LB, Kunde MA, Bastos PW, Teer R, et al. Chronic pain: mechanism based management. Acta Méd. 2018: 39(1):13-21.
4. Maia Costa Cabral D, Sawaya Botelho Bracher ES, Dylene Prescatan Depintor J, Eluf-Neto J. Chronic pain prevalence and associated factors in a segment of the population of São Paulo City. J Pain. 2014;15(11):1081-91.
5. de Souza JB, Grossmann E, Perissinotti DMN, de Oliveira Junior JO, da Fonseca PRB, Posso IP. Prevalência de dor crônica, tratamentos, percepção e interferência nas atividades da vida: pesquisa de base populacional brasileira. Pain Res Manag. 2017;2017:4643830.
6. Kalso E, Edwards JE, Moore RA, McQuay HJ. Opioids in chronic non-cancer pain: systematic review of efficacy and safety. Pain. 2004;112(3):372-80.
7. Kraychete DC, Garcia JB, Siqueira JT. Recommendations for the use of opioids in Brazil: Part IV. Adverse opioid effects. Rev Dor. 2014;15(3):215-23.
8. Trescot AM, Boswell MV, Atluri SL, Hansen HC, Deer TR, Abdi S, et al. Opioid guidelines in the management of chronic non-cancer pain. Pain Physician. 2006;9(1):1-39.

9. Webster LR, Webster RM. Predicting aberrant behaviors in opioid-treated patients: preliminary validation of the Opioid Risk Tool. Pain Med. 2005;6(6):432-42.
10. Barclay JS, Owens JE, Blackhall LJ. Screening for substance abuse risk in cancer patients using the Opioid Risk Tool and urine drug screen. Support Care Cancer. 2014;22(7):1883-8.
11. Krawczyk N, Greene MC, Zorzanelli R, Bastos FI. Rising trends of prescription opioid sales in contemporary Brazil, 2009–2015. Am J Public Health. 2018;108(5):666-8.
12. Moreira de Barros GA, Calonego MAM, Mendes RF, Castro RAM, Faria JFG, Trivellato SA, et al. The use of analgesics and risk of self-medication in an urban population sample: cross-sectional study. Rev Bras Anestesiol. 2019;69(6):529-36.
13. Carvalho RC, Maglioni CB, Machado GB, Araujo JE, Silva JR, Silva ML. Prevalence and characteristics of chronic pain in Brazil: a national internet-based survey study. Rev Dor. 2018;1(4):331-8.
14. Castro MM, Quarantini L, Batista-Neves S, Kraychete DC, Daltro C., Miranda-Scippa A. Validity of the hospital anxiety and depression scale in patients with chronic pain. Rev Bras Anestesiol. 2006;56(5):470-7.
15. Hurstak EE, Kushel M, Chang J, Ceasar R, Zamora K, Miaskowski C, et al. The risks of opioid treatment: perspectives of primary care practitioners and patients from safety-net clinics. Subst Abus. 2017;38(2):213-21.
16. Vieira EB, Garcia JB, Silva AA, Araújo RL, Jansen RC, Bertrand AL. Chronic pain, associated factors, and impact on daily life: are there differences between the sexes. Cad Saude Publica. 2012;28(8):1459-67.
17. Rosen S, Ham B, Mogil JS. Sex differences in neuroimmunity and pain. J Neurosci Res. 2017;95(1-2):500-8.
18. Jones JD, Vogelman JS, Luba R, Mumtaz M, Comer SD. Chronic pain and opioid abuse: factors associated with health-related quality of life. Am J Addict. 2017;26(8):815-21.
19. Fayaz A, Croft P, Langford RM, Donaldson LJ, Jones GT. Prevalence of chronic pain in the UK: a systematic review and meta-analysis of population studies. BMJ Open. 2016;6(6):e010364.
20. Refshauge KM, Maher CG. Low back pain investigations and prognosis: a review. Br J Sports Med. 2006;40(6):494-8.
21. Rayner L, Hotopf M, Petkova H, Matcham F, Simpson A, McCracken LM. Depression in patients with chronic pain attending a specialised pain treatment centre: prevalence and impact on health care costs. Pain. 2016;157(7):1472-9.
22. de Castro S, Cavalcanti IL, Barrucand L, Pinto CI, Assad AR, Verçosa N. Implementing a chronic pain ambulatory care: preliminary results. Rev Bras Anestesiol. 2019;69(3):227-32.
23. Hooten WM. Chronic pain and mental health disorders: shared neural mechanisms, epidemiology, and treatment. Mayo Clin Proc. 2016;91(7):955-70.
24. Sullivan MD, Edlund MJ, Zhang L, Unützer J, Wells KB. Association between mental health disorders, problem drug use, and regular prescription opioid use. Arch Intern Med. 2006;166(19):2087-93.
25. Cunningham JL, Craner JR, Evans MM, Hooten WM. Benzodiazepine use in patients with chronic pain in an interdisciplinary pain rehabilitation program. J Pain Res. 2017;10:311-7.