

Opioid for in-hospital admitted patient analgesics; which demographics and psychiatric profiles need more pain drugs?

Tahereh Mohammadi ¹, Elham Sharafi ², Atieh Sadeghniiat-Haghighi ^{1, *}, Farzan Vahedifard ³, Arghavan Shafiee-Aghdam ⁴ and Mohammad Arbabi ⁵

¹ Department of Psychiatry, Roozbeh Hospital, Tehran University of Medical Science, Tehran, Iran.

² Psychosomatic Fellowship, Tehran University of Medical Science, Tehran, Iran.

³ Department of Diagnostic Radiology and Nuclear Medicine, Rush Medical College, Chicago, USA.

⁴ Department of Psychiatry, Razi Hospital, University of Social Welfare and Rehabilitation Sciences, Tehran, Iran.

⁵ Department of Psychiatry, Brain, and Spinal Cord Injury Research Center, Neuroscience Institute, Tehran University of Medical Sciences, Tehran, Iran.

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Abstract

Introduction: The prevalence of substance use disorders is higher in patients receiving opioid analgesics, and pain management in these patients is more challenging. This study aimed to investigate the pattern of analgesic drug administration and evaluate the associated factors.

Method: The cross-sectional study was performed on 230 patients admitted to General Hospital (internal medicine, surgery, and cancer wards).

Result: The most used analgesic drug was morphine (59.4%), and a mean dose of 27 mg, then pethidine and methadone. Most pain control methods were intravenous (68.1%) and PRN pattern (61.1%). Using analgesics in patients who do not have risk factors for drug abuse, or addiction, can be considered safe. In our subjects, 95.6% of analgesic users did not become addicted or had any misuse.

Discussion and Conclusion: For effective and low-risk treatment of these patients, there is a need for clinical skills, knowledge of opioid administration, assessment, and risk management of substance abuse and addiction. In patients with substance abuse, analgesics should be prescribed in a particular setting, under supervision, and with careful monitoring. Structured and planned administration of opioid agonists (such as methadone or buprenorphine) seems appropriate according to a structured schedule. These plans are recommended:

- Increasing the awareness of clinicians about prescribing narcotic analgesics.
- Prescribing narcotic analgesics with a regular pattern against PRN.
- Evaluating patients for a history of substance abuse.
- Closely monitoring them, and if necessary.
- Counseling.

Identifying high-risk groups such as women, youth, and psychiatric patients are also recommended, and performing early interventions.

* Corresponding author: Atieh Sadeghniiat Haghighi

Department of Psychiatry, Roozbeh Hospital, Tehran University of Medical Science, Tehran, Iran. Email: asadeghniiat@razi.tums.ac.ir

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1. Introduction

Pain is an integral part of life that almost everyone experiences to varying degrees throughout their lives, and its prevalence is higher than diabetes, cancer, and heart disease [1]. Pain is one of the most common causes of emergency room visits [2]. All pain complaints can affect a person's performance and quality of life, so they should be thoughtfully and carefully evaluated [3]. The untreated pain leads to unnecessary suffering, prolonged hospital stays, increased treatment costs, and may progress to chronic pain [4]. Some studies indicate inadequate treatment of pain in hospitalized patients, especially in Cancer-Related Pain [5, 6].

Multiple classes of analgesics are used to relieve acute and severe pain, such as narcotics, which are mainly used in the form of injections. Inappropriate analgesia usage may be associated with side effects and complications, such as excessive or inadequate dosing, prolonged interval administration, drug abuse, long-term unnecessary prescribing, and the occurrence of drug dependency [7, 8]. Arbitrary use or overdose of opioids has been associated with the opioid crisis, which has imposed a heavy cost on the health care system. An extensive research budget has been allocated to the NIH for the opioid crisis [6, 9-11]. Pain management has become a clinical challenge for physicians [10]. Improper pain management may lead to significant burnout and long-term suffering for the patient, especially in patients with substance abuse or who routinely use opioids to control pain. Pain management has become more complicated with background diseases [12-14]. Substance abuse is another critical health issue in Iran and other countries, with a significant prevalence rate. Also, the importance of substance abuse is often overlooked when it is not the primary problem.

Despite the high prevalence of opioid-related disabilities and the availability of management methods, substance abuse and lack of appropriate treatment are still seen in hospitalized patients. Public hospitals, in particular, can be an efficient place to make an initial diagnosis and interventions for substance-related disorders. In addition, physical diseases are prevalent among substance abusers, which affects the rate of analgesic use. Therefore, research on the extent of substance abuse in public hospitals with physical complaints may change their pain management.

Substance use is prevalent in hospitalized patients, and sufficient studies have not been conducted on the pattern of opioid use in hospitalized patients and substance abusers. Therefore, this study aimed to investigate the pattern of analgesic drug administration and evaluate the factors associated with using analgesics, and substance abuse. The demographic and psychiatric profile of patients requiring analgesic drug administration was also assessed.

2. Material and methods

This cross-sectional study was performed on patients admitted to Imam Khomeini Hospital (excluding ICU and operating rooms) in 2018. The information related to the prevalence of substance abuse was calculated separately for internal medicine, surgery, and cancer wards.

To calculate the sample size, we first did a pilot study on 100 patients from the mentioned wards. To calculate the total prevalence of substance abuse, the calculated prevalence values in the mentioned sections were weighted based on the sample size taken from each ward. Finally, the prevalence of total weight was estimated to be 13.9%. Using the formula for calculating the sample size to estimate the ratio in a community and considering the error of 0.05 and the value of 95% Z, the sample size was estimated to be 184 people.

2.1. Inclusion criteria

Age over 16 years, fluency in Persian, lack of consciousness, and lack of narcotic analgesia.

2.2. Exclusion criteria

Uneducated, not cooperative

Information about patients' demographic characteristics was obtained through a questionnaire. This questionnaire was developed by the researcher and is based on study variables.

The WHO-Assist questionnaire was used to assess the underlying substance abuse. In this questionnaire, patients are first given an answer-materials card explaining the materials and scoring. Then for each subject (A to Z), the points received for questions 2 to 7 are added together.

Based on the patient's involvement score with each substance, the amount of intervention is determined: 0-3: without intervention, 4-26: short therapeutic intervention, and above 27: more specialized intervention. The Assist Questionnaire was first developed by Knight et al. To identify psychotropic drug abusers and related problems in primary patient care for the World Health Organization and translated and validated into Persian by Nouri et al. [15].

Evaluation of response to analgesic treatment following drug use was performed based on the Numeric pain rating scale. Accompanying psychiatric issues, including anxiety and depression, were assessed by HADS [16, 17]. There are different trending modalities for depression and anxiety, from traditional drugs and also new neuromodulators [18-20], which have fewer side effects than opioids.

Other relevant information was obtained through pharmacy drug offices, referrals to hospital wards, patient records, nursing reports, admissions and discharge office notes, direct contact with patients during the treatment course, and questionnaires.

Numbers and percentages were used to describe qualitative variables. The distribution of quantitative variables was first tested using the Kolmogorov-Smirnov test. The patient age variable (which followed the normal distribution) was described with mean and standard deviation indices. Other quantitative variables in this test did not follow the normal distribution, so the description of these variables was done by presenting the amplitude of the variable (minimum and maximum value) and the median and interquartile range.

3. Results

3.1. Demographic information

Our calculated sample size was 230 subjects (final number= 229). The average age of the subjects was 46.7 years. The majority of the samples were married (76%), male (74.7%), and undergraduates. A summary of this information is shown in Table 1.

Table 1 Demographic characteristics of the studied samples

Variables	Numbers (%)
Mean age + - standard deviation	46.7 ± 17.1
Gender	
Female	58 (25.3)
Man	171 (74.4)
marital status	
Single	49 (21.4)
Married	174 (76.0)
Widow	2 (1.0)
divorced	4 (1.8)
Level of Education	
illiterate	19 (8.3)
Lower than diploma	118 (51.5)
Diploma	68 (29.7)
College education	23 (10.1)
Unknown	1 (0.44)

3.1.1. What was the type of narcotic analgesics, and the reason for administration?

Table 2 Type and method of narcotic analgesia use for the studied patients

Variable	Numbers (%)
Type of Substance	
Morphine	136 (59.4)
Pethedine	75 (32.8)
Methadone	17 (7.4)
Opium	1 (0.4)
Method of Use	
Intravenous	156 (68.1)
Muscular	34 (14.9)
Oral	2 (0.9)
Subcutaneous	(16.2)

The most commonly used analgesic was morphine (59.4%), and the most commonly used method was intravenous (68.1%). In all patients, the reason for the opioid administration was pain relief. Additional information is given in Table 2.

3.1.2. What was the dose of used analgesics, and what was the prescription pattern?

The median dose (equivalent to morphine) in patients was 27 mg. Prescribing intervals have been mostly non-fixed, as needed, or PRN (Table 3)

Table 3 Amount and intervals of drug analgesia for patients studied

Dosage (mg)	
Medium (interquartile range)	27 (12-90)
Prescribing intervals	Numbers (%)
PRN	140 (61.1)
TDS	37 (16.2)
BD	30 (13.1)
QID	20 (0.9)
Daily	(0.1)

3.1.3. How was the dose of opioid analgesics related to the patients' demographic variables (such as age, gender, marital status, and level of education)?

The highest dose was reported in the age of 51-60, then 41-50 years (Figure 1). There is no linear relationship between age and the amount of used analgesics in hospitalized patients (Spearman correlation coefficient: 0.0702, P-value: 0.2905).

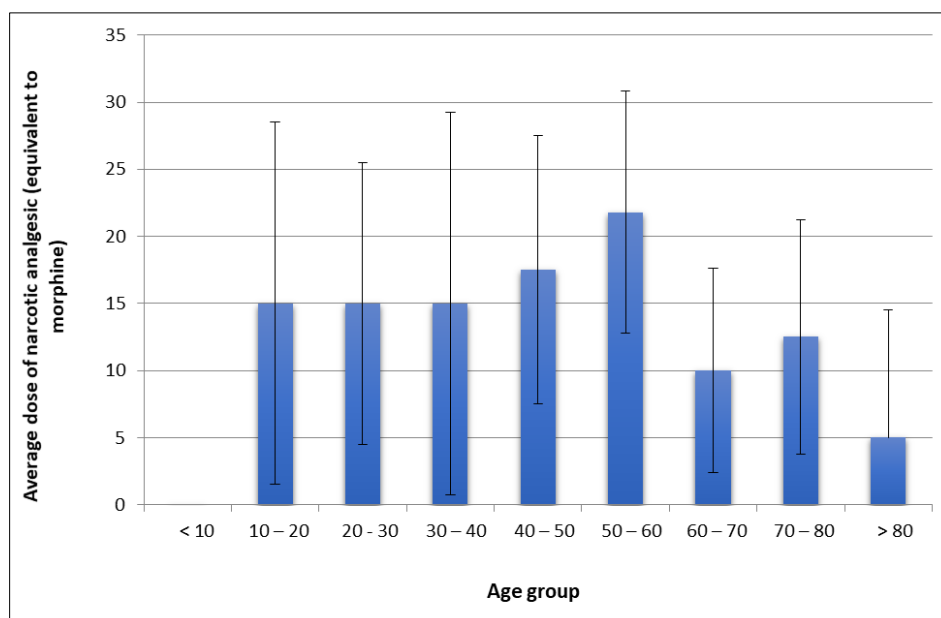


Figure 1 Average use of narcotic analgesics (morphine equivalent) by age group of the samples

The amount of opioid analgesics used in male patients was higher than in female patients. This difference was statistically significant on the borderline (Pearson X2: 3.2, P-value: 0.074).) (Table 4)

Table 4 Average consumption of analgesics (equivalent to morphine) by sex of the patients

P-value	Pearson X2	interquartile range	Middle	Gender
0.074	3.2	6 – 22.5	12	Female
		9-30	18	Male

* Mann-Whitney U test

The lowest mean dose of the drug was in single patients. This rate increased in married, widowed, and divorced patients, respectively, and this difference was also statistically significant (P-value = 0.04).) (Table 5 and Figure 2)

Table 5 Average consumption of narcotic analgesics (morphine equivalent) by marital status of the studied samples

Marital status	Middle	Interquartile range	P-value*
Single	15	35 – 7.5	0.04
Married	17.5	9-30	
Widow	27	24-30	
divorced	90	40-150	

* Kruskal Wallis test

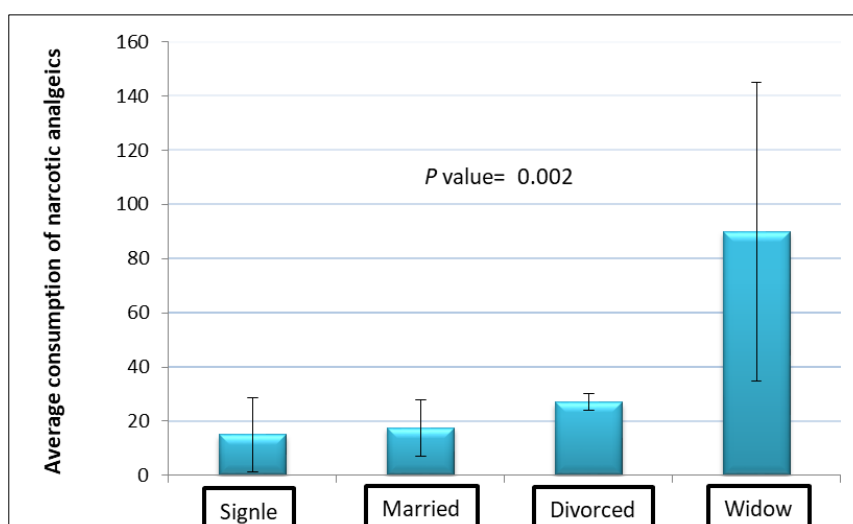


Figure 2 Average consumption of narcotic analgesics (morphine equivalent) by marital status of the studied samples

3.1.4. What were the underlying medical diseases in patients included?

Twenty-one percent (48 subjects) were hospitalized in surgical wards, and the remaining were in internal medicine wards. 121 of 181 internal medicine patients, 32 of 48 surgical patients, had cancerous pain, and the rest had other diseases. The information on the ward and the type of disease in patients can be seen in Table 6.

Table 6 Study samples categorized by ward

Variable	Number (percent)
Patients admitted to each ward	
Admitted to Internal medicine ward	181 (79.1)
Admitted to Surgical ward	48 (21.0)
Type of pain	
Patients in the Internal medicine ward	
Cancerous	121 (53.1)
Non-cancerous	59 (25.9)
Patients in the surgery ward	
Cancerous	32 (14.0)
Non-cancerous	16 (7.2)

3.1.5. How many analgesics were used in different hospital wards and patients with various underlying diseases?

In the internal medicine department, cancer and non-cancer patients did not significantly differ in the amount of analgesic drug received (P -value = 0.303). This finding was also observed for cancerous and non-cancerous patients admitted to surgical wards (P -value = 0.540). However, the average intake of opioid analgesics in surgical patients was significantly higher than in internal medicine patients (P -value = 0.001.) (Table 7).

Table 7 Comparison of the average analgesic dose received (equivalent to morphine) by the underlying disease

Type of underlying diseases	Min-max	Medium) (range between quarters	Test X ² *	P-value
Internal medicine ward			1/1	0.303
Non-cancerous	2-150	15 (8-27)		
Cancerous	2.5-210	15 (7.5-30)		
Surgery ward			0.4	0.540
Non-cancerous	3-130	23.3 (13.5-58.8)		
Cancerous	5-330	37.5 (20-70)		
Internal medicine ward	2-210	15 (7.5 – 27)	11.7	0.001
Surgery ward	330 - 3	25 (15 – 60)		

* Mann-Whitney U test

3.1.6. What type of intervention was required for substance abuse in the studied patients?

The prescribing of analgesics via a specialized intervention (by a psychiatrist) differs from the general intervention (general practitioner or nursing staff). So the pattern of prescribed analgesics, is probably affected by specialized versus general intervention. Therefore, we examined the required intervention for patients (specialized/ general) as a significant factor. To treat substance dependence, and among the patients who received opioid analgesics, ten (4.4%) needed specialized interventions, and 76 (33.2%) needed general interventions. 143 people (62.4%) did not need special action in this regard. (Table 8).

Table 8 Type of intervention required for substance abuse in the studied samples based on the results of the questionnaire Assist

Number (percent)	Drug use (according to the Assist questionnaire)
143 (62.5)	No need for intervention
76 (33.2)	General intervention
(4/4)	Specialized intervention

3.1.7. Is there any connection between the use of analgesics and psychiatric disorders in patients?

There was no linear relationship between anxiety scores (Spearman correlation coefficient: 0.07, P-value: 0.3134), depression (Spearman correlation coefficient: 0.002, P-value: 0.96), and total score of HADS (Spearman correlation coefficient: 0.06, P-value: 0.36) with the dose of analgesic drugs in admitted patients. Table 9 shows the average total scores and two groups of depression and anxiety sub-groups in the samples.

Table 9 Prevalence of anxiety and depression disorders in the studied samples, based on the HADS tool

Variable	Min-max	Mean ± SD	Middle (range between quarters)
Total HADS questionnaire score	0 - 24	7.4 ± 12.4	15 (7 - 18)
Anxiety scores from the HADS index	0 - 15	4.7 ± 5.8	5 (2 - 10)
Depression Score from the HADS Index	0 - 16	4.8 ± 6.6	7 (2 - 10)

3.1.8. Did the analgesic treatment was effective in reducing patients' pain?

The average patient's pain after receiving an analgesic has significantly decreased. (Table 10).

Table 10 Response to analgesic therapy following drug use based on Visual Analogue Scale

Before prescribing		After prescribing		P-value*
Middle (range between quarters)	Mean (standard deviation)	Middle (range between quarters)	Mean (standard deviation)	
8 (8 – 7)	7.8 (9/0)	3 (2 – 3)	2.8 (1.3)	<0.0001

*Wilcoxon signed-rank test

4. Discussion

In this study, we investigated the pattern of analgesic drug usage in 229 inpatient subjects. Also, we evaluated the patients' associated factors (substance abuse), demographic, and psychiatric profile. The most commonly used analgesic drug was morphine (59.4%), and a mean dose of 27 mg, then pethidine and methadone. Most pain control methods were intravenous (68.1%) and PRN pattern (61.1%). Using analgesics in patients who do not have risk factors for drug abuse or addiction, can be considered safe. In our subjects, 95.6% of analgesic users did not become addicted or had any misuse.

In comparison, in the study of Zin and colleagues in the UK, the most used analgesic was morphine, mainly with a dose of less than 50 mg/day. Also, the administration of other analgesics - oxycodone, buprenorphine, and fentanyl- has also increased over time. However, our study's prescribed dose of analgesics is far less than the above study. In another study by Neo et al. in Singapore, morphine was the most commonly used drug in one-third of pain patients [21].

On the other hand, in the study of George et al. in Singapore [22], the most prevalent analgesic was methadone (45.2%), and then morphine (38.1%). The causes of this variance are related to these two drugs' effects, complications, pharmacodynamics, pharmacokinetics, and differences in external conditions (prices, access, and experience of treatment staff with a particular drug). Also, only patients with chronic non-disposable pain have been investigated. The average dose of methadone consumption in this study is similar to the current study: For 36% of subjects, the morphine dose was between 1-30 mg, and for 36% of subjects was between 31-60 mg. The present study calculates the average dose of opioid drugs at 27 mg of morphine.

There seems to be a greater tendency to use morphine as an analgesic for various reasons, such as being effective, inexpensive, and available. However, with increased access to drugs with newer formulations, greater efficacy, and fewer side effects, more investigation is needed on drug options, considering physician preference, patient ease of use, and availability.

4.1. Method and pattern of using analgesics

The highest consumption pattern was PRN in most similar studies. Skinner et al. [23] reported the highest practice of analgesic use in PRN (49%) and then regular use (31%) in the United States, which is consistent with our study.

The symptomatic use of opioid analgesics was associated with pain-related, poor mental health, and using analgesics in a planned pattern is associated with better mental health. Interventions and encouragement of strategic or planned use of opioids have been suggested to improve pain control outcomes with opioids.

4.1.1. This PRN prescribing model has some weaknesses and challenges:

The PRN prescription places the responsibility for pain management on the nurse, which sometimes leads to prescribing the minimum dose required and ignoring patients' actual needs.

Some patients cannot request medication due to their disability, and some may refuse to apply for housing for fear of drug dependence.

This pattern also leads to fluctuations in the blood levels of the drug, which may increase the demand.

In many cases of the PRN method, re-evaluation has not been done after prescribing, and there are problems in recording cases in the files. For example, in the study of Hajebi et al., the opioid analgesics prescribed by the surgeons differed from the type of analgesic medication used by the nurses. In our study, there were many discrepancies between

the doses of the drug received by patients, the instructions of the in-charge physician, and the drug information center, which in some cases made it difficult to judge the amount of drug used by the patient.

The dose of opioid analgesics in this study was not significantly related to the age of the samples. However, a slightly higher dose was prescribed in male patients, which is statistically significant at the border. Narcotic analgesics are less commonly used in single patients, more commonly in married patients or slightly widowed men, and significantly more common in divorced women. Lower education in this study was associated with more use of these drugs. In a 2007 study by Hajebi et al. [24], women used more opioid analgesics than men, and most recipients were younger. In Sanchez et al.'s [25] study, there was no significant difference in the morphine response effect between the two sexes. However, women reported more drug side effects, contradicting our clinical and experimental findings, indicating that women respond more to opioids than men. Taking more opioid analgesics in men may be due to their lower response to opioids and greater tolerance to side effects.

- Forty-eight of our patients were in the surgical ward, and the rest were in the inpatient wards. There were 181 internal patients (121 with cancer), and 48 surgical patients (32 with cancer). Cancer and non-cancer patients did not differ significantly in the amount of analgesic drugs received in both internal and surgical departments. However, the average intake of opioid analgesics in surgical patients was significantly higher than patients in the internal medicine ward.
- The patients in our study expressed pain intensity on average in the range of + 0.9 – 7.85. This rate was higher than Noorbala et al.'s study, which studied the prevalence of substance abuse in the inpatient wards of Imam Khomeini Hospital in 2016. 5.8 ± 1.5 (which indicates more severe pain in patients receiving opioid analgesics). Also, in our study, opioid analgesics significantly reduced patients' pain based on the Numeric pain rating scale. In 2006, Forlan et al. Conducted a meta-analysis to compare the effects of different types of narcotic analgesics with each other, other analgesics, and placebo for chronic non-cancerous pain [26]. They found that opioid analgesics were superior to placebo in relieving nociceptive pain (such as osteoarthritis, rheumatoid arthritis, and low back pain), and neuropathic pain (such as post-herpetic neuralgia, diabetic neuropathy, and phantom limb pain), and fibromyalgia-related pain. In a total of 41 studies in 6019 patients, only potent drugs (tramadol, codeine, and propoxyphene) were superior to non-narcotic analgesics such as naproxen and nortriptyline. This difference was not seen for weak drugs (morphine and oxycodone).
- The results of using the ASSIST questionnaire showed that ten patients (4.4%) of patients who received opioid analgesics need specialized interventions to treat substance dependence, 76 patients (33.2%) should receive general interventions, and 143 patients (62.4%) do not need any particular action in this regard. Overall, 37.6% of patients needed intervention for substance abuse. In a similar study by MalarRabie et al., this number was reported to be 29.6%, indicating a higher prevalence of substance abuse in patients receiving opioid analgesics.
- A study by Sharifi et al. in 2015 [27] showed that the prevalence of substance dependence in the general population of Iran is estimated at 2.8%. Compared to the present study (4.4% requiring specialized interventions based on ASSIST), patients receiving opioid analgesics appear more likely to have substance abuse disorders. This finding has been confirmed in other studies. Adland et al. [28] showed that recipients of opioid analgesics for non-cancerous pain were more likely to have substance-related disorders such as opioid abuse. A similar result was obtained among the abused substances; the highest prevalence was related to nicotine and opium, consistent with other studies in this field.

Using the HADS tool, it was also found that there is no linear relationship between the scores of anxiety, depression, and the dose of analgesic drugs. A 2006 study by telephone and longitudinally, conducted from 1998 to 2001 on 6,439 patients on opioid prescriptions, found that among patients taking opioid analgesics were those with psychiatric disorders (including MDD, GAD, dysthymia, and panic) were more likely to continue opioid use after these three years. Of course, comparing these two studies seems difficult due to different designs, tools, cultural and social differences in drug use patterns, and many other factors.

A 2007 study by Wasan et al. [29] Examined patients taking opioid analgesics for non-cancerous pain and found that high-risk groups were also at higher risk for opioid abuse in terms of psychiatric disorders. Our study found no relationship between the dose of opioid analgesia and recent depression and anxiety based on HADS. However, due to the cross-sectional nature of this study, it is not easy to generalize the results and compare the two studies.

A retrospective cohort of Bantagreen et al. [30] was performed on 704 chronic opioid patients in the United States. It was seen that among the three groups defined based on Latent Class Analysis: the normal group (light pain + moderate psychiatric symptoms) had a lower average drug dose than the other two groups. The other two groups, the group with

addictive behaviors (severe psychiatric disorders + substance abuse+ light pain) and a group with dysfunction due to pain (severe pain + severe psychiatric disorders + substance abuse), had higher mean drug doses. Pain does not seem to be an independent factor, and the psychiatric background is a better predictor of substance abuse and higher doses of narcotic analgesics. Part of the reason for not confirming such a result in the present study can be attributed to the mildness of the disorders studied in the present study (depression and anxiety). A 2013 study by Fiellin et al. [31] found that young men with a history of substance abuse such as smoking, alcohol, and cannabis, and young women with a history of cannabis abuse, were more likely to use prescribed opioids for controlling pain.

5. Conclusion and suggestions

The prevalence of substance use disorders is higher in patients receiving opioid analgesics, and pain management in these patients is more challenging. For effective and low-risk treatment of these patients, there is a need for clinical skills, knowledge of opioid administration, assessment, and risk management of substance abuse and addiction. A complete history and physical examination of all patients should be made, including an evaluation of psychosocial factors and family history, to assess the risk of treatment. Personal and family history of alcohol use, young age, and the presence of underlying psychiatric illness (especially PTSD) should be carefully evaluated, as they can strongly predict future drug abuse. Due to the low dose of narcotics in this study compared to other studies, clinicians should consider whether the patient's pain may respond effectively to non-opioid drugs?

- In patients with substance abuse, societyenviro should be prescribed in a special setting, under supervision, and with careful monitoring (especially in cases where the patient uses other substances and non-prescription drugs simultaneously). A thorough evaluation of the benefits and harms of treatment should be done. Counseling and referral for comorbidity management should be performed in patients with substance use disorder criteria.

Structured and planned administration of opioid agonists (such as methadone or buprenorphine) seems appropriate according to a structured schedule. Studies have shown that general guidelines improve pain management, even in people with a history of substance abuse. Also, patients with a history of addiction can benefit from narcotic analgesics with strategies such as contracting with the patient, setting appropriate therapeutic goals, prescribing appropriate amounts of medication, careful monitoring, and recording.

In general, some measures and interventions can be taken for better and fewer complications of pain control in non-psychiatric wards, such as: increasing the awareness of clinicians about prescribing narcotic analgesics, prescribing narcotic analgesics with a regular pattern against PRN, evaluating patients for a history of substance abuse, closely monitoring them, and if necessary, counseling. Identifying high-risk groups such as women, youth, and psychiatric patients are also recommended, and early interventions should be performed on them

Compliance with ethical standards

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Disclosure of conflict of interest

There is no conflict of interest for any of the authors

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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