Title: Investigating the Dimensions of Quality of Life, Depression, Anxiety, Stress, and Substance Craving in People with Opioid Use Disorders, Methadone-Maintained Subjects, and Narcotics Anonymous Members

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ABSTRACT

Background: Opioid use disorder (OUD) is a major public health concern, and different approaches for its treatment such as maintenance therapy or group therapy have been proposed. The effectiveness of these therapies in the improvement of the psychological and mental state of the patients is always a topic of research and evaluation. This study aimed to compare the dimensions of quality of life, depression, anxiety, stress, and substance control-related factors in OUD subjects and those who have entered methadone maintenance treatment or Narcotics Anonymous (NA) group therapy in comparison to control subjects who had never used opioids.

Methods: Participants (n = 80) in this cross-sectional study were all male subjects comprised of four groups (n = 20 in each group): OUD subjects, NA members with a history of OUD, methadone-maintained individuals previously involved with OUD and a healthy control group. The three first groups were recruited from substance use disorder treatment centers and community groups in Tehran, Iran. All participants completed the validated Farsi version of questionnaires WHOQOL-BREF, DAS-21, and DDQ. MANOVA followed by LSD was used for assessing the differences between groups.

Results: Data showed that for the DASS-21 scale, the differences between OUD subjects with each of the other three groups for all variables of the scale were statistically significant except for the difference between OUD and MMT subjects for the stress variable that was not significant. For the DDQ and WHOQOL-BREF scales, the differences between the OUD group and NA or control subjects for all variables of the scale*s* were significant. However, no significant differences were observed between OUD and MMT groups in terms of these variables.

Conclusion: The results of our study suggest that entering NA programs may be a more effective treatment option than consuming methadone for individuals with OUD in terms of improvement in the mental and psychological state of the patient which may need to be further evaluated in the future.

Keywords: OUD, MMT, NA group therapy, DDQ, WHOQOL-BREF, DASS-21

Introduction

Substance use disorder (SUD) is a chronic and recurring condition characterized by obsessive substance seeking and use regardless of the negative effects (1). It is a complicated and difficult problem that impacts individuals, families, and communities all around the world (2). Opioid use disorder (OUD), in particular, has become a major public health concern in recent years, with rates of abuse and overdose deaths rising at an alarming frequency (3). OUD was predicted to affect 26.8 million people worldwide in 2016, and over 100,000 people die from opioid overdoses each year, including over 47,000 Americans in 2017 (4).

OUD is associated with a range of physical health consequences, including respiratory depression, constipation, and an increased risk of infectious diseases such as HIV and hepatitis C (5, 6). In addition to the physical health complications, individuals with OUD may encounter a variety of psychological and social challenges that can significantly impact their quality of life (7). For example, OUD can result in mental health issues such as depression and anxiety, as well as social isolation, relationship problems, financial difficulties, and legal issues (7-10). Quality of life is a multidimensional construct that encompasses physical, psychological, social, and environmental elements that contribute to an individual's overall well-being (11). In the context of OUD, quality of life may be negatively impacted by a range of factors, including chronic pain, impaired functioning, financial difficulties, and social stigma (12). Besides, a person's quality of life can be greatly impacted by typical mental health issues such as depression, anxiety, and stress, which are also experienced often by people involved with OUD.

Opioid craving is a fundamental feature of OUD and is defined as an intense urge or desire to use drugs (13). The desire can be so strong that it can overcome a person's willingness to regulate his/her drug use, ultimately resulting in a relapse (14). Craving is considered one of

the major barriers to long-term recovery from OUD (13) and can be caused by both physiological and psychological factors. Physiologically, it is related to changes in brain function and the release of neurotransmitters, such as dopamine, which are associated with reward and pleasure (15). Psychologically, it can be triggered by a range of external and internal cues, such as stress, negative emotions, physical withdrawal symptoms, and drug-related environments or stimuli (16, 17). Understanding the factors that contribute to substance craving can help individuals and healthcare providers develop effective treatment plans to overcome SUD. The psychological component of craving can be related to the individual's thoughts, emotions, and memories related to drug use (18). Therefore, effective addiction treatment should address both the physiological and psychological aspects of substance craving to help people manage their urges and achieve and maintain recovery.

A variety of treatment approaches, such as medication-assisted treatment (MAT) and support groups like Narcotics Anonymous (NA), are available for patients involved with OUD (19, 20). In MAT, medications such as methadone, buprenorphine, or naltrexone are used to manage withdrawal symptoms and diminish craving (21). Supportive groups such as NA provide a beneficial community for individuals in recovery and can help to reduce social isolation and stigma of OUD and improve the patient's quality of life without using replacement medications (22).

It is always a subject of research which one of the mentioned approaches for the treatment of OUD could better overcome mental health issues like depression, anxiety, and stress in patients. In addition, the superiority of different treatment methods regarding the dimensions of quality of life and substance craving is an important question raised by healthcare providers. The current study was designed to investigate such questions by comparing OUD, MMT, and NA groups

with control subjects regarding the scales of mental health issues, quality of life, and substance craving.

Materials and Methods:

Participants

This cross-sectional study was performed in 2020 and included 80 male participants between the ages of 20 and 45, with 20 participants in each of the following four groups: 1) subjects with OUD, 2) Narcotics Anonymous (NA) members previously involved with OUD who were drug-free for at least one year at the time of enrollment in the study, 3) individuals receiving methadone maintenance treatment previously suffering from OUD who were consuming methadone for at least six months and 4) control people without a history of OUD. MMT clinics and NA communities in Tehran were used to recruit participants for the first three groups. Control subjects were selected from students and staff of the Tehran University of Medical Sciences. The sample size was determined using power analysis, which was based on the effect size of previous studies that examined the same or similar variables, with a power of 0.80 and an alpha level of 0.05. Inclusion criteria of the study were: male individuals aged 20 to 45 years, opioid addiction or NA membership or methadone use (for the corresponding groups), and no history of substance use disorder (for the control group). Exclusion criteria were: having a history of psychotic disorder or severe mental illness and being currently in an acute phase of withdrawal.

All participants provided written informed consent before enrollment in the study. The protocols and processes were all approved by the ethics committee for human studies at the Tehran University of Medical Sciences.

Measures:

Quality of life

Quality of life was measured using the World Health Organization Quality of Life-BREF (WHOQOL-BREF) scale which is also validated in Iranian subjects (23).

The WHO defines quality of life as a person's perception of their place in life concerning their goals, aspirations, standards, and concerns in the context of the culture and value systems in which they live (24). These qualities are classified into variables such as physical health, mental health, social relationships, and environmental health. The questions are ranked on a Likert scale with items scoring between 1 and 5. The WHOQOL-BREF has been found to have good internal consistency, with Cronbach's alpha coefficients ranging from 0.66 to 0.82 across different domains and cultures. Test-retest reliability of the tool is high, with intra-class correlation coefficients ranging from 0.70 to 0.90 (25). A study to examine the Persian version of the questionnaire in Iran found that the WHOQOL-BREF scale had good reliability, with Cronbach's alpha ranging from 0.76 to 0.82 for the domains measured. In addition, the intra-class correlation exceeded 0.7 for all domains (23).

Depression, anxiety, and stress

Depression, anxiety, and stress were measured using the Depression Anxiety Stress Scale (DASS-21) (26) which is a widely used tool for measuring symptoms of depression, anxiety, and stress. It consists of 21 items, with seven items for each domain (27). The DASS-21 has been found to have good reliability and validity in numerous studies. Internal consistency is high for all three domains, with Cronbach's alpha coefficients ranging from 0.78 to 0.97 (28). Also in the Persian version, the DASS-21 has been found to have good reliability and validity. Internal

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consistency for all three domains is high, and Cronbach's alpha coefficients range from 0.82 to 0.95 (29, 30).

The Desire for Drug

The Desire for Drug Questionnaire (DDQ) (Persian version) includes 13 questions that measure three main components of drug craving: desire and intention to use (7 questions), negative reinforcement (4 questions), and control (2 questions). One question was added to enhance the internal consistency of the negative reinforcement component. The questionnaire uses a seven-point Likert scale to rate the intensity of feelings or thoughts related to drug use, ranging from "not at all" to "approximately complete".

The internal consistency of the measured variables was high for the first two factors, with coefficients of 0.89 and 0.79. However, the third factor had a low internal consistency with a coefficient of 0.4. in the Persian version (31).

Procedure:

WHOQOL-BREF, DASS, and DDQ scales were completed in a face-to-face setting at a clinic. The questionnaires were filled in by a trained research assistant who was available to answer any query raised by the participants. The completion of the scales took approximately 30-45 min. Ethical considerations were taken into account in this study, including protecting participants' privacy and confidentiality and minimizing potential inconveniences for participants.

Data analysis

The data obtained from the scales were analyzed using multivariate analysis of variance (MANOVA) to examine differences between the four groups on the dependent variables. Data analysis was performed using SPSS 21 and the significance level was set at 0.05.

Results

The demographic data of participants is shown in Table 1. We did our best to select subjects in a way that the characteristics such as age, employment, education, and marital status that could affect the variables assessed in the questionnaires be similar between groups with no significant differences. Multivariate analysis of variance (MANOVA) was conducted to determine whether there were significant differences between the four study groups in terms of each of the study variables. The results of Levene's test indicated that the variances of all study variables were equal across the four groups (P > 0.05). The Wilks' Lambda test was used to examine the differences between the groups, and the results showed that there was a significant difference between the groups (F = 10.39, P < 0.001), supporting the overall hypothesis of the study. In other words, the results suggested that there was a significant difference in at least one of the research variables among the four groups. The variable amounts of the DASS-21 questionnaire for all study groups are presented in Table 2. Tables 3 and 4 demonstrate the descriptive statistics of research variables for the WHOQOL-BREF and DDQ scales, respectively.

The outcomes of a multivariate analysis of variance with a comparison of study variables are shown in Table 5. The results demonstrated significance in all variables (P < 0.05). To determine the differences between the four groups in terms of the desired variables, the LSD (Least Significant Difference) post-hoc test was conducted, given the significance of the differences.

For the DASS-21 scale, the differences between OUD subjects with each of the other three groups for all variables (depression, anxiety, and stress) were statistically significant except for the difference between OUD and MMT groups for the stress variable that was not significant. For the DDQ scale, the differences between the OUD group and NA or control subjects for all three variables of the scale (Desire and intention to drug use, Negative reinforcement, and drug control) were significant. However, no significant differences were observed between the OUD and MMT groups in terms of these variables. The same state was observed for the WHOQOL-BREF scale: the variables of the questionnaire were statistically different between OUD and NA or control groups, however, the difference between OUD and MMT subjects was not statistically significant. The detailed results are presented in Table 6.

Table 1. Demographic data of the study participants

Group	Age (years, means ± SD)	Duration of drug use (years, mean± SD)	Duration of methadone maintenance (years, mean± SD)	Duration of abstinence (years, mean± SD)	Dose of administered methadone (mg/day)	Marital status		Employment status		Education		
						Married	Single	Employed	Unemployed	High school	BA	MS
OUD	32 ± 4.2	13.9 ± 7.4	---	---	---	16	4	20	0	15	4	1
NA	32 ± 7.1	12.1 ± 5.2	---	3.85 ± 1.16	---	17	3	19	1	16	3	1
MMT	35 ± 4.5	11.3 ± 6.1	8.5 ± 2.3	---	70 ± 15	15	5	19	1	17	2	1
Control	33 ± 5.4	---	---	---	---	15	5	19	1	14	4	2

Table 2. Descriptive statistics of research variables of the DASS-21 questionnaire

Variable / Groups	Depression (Mean ± SD)	Anxiety (Mean ± SD)	Stress (Mean ± SD)
OUD	21.10 ± 5.78	21.3 ± 9.52	21.50 ± 5.87
MMT	16.20 ± 9.10	11.40 ± 6.90	18.60 ± 6.87
NA	10.09 ± 10.22	8.6 ± 8.49	12.19 ± 10.6
Control	4.10 ± 2.78	2.94 ± 2.24	3.05 ± 2.34

SD: Standard Deviation

Table 3. Descriptive statistics of research variables for the WHOQOL-BREF scale

Variable	Mental Health (Mean ± SD)	Social Relationships (Mean ± SD)	Physical Health (Mean ± SD)	Environmental Health (Mean ± SD)
Groups				
OUD	17.0 ± 5.00	10.9 ± 1.48	20.1 ± 4.33	25.00 ± 3.043
MMT	18.0 ± 3.99	10.75 ± 2.57	22.40 ± 3.36	25.65 ± 4.47
NA	21.33 ± 2.394	12.57 ± 1.59	23.42 ± 2.73	29.33 ± 3.69
Control	22.8 ± 2.03	12.57 ± 2.11	24.31 ± 4.29	30.89 ± 4.306

SD: Standard Deviation

Table 4. Descriptive statistics of research variables for DDQ scale.

Variable	Desire and intention to drug use (Mean ± SD)	Drug control (Mean ± SD)	Negative reinforcement (Mean ± SD)
Groups			
OUD	41.95 ± 5.26	9.2 ± 0.65	18.9 ± 4.817
MMT	39.8 ± 8.677	8.25 ± 0.648	16.2 ± 7.517
NA	14.0 ± 8.71	2.4 ± 0.73	8.52 ± 6.918
Control	5.47 ± 3.5	1.3 ± 0.51	3.26 ± 2.05

SD: Standard Deviation

Table 5. The results of multivariate analysis of variance to compare research variables.

Scale	Variable	df	Mean Square	F	P value
DASS-21	Depression	3	3197.2	18.2	.000
	Anxiety	3	3469.5	21.12	.000
	Stress	3	3893.8	25.2	.000
DDQ	Negative reinforcement	3	3028.5	30.1	.000
	Desire and intention to drug use	3	19898.5	136.3	.000
	Drug control	3	966.8	38.4	.000
WHOQOL-BREF	Environmental health	3	479.7	10.4	.000
	Mental health	3	443.2	11.5	.000
	Physical health	3	191	4.59	.005
	Social relationships	3	3197.2	5.2	.003

Table 6. The results of the LSD post hoc test for study variables.

Scale	Variable	(I) GROUP	(J) GROUP	Mean Difference (I-J)	Std. Error	P value
DASS-21	Depression	OUD	MMT	4.9*	2.4	.046
			NA	11***	2.38	.000
			Control	16.99***	2.44	.000
	Anxiety	OUD	MMT	9.9***	2.33	.000
			NA	12.63***	2.31	.000
			Control	18.35***	2.37	.000
	Stress	OUD	MMT	2.9	2.26	.205
			NA	9.3***	2.24	.000
			Control	18.44***	2.29	.000
DDQ	Negative reinforcement	OUD	MMT	2.7	1.83	.144
			NA	10.42***	1.80	.000
			Control	15.68***	1.85	.000
	Drug control	OUD	MMT	0.95	.91	.303
			NA	6.81***	.90	.000
			Control	7.93***	.92	.000
	Desire and intention to drug use	OUD	MMT	2.15	2.20	.333
			NA	27.95***	2.17	.000
			Control	36.47***	2.234	.000
WHOQOL-BREF	Social relationships	OUD	MMT	0.15	.62	.812
			NA	-1.67**	.62	.009
			Control	-1.67**	.635	.010
	Environmental Health	OUD	MMT	-0.65	1.23	.601
			NA	-4.33***	1.22	.001
			Control	-5.89***	1.25	.000
	Mental health	OUD	MMT	-1.05	1.125	.354
			NA	-4.20***	1.125	.000
			Control	-5.90***	1.12	.000
	Physical health	OUD	MMT	-2.25	1.17	.060
			NA	-3.27**	1.16	.006
			Control	-4.16***	1.19	.001

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Discussion

The current study aimed to compare the quality of life, the desire for drug, and the mental health status of individuals with OUD in comparison to MMT, NA, and control subjects to estimate the efficacy of these treatment methods in terms of mental and psychological parameters. A great deal of focus has been placed on the health and quality of life of people involved with substance use disorders (32). Several studies have found that these people have a less wealthy quality of life than normal individuals (33-35). Some studies have also reported that maintenance treatment with methadone or buprenorphine could improve users' quality of life (36).

The findings of our study showed a significant difference in the level of anxiety and depression between the OUD group and normal individuals, as well as MMT and NA subjects. This is consistent with previous research that has shown a high prevalence of anxiety and depression among individuals with OUD (37-39). We also observed that the difference in stress levels between MMT and OUD subjects was not significant. This contrasts with some previous studies reporting that maintenance treatment with methadone can reduce stress levels in individuals with OUD (40, 41). This discrepancy may be due to differences in sample size and study design. Nonetheless, our study's findings regarding the beneficial effects of methadone in reducing anxiety and depression are consistent with previous research (41). A previous study has also reported that NA groups are more effective than medication-assisted treatment programs in reducing anxiety and depression in individuals with OUD (42). According to our findings, the level of depression and anxiety in the NA group was like the control group. Attending NA meetings has been linked to lower levels of anxiety and depression in some studies (42). Other studies have found mixed results or no significant differences between NA and other treatments for OUD.

The analysis of the quality of life parameters across different groups suggested that having a history of OUD could harm one's quality of life, which is consistent with previous research (43). However, the findings of our study indicated that attending NA meetings can positively affect the quality of life, as there was a significant improvement in all aspects of quality of life (including physical health and social relationships) for individuals in the NA group. On the other hand, the data indicated no significant improvement in any of the quality of life scales for the MMT group. Our findings challenge prior studies that have suggested that methadone therapy could improve the quality of life in areas such as physical health and social functioning (44, 45). The lack of significant improvement in quality of life among our MMT individuals may be due to various factors, such as the dose and duration of methadone treatment, as well as individual differences in adherence to treatment and engagement in other forms of care. More studies with larger case numbers are needed to be performed in the future to clarify the reasons.

Our data also revealed a significant difference between the OUD group and both the control and NA subjects in the negative reinforcement subscale of the DDQ, which suggests that opioid users may be more likely to use drugs to avoid negative feelings or experiences, such as withdrawal symptoms or anxiety. This finding is consistent with previous research showing that substance use disorder can be driven by negative reinforcement, which is the desire to avoid or alleviate negative feelings or experiences (46, 47). In a previous study using the DDQ scale to assess individuals with cocaine use disorder, it was found that these people had higher scores on the negative reinforcement subscale of the DDQ compared to non-drug-using controls, suggesting that negative reinforcement plays an important role in drug use disorders (47). Previously, Koob and Le Moal proposed the "dark side" of addiction, which refers to the negative emotional state that can arise during drug withdrawal and contribute to drug-seeking behavior. The authors have

hypothesized that the negative reinforcement model of addiction, which emphasizes the role of negative affect in driving drug consumption, may be more accurate than the traditional model of drug use disorder which focuses on the rewarding properties of drugs (48, 49). There was no significant difference in the negative reinforcement subscale of the DDQ between the OUD and MMT groups. A possible explanation might be that in this study, the individuals using methadone had a history of long-term use of other drugs. Furthermore, it is probable that replacement therapy with agonists like methadone which have a similar underlying mechanism of action (50), may not adequately modify the molecular pathways involved in the pathogenesis of OUD. Nevertheless, it seems that NA groups are more effective in the reduction of negative reinforcement, desire to consume, and impulse control of OUD subjects to maintain abstinence and reduce drug use.

Conclusion

In summary, the findings of the comparison across the four groups of OUD, MMT, NA, and control demonstrated that supportive NA groups have higher performance and outcome than methadone in terms of quality of life and the number of indicators that induce relapse, such as negative reinforcement and the urge to use, and cognitive control. Of course, methadone has been shown to enhance some of these signs; for example, there is a significant decrease in anxiety and depression in the methadone group as compared to the OUD subjects. However, because of the limited sample size of this study, the findings should be considered with caution when generalizing the results.

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Conflict of interest:

The authors declare no conflict of interest.

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