

Factors Associated with Sustained Remission among Chronic Opioid Users

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Original Article

Abstract

Background: Chronic opioid use is a major public health problem with significant morbidity. The aim of this study was to investigate factors associated with sustained remission among a sample of Iranian chronic opioid users in Shiraz, Iran.

Methods: This was a cross-sectional study to evaluate sustained remission among chronic opiate users aged 20-60 years. Participants included two groups: 365 people who have been in sustained remission for the past year, and 187 persons who did not achieve remission for the past one year. Then, demographic and factors related to drug use pattern and previous treatments were compared between two groups. Pearson chi-square test was used for univariate analysis and backward stepwise logistic regression was used to estimate adjusted odds ratios (AORs).

Findings: Our findings showed that sustained remission was associated with Narcotic Anonymous (NA) participation [AOR = 3.28, 95% confidence interval (CI): 2.19-4.89, $P < 0.001$], male gender (AOR = 2.53, 95% CI: 1.45-4.43, $P = 0.001$), younger age of onset (AOR = 1.63, 95% CI: 1.03-2.58, $P = 0.037$), higher total years of opioid use (AOR = 2.13, 95% CI: 1.42-3.19, $P < 0.001$), no history of imprisonment (AOR = 2.11, 95% CI: 1.16-3.85, $P = 0.015$), and family support (AOR = 2.58, 95% CI: 1.33-5.01, $P = 0.005$).

Conclusion: Participation in self-help groups can be a suitable alternative in predicting sustained remission among chronic opiate users. Chronic opioid users should be encouraged by the physicians who are involved in the treatment of drug addiction to participate in NA programs.

Keywords: Drug addiction; Opioids; Substance use disorders; Opiate substitution treatment

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Introduction

Chronic opioid use is a major public health problem with significant morbidity that affects more than 21 million people worldwide.^{1,2} The natural course of chronic opioid use includes opioid dependency, repeated attempts to stop substance use, and frequent relapse.³

Opioids are the most commonly used drugs in Iran with the highest rate of opiate use in the world.^{4,5} In addition to opium, which is traditionally the main drug of abuse in Iran, there has been an increase in the use of heroin among Iranian opiate users within the last decades,^{6,7} and more than 80% of drug abuse treatment cases were related to opiate addicts who were seeking treatment.⁴

Abrupt cessation of opioids without any treatment is less likely and a substantial number of chronic addicts resort to therapeutic modalities. Findings from prospective studies indicate that participation in formal and prolonged treatment is generally associated with better outcomes.^{8,9} A variety of treatment methods are used by chronic opioid users to control their addiction, often with a multiple stop-and-start pattern.¹⁰ Harm reduction and abstinence-oriented policies are the two strategies to control opioid use disorder (OUD). Many opioid addicts experience single or combined treatment methods to overcome their addiction; hence, the efficacy of a single method cannot be measured accurately.⁸

The most common pharmacological methods for treatment of opioid addiction are detoxification and maintenance therapy with drugs such as opioid agonists and antagonists, and alpha-2-adrenergic agonists. Agonist maintenance therapy is one of the most common types of treatment because of the better outcomes attained in comparison with other drug therapies.¹¹ Moreover, participation in 12-step or Narcotic Anonymous (NA) groups is another common method used by opioid addicts to control opioid use.¹²

Although drug addiction is defined as a chronic relapsing disease, which has periods of exacerbation and remission,^{13,14} duration of remissions is an important factor for predicting future physical and mental health of patients. The longer the periods of remission, the better would be the physical, psychological, and social function

and ultimate prognosis.¹⁵

Factors associated with remission from alcohol dependence have been extensively studied, but few studies have investigated factors associated with sustained remission from other substances including opiates.^{16,17} Follow up of patients after outpatient treatment programs indicates that better outcomes are associated with older age, lower severity of addiction, less psychiatric comorbidity, longer duration of treatments, and participation in 12-step programs.^{18,19} In addition, gender, race/ethnicity, educational attainment, income, marital status, comorbid substance use disorders (SUDs), and drug treatment utilization have been associated with sustained remission.^{20,21}

In the present study, we compared two groups of opiate addicts: chronic opioid users who maintained remission and those who did not achieve remission for the past one year.

Methods

This cross-sectional study with a control group was carried out between June to August 2017 in Shiraz, Iran. Study population included people aged 20-60 years with a history of at least two years of continuous use of opium or heroin, and involvement in at least one formal treatment program to stop their addiction. All of the participants stated opium or heroin as their primary drug of choice. Pure users of cannabis, methamphetamines, and prescription opioids such as tramadol or methadone were excluded from the study. According to The Diagnostic and Statistical Manual of Mental Disorders-5th Edition (DSM-5) criteria for SUDs, sustained remission is defined as ≥ 12 months without meeting SUD criteria, except craving.²² Considering the cross-sectional design of this study, we considered sustained remission as not meeting the DSM-5 criteria at the time of the study and no self-reported relapse during the last year. We used outpatient clinics and self-help groups sessions as settings to access chronic opioid users who were seeking treatment modalities. The sample size was calculated by assuming $\alpha = 0.05$, a population proportion of 50%, and a precision of 0.05, and was estimated as at least 384 patients. There are 60 outpatient addiction treatment clinics and 13 NA self-help groups in the inner city of Shiraz which were numbered and then fifteen

outpatient addiction treatment clinics and six NA self-help groups were selected by simple random sampling. Following a screening interview to determine eligibility for the study with more than 1500 patients of selected centers and groups, 552 people were identified as eligible. Data collection was performed by a team including a physician who checked the eligibility of participants. Eligibility was based on patients' self-report. Participants included two groups: 365 people who have been in sustained remission for the past year, and 187 persons who met SUD criteria and had at least one substance use relapse during the past year. A written informed consent was obtained after the study was explained to all the participants. The study received ethical approval from the local Ethics Committee of Shiraz University of Medical Sciences (code: IR.SUMS.MED.REC.1395.08).

The research instrument was an interviewer-administered structured questionnaire that contained demographic characteristics (age, gender, marital status, educational level, and job) and substance-related questions including age of the onset, primary drug of use, total years of opioid use, history of injection drug use (IDU), opioid use among first degree relatives, number and type of treatment programs (including agonist therapy and participation in self-help groups) and also history of imprisonment. Data were analyzed with the use of SPSS software (version 19, SPSS Inc., Chicago, IL, USA). Comparisons were made by means of independent t-test for continuous variables and chi-square test for categorical variables. For univariate analysis, continuous variables were dichotomized at median values. Subsequently, multivariate logistic regression with backward elimination of variables was performed. Adjusted odds ratios (AORs) and 95% confidence intervals (CIs) were calculated. Significance level of 0.05 was considered to be statistically significant.

Results

Study participants were opiate users residing in Shiraz City, with at least two years of regular opiate use. The majority of participants were male (87.0%), married (59.6%), had less than 12 years of education (76.8%), employed (65.0%), started opiate use after age of 20 (71.6%), used opiates for more than 5 years (65.9%), and reported opium as

their primary drug of use (69.4%). Some participants reported history of IDU (21.2%) and opiate use among first-degree relatives (39.3%). More than one third of participants (37.9%) had tried five times or more episodes of treatment. The most commonly used treatment program was opioid agonist therapy (OAT) (71.9%). There was also a significant proportion of patients (66.5%) who had participated in self-help groups.

Characteristics of study subjects are summarized in table 1. The mean age of those with sustained remission was 42.12 ± 8.48 and of those without it was 41.23 ± 8.02 ($P = 0.441$).

Those patients who did not achieve sustained remission were more likely to be female patients, with 2-5 years of opioid use and history of imprisonment, and they had commonly used OAT. Those with sustained remission had lower age of onset and positive family support, and had more commonly participated in NA programs.

According to univariate analysis, sustained remission was predicted by male gender (OR: 3.03, CI: 1.83-5.02, $P < 0.001$), age of onset of opioid use before 20 years (OR: 2.08, CI: 1.36-3.18, $P = 0.001$), more than 5 years history of opioid use (OR: 2.72, CI: 1.88-3.93, $P < 0.001$), family support (OR: 3.18, CI: 1.71-5.91, $P < 0.001$), no history of imprisonment (OR: 1.85, CI: 1.08-3.15, $P = 0.032$), and participation in self-help groups (OR: 4.23, CI: 2.89-6.18, $P < 0.001$). It was inversely related to a history of agonist therapy (OR: 0.57, CI: 0.37-0.86, $P = 0.007$). Sustained remission was not associated with age ($P = 0.564$), marital status ($P = 0.271$), education ($P = 0.832$), job status ($P = 0.510$), primary drug of use ($P = 0.172$), history of IDU ($P = 0.154$), and number of treatment episodes ($P = 0.926$) (Table 1).

The results of multivariate regression analysis have been shown in table 2. The model explained approximately 26% of the observed variance (pseudo- $R^2 = 0.257$), and the overall accuracy of the model to predict sustained remission was 66.1%. According to the model, sustained remission was associated with NA participation (AOR = 3.28, 95% CI: 2.19-4.89, $P < 0.001$), male gender (AOR = 2.53, 95% CI: 1.45-4.43, $P = 0.001$), younger age of onset (AOR = 1.63, 95% CI: 1.03-2.58, $P = 0.037$), more total years of opioid use (AOR = 2.13, 95% CI: 1.42-3.19, $P < 0.001$), no history of imprisonment (AOR = 2.11, 95% CI: 1.16-3.85, $P = 0.015$), and family support

(AOR = 2.58, 95% CI: 1.33-5.01, P = 0.005). The model showed that being a female and having a

history of imprisonment were inversely related to sustained remission (Table 2).

Table 1. Univariate analysis of factors associated with sustained remission among chronic opiate users, Shiraz, Iran

Variable	Total (n = 552) [n (%)]	Not in remission (n = 187) [n (%)]	In sustained remission (n = 365) [n (%)]	OR (95% CI)	P
Age (year)					
20-39	374 (67.75)	130 (69.50)	244 (66.80)	1.13 (0.77–1.65)	0.564
40-60	178 (32.25)	57 (30.50)	121 (33.20)	1	
Sex					
Male	480 (86.95)	146 (78.10)	334 (91.50)	3.03 (1.83–5.02)	< 0.001
Female	72 (13.05)	41 (21.90)	31 (8.50)	1	
Marital status					
Married	329 (59.60)	105 (56.10)	224 (61.40)	1.24 (0.87–1.77)	0.271
Single/divorced/widowed	223 (40.40)	82 (43.90)	141 (38.60)	1	
Age of onset of opioid use (year)					
< 20	157 (28.44)	36 (19.30)	121 (33.20)	2.08 (1.36–3.18)	0.001
≥ 20	395 (71.56)	151 (80.70)	244 (66.80)	1	
Family support					
Yes	83 (15.03)	13 (7.00)	70 (19.20)	3.18 (1.71–5.91)	< 0.001
No	469 (84.97)	174 (93.00)	295 (80.80)	1	
Education (years of schooling)					
≥ 12	128 (23.19)	42 (22.50)	86 (23.60)	1.06 (0.69–1.62)	0.832
< 12	424 (76.81)	145 (77.50)	279 (76.40)	1	
Having a job					
Yes	359 (65.03)	122 (65.20)	237 (64.90)	0.97 (0.68–1.43)	0.510
No	193 (34.97)	65 (34.80)	128 (35.10)	1	
Primary drug of use					
Opium	383 (69.38)	137 (73.30)	246 (67.40)	1.33 (0.89–1.96)	0.172
Heroin	169 (30.62)	50 (26.70)	119 (32.60)	1	
Opioid use in first degree relatives					
Yes	217 (39.31)	63 (33.70)	154 (42.20)	0.69 (0.48–1.01)	0.054
No	335 (60.69)	124 (66.30)	211 (57.80)	1	
Total years of opioid use					
> 5	364 (65.94)	95 (50.80)	269 (73.70)	2.72 (1.88–3.93)	< 0.001
2-5	188 (34.06)	92 (49.20)	96 (26.30)	1	
History of IDU					
Yes	117 (21.20)	33 (17.60)	84 (23.00)	0.72 (0.46–1.12)	0.154
No	435 (78.80)	154 (82.40)	281 (77.00)	1	
History of imprisonment					
No	490 (88.77)	158 (84.50)	332 (91.00)	1.85 (1.08–3.15)	0.032
Yes	62 (11.23)	29 (15.90)	33 (9.00)	1	
NA participation					
Yes	367 (66.49)	84 (44.90)	283 (77.50)	4.23 (2.89–6.18)	< 0.001
No	185 (33.51)	103 (55.10)	82 (22.50)	1	
History of agonist therapy					
Yes	397 (71.92)	148 (79.10)	249 (68.20)	0.57 (0.37–0.86)	0.007
No	155 (28.08)	39 (20.90)	116 (31.80)	1	
Treatment episodes					
1-4 times	343 (62.14)	117 (62.60)	226 (61.90)	1.03 (0.71–1.48)	0.926
≥ 5 times	209 (37.86)	70 (37.40)	139 (38.10)	1	

OR: Odds ratio; CI: Confidence interval; IDU: Injection drug use; NA: Narcotic anonymous

Table 2. Multivariate analysis of factors associated with sustained remission among Iranian chronic opiate addicts, Shiraz, Iran

Variable	B	SE	Wald	df	AOR (95% CI)	P
NA participation						
Yes	1.188	0.204	33.779	1	3.28 (2.19–4.89)	< 0.001
No					1	
History of imprisonment						
No	0.746	0.307	5.894	1	2.11 (1.16–3.85)	0.015
Yes					1	
Primary drug of use						
Opium	0.226	0.228	0.986	1	1.25 (0.80–1.96)	0.321
Heroin					1	
Sex						
Male	0.930	0.285	10.655	1	2.53 (1.45–4.43)	0.001
Female					1	
Age of onset of opioid use (year)						
< 20	0.489	0.235	4.338	1	1.63 (1.03–2.58)	0.037
≥ 20					1	
Family support						
Yes	0.947	0.339	7.809	1	2.58 (1.33–5.01)	0.005
No					1	
Total years of opioid use						
> 5	0.756	0.207	13.338	1	2.13 (1.42–3.19)	< 0.001
2-5					1	
History of agonist therapy						
Yes	-	0.233	1.342	1	0.72 (0.46–1.13)	0.155
No	0.331				1	

AOR: Adjusted odds ratio; CI: Confidence interval; SE: Standard error; df: Degree of freedom; NA: Narcotic anonymous

Discussion

Our findings showed that male opioid addicts were more likely to achieve sustained remission and to stay sober compared to female patients. There was a significant gender difference in prevalence rates, health service use, treatment outcome, and physiological consequences of SUDs. Evidence suggests that female addicts suffer more severe emotional and physical consequences in comparison to men. They usually face numerous barriers including limited access to treatment, stigma, and fear of legal problems.^{23,24} These factors may affect the frequency and duration of remissions.

Another finding of the present study showed that people with earlier age of onset and higher total years of opiate use were more likely to report sustained remission. This finding is in contrast to previous reports which had implied that early age of onset was associated with a higher prevalence of dependency, increased clinical severity, and worsened consequences.^{25,26} However, at the same time, some reports were in line with our findings. For example, in a cohort study on people with different drug addictions, duration of remission

was significantly higher in those with age of onset of below 21 years. Moreover, according to this study on heroin addicts, substance cessation attempts 10-20 years after first drug use were more successful.¹⁶ In studies of community and treatment populations, about 60 percent of patients with a SUD eventually achieved sustained recovery at some time in their lives.²⁷ Whether this is due to experience obtained by repeated cessation attempts or a blunted dopaminergic system is questionable. It has been suggested that chronic drug use might down-regulate dopamine receptors and production in the brain reward system that might help patients to reduce or stop substance use.²⁸

Social support from family has been consistently found to predict positive outcomes among drug addicts.^{9,29} The results of our study also supported the association of family support with sustained remission among opioid addicts. It seems that emotional and economic burden and relationship distresses and conflicts can be relieved by a supporting family.

A substantial proportion of people with OUDs experiences imprisonment. A history of

imprisonment is associated with an ongoing elevated risk of negative outcomes. Almost 75% of prisoners with OUD do not maintain remission 3 months after release from jail.^{30,31} In the present study, lack of history of imprisonment was found to be predictive for sustained remission.

A notable finding of this study was that participation in self-help groups was a significant predictor of sustained remission among chronic opiate users. Some other studies have similarly shown that self-help group participation promoted sustained remission among different drug users.¹⁰ As an abstinence-based method of addiction treatment, 12-step program helps opioid addicts to stay clean through spiritual practices.³² Although this treatment method also follows a multiple stop-and-start pattern,¹⁰ the present study showed that those with a history of participation in self-help groups were more likely to stay in sustained remission. In some treatment programs, NA meetings are used as a complementary treatment, which has shown to enhance maintenance of the relapse-free state.³³ It seems that participation in 12-step programs promotes positive psycho-emotional changes that help opioid addicts to stay in remission for longer periods of time.

The present findings suggest that OAT, despite its considerable benefits, is not significantly associated with sustained remission. Maintenance treatment with methadone reduces injecting practice, crime, risk of blood borne viral infections, and drug overdose, and improves social function.³⁴⁻³⁶ At the same time, relapses are common with this modality, and according to a prospective study, just 27% of opiate addicts under methadone therapy had 4 months or longer periods of remission.¹⁶ As a substitute method, agonist therapy is an appropriate tool for controlling opioid addiction as far as the substitute drug is used, but it does not seem to significantly affect the rate of sustained remission.

Most chronic addicts, who achieve sustained recovery, do so after at least one episode of formal treatment.²⁷ Our findings showed that there was no association between the number of previous

treatment episodes and the experience of sustained remission. A longitudinal study on 1326 patients for 9 years showed a negative association between number of treatment episodes and sustained remission. In the aforementioned study, after the initial 6 months of treatment, the likelihood of sustained remission decreased as the number of subsequent treatment episodes increased.¹⁵ Maybe the quality and type of treatments and use of complementary methods like 12-step programs, as our findings showed, are more important determinants of sustained remission.

There are some limitations to our study. First, this was a cross-sectional study based on participants' self-report. The validity of self-reported data cannot be established and the collected information is subject to bias. Second, we did not assess factors such as mental distress and duration of retention in treatments. Third, we considered drug addicts who were seeking treatments; therefore, the enrolled population might not be representing all chronic opiate addicts.

Conclusion

According to our findings, participation in self-help groups can be a suitable alternative in predicting sustained remission among chronic opiate users. Moreover, male chronic opiate addicts with earlier age of onset of drug use and longer history of opioid use are more likely to report sustained remission. Chronic opioid users should be encouraged by the physicians who are involved in the treatment of drug addiction to participate in NA programs.

Conflict of Interests

The Authors have no conflict of interest.

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بررسی عوامل مرتبط با بهبود پایدار در مصرف‌کنندگان مزمن مواد اپیوئیدی

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مقاله پژوهشی

چکیده

مقدمه: مصرف مزمن مواد اپیوئیدی، مشکل عمده سلامت جامعه است که با عوارض قابل توجهی همراه می‌باشد. پژوهش حاضر با هدف بررسی عوامل مرتبط با بهبود پایدار در نمونه‌ای از مصرف‌کنندگان مواد اپیوئیدی شهر شیراز انجام شد.

روش‌ها: این مطالعه از نوع مقطعی بود که جهت ارزیابی بهبود پایدار در مصرف‌کنندگان ۲۰ تا ۶۰ ساله مواد اپیوئیدی انجام گردید. شرکت‌کنندگان شامل دو گروه بود؛ ۳۶۵ نفر که طی یک سال گذشته در بهبودی به سر برده بودند و ۱۸۷ نفر که طی این مدت بهبودی به دست نیاورده بودند. خصوصیات دموگرافیک و شاخص‌های مرتبط با الگوی مصرف و درمان‌های قبلی بین دو گروه مقایسه گردید. جهت آنالیز تک متغیره، آزمون χ^2 Pearson و جهت برآورد نسبت شانس سازگار شده نیز روش Logistic regression گام به گام مورد استفاده قرار گرفت.

یافته‌ها: بهبود پایدار با شرکت در جلسات معتاد گمنام [$P < 0/001$ ، $OR = 2/53$ ، $CI = 1/45 - 4/43$ ، $P = 0/001$]، جنس مذکر ($OR = 1/63$ ، $CI = 1/03 - 2/58$ ، $P = 0/037$)، سن کمتر شروع مصرف ($OR = 2/13$ ، $CI = 1/42 - 3/19$ ، $P < 0/001$)، نداشتن سابقه زندان ($OR = 2/11$ ، $CI = 1/16 - 3/85$ ، $P = 0/015$) و حمایت خانواده ($OR = 2/58$ ، $CI = 1/33 - 5/01$ ، $P = 0/005$) ارتباط معنی‌داری داشت.

نتیجه‌گیری: شرکت در گروه‌های همیار می‌تواند جایگزین مناسبی برای پیش‌بینی بهبود پایدار در مصرف‌کنندگان مزمن مواد اپیوئیدی باشد. پیشنهاد می‌شود پزشکی که به درمان اعتیاد می‌پردازند، مصرف‌کنندگان مزمن مواد اپیوئیدی را به شرکت در برنامه‌های معتادان گمنام تشویق نمایند.

واژگان کلیدی: اعتیاد به دارو، اپیوئید، اختلالات سوء مصرف مواد، درمان جایگزین اپیوئید

ارجاع: شیرالی رامین، تقوا مریم. بررسی عوامل مرتبط با بهبود پایدار در مصرف‌کنندگان مزمن مواد اپیوئیدی. مجله اعتیاد و سلامت ۱۳۹۷؛ ۱۰ (۲): ۹۴-۸۶.

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