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RESEARCH ARTICLE

CALCULATOR OF PRESCRIBED OPIOID ADDICTION RISK FACTORS: OPI-CALC

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ABSTRACT

In recent years there is a growing tendency to prescribe opioid analgesics. Opioids are not the first-line treatment of chronic non-cancer pain, but it is becoming more frequent to see their prescription and, at the same time, they increase issues associated with them, such as side effects, risk of abuse / misuse and addiction, and deaths due to about dose. Because of this, it is fundamental to a patient with pain to perform a complete clinical history that allows us to assess the risk of future addiction that patient will have. As this evaluation is not always possible to perform correctly, and risk assessment tools are not diagnostic tools, we present a rapid, simple opioid addiction risk calculator, useful both for health professionals and for patients and based on evidence.

INTRODUCTION

International Association for the Study of Pain, (IASP, 2007) defines pain as "an unpleasant sensory and emotional experience, associated with real or potential organic injury, or that is described as caused by said injury". It is, therefore, a vital physical, cognitive, evaluative and emotional experience. It is not necessary to remember that chronic pain is a problem of first sanitary magnitude due to its high prevalence and the intense physical, emotional and social impact it causes in people who suffer from it. Pain relief is an ethical-care imperative and has been established as a priority objective of 21st century medicine (Hastings Center Report, 1996). The IASP's Montreal declaration in 2010 formally ratified the inclusion of access to analgesic treatment as a Fundamental Human Right (IASP, 2010). Population studies show that 19% of Europeans suffer from chronic pain (Spain is somewhat below the European average with 17%) (Torralba *et al*, 2014) and that in 34% of these the intensity the pain was classified as intense. The duration of chronic pain was greater than two years in 59% of cases, in 20% depressive symptoms were associated and in 19% there was loss of work due to this cause. 5% of patients with chronic pain, considered globally, required analgesia with major opioids. The experts considered in the light of these data that about 40% of patients did not receive adequate analgesic treatment (Collett *et al*, 2006). In recent years we have observed, in general and in different countries, an increase in the use of opioid drugs for the treatment of pain, especially chronic non-cancer pain. Sometimes, this use is justified by the relief it represents for the person to diminish or abolish the nociceptive sensation.

For this same reason, its use has spread and has become popular to extremes sometimes unjustifiable. Not all types of pain should be treated with this class of analgesics and it is always convenient to start in a phased manner, depending on the underlying pathology and using the most appropriate drug in each case. Opioids are very effective drugs for pain, but they are not exempt from complications; for example, they can produce a rebound effect and cause more pain instead of relieving it or they can even cause an addiction. Over the last two decades, there has been a radical change in the perspective of opioid analgesia. We have gone from a kind of opiophobia, with a restrictive medical use of opioid analgesics, to an opiophilia, with a substantial increase in its prescription throughout the world, especially for the treatment of non-cancer chronic pain (Angst *et al*, 2006). In this regard, it should be noted that, although there is clear evidence of the efficacy of opioids in severe acute pain, post-surgical pain and cancer pain, its effectiveness, especially in the long term, in chronic non-cancer pain. It is still controversial, since the follow-up studies do not go beyond eight months, much less than the usual treatment with opioids in most patients with chronic pain (Kalivas *et al*, 2005). Maintaining a balance between these two perspectives of opioid analgesia is complicated. The increase in the medical use of these drugs has clearly improved the treatment of many patients with chronic pain. But this increase in prescription has been accompanied by a marked increase in problems related to its long-term use (abuse, abuse, addiction and even deaths related to overdose in some countries). In the United States, this has become a serious public health problem of epidemic proportions, with very high direct health costs and with important social, psychological and physical repercussions for patients. This increasing problematic use of prescription opioid analgesics is a worldwide problem that affects many countries

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to varying degrees. There is even more concern that the global extent of the problem may be underestimated, since there is no reliable data on the medical and non-medical use of these drugs in much of the world. In the United States, the turning point of this change in the perspective of opioid analgesia we have to place it in the nineties, when the American Pain Society began to consider pain as the fifth vital sign and established that the strategies for The pain control that had been used until then did not present an optimal profile. Therefore, the experts advocated a greater use of opioid analgesics for the treatment of pain. From 1996 to 2012, in the USA UU there was an exorbitant increase in opioid production. But at the same time, this increase in the use of these drugs has been accompanied by an increase in side effects and related complications, including misuse, abuse and opioid addiction. A 2011 CDC report (Centers for Disease Control and Prevention) noted that prescription opioid analgesic sales were multiplied by fourteen in the period from 1999 to 2010 (Case *et al*, 2015). In 2011, 116 million Americans were treated with opioids and prescription is on the rise (Institute of Medicine, Relieving Pain in America, 2011). A meta-analysis published in 2015 estimated a prevalence of opioid analgesic addiction in the US population around 8-12% (Rudd *et al*, 2016).

Over the last decade, in the USA UU mortality rates from opioid overdoses have tripled, opioid-related emergencies increased by 153% and initiation of treatment for opioid use other than heroin increased by 236% (Jones *et al*, 2015). Although the prescription of opioid analgesics and the complications derived from their abuse and abuse in Europe have not reached the figures of EE. UU., These two parameters have increased enough to be considered something worrisome and priority. In 2013 it was estimated that some 455,000 people in Europe had criteria for addiction to prescription opioid analgesics, with the United Kingdom being the country with the highest rates, with a prevalence rate of 0.30%, followed by the Nordic countries (0, 15%), Germany (0.13%) and Spain (0.07%) (Hannu, 2013). In 2016, a study on the prevalence of the abuse of opioid nalgesics in five countries of the European Union (Germany, Denmark, Spain, United Kingdom and Sweden) placed Spain in first place in terms of prevalence both in the previous year and throughout life (Table 1).

Table 1. Prevalence of the abuse of prescription opioids

	Past Year %(DE)	Troughout Life %(DE)
Denmark	4,4 (0,5)	11,6 (0,8)
Germany	2,9 (0,2)	9,6 (0,4)
U.K.	6,2 (0,5)	14,6 (0,7)
Spain	6,8 (0,5)	18,3 (0,7)
Sweden	3,8 (0,5)	11,3(0,7)

(Hannu, 2013)

In the European Report on Drugs of 2016, (EMCDDA, 2016) the problem of opioids in Europe remains a fundamental issue, with a worrying increase in mortality related to these drugs. Up to eighteen European countries reported that more than 10% of patients who started treatment for opioid use had problems related to opioids other than heroin, with opioids most involved being methadone, buprenorphine, fentanyl, codeine, morphine, Tramadol and oxycodone. The Spanish Agency for Medicines and Health Products (AEMPS, 2017) has published two reports on the use of opioid drugs, based on data from the National Health System. The first report includes

the data for the period between 1992 and 2006, and the second shows the data for the period from 2008 to 2015. Over the last two decades there has been a substantial growth in the use of opioid analgesics in Spain, as has happened in other countries in Europe and the rest of the world. The role of opioid analgesics for the management of severe acute pain, postoperative pain and cancer pain is clearly established. But its long-term effectiveness in non-cancer chronic pain remains controversial, since most studies on its efficacy do not exceed twelve weeks and safety studies do not go beyond one year (Reuben *et al*, 2015). Therefore, major opioids should be reserved for chronic non-cancer pain in those cases in which the first two steps of the WHO analgesic scale have failed, and only if the expected benefits in relation to pain and functionality exceed those risks. Some neurosurgical techniques, including neurostimulation, nerve blocks, or neurolysis, have also been shown to be effective in this type of pain. In any case, regardless of the type of pain, the prescription of opioid analgesics must be adequate, prudent, safe and controlled (ASIPP, 2012). Although no absolute contraindication has been established for the use of these drugs in the treatment of pain, there is evidence that in certain cases it is advisable to avoid their use (Just *et al*, 2016). As a general rule, for the treatment of non-cancer chronic pain, it is recommended to follow the analgesic scale with a progressive approach, elaborating an individualized treatment plan that includes, from the beginning, pharmacological and non-pharmacological measures (Dowell *et al*, 2016). Opioids in non-cancer chronic pain should only be initiated if: another alternative therapy has not been efficient in terms of pain reduction AND pain significantly affects the functionality and / or quality of life of the patient AND the potential of the benefits of its prescription exceeds the damages. Opioids should only be maintained in continuation treatment when it has been well demonstrated that there is efficacy in terms of pain (after having made a therapeutic trial) (Chou *et al*, 2009), (Frieden *et al*, 2016). When possible, opioids should be combined with non-pharmacological therapies and non-opioid drugs at the lowest dose that achieves effectiveness (Dowell *et al*, 2016). Opioids should be considered as a chronic-based treatment only if there is a low risk of developing substance abuse disorder and the persistence of pain has not responded to treatment with non-opioid analgesics and antidepressants. It must be borne in mind that the evidence for the maintenance of long-term opioid therapy is limited and that the risk of overdose increases with increasing doses (Passik *et al*, 2009).

The risk assessment of therapy

Before starting opioid treatment in chronic non-cancer pain, clinicians should expose patients to the risks of overdose and developing an opioid use disorder (Chou *et al*, 2009), (Dowell *et al*, 2016). In addition, another of the important points of the therapy is to assess the risk / benefit of the prescription. There are instruments to identify those patients with potential risk of misuse / abuse of opioids prescribed at the beginning of treatment: The Screening goes Opioid Assessment for Patients with Pain (SOAPP), consists of 14 items, is self-administered and detects the first signs of a possible use / aberrant behavior in the future. It identifies 91% of patients at high risk (Butler *et al*, 2004). A revised version (SOAPP-R) consists of 24 questions and can also be used (Butler *et al*, 2008); The Opioid Risk Tool (ORT), is brief, self-administered, consists of 5 items with a dichotomous response (affirmative / negative). Its

items are: family and personal history of substance use, age, history of sexual abuse in preadolescence and psychopathology. Results from 0 to 3 are associated with low risk; from 4 to 7 with moderate risk, and results greater than 8 with high risk. Although it is easy and brief in its administration, it runs the risk of not being reliable in its results (Webster *et al.*, 2005). This instrument provides excellent discrimination between high and low risk patients and between men and women, showing in the analyzes carried out a capacity of 90.9% to predict abuse of opioid drugs in high risk patients and 94.4% to predict no abuse in patients with low risk. We have seen that there are tools for risk assessment at the beginning of treatment, but there are few studies that demonstrate its efficacy (Chou *et al.*, 2009), (Lawrence *et al.*, 2017). These instruments are not diagnostic tools. But some prescribers use this type of tool in every review query. (Butler *et al.*, 2007).

In general, the clinical interview is the most sensitive when predicting risk; the questionnaires only have an indicative value. (Jones, 2012) (Moore, 2009). Risk assessment tools during treatment: The current Opioid Misuse Measure (COMM) can help to identify patients who during long-term opioid treatment show aberrant behavior with misuse of medication (Butler *et al.*, 2007). The Diagnosis, Intractability, Risk, Efficacy (DIRE) store was designed to predict analgesia and adherence during long-term treatment, but it can also be used during its continuation. Each category (diagnosis, difficulty, efficacy and risk of psychopathological disease, chemistry, reliability and social support) is graded between 1 and 3. Higher scores indicate a greater chance of success with opioid therapy. It requires a good clinical history and a good doctor-patient relationship, so it can be completed in less than 2 minutes (Belgrade *et al.*, 2006).

The Addiction Behavior Checklist (ABC) can also be useful in the evaluation of adverse and inappropriate behaviors in the use of long-term opioids (Wu *et al.*, 2006).

Proposed variables as risk factors of abuse or addiction to opioid analgesics

As mentioned before, the assessment of the risk of future addiction when starting opioid treatment is clinical. For this reason, it is essential to carry out a complete clinical history, including the history of toxic consumption, even by doctors who are not dedicated to the field of drug addiction. Numerous variables have been described associated with an increased risk of misuse or abuse. opioid abuse (Table 2). (Manchikanti *et al.*, 2012), (National Opioid Use Guideline Group, 2017), (Chou *et al.*, 2009), (Celaya *et al.*, 2014), (Liebschutz *et al.*, 2010), (Wilsey *et al.*, 2008). Taking into account the importance of pain as "the fifth constant", the growing tendency to use opioids in chronic non-cancer pain, the demands for care on the part of patients, not always justified (we cannot objectify pain, is a subjective parameter), the available screening batteries and the need for consultation time for the completion of a complete clinical history, it is common for some clinicians to fall prey to a not always correct prescription of analgesic opioids. Therefore, the objective of this work is to create a tool that allows the clinic in a few minutes to determine, with certainty, the probability of risk of opioid addiction in a patient with chronic non-cancer pain.

MATERIALS AND METHODS

To carry out this work, three methodologies have been carried out: 1) a bibliographic search to determine what risk factors are proposed in the literature; 2) a retrospective study was carried out analyzing the variables and establishing or not possible risk factors based on the population characteristics of our health area and; 3) Scale items and existing questionnaires for risk assessment have been used to complete possible variables to be taken into account in an exploration of chronic non-cancer pain.

Literature Review

A bibliographic search was performed in the MEDLINE search engine, including the following terms: "risk factors opioids dependence"; "Risk factors misuse opioid"; "Risk factors opioid use disorder"; "risk factors opioid abuse". In addition, the inclusion of Boolean parameters has been carried out for its association with the term "chronic non-cancer pain".

Study of patients

We performed a retrospective study on a sample of 80 patients (54 women, 26 men; mean age: 55 years). The data were collected in psychiatry from November 2015 to March 2017. The patients included in the sample have special characteristics that are being monitored in our clinic's Pain Unit. All patients had been previously evaluated in the anesthesia or rheumatology clinic and were grouped according to following diagnoses: 1. Fibromyalgia (FB), 2. chronic non-cancer pain with associated psychopathological comorbidity, 3. chronic non-cancer pain with suspected opiate dependence, or 4. chronic non-cancer pain and do not respond adequately to their usual treatment. Statistical analysis was carried out using the MEDCALC program (https://www.medcalc.org/calc/odds_ratio.php) and sociodemographic variables such as age, sex, place in fraternity (position he occupies among his siblings, being the older, younger or middle brother / s), environmental factors (such as exposure to stress or trauma), psychiatric diagnosis and history prior to the assessment within the Pain Unit (history of drug addiction are included), psychiatric and toxicological background, Fibromyalgia, diagnosed Failure Back Syndrome (FBS), location of pain (one or two points or diffuse localization), and factors related to the treatment of opioids (if prescribed, the daily dose of MME is identified). Descriptive data and associated risk factors have been studied (Odds Ratio (OR), $p < 0.05$).

Assessment of questionnaires and scales

The scales and questionnaires used were chosen for their sensitivity and specificity, for their ease of realization and for being able to be completed by the prescribing physician, avoiding self-application bias on the part of patients (except ORT that is self-applied, but can be completed by the clinician). In addition, we have chosen a questionnaire for each phase of the therapy, that is, one that assesses the risk before the prescription (ORT: 5 items.) The higher the score, the higher the risk, and can be classified as: 0-3 points (low risk), of 4-7 points (moderate risk) and superior to 8 points (high risk)) and another, that evaluates the risk during the prescription of opioids (DIRE: graduates between 1 and 3).

Table 3. Stratification of the risk of addiction to opioid analgesics

	LOW RISK	MEDIUM RISK	HIGH RISK
PAIN	located	In less than three zones	Diffuse
SIGNS AND SYMPTOMS	present	present	missing
PAIN EXACERBATION	missing	rare	Frequent
PSYCHIATRIC COMORBIDITY	Missing or minor	Moderate	Severe or not controlled
ORGANIC DISORDER	Missing or minor	Moderate	Severe or not controlled
FAMILY HISTORY – ADDICTION RELATED	No	Controlled	Active and Consumption
PERSONAL HISTORY - ADDICTION	No	Controlled	Active and Consumption
TOLERANCE	Missing	Low	Significant
PHYSICAL DEPENDENCY	Missing	Missing	Present
HYPERALGESIA	Missing	Missing	Present
ABUSE	Missing	Missing	present
PAIN ACCEPTATION	High	Moderate	Low
COPING STRATEGIES	adaptive	Adaptive Unadaptive	Unadaptive
FUNCTIONALITY	Functional or almost functional	Dysfunctional with	Clearly Dysfunctional
MULTIMODAL TREATMENT ACCEPTATION	Yes	Yes	No

Adaptation of Consensus Guide for the proper use of opioid analgesics (Socidrogalcohol, 2017)

Table 4. Studies on risk factors for opioid addiction in chronic non-cancer pain

Estudies	Results
Ives <i>et al</i> , 2006	<ul style="list-style-type: none"> Age Cocaine / alcohol / abuse
Boscarino <i>et al</i> , 2010	<ul style="list-style-type: none"> Depression OR 1,29 Use of psychopharmacology OR: 1,73 Age <65 years OR: 2,33 Opioid Use Disorder History OR: 3,81 Combination of previous variables: OR: 8,01 Combination variables/ opioids abuse OR: 56,36
Boscarino <i>et al</i> , 2010	<ul style="list-style-type: none"> Depression Substance Use Disorder (including alcohol)
Edlund <i>et al</i> , 2014	<ul style="list-style-type: none"> Long-term opioid use (>3 months)
Chou <i>et al</i> , 2014	<ul style="list-style-type: none"> Daily dose >100MME*

* MME: Morphine Milligrams Equivalents

Table 2. Variables proposed as risk factors for abuse / misuse of opioids in chronic non-cancer pain

Sociodemographic Variables	Age	Young (16-45 years)
	Gender	Women
Pain related variables	Multiple variables Located pains	Subjective complains More functional limitation
Genetic variables		Polymorphism of certain genes
Psicopatological variables	Severe psychosocial stress	Emotional pain Psychiatric comorbidity
	High doses Beta agonists	Fast acting formulation
Opioids related variables	Via parenteral o transmucosal	Multiple opioids prescription

The higher scores indicate greater possibility of success of opioid therapy). We have included the risk stratification of the Consensus Guide for the proper use of opioid analgesics (Socidrogalcohol, 2017), since it graduates according to whether or not the variables are present in terms of psychiatric, toxicological and painful history, at risk low, medium and high. Table 3. To compare this stratification to the scores of the other scales, we have chosen to assign a number to each degree of risk, resulting in: 1 (low risk), 2 (medium risk) and 3 (high risk). Finally the results have been grouped. As on the one hand we have obtained cardinal numbers (those corresponding to the scales) and on the other, decimals (those corresponding to the literature and the field study), we have maintained this heterogeneity. All the values have been included and have been coded in java language in order to obtain the risk calculator.

RESULTS

Summary of the bibliography: Opiate abuse frequently occurs in patients with chronic pain. Patients with a history of alcohol or cocaine abuse should be carefully evaluated and reviewed if it is decided to prescribe opiates.

Structured monitoring should be conducted for the abuse of opioids. (Ives, 2006). According to studies and reviews of the literature, the prevalence and association between chronic pain and opiate abuse exist, but they vary (Table 4):

- Average age of the patients was 52 years. 55% males. 32% misused opiates. Abusers were more likely to be younger (48 years old). Age, previous history of cocaine and / or alcohol abuse, were predictors of misuse. Pain scores were not related to misuse (Ives 2006).
- According to meta-analysis performed in patients with chronic back pain: the prescription of opioids in the treatment varies between 3-66%. Compared with placebo or non-opioid treatment, pain reduction was not observed. Long-term efficacy (more than 16 weeks) is unclear. The prevalence of disorders due to the use of substances throughout life was between 36-56%, the prevalence at the time of the study was 43%, and the aberrant behaviors in the taking of the medications were between 5% and 5%. and 24%. (Martell, 2007)

Table 5. Results obtained with the study of the area

OPIOID DEVELOPMENT ADDICTION	LOCATION OF THE PAIN	5,34(CI 95%: 2,52-11,33)
	PHRATRY POSITION	3,71 (CI 95%: 1,53-9,00)
	OPIOIDS PRESCRIPTION	3,25 (CI 95%: 1,64-6,42)
	CONSIDERS HAS SUFFER A TRAUMATIC EXPERIENCE	2,08 (CI 95%: 1,09-3,95)
	FEMALE GENDER	1,93 (CI 95%: 1,02-3,65)
	PAIN LOCATION	14,38 (CI 95%: 6,32-32,68)
	PHRATRYPOSITION	10,00 (CI 95%: 3,87-25,81)
	CONSIDERS HAS SUFFER A TRAUMATIC EXPERIENCE	5,60 (CI 95%: 2,72-11,52)
	FEMALE GENDER	5,19 (CI 95%: 2,53-10,66)
	HAS PERSONAL PSYCHIATRY BACKGROUND	3,83 (CI 95%: 1,89-7,74)
	TAKES OPIOIDS >6MESES	3,21 (CI 95%: 1,60-6,50)
	SOMATOFORM DISORDER	3,12 (CI 95%: 1,55-6,30)
	FB	2,97 (CI 95%: 1,47-5,99)
	FBS	4,84 (CI 95%: 2,41-9,68)
	PAIN LOCATION	4,47 (CI 95%: 2,10-9,52)
	PHRATRY POSITION	3,11 (CI 95%: 1,27-7,59)
	OPIOIDS CONSUMPTION	2,72 (CI 95%: 1,37-5,40)

Table 6. Opioid addiction risk calculator in chronic non-cancer pain

VARIABLES	WOMEN	MEN
Gender**	1,93	0,52
Age	Is the patient older than 65?*	Yes OR: 0,43 No OR: 2,33
Phratryposition	Is the patient the oldest brother? **	Yes OR: 0,27 No OR: 3,71
Considers has suffer a traumatic experience	Have you suffer a traumatic experience in your life? **	Yes OR: 2,08 No OR: 0,48
Personal Child Abuse History	Have you been victim of child abuse?	Yes: 3 No: 0
Location and characteristics of the pain	Is there any back pain? **	Yes OR: 5,34 No OR: 0,187
	FBS: Does he have FBS? **	Yes OR: 3,06 No OR: 0,33
	Where is the pain? ###	1: One Place 2: Several Places 3: Diffuse
	Are there signs and objective symptoms? ###	Yes: 1 No: 3
	Is pain exacerbation frequently? ###	Yes: 3 No: 1
	Is there organic disorder that justifies the pain? ###	Yes, severe: 3 Yes, medium: 2 No: 1
Attitude on the pain	What pain acceptance does the patient have? ###	High: 1 Medium: 2 Low: 3
	Are there any pain resistance strategies? ###	Yes: 1 No: 3
	What is the functionality level? ###	Normal: 1 Tries: 2 Dysfunctional: 3
	Does he accept multimodal or non pharmacological treatment? ###	Yes: 1 No: 3
Personal Psychiatry Background	Does he have depression, dysthymia or adaptive disorder?	Yes OR: 3,06 No OR: 0,33
	Does he take anxiolytics?	Yes OR: 1,73 No OR: 0,58
	Has he been diagnosed with somatoform disorder?	Yes OR: 2,82 No OR: 0,354
	Does he have severe psychiatric comorbidity, Schizophrenia, Bipolar disorder?	Yes OR: 3,97 No OR: 0,252
	Is there any personal background on drug abuse?	Yes OR: 3,81 No OR: 0,262
	Is there any personal background on addiction?	Yes: 4 No: 0
	Is there any personal background on drugs prescribed?	Yes: 5 No: 0
	Is there any personal background on alcohol addiction?	Yes: 3 No: 0
Family background (addiction)	Does he have family background related to addictions?	Yes: 4 No: 0
	Is there any family background on drugs prescription addiction?	Yes: 4 No: 0
Others	Does he have tensional headache or non-specific dizziness?	Yes: 3 No: 0
	Does he have vital disorganization? ##	Yes: 3 No: 0
	Does he have FB? ##	Yes: 3 No: 0
	Are they degenerative changes on the spine?	Yes: 2 No: 0
	Is there any neuropathic pain? ##	Yes: 2 No: 0
	Is there any car accident background? ##	Yes: 2 No: 1
	Is he chronic unemployed? ##	Yes: 2 No: 1
After the Opioids treatment has been initiated	What is the dosage regimen? *	20-49MME à OR: 1,44 >50 MMEà OR: 3,73 >100MMEà OR: 8,87 Not prescribed yet: 0
	How much time has he been taking opioids? *	<3 monthsà 1 Between 6 y 3 monthsà 2 >6 monthsà 3
	Does he have developed tolerance? ###	Missing: 1 Low: 2 Significant: 3 Not prescribed yet: 0
	Does he have hyperalgesya? ###	Yes: 3 No: 1 Not prescribed: 0
	Are they any withdrawal symptoms if he is late for his dose? ###	Yes: 3 No: 1 Not prescribed yet: 0
	Does he use opioids against stress? ##	Yes: 2 No: 1 Not prescribed: 0
	Does he have guideline disorder? Does he loses his dose? ##	Yes: 3 No: 1 Not prescribed Yet: 0
	Is there any pain reduction with treatment? ##	Yes, better quality of life: 1 Low, but maximum dose has not been exhausted: 2 Not responding even on high dose: 3
	Is there any abuse/misuse? ###	Not prescribed: 0 Yes: 3 No: 1 Not prescribed: 0

- According to a study by the United States health system in 2010: opioid dependence in DCNO would be 26% (95% CI: 22-29.9). Dependence was associated with variables such as: age <65 years OR: 2,33; history of opioid abuse OR: 3.81; depressive disorder OR 1,29; use of psychoactive drugs OR: 1,73. The combination of the previous variables together with pain deterioration had OR: 8.01, and its combination with a history of opioid abuse was OR: 56,36. (Boscarino *et al*, 2010)
- Evaluating the prescribed opioids and the mean daily dose as variables for the development of opioid disorder, it was determined that: in patients with OCD, the prescription of opioids was a strong risk factor for developing substance use disorder. The magnitude of the effects were great. The duration of the therapy was more important than the daily dose administered to determine the risk (Edlund, 2014).

Results of the study

The values that had OR greater than value 1 were chosen, and have been grouped according to the variable from which they could be a risk factor. Within the chosen values, they have been ordered ascending according to the strength of association between one variable and another. Only the OR figures and their confidence interval are included in the table. The type of association between the variables is determined in the fourth column, being a risk factor when the lower and upper limit of the confidence interval are both greater than 1. In case the lower limit of the interval is less than 1, the association It is not significant and has not been included in the results table Table 5.

Scales and questionnaires

As explained in the methodology, the categorization of the scales would be as follows:

- ORT: 0-3 points (low risk), 4-7 points (moderate risk) and more than 8 points (high risk).
- DIRE: graduated between 1 and 3 points. Higher scores indicate a greater chance of successful opioid therapy).
- Socidrogalcohol, 2017: 1 point (low risk), 2 points (medium risk) and 3 points (high risk).

The final result, with the combination of all the variables and their numerical assignment, whether cardinal or decimal, according to the type of question issued is shown in Table 6. If there were data obtained by the literature review and by the study field, has chosen to take the greater result, in order to increase sensitivity. The variables were grouped by: age, position in the phratry, consider having suffered a trauma, history of abuse, pain characteristics, attitude to pain, personal psychiatric history, psychiatric family history, other variables and finally, the group that it refers to the characteristics of a possible opioid treatment. Since it is not always possible not to treat, for those cases of secondary prevention, questions related to the monitoring of the treatment are included in the calculator. In case of finding ourselves in front of a first assessment, primary prevention, these questions would be answered with the answer "they have not been prescribed". The difference between this work and other scales, is that in our case, being prepared for your computer application,

automatically calculates both the risk in cardinal numbers and the risk according to OR. Its interpretation is shown in Table 7.

Table 7. Interpretation and risk stratification according to the results of the calculator.

	LOW RISK	MEDIUM RISK	HIGH RISK
Cardinal Results	<1	Between 1-2	>2
Decimal Results	<1	Between 1-2	>2

DISCUSSION

There is a growing concern throughout the world to ensure the proper, equitable and homogenous use of opioid analgesics. The events that have occurred in recent years in the USA have contributed to this interest. Related to an excess of inadequate indications of opioid analgesics and even referral to a later use of heroin as a substitute for these drugs. In Spain, the use of analgesics in general, and opioid analgesics in particular, has grown significantly. In most cases it is a reflection of an adequate and more exhaustive use of the diverse arsenal available to the clinician and its application is in accordance with the generally accepted criteria. However, we cannot ignore that a part of the indications that are established do not correspond to protocols and guides of good practice. In some as in other indications, being familiar with the use of opioid drugs can mean the difference between obtaining the expected benefit of the therapy applied or magnifying to intolerable limits the risks for the patient. It is necessary to achieve a more balanced use of opioids, which allows the availability of these drugs for those patients who can benefit from them and limits as far as possible an inappropriate use that supposes a greater risk of the associated negative consequences. Those patients who present criteria for the misuse, abuse or addiction of prescription opioids require a comprehensive and multidisciplinary treatment that includes adequate management of both pain and opioid use disorder (Gregg, 2105). However, this risk stratification is not always easy for professionals who are not specialists in opioid analgesia. There are so many possibilities for combining the proposed risk factors that it is difficult to calculate the risk of possible addiction in a consultation. Although in general it is considered that both sexes have the same risk, some studies indicate that the risk could be higher in women for various reasons, related both to the characteristics of pain, as well as to psychopathology and addiction. Regarding pain, women seem to present more frequent, more intense, more lasting and less localized pain; they need a higher prescription of analgesics at high doses and for a longer time; they require more prescription opioid analgesics, in addition, they have a greater concomitant use of hypnotics and sedatives and, greater dysfunction in their daily lives (Brady *et al*, 2015) (Campbell *et al*, 2010) (Campbell *et al*, 2015) (Greenspan *et al*, 2007) (Mendrek *et al*, 2014). Regarding psychopathology, women have higher levels of pain-related anxiety, more maladaptive coping strategies, higher incidence of anxiety disorders, depressive disorders and post-traumatic stress disorder, and higher incidence of psychiatric comorbidity. traumatic events (physical abuse, sexual abuse) (Back *et al*, 2009 and 2011), (Beck *et al*, 2011), (Cicero *et al*, 2008), (Keogh *et al*, 2006 and 2014), (Manubay *et al*, 2015), (Davidson *et al*, 2015), (Weissman *et al*, 2006). Regarding the factors related to opioid abuse or addiction, women seem to present greater use and abuse of opioid analgesics, more self-medication in response to emotional stress, greater sensitivity to the effects of opioids

and a more rapid progression of abuse. to addiction (Cicero *et al*, 2008), (Manubay *et al*, 2015) (Back *et al*, 2011 and 2010), (Jamison *et al*, 2010). In addition to these differences shown in the literature, we have been able to objectify them both in the field study (OR women: 1.93 (CI: 1.02-3.65)), and in the graduations of the scales, since in the In the case of ORT, being a man scores 0 in the question referring to abuse in childhood (value 0 in the answer both affirmative and negative). Based on the above, the fact of stratifying the risk helps us to plan a therapeutic journey. This will favor an individual treatment plan according to the characteristics of each patient. But nonetheless, the calculator allows us to group patients into three large groups:

- Low risk: patients without personal or family history of alcohol or substance, without associated psychiatric disorder, and with low risk scores in the initial assessment instruments. These patients can be managed from Primary Care with adequate monitoring.
- Moderate risk: patients who have risk factors for misuse (family history of alcohol or substance use). In addition, they can associate personal history of mental disorder (Gourlay *et al.*, 2005). In case of prescription, they should have a closer and more exhaustive control and follow-up. They will have to be referred to Specialized Care as they need.
- High risk: patients with a personal history of substance abuse, severe mental disorder or overdose. In case of needing opioid therapy, they will have to have a prescription with strict care and in need of joint follow-up with unit of addictive disorders.

The prescription of opioids is exceptional for patients with a high risk of misuse of treatment. For patients with moderate-low risk, monitoring strategies will be used during the course (Dowell *et al*, 2016).

Conclusion

As demonstrated previously, it is not easy to make a complete assessment of a patient with chronic non-cancer pain and, even less, to assess their prognosis and risk of opioid addiction if prescribed. That is why we created this tool, the risk calculator, to make it easier for clinicians, whether specialists in pain or drug addiction, or for primary care physicians, or anyone not familiar with analgesic opioids, the way quick, simple and based on evidence, to predict an addiction to analgesic opioids and to assess their evolution in case of prescribing them.

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