

Article

Predictors of relapse among patients with opioid use disorder treated with relapse prevention based cognitive behavior therapy: a prospective study

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Abstract

Background: Opioid use disorder is defined as persistent opioid use that produces clinically substantial distress or impairment and necessitates effective treatment. According to epidemiological studies, 26–36 million persons globally abuse opiates, with extremely high relapse rates. Effective recovery is possible with sufficient therapy, but with a persistent propensity to relapse. The purpose of this study was to investigate the pretreatment patient's characteristics that might predict relapse among patients with opioid use disorder after treatment with relapse prevention based cognitive behavior therapy for 12 weeks. **Methods:** this was a prospective cohort study of 50 Egyptian opioid dependent patients who underwent detoxification with clonidine drug followed by assigning to relapse prevention based CBT sessions at outpatient psychiatry and addiction clinic of Alexandria main university hospital for 12 weeks then relapse into opioids was assessed at end of psychotherapy by urine screen test for opioids. **Results:** of the 50 recruited patients, 15 patients didn't complete the study with dropout rate 30%. 16 patients remained abstinent with negative urine test for opioids at end of CBT program while 19 one relapsed to opioid use with positive urine test. Statistical analysis of the results showed that having family history of substance abuse, using high doses of heroin per day and injection route of

use were significantly associated with relapse at follow up while using high doses of heroin per day pretreatment was the most independent variable associated with relapse. *Conclusion:* identification of predictors of relapse and hence high risk patients might be helpful in designing more effective and focused treatment plan to reduce relapse.

Keyword: relapse prevention, predictors, opioid use disorder, cognitive behavior disorder

Introduction

Opioid use disorders are described as a pattern of opioid use that is coupled with a variety of physical, mental, social, and legal difficulties, as well as increased mortality, resulting in clinically significant impairment or distress. (1) Over 16 million individuals worldwide suffer from opioid use disorders, including 2.1 million in the United States, and opioids are responsible for over 120,000 fatalities each year. (2) It has been documented in the United States that nonmedical use of prescription opioids is associated with a significant upsurge in mortality and the hazard of switching to heroin usage. (3) Opioid misuse, particularly heroin, can be caused by a variety of causes; experimentation, mimicking friends, or submitting to peer pressure are all possibilities. It often starts with the user taking opioids as prescribed and progresses to the user taking the medications differently than intended or acquiring opioids given to someone else. (4) Opioids are abused for their analgesic and rewarding characteristics; those who are physically addicted to heroin may also abuse them to avoid withdrawal symptoms. The capability of opioids to raise the activity of dopamine neurons in the ventral tegmental area and increase dopamine release in the nucleus accumbens explains why they are used for their rewarding effects. (5) Data on the factors in relation with the development of opioid use disorder are frequently based on case-control studies.

According to these research, risk factors for prescription opioid usage include previous history of substance abuse, being younger, experiencing more severe pain, and having co-occurring mental issues.(6) Furthermore, a history of childhood maltreatment (e.g., sexual, physical, or emotional abuse or neglect) is regarded as a risk factor for opioid use disorder.(7) Relapse is recognized as a breakdown in a person's attempt to change drug use habits, return to pre-treatment drinking levels, or continue using substances after an interval of sobriety, or a setback in a person's attempt to alter or modify any target behavior.(8) Substance use following successful detoxification and recovery is a global concern, and it is more prevalent in low and middle-income nations than in high-income countries.(9) Relapse rates for opioid addiction are higher than for any other drug addiction, with one study estimating that up to 91 percent of those in recovery will relapse. The study also found that at least 59 percent of those who relapsed would do so within the first week of sobriety, and 80 percent would relapse within a month after leaving a detox program. (10) Because the relapse rate following opioid detoxification and rehabilitation is so high, the purpose of this study was to investigate the pre-treatment patients' characteristics that

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may predict relapse among patients with opioid use disorder after treatment with relapse prevention based cognitive behavior therapy for 12 weeks.

Methods

Study design, setting and participants

The present study was prospective cohort study conducted on 50 patients diagnosed with opioid use disorder according to Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria. (11) They were referred from the outpatient clinics of Alexandria main university hospital and from two private outpatients' addiction clinics through the period of 1st of April 2020 till 30th of August 2021. All participants were assigned to relapse prevention based cognitive behavioral therapy group sessions after being detoxified with alpha 2 agonist drug, clonidine, and had naltrexone challenge test negative. Patients were selected according to inclusion and exclusion criteria. Our inclusion criteria were being a male patient, age between 18-45 years, meeting DSM-5 criteria of opioid use disorder while exclusion criteria were Serious or unstable medical condition in the past 6 months (infective endocarditis, HIV, viral hepatitis C or B), participants with intellectual disability.

Data collection and assessment

All patients were evaluated pretreatment by a pre-designed structured interview questionnaire to collect socio-demographic data as age, residence, marital state and occupation, medical and psychiatric history and by Arabic version of addiction severity index (ASI). (12) The ASI is a face-to-face structured clinical interview that was created to meet the demand for a dependable, valid, and standardized diagnostic and evaluation tool in the field of alcohol and drug misuse. This Arabic version was translated for use in a medical doctorate candidate's thesis by a senior physician at the Institute of Psychiatry, Ain Shams University Hospital. Urine screening test for opioid was performed to all participants at end of cognitive behavioral therapy program (at 3 months) to detect relapse.

Relapse prevention based Cognitive behavioral therapy (CBT) (13)

All patients were subjected to relapse prevention based CBT group sessions (12 sessions) at outpatient addiction clinic of Alexandria main university hospital, one session per week and each session was lasting for 90 minutes. Each group included (8-12) participants. Sessions were covering the following aspects: Psycho-education about pathophysiology of addiction, stages of recovery and basic concepts of RP based CBT for addiction. Illustration of cognitive model of addiction and training on techniques of cognitive therapy (thought stopping techniques). Identifications of triggers either external or internal and risky situations. Understanding the craving and techniques to cope with it. Teaching and practicing drug refusal skills. Crisis

intervention and problem solving skills training for managing general life problems. Understanding the role of abstinence violation syndrome in relapse and strategies for relapse prevention.

Statistical analysis of the data

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp). Categorical data were represented as numbers and percentages. Chi-square test was applied to investigate the association between the categorical variables. Alternatively, Fisher's Exact correction test was applied when the expected cell counts were less than 5. For continuous data. Distributed data were expressed as range (minimum and maximum), mean, standard deviation and median. Logistic regression analysis was used to detect the most independent factor for affecting relapse at follow up post treatment. Significance of the obtained results was judged at the 5% level.

Ethical considerations

Prior to conducting this research, ethical approval was obtained from the ethical committee (EC) of Alexandria University Faculty of Medicine. This EC has a federal wise assurance (FWA) for more than 20 years now. (14) It operates according to the International Conference of Harmonization Good Clinical Practice (ICH GCP) and applicable local and institutional regulations and guidelines. (15)

Informed consent

An informed consent was obtained from all patients to use their anonymous data for research purpose.

Results

Descriptive analysis

Regarding the sociodemographic and some abuse relevant variables of the 50 recruited patients, mean of age was (32.3 ± 7.6) . 60% of patients were living in urban areas while 40% in rural areas. 48% were single, 32% were married while 20% were widow/ divorced. 56% were employed versus 44% unemployed. 54% had family history of substance abuse among first degree relatives. 26% of patients were only opioid dependent while 74% were poly drug dependent. Regarding route of opioids use, 48% were using opioids via smoking, 30 % via snorting / sniffing while 10 % were via injection. 66 % of patients were using gram or more of heroin per day versus 34% using less than one gram per day. **(Table 1)**

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Table (1): Distribution of the studied cases according to demographic data and some abuse relevant variables (n = 50)

	No. (%)
Age (years)	
Mean \pm SD.	32.3 \pm 7.6
Median (Min. – Max.)	32.5 (19 – 45)
Residence	
Urban	30 (60%)
Rural	20 (40%)
Marital state	
Single	24 (48%)
Married	16 (32%)
Widow/ Divorced	10 (20%)
Occupation	
Unemployed	22 (44%)
Employed	28 (56%)
Family history of substance abuse among first degree relatives	
	27 (54%)
Pattern of use	
Opioids mono drug use	13 (26%)
Poly drug use (opioids plus other substances)	37 (74%)
Route of opioids use	
Smoking	24 (48%)
Sniffing/ snorting	15 (30%)
Injection	11 (22%)
Dose of heroin /day	
Less than one gram/day	17 (34%)
Gram or more	33 (66%)

SD: Standard deviation

The Mean \pm SD and Median of composite scores of the seven domains of the addiction severity index of the recruited patients were demonstrated in **Table 2**.

Table (2): Descriptive analysis of the studied cases according to ASI composite scores (n = 50)

	Mean ± SD.	Median (Min. – Max.)
Medical status	1 ± 1.9	0 (0 – 9)
Employment/ support status	3.3 ± 1.8	3 (0 – 7)
Alcohol	1.4 ± 1.6	1 (0 – 6)
Drug	5.3 ± 1.6	5 (2 – 9)
Legal status	1.4 ± 1.6	1 (0 – 6)
Family/ social relation ships	3.4 ± 2	4 (0 – 7)
Psychiatric status	4.6 ± 3	6 (0 – 9)

SD: Standard deviation

Post treatment urine screening test (at 3 months) was only done for 35 (70%) of the recruited patients, as 15 (30%) didn't complete the study and dropped out from CBT program sessions. Of the 35 patients who completed the study, 16 (32%) patients had negative urine test for opioids (remain abstinent) while 19 (38%) had positive one (relapsed into opioid use). (**Table 3**)

Table (3): Distribution of the studied cases according to replace and dropped out rates at end of therapy (at 3 months) (n = 50)

Urine Screen Test	No. (%)
Abstinent (Negative)	16 (32%)
Relapsed (Positive)	19 (38%)
Dropped out	15 (30%)

#: Relapse confirmed by positive urine test

Relation between occurrence of relapse at 3 months follow up and some abuse relevant data

Table 4 depicts that having family history of substance abuse among first degree relatives, using opioids via injection and using high doses of heroin per day (gram or more) were significantly associated with relapse to opioid use at 3 months follow up ($p \leq 0.05$) while being poly drug dependent pretreatment didn't show the same significant association with relapse. ($FEP=1.000$).

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Table (4): Relation between relapse at end of therapy and some relevant abuse data (n = 35)

	Urine Screen Test		χ^2	P
	Abstinent (Negative)	Relapsed (Positive)		
	(n = 16)	(n = 19)		
Family history of substance abuse	4 (25%)	13 (68.4%)	6.556*	0.010*
Pattern of use				
Opioids mono drug use	5 (31.3%)	5 (26.3%)	0.104	^{FE} p=1.000
Poly drug use (opioids plus)	11 (68.8%)	14 (73.7%)		
Route of opioids use				
Smoking	9 (56.3%)	6 (31.6%)	2.159	0.142
Sniffing/ snorting	6 (37.5%)	5 (26.3%)	0.504	0.478
Injection	1 (6.3%)	8 (42.1%)	5.846*	^{FE} p=0.022*
Dose of heroin /day				
Less than one gram/day	13 (81.3%)	3 (15.8%)	14.998*	<0.001*
Gram or more	3 (18.8%)	16 (84.2%)		

χ^2 : Chi square test FE: Fisher Exact

p: p value for comparing between **Abstinent (Negative)** and **Relapsed (Positive)**

*: Statistically significant at $p \leq 0.05$

Regression analysis of factors predicting relapse to opioid use at 3 months

Univariate and multivariate regression analysis were performed on the significant findings from relation analysis to identify their independent effect on relapse. Univariate regression showed a significant association between the relapse at 3 months and most of the analyzed variables i.e., family history of substance abuse among first degree relatives, using opioids via injection and pretreatment using high doses of heroin per day ($p < 0.05$). On multivariate regression, pretreatment using of high doses pf heroin per day (gram or more) was the most independent factor to affect the relapse into opioid use at 3 months (OR 14.003, 95% CI 1.778 – 110.30; $p = 0.012^*$).

(Table 5)

Table (5): Univariate and multivariate Logistic regression analysis for the parameters affecting relapse (n = 19 vs. 16)

	Univariate		#Multivariate	
	p	OR (95%C.I)	p	OR (95%C.I)
Family history of substance abuse	0.014*	6.500 (1.467 – 28.804)	0.322	2.897 (0.353 – 23.769)
Pattern of use				
Opioids mono drug use		1.000		
Poly drug use (opioids plus)	0.748	1.273 (0.293 – 5.534)		
Route of opioids use				
Smoking	0.146	0.359 (0.090 – 1.430)		
Sniffing/ snorting	0.479	0.595 (0.141 – 2.507)		
Injection	0.035*	10.909 (1.185 – 100.41)	0.070	13.008 (0.813 – 208.02)
Dose of heroin /day				
Less than one gram/day		1.000		1.000
Gram or more	<0.001*	23.111(3.977 – 134.29)	0.012*	14.003 (1.778 – 110.30)

OR: Odd's ratio

C.I: Confidence interval LL: Lower limit UL: Upper Limit

#: All variables with $p < 0.05$ was included in the multivariate*: Statistically significant at $p \leq 0.05$

Discussion

In this study, we evaluated the predictors of relapse into opioid use among opioid dependent patients treated with relapse prevention based cognitive behavioral therapy program for 3 months. The main findings were that having family history of substance abuse, taking opioids via injection route and pretreatment using high doses (gram or more) of heroin per day were significantly associated with relapse at 3 months follow up ($p \leq 0.05$) while pretreatment using high doses of heroin per day was the main independent factor of relapse ($p=0.012^*$). This is in line with the data reported from most of the literature study. (16-18) For instance, Harsh et al. observed that relapsed patients abused more and used injections more frequently than non-relapsed patients in their investigation of pretreatment patient characteristics of 466 opioid using patients to identify the predictors of relapse through a 1-year follow-up study. Also, during a one-year follow-up after inpatient opioid detoxification, patients with a family history of alcohol misuse (parental or first degree) had a worse chance of maintaining remission. (16) Although treatment used in Harsh et al study was only detoxification, their results were agreed with our results. Another study of 34 patients for relapse to heroin use during 6 months of Buprenorphine (BUP) treatment found that those who used low doses of heroin before the study were more likely

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to submit an opioid-negative urine sample during initial outpatient BUP maintenance and had a lower risk of relapse than those who used high doses.(17) Previous studies reported significant association between pattern of opioid use before treatment and relapse to opioid use where being poly drug dependent carry more risk of relapse than being opioid mono drug use. (19,20) We, however, failed to prove this association in our cohort study. This can be explained by the different methodologies used that make the comparison between these studies and ours challenging.

Conclusion

To conclude, early identification of relapse predictors and therefore high-risk patients may aid in the development of a more successful and targeted treatment strategy. More research is needed to explore patient characteristics based on our study which may help to reduce relapse following treatment with relapse prevention based cognitive behavioral therapy.

The main limitation of our study is unavailability of similar studies investigating relapse among opioid patients after treatment with CBT in literature that make comparison of our results is challenging.

Funding

This research received no external funding and no one other than the authors contributed to it.

Acknowledgment

I would like to thank all staff members of psychiatry and addiction department of Alexandria faculty of medicine for their valuable advice, guidance and constructive criticism.

Conflict of interest

The authors declare no conflict of interest

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