

Observational Study

Can We Predict Addiction to Opioid Analgesics? A Possible Tool to Estimate the Risk of Opioid Addiction in Patients with Pain

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Background: The use of opioid analgesics in the treatment of chronic pain conditions has long been controversial. They have been reported to be relatively safe when prescribed with caution, but a brief and valid instrument to estimate a person's risk of addiction is still missing.

Objective: The aim of this study was to investigate a self-rating questionnaire allowing an estimation of a person's risk of addiction to opioid analgesics.

Study Design: Retrospective review.

Setting: Four Austrian hospitals.

Methods: Seven hundred forty-one patients were interviewed. Of these, 634 patients were affected with chronic pain while 107 patients had a history of opioid addiction. Patients were interviewed about alcohol and nicotine consumption and family history of psychiatric disorders. Attitudes towards medication and the origin of pain were examined. We asked patients with an opioid addiction and patients suffering from chronic pain to complete a short questionnaire intended to help screen for addiction potential.

Results: Compared to the patients suffering from chronic pain, patients with an opioid addiction significantly more often had alcohol- and nicotine-related pathologies and psychiatric comorbidity. A family history of mental illness and developmental problems were significantly more frequent in this group. Compared to those not addicted, those with an opioid addiction had significantly higher expectations concerning the potential of medication to change one's mental state; they thought that psychological factors might contribute to the pain they feel.

Limitations: The main limitation of this study is the use of a self-rating instrument which reduces objectivity and introduces the possibility of misreporting. Also, the 2 groups differ in number and are not homogenous.

Conclusion: We found differences in questionnaire responses between patients with an opioid addiction and patients suffering from chronic pain to be dependent upon the prevalence of current or former addiction, psychiatric history, attitudes towards medication, and ideas about the origin of pain. We believe these factors have predictive value in estimating a patient with pain's risk of addiction.

Key words: Pain, opioids, analgesics, addiction, questionnaire, self-rating, screening

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Chronic pain conditions are a major health issue in developed countries, affecting up to 25% of the US population (1) and up to 19% of Europeans (2). Furthermore, chronic pain has become the most frequent cause of disability in the US (3). Concerning the pharmacological treatment of chronic pain, consensus has been reached that pain has to be treated successfully whenever possible in order to improve the quality of life of those concerned, reduce the social impact of disabilities caused by conditions accompanied by chronic pain, and to limit suffering from chronic, fatal diseases (1).

Opioids are known to be effective in the management of both acute and chronic pain (4). Despite side effects like nausea, constipation and negative effects on cognition and psychomotor functions, they are widely used for the treatment of cancer pain and chronic non-cancer pain. The major fear concerning these substances is related to the risk of abuse, addiction, and diversion. Numerous studies have dealt with the question of the danger of addiction when prescribing opioid analgesics and the overall risk of the nonmedical use of opioids seems to be extensive (5,6,7). Although a higher chance of aberrant drug behavior seems to exist in patients with a family or personal history of substance abuse or a history of legal problems (8), most studies found out that, when taking these factors into account, the risk of addiction is very low. Fishbain et al's (6) review showed that, when preselected for no previous history of abuse or addiction, the percentage of patients developing an addiction to opioid analgesics is as low as 0.19% (6). But evidence for the efficacy and safety of opioid analgesics is still not really sound (9), and so opioid analgesics are still often prescribed somewhat unassertively (10) and misconceptions about the prescribing of opioids remain frequent (11). Furthermore, confusion about the definition of drug use (use without physical or psychological dependence), physical tolerance (physical need to consume a substance without psychological dependence), and addiction (physical and psychological need to consume a substance) persists and additionally renders physicians uncomfortable to prescribe opioids for long-term use (12).

Many different risk factors for the development of addictive disorders have been described. Among these are a genetic vulnerability, different biological and sociological factors, and a number of psychological features (13,14). Consequently, assessing risk factors, like a personal or family history of addiction, has been recommended to estimate a person's risk of developing

addiction to opioid analgesics (15,16). Stratification of patients into different risk categories by using existing screening tools has recently been suggested (17). This approach, although apparently useful, is however time-consuming, as it combines different screening tools and trained staff are required to perform some of the ratings. A single screening tool that can be applied universally is still unavailable (18).

METHODS

Aims of the study

We sought to develop a self-rating questionnaire for estimating a person's risk of addiction to opioid analgesics. Knowing that a history of psychiatric illness, substance abuse, developmental problems, psychiatric family history, and anticipated effect of medication on psychological wellbeing can be predictive factors for the development of addiction, we included questions concerning these items (Table 1).

We expected to find differences in socioeconomic background, substance use behavior, and expectations towards medication. We also expected to find different conceptions about the origin of pain between the groups.

Overview, sample, procedures

From September 1, 2008, through December 31, 2010, a total of 741 patients were investigated using a self-rating questionnaire (Table 1). Of the participating patients, 634 were affected with chronic pain and were at the beginning of treatment. All of them were in a state where opioids are normally considered, but for different reasons not all of them were prescribed opioid analgesics. Another 107 patients who were investigated were suffering from chronic opioid addiction according to ICD-10. All patients were asked to complete the questionnaire during a routine appointment. The patients suffering from chronic pain were investigated in 4 different Austrian hospitals in units specialized in treating chronic pain conditions. Patients with prior opioid addiction were investigated in a large center specializing in the treatment of opioid addiction in Vienna, Austria, where they were under current treatment for their addiction disorder.

We chose to compare patients with an opioid addiction to patients suffering from chronic pain conditions because risk factors for addiction to opioids could be assumed to be exhibited very strongly in the group of patients with an opioid addiction who had, regardless

Predicting Opioid Addiction in Patients with Pain

Table 1. Questionnaire to help estimate the risk of addiction at the beginning of treatment with opioid analgesics.

Nicotine-Addiction (Heavy Smoking Index)		Risk of Addiction	
How soon after waking do you smoke your first cigarette?	<input type="checkbox"/> Within 5 minutes = 3 Points <input type="checkbox"/> 6-30 minutes = 2 Points <input type="checkbox"/> 31-60 minutes = 1 Point <input type="checkbox"/> Longer than 60 minutes = 0 Points	A total of 4 points or more	
How many cigarettes do you smoke per day?	<input type="checkbox"/> 10 or less = 0 Points <input type="checkbox"/> 11-20 = 1 Point <input type="checkbox"/> 21-30 = 2 Points <input type="checkbox"/> 31 or more = 3 Points		
Alcohol-dependence (CAGE-Questionnaire)			
Have you ever felt you needed to cut down drinking?	<input type="checkbox"/> yes <input type="checkbox"/> no	A total of 2 points or more	
Have people annoyed you by criticizing your drinking?	<input type="checkbox"/> yes <input type="checkbox"/> no		
Have you ever felt guilty about drinking?	<input type="checkbox"/> yes <input type="checkbox"/> no		
Have you ever felt you needed a drink first thing in the morning (eye-opener) to steady your nerves or get rid of a hangover?	<input type="checkbox"/> yes <input type="checkbox"/> no		
Psychiatric History			
Is there any history of psychiatric illness or addiction (ie. alcohol) in your family (parents or siblings)?	<input type="checkbox"/> yes <input type="checkbox"/> no	One question or more answered with "yes"	
Before the age of 14, have you experienced psychological strain and/or suffered from a cerebral lesion or disease that had negative influence on your development (resulting in difficulties at school, changes in behaviour or stuttering)?	<input type="checkbox"/> yes <input type="checkbox"/> no		
Are you or have you ever been suffering from a Depressive Disorder or Anxiety Disorders?	<input type="checkbox"/> yes <input type="checkbox"/> no		
Evidence of former or current Abuse of or Addiction to illicit drugs?	<input type="checkbox"/> yes <input type="checkbox"/> no		
Expected Effect of Analgetic Medication			
Do you think that a drug can make you happier, more content or more self-secure?	<input type="checkbox"/> yes <input type="checkbox"/> no	One or both questions answered with "yes"	
Do you think that a drug can help you unwind and/or reduce stress?	<input type="checkbox"/> yes <input type="checkbox"/> no		
Attribution of Origin of Pain			
In your opinion, is your pain mainly due to organ damage or could psychological factors or psychosocial stress lead to contractions and thus to pain?	My pain is caused by somatic reasons only	My pain is caused by psychological reasons only	The more the pain is attributed to psychological factors, the higher the risk

of physical condition and medical intervention, already developed addictive disorder.

The study was approved by the Ethics Committee of the Medical University of Vienna.

Measures

Nicotine use

Smoking status was assessed and smoking severity was determined using the Heaviness of Smoking Index (HSI). The HSI is a short 2-item questionnaire of nicotine dependence originally derived from the Fagerström Tolerance Questionnaire. It measures smoking heaviness using self-reported time to the first cigarette of the day and the number of cigarettes smoked per day (19,20).

Validation studies show favorable scale properties of the HSI (21) for screening for biological dependence at cut-off ≥ 4 .

Alcohol use

To screen for alcoholism the CAGE questionnaire ("Cutting down," "Annoyance by criticism," "Guilty feeling," and "Eye-opener") was used. The CAGE questionnaire has good sensitivity and specificity for alcohol dependence at cut-off ≥ 2 (22).

Psychiatric comorbidity

Patients were asked about developmental problems during childhood and adolescence. A history of affective disorder, anxiety disorder and addiction, and

a family history of psychiatric illness were assessed using a self-rating questionnaire. If one or more questions were answered with "yes," this was considered a risk factor for addiction. These factors have been found to be of prognostic potential in alcohol dependence (23).

Attitudes towards medication and origin of pain

Attitudes towards medication were examined by asking the following questions: "Do you think that a drug can make you happier, more content or more self-secure?" and "Do you think that a drug can help you unwind and/or help you reduce stress?" Attributing pain to physical or somatic reasons was examined by asking patients to complete a line test that asked them to point out where between the poles of "The pain I am encountering is only due to a physical condition" and "The pain I am encountering is only due to psychosocial reasons" they find themselves. Since most patients with an opioid addiction who were investigated were not suffering from pain at the moment of

investigation, they were asked to imagine or remember a painful condition.

We used validated instruments for tobacco and alcohol use, but there are no such well-validated tools for psychiatric comorbidity, attitude towards medication, and the origin of pain. In these parts we intended to develop new items with predictive potential concerning future addiction.

The questionnaire is in Table 1.

Statistical Analysis

Due to incomplete data in some parts of the questionnaire, percentages in Table 2 do not add up to 100% (n = 741). Therefore subsequent analyses were based on slightly different cell counts. Differences in characteristics between patients with an opioid addiction and patients without an opioid addiction were assessed by t tests and Mann-Whitney-U tests for nonparametric variables. *P* values at the level < .05 were considered significant. The data were analyzed with SPSS Statistics 19.0 software (IBM Corporation, Armonk, NY).

Table 2. *Patient characteristics.*

	Pain Patients n = 634	Opioid Addicts n = 107	P values
Sex			
Female	55.7% (n = 334)	29.2% (n = 31)	< 0.001
Age			
Mean age (years)	58.98 (SD 14.1)	27.06 (SD 5.2)	
Educational Status			
Graduation from school	97.4% (n = 565)	96.3% (n = 103)	n.s.
Graduation from apprenticeship training	61.2% (n = 353)	46.7% (n = 50)	= 0.005
Graduation from University	6.9% (n = 40)	3.7% (n = 4)	n.s.
Smoking			
Smoker	34.5% (n = 219)	98.1% (n = 105)	< 0.001
Exsmoker	19.4% (n = 121)	1.9% (n = 2)	< 0.001
Nonsmoker	45% (n = 285)	0% (n = 0)	< 0.001
Alcohol			
CAGE ≥ 2	7.3%	28.0%	< 0.001
Psychiatric illness			
Developmental Problems	6.7% (n = 41)	26.2% (n = 28)	< 0.001
Comorbidity Depression/Anxiety	32.8% (n = 200)	54.2% (n = 58)	< 0.001
Family history of mental illness/addiction	11.1% (n = 68)	44.9% (n = 48)	< 0.001
Attitudes towards medication			
I think that a drug can make me happier, more content or more self-secure	24.8% (n = 149)	50.5% (n = 54)	< 0.001
I think that a drug can help me unwind and/or help you reduce stress	38.2% (n = 224)	73.3% (n = 77)	< 0.001

RESULTS

Sociodemographic data

Groups differed significantly in gender with a higher proportion of men in the group of patients with an opioid addiction. Patients with an opioid addiction were on average markedly younger than patients without an opioid addiction, with a mean age difference of 31.9 years. No difference was found concerning graduation from high school and, interestingly, from a college or university, but a significantly smaller proportion of the patients with an opioid addiction had finished apprenticeship training.

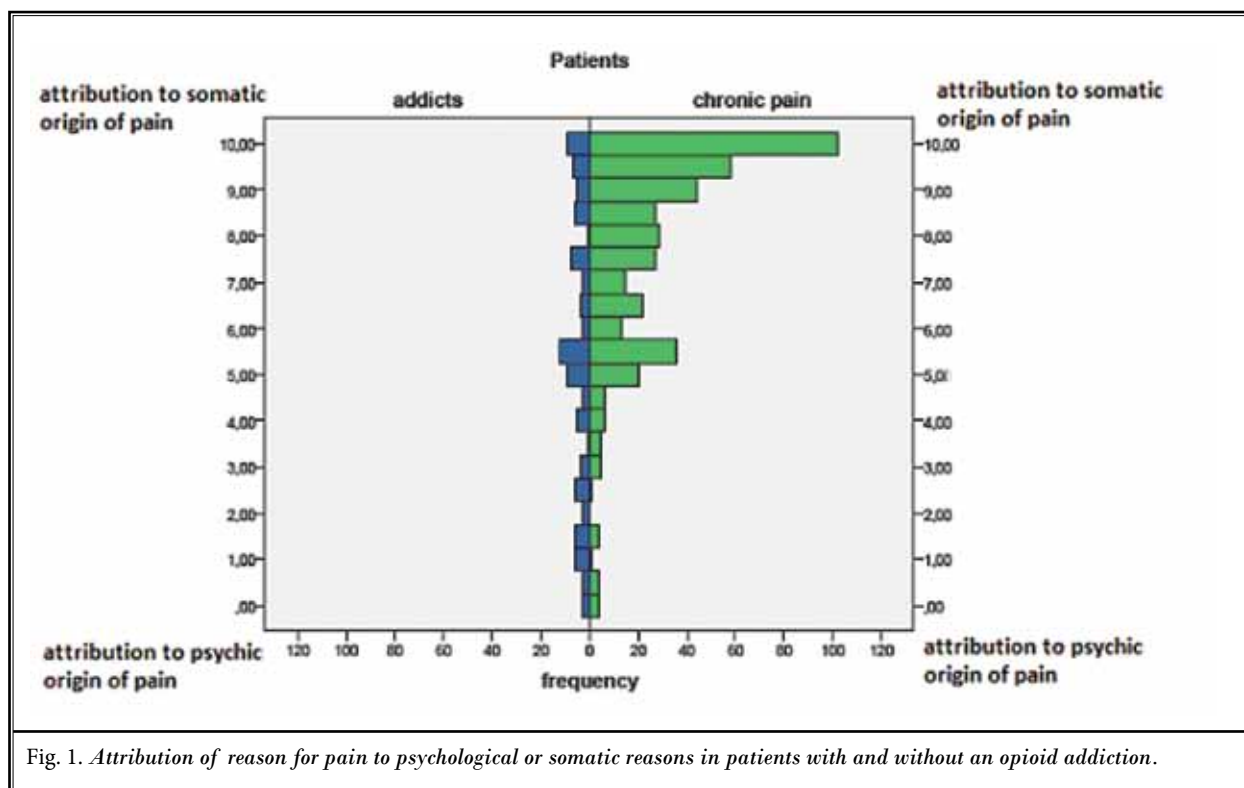
Assumed risk factors

As expected, there were huge differences between the groups in alcohol and nicotine consumption as well as in psychiatric comorbidity. Concerning smoking status, significant differences were found with 98.1% of patients with an opioid addiction being smokers versus 34.5% of patients without an opioid addiction being smokers. Significantly more patients without an opioid addiction were ex-smokers (19.4% versus 1.9%) or non-

smokers (45% versus 0%). Significantly more patients with an opioid addiction exhibited problematic alcohol consumption (28.0% versus 7.3%) and developmental problems (26.2% versus 6.7%). Comorbid anxiety or depressive disorders were reported by 54.2% of all patients with an opioid addiction compared to 32.8% of patients without an opioid addiction and a family history of mental illness was also present significantly more often in this group (44.9% versus 11.1%).

Patients with an opioid addiction had significantly higher expectations concerning the potential of medication to change their mental state and significantly more often considered a drug apt to make them happier or help them unwind. When asked to estimate what percentage of their pain is being caused by somatic or psychological reasons, patients with an opioid addiction rarely considered somatic conditions as the main or only reason for chronic pain conditions. In contrast, most patients without an opioid addiction perceived their pain as being caused only or mainly by somatic factors (Fig. 1).

For sample characteristics also see Table2.



DISCUSSION

Although abuse and addiction are potential dangers of long-term therapy with opioid analgesics, consensus has been reached that therapeutic access to this treatment has to be maintained for patients with legitimate medical need. Numerous strategies to improve pain management while minimizing opioid abuse have been established. These include the assessment of a history of addiction, the selection of the most appropriate opioid therapy, monitoring of treatment, and early detection of abuse or addiction (24-29).

Screening for a personal or family history of addiction to minimize the risk of abuse or addiction is usually recommended when considering treatment with opioid analgesics. Such an approach is certainly useful but might both unjustifiably render access to opioid analgesics impossible to some patients and miss out evidence for addiction potential in others.

At present, a thorough and ongoing assessment is recommended to help tailor an individual therapy and identify patients who exhibit aberrant behavior (30). However, this approach necessitates a multidisciplinary team including at least one psychiatrist or psychologist who regularly monitors the patient for signs of addiction. In daily practice, however, treatment often has to be managed by family physicians, internal specialists, or anesthesiologists who have to work without a psychiatrist at hand. Prescribing physicians are thus usually confronted with the problem of estimating a person's risk of addiction without being able to rely on reference values. These physicians would profit from a scale telling them roughly how high the risk of addiction is for a patient.

A complicating factor in the therapeutic use of opioids is their bad reputation for addiction potential. Nowadays they are, however, increasingly used for the treatment of non-cancer pain (31), so the question of safety and addiction potential of this group of substances has again become important. Recent studies depicted certain personality traits, young age, family or personal history of addiction, and traumatic events or psychiatric illness other than addiction as criteria underlying the development of addiction disorders (15,16,31-39). Further complicating the issue, both addiction and chronic pain have a multifactorial etiology, and chronic pain is often accompanied by psychiatric comorbidity (40).

It is known that the most important factor in the assessment of addiction potential is the patient's susceptibility, rather than the particular drug prescribed.

(35-39). When discussing the possible addictive potential of opioid analgesics, we must focus on the person receiving the drug and his or her potential to develop an addictive disorder. Meeting criteria of former or current addiction might be helpful in the identification of patients at special risk, but identification of personality traits or attitudes towards medication could be of even greater importance. In comparing possible risk factors of addiction in patients with an opioid addiction and patients suffering from chronic pain conditions without an opioid addiction, we intended to see whether these factors are indeed more pronounced in patients with a history of addiction.

By designing a short questionnaire that included factors known to correlate with an elevated risk of addiction, we tried to develop an easily applicable tool to estimate the risk of addiction to opioid analgesics in patients with pain. While we applied validated instruments for tobacco and alcohol use, the questions used for investigation of psychiatric comorbidity and attitudes towards medication are not yet validated. By including these questions into the questionnaire we intended to compile a new instrument exhibiting predictive potential for future aberrant drug behavior in patients in need of opioid therapy. In this study we investigated this questionnaire for the first time comparing 2 distinctive groups. We hypothesized we would find a higher prevalence of the items we considered risk factors in the group of patients with an opioid addiction than in the group of patients suffering from chronic pain who did not have an opioid addiction.

Looking at the results we found strong differences in social and environmental factors. Groups also differed strongly in age and gender distribution. Interestingly, we found no significant difference between the groups in graduation from high school and graduation from a college or university, the latter being a fact that we cannot explain.

Each of the items proposed as possible risk factors scored markedly higher in the group of patients with an opioid addiction. As expected, a family history of psychiatric disorder was far more frequent in the patients with an opioid addiction than in the patients without an opioid addiction. We found significantly higher incidences of alcohol and nicotine addiction in this group. Developmental problems and depressive or anxiety disorders were also present significantly more often in the group of patients with an opioid addiction. Expectations concerning medication effects on

psychological well-being differed significantly between the groups with the patients with an opioid addiction anticipating higher benefit concerning relaxation and stress reduction. These patients were also more likely to consider their pain to be influenced by psychological reasons than those without an addiction (Fig. 1).

Although these results are clear, we should not forget that pain and opioids can mutually influence each other. While addiction and many other psychiatric disorders, including somatoform disorders, generalized anxiety, and depression play complex roles in the initiation, maintenance, and severity of chronic pain (41,42), tolerance to opioids enhances pain perception and pain sensitivity, but usually decreases with detoxification (43). In our sample, comorbid anxiety or comorbid depressive disorder was as frequent as 32% in the group of patients without an opioid addiction and although the occurrence of psychiatric disorders in this group is significantly lower than in the group of patients with an opioid addiction, it is still higher than in the general population (44). The possibility or danger of iatrogenic misuse of opioids for mood control in these patients also has to be considered. A prescribing physician should also attend to the differentiation of anxious or depressed mood and insufficient pain control. Interestingly, the patients with an opioid addiction considered psychological influence on pain conditions far more than did patients without an opioid addiction (Fig. 1). Although this psychosomatic connection is more frequently seen in psychiatric disorders other than addiction, it seems to be perceived by patients with an opioid addiction rather than by psychiatrically healthy patients. Following the more "holistic view" patients with an opioid addiction in our sample obviously have towards the origin of their pain, it is not surprising they expect a psychosomatic benefit from the drug they receive to treat this condition. The concept of experiencing instant relief both of physical and of psychological symptoms by taking a pill is very often found in patients with an opioid addiction but can also evolve in psychiatrically healthy persons during treatment for pain conditions.

Regular controls and monitoring for aberrant drug use will always remain indispensable in the course of treatment with opioid analgesics. Still, we hope that estimating a person's risk of addiction to opioid analgesics by means of a questionnaire will be helpful in deciding whether or not to put a person suffering from chronic pain on opioid analgesics. In this study,

however, the tool was applied to 2 completely different populations and patients were not followed long enough to determine who developed problematic use of opioids. Extrapolating these results is thus currently not appropriate. A second study is now needed applying this tool to patients with chronic pain to see if it really can distinguish future opioid abusers from those taking opioids responsibly.

Limitations

The main limitation of this study is the use of a self-rating instrument, which reduces objectivity and introduces the possibility of misreporting. The groups differed in number and were not homogenous. This study presents preliminary data of a potentially promising tool. Until this tool is validated in a population of patients with chronic pain by distinguishing abusers from those legitimately using opioids, it cannot be applied in clinical practice.

CONCLUSION

The risk of addiction to opioid analgesics in patients suffering from chronic pain is an important area of active investigation. A great many factors contribute to the development of addiction. While family history and a history of substance abuse are 2 of them, other individual, biological, and social factors also play an important role.

Although many efforts have been undertaken to identify and manage misuse and dependence in primary care (15-18,28-39,45,46), a validated, reliable, and easily applicable scale to predict the risk of addiction in persons suffering from chronic pain is currently not available. In this study we describe a questionnaire we believe useful in predicting a patient with pain's risk of addiction to opioid analgesics, and that shows differences in responses between patients with an opioid addiction and patients without an opioid addiction in treatment for chronic pain. Such an instrument could be very helpful for prescribing physicians confronted with someone in need of opioid therapy. As the tool cannot be utilized before its validation, prospective studies to investigate metric properties and predictive potential of this questionnaire are needed.

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Statement concerning each author's contribution

Skala K, Lesch OM, and Walter H designed the study and wrote the protocol. Skala K also wrote the first draft of the manuscript. Ilias W, and Grögel-Aringer G, and Herrmann P supervised data acquisition

and procession. Likar R and Wallner C managed data acquisition and engaged in literature searches. Reichl L managed literature searches and performed statistical analysis. Schlaff G critically reviewed the manuscript.

All authors contributed to and have approved the final manuscript.

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