Study of sociodemographic correlates, anxiety, and depression among opioid dependents admitted in treatment centres in Sikkim, India

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Abstract

Background: People with opioid use disorder have significant anxiety and depression which can be because of neuroplastic changes due to use of opioid or because of use as a self-medication to relieve depression and anxiety. During the last one decade, opioid use has reached an alarming proportion in Sikkim, India; but, any research related to anxiety and depression among opioid users has not been done.

Aims: To assess for depression and anxiety disorders among the opioid dependence syndrome (ODS) participants and its severity, and to find the association with the sociodemographic characteristics.

Method: One hundred participants from three different drug detoxification and rehabilitation centres who were diagnosed with ODS as per the ICD-10, Diagnostic Criteria for Research were assessed cross-sectionally with the Addiction Severity Index to find out the substances abused and psychiatric morbidity. Anxiety, depression, and mania were graded with the Hamilton rating scales for anxiety and depression, and the Young Mania Rating Scale.

Results: Mean age of participants was 29.6 (±6.24) years. Ninety six per cent were males. Most of the participants were using multiple opioid preparations. Thirty four per cent were using dextropropoxyphene containing pain killer followed by six per cent using codeine containing cough syrup. Eighty two per cent had depression; however, only 13% were found to have severe depression. Fifty six per cent had anxiety and six per cent were found to have mania. Most of the

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participants with ODS were single, attended at least secondary education, from urban locality, and were from high socioeconomic status.

Conclusion: anxiety and depression are highly prevalent among ODS people. Treatment should not be limited to management of ODS but also the comorbid psychiatric illness.

Keywords

Self Medication; Rehabilitation; Mania; Dextropropoxyphene; Codeine; Sikkim

INTRODUCTION

Opioids are a group of substances that act on opioid receptors, generally used to control pain and which have significant abuse potential.[1] Opium is a word derived from the Greek word *opos* which means "juice". Opiate refers to any compound which is structurally related to products found in opium. Natural opiates are obtained from the resin of the plant *Papaver somniferum*. Opiate includes plant alkaloid morphine, codeine, thebaine, and other psychoactive compounds that can be derived from them. Opioid refers to any substance that has the pharmacological and functional properties of an opiate.[2] It includes fully synthetic compounds like methadone and fentanyl, and endogenous compounds such as endorphins, enkephalins, and dynorphins.[3] The opioid receptors are present in the central nervous system and the peripheral tissues. These receptors are named with Greek letter based on their prototype agonist. Mu (μ) (agonist morphine) receptors are found in the brainstem and the medial thalamus. Mu1 is related to analgesia and Mu2 is related to anorexia, respiratory depression, decreased gastric motility, and dependence. Kappa (κ) (agonist ketocyclazocine) are distributed in the limbic and diencephalic area, brainstem and spinal cord, and are responsible for spinal analgesia, sedation, dyspnoea, dependence, and respiratory depression. Delta (δ) (agonist delta-alanine-delta-leucine-enkephalin) receptors mainly fund in the brain are responsible for psychomimetic and dysphoria.[4]

There had been a widespread traditional use of opium in some parts of India. As reported by Ganguly *et al.*,[5] opium was used in different forms in the North-Western region of the country. The consumption was done in social gathering and to get relief from worries. Mothers often introduced opium to children. Only ten per cent were considered deviant and the rest were well-integrated to society. Mahanta *et al.*[6] also reported traditional use of opium in Assam for holy purpose, healing, increasing physical capacity, and to relieve mental stress.

Decreasing trend over last few years in the use of opium has been witnessed; but, at the same time, it has been observed that there is increased use of opioids like dextropropoxyphene, codeine, and injectable buprenorphine.[6,7] In Sikkim, a small state in the North-East part of India, among patients attending emergency services in a tertiary care centre for substance-related complications, 14.8% were identified as opioid abusers and the common opioids they abused were codeine, dextropropoxyphene, and pentazocine.[8]

A large number of people who are abusing opioids have other psychiatric comorbidity. The relationship between mood and anxiety disorder and opioid use can emerge in one or more

non-exclusive ways. Behavioural and neuroplastic changes arising out of chronic use of substance can result in mood and anxiety disorder; mood and anxiety disorder can lead to use of opioids as self-medication to relieve the symptoms; or because of susceptibility to both the reasons.[9] In a Spanish study,[10] where 621 patients who were enrolled for opioid agonist treatment (OAT) programme, 53% had anxiety disorder, 48% had mood disorder, 41% had sleep disorder, and 36% substance-related disorder. In an Indian study done by Arora and Kaur,[11] 65.2% of the participants were having mood disorder. Only 29% of all the participants were diagnosed with substance-induced depression and the rest were having an independent diagnosis of mood disorder. The second most common diagnosis was generalized anxiety disorder (17.6%).[11]

Sikkim is connected to the rest of India through the famous 'Siliguri Corridor'. This corridor connects North-East part of India to other parts of the country. Nepal and Bangladesh lies on either side of the corridor, and Bhutan on the Northern side. This corridor act as a major route for transportation of drugs and Sikkim being one of the connected states is affected with the drug nuisance. Study on mood and anxiety disorder among the opioid users in Sikkim has never been done, and whether the finding of other studies holds true among the population in Sikkim was never explored. This study tries to fill the gap.

Aims and objectives

- To find out the presence of mood and anxiety disorders in people with ODS taking treatment in Sikkim.

- To assess and grade the severity of the illnesses under study among the participants.

- To assess the distribution of the problem across various sociodemographic divides.

MATERIALS AND METHODS

This is a cross-sectional observational study done in hospital and drug-deaddiction centre. The participants included were from the Sikkim Manipal Institute of Medical Sciences, Sir Tashi Namgyal Memorial Hospital, and Sikkim Rehabilitation Centre, Nimtar. The study period was from December 2013 to December 2014. The participants were selected by convenience sampling and data from 100 participants were included for assessment. Approval from the Institutional Ethics Committee, Sikkim Manipal Institute of Medical Sciences was obtained before data collection.

Case selection and definition

Patients diagnosed with ODS of either sex were selected for this study. Patients who fulfilled the criteria of any other substance except for tobacco or suffering from any major physical illness were excluded from the study. The criteria used to diagnose ODS were those as laid down by the ICD-10, Diagnostic Criteria for Research.[12] The cases that fulfilled the criteria for ODS only were chosen and an informed consent was taken from them. Each

participant was explained the nature of the study, its purpose, and had assured her or his confidentiality. The participation in the study was voluntary.

Tools used

The following questionnaires were administered on the cases-

The Addiction Severity Index (ASI)[13] was used for screening and assessment of the subjects for dependence to opioids and also to rule out any comorbid medical condition. ASI is a relatively brief, semi-structured interview designed to provide important information about aspects of a patient's life which may contribute to his/her substance abuse syndrome. It is one of the most widely used addiction assessment tools used in the addiction field internationally. It collects information on 200 items across seven domains: medical status, employment status, drug use, alcohol use, legal status, family/social status, and psychiatric status.

The Hamilton Depression Rating Scale (HDRS) was used to grade the depression in the cases selected. The Hamilton Rating Scale for Depression (HRSD), also called HDRS, abbreviated HAM-D, is the most widely used clinician administered depression assessment scale. The original version (which was used in the present study) contains 17 items pertaining to the symptoms of depression experienced over the past week. It is used to provide an indication of depression, and also as a guide to evaluate recovery. The scoring on HAM-D is as follows: zero to seven (no depression), eight to 17 (mild depression), 18–23 (moderate depression), and 24 and above (severe depression).[14,15]

The Hamilton Anxiety Rating Scale (HAM-A) was used to assess and grade the anxiety in the cases selected. It is a clinician-rated evaluation composed of 14 items. The scores on this scale range from zero to 56. The scoring is done as follows: 14–17 (mild anxiety), 18–24 (moderate anxiety), and 25–30 (severe anxiety).[16]

To evaluate mania in the cases selected, the Young Mania Rating Scale (YMRS)[17] was employed. The YMRS is an 11-item clinician-rated scale designed to assess the severity of manic symptoms. The gold standard of mania rating scales, this instrument is widely used in both clinical and research settings. Four of the YMRS items are rated on a zero to eight scale, with the remaining five items being rated on the zero to four scale. A score of 12 or more was taken as suggestive of presence of mania.

Socioeconomic status of the participants was assessed by using the Modified BG Prasad's Classification for 2014.[18]

Statistical analysis

Sociodemographic and clinical variables were described using mean and standard deviation (SD) for continuous variables while categorical variables were represented using percentages. Association of opioid dependence was analysed for all the sociodemographic factors to ascertain the distribution of the disease across the divides. The severity of depression and anxiety, and the presence of mania was also analysed using the same sociodemographic parameters. Student's t-test was used for continuous variables and Chi-

square test for categorical variables except when at least one box had expected frequency of less than five, in which case Fisher's correction was applied. All statistical analyses were done using Statistical Package for the Social Sciences (SPSS version 17.0).[19] A statistical significance level of 0.05 was used for all comparisons.

RESULTS

Participants' characteristics

A total of 100 patients from the three centres were assessed. The mean age of the participants was 29 years with SD of 6.24 years. Majority of them were male (96%) and Hindu (51%). Though 31% of the participants were unemployed, majority belonged to class I socioeconomic status (74%). Most of the participants were single (54%) and from urban locality (84%). Except three per cent (N=three) who never attended school, all participants had received formal education as shown in Table 1.

In the study population, most of the participants used more than one opioid (multiple opioids use) (N=57 [57.0%]) which included 55 (55.0%) males and two per cent females (Table 2). Apart from multiple opioids use, the single most commonly used opioid was found to be dextropropoxyphene containing pain killers (spasmoproxyvon) with N=34 (34%), of which 33 (33.0%) males and one per cent female. Both the sexes were found to be significantly using drugs containing different opioids together as compared to single opioid containing drug alone (χ^2=24.47, df=5, p<0.0002).

Psychiatric comorbidity

Depression was found in 82% of the participants. As per HAM-D score, 13% had severe depression (Table 3). No significant difference was found between the two sexes with opioid dependence and diagnosis and severity of depression (p>0.742). Similarly, no significant difference was found between different religions, socioeconomic status, marital status, educational status and diagnosis and severity of depression.

Fifty six per cent of the participants had anxiety (Table 4). There was no statistically significant difference found between the presence of anxiety or its severity among the participants with opioid dependence among different groups of sociodemographic variables.

Six participants were found to have manic symptoms with YMRS score>12 (Table 5). All these patients were male. Significant association was found between manic symptoms in participants with opioid dependence and Nepali community (Chi-square value=16.273, df=4, p-value=0.003).

DISCUSSION

In the present study, we found that among the participants with ODS, 57% had been using more than one opioid preparation before treatment. Thirty four per cent were using dextropropoxyphene containing oral prepartion followed by six per cent of the participants using codeine containing cough syrup. Depression was found in 82% of the participants with ODS. Thirteen per cent of the participants were found to have severe depression. More than

50% of the participants were also having anxiety and in majority among them, the anxiety was mild in severity. We also found that participants with ODS who had manic symtoms were more likely from the Nepali community.

Prevalence of depression

In the current study, 82 of the 100 patients (82.0%) were having depression. Out of which 21% had mild, 48% had moderate, and 13% had severe depression. Arora and Kaur[11] had found a prevalence of 29% and 8.2% of the participants having substance-induced depression and major depressive disorder respectively. Though the difference apparently is not much if we consider the prevalence of only major depression, Arora and Kaur[11] had a sample size of 500 and all the participants were examined in outdoor department whereas the participants in our study were in rehabilitation centres and were staying away from home, some, for months, with all the restrictions in the centres which did possibly play a role in the higher reporting of depressive symptoms in our study. Moreover, it was reported that opioid addicts in the community are more functional and less depressed than those who seeks treatment,[20] which may explain the high prevalence in our study participants.

Prevalence of anxiety

Fifty six per cent of the participants were found to have anxiety which is similar to as reported by Passik *et al.*,[21]where they surveyed prospectively prescription drug abusers and had almost same number of participants (N=109) as that of our study, and they found a prevalence of 55% in their participants. Roncero *et al.*[10] also reported a prevalence of anxiety as 53% in their 621 participants and they had used the European version of ASI (EuropASI). Frei and Rehm[22] reported a prevalence of 26% in their sample of 85 participants; the difference may be due to the use of different diagnostic instrument as well as difference in the mean age of the participants which was 32.6 years.

Prevalence of mania

In the current study, the prevalence of mania was six per cent. Ahmadi *et al.*[23] found that of the 500 opioid dependent patients, three (0.6%) received a diagnosis of bipolar mood disorder type I. The difference in the prevalence of mania in the study mentioned and the current study could be due to the difference in the sample size (N=500) and also due to the fact that their study used the structured clinical interview for DSM-IV Axis I Disorders (SCID-I) for assessment of subjects while in the present study ASI was used for assessment purpose and the presence of mania was established with the help of YMRS. In an Indian study done by Arora and Kaur[11] of the 500 participants, five (one per cent) were diagnosed with bipolar mood disorder type I and two (0.4%) were diagnosed as having bipolar mood disorder type II. This is comparable to the findings of the present study.

Sociodemographic correlates

Age—In the present study of 100 cases, the mean age of the study population was found to be 29 years with a SD of 6.24 years. Majority of the cases belonged to the age group of 21 to 40 years. This is in accordance to the finding of Arora and Kaur,[11] where 37.4% of the ODS participants were in the age group 26–35 years followed by 21% in 36–45 years group.

Prasant *et al.*[24] also found that 72% of the ODS participants were below 30 years of age. These studies including the present study show that opioid dependence is a problem area of the youth populace. Certain factors such as peer pressure, sensation seeking behaviour along with poor coping skills, especially in context to Sikkim where the statistics show high suicide rates and excessive dependence and inclination towards Western culture leading to gradual decline of family values and ethos, increased competition, unemployment could be responsible for the observed trend in the youth.

Gender—Among 100 participants with ODS, 96% were male and rest were females. Similar findings has been reported in different studies.[23,25,26] Results showed that males have higher incidence for both non-dependent and dependent use for opioids.[27] Possible reasons for very low prevalence of opioid dependence could be pointed to the greater presence of stigma and taboo towards females having opioid dependence especially when it comes to reporting the same to healthcare providers. Another significant reason could be the fact that the deaddiction centres from where considerable number of subjects were recruited for the present study have limited provision for keeping female subjects battling with opioid dependence.

Socioeconomic status—Seventy four per cent (N=74) of the subjects belonged to the class I of BG Prasad scale for socio-economic status and also most number of cases suffering from depression belonged to this group only. However, in one study, opioid ever-use and current-use were found across all income spectrums.[26] Similarly, in the study done by Fischer *et al.*,[28] non-medical prescription opioid use (NMPOU) and key socioeconomic variables (i.e. sex, age, aboriginal ethnicity, household location, income, subjective social status) were measured based on multivariate analyses; it was found that NMPOU is widely distributed across sociodemographic and socioeconomic strata. A plausible explanation for higher prevalence of opioid dependence in the present study could be that the state of Sikkim's per capita income is among the highest in India,[29] and the findings of the current study concurs with this data. Another possible explanation for this finding could be due to easy accessibility, availability, and higher purchasing capability of the subjects belonging to this group.

Level of education—In the current study, 48% (N=48) of the cases had educated up to secondary level. This finding is fairly consistent with the study done by Ahmadi *et al.*,[26] who found that out of 496 subjects, 322 had elementary or high school education. Another study of Ahmadi *et al.*,[23] out of 500 patients dependent on opioids, more than half (59.8%) had education up to the level of primary or high school. However, Datta *et al.*,[25] who conducted their study in Sikkim found that out of 224 participants who were actively using opioids, 69 (30.8%) had completed 12th standard of education which completely matches to our finding.

Marital status—In the present study, most cases were unmarried (N=54, 54%); on the other hand, the number of married and divorced were 38 (38.0%) and eight (8.0%) respectively. The findings of this study match with the findings of the study done by Dutta *et al.*,[25] where they found that 65% of the subjects were unmarried. A possible explanation

to the less prevalence of married subjects having opioid dependence could be that the institution of marriage might provide a strong support system which could prevent dependence to opioids.

Place of residence—With respect to the place of residence it was found that 84 (84.0%) of the cases were from urban area. This finding is like the finding of a study from India done by Mattoo *et al.*,[30] where it was found that all patients of the study were from urban backgrounds (80%). Datta *et al.*[25] also found that of the 224 participants primarily dependent on opioids, 57.6% (n=129) prescription opioid abusers belong to urban community. One possible cause for this is that many of the study population were taken from the drug deaddiction centres which are in close proximity to Gangtok city. There were other deaddiction centres in and around rural areas also; but, the subjects in those centres were not included in the present study.

Type of opioids use

In the present study, most of the cases used more than one opioid (multiple opioids use); 57 (57.0%) used more than one opioid. Dextropropoxyphene containing pain killers (spasmoproxyvon) (34 [34%]) was the single most commonly used opioid. This finding is similar to the trend found at by Basu *et al.*,[31] who found that there was a trend of shifting to synthetic opioids use from the natural forms over the last three decades. Subjects using natural opioids decreased over the three decades (47.4, 26.5, and 18.3%).[6,7,31]

Similar findings were reported by Sproule *et al.*,[32] where it was observed that in 58 patients who received diagnosis of opioid dependence, most frequently used opioids were prescription opioids such as codeine (52%) and oxycodone (40%).

Strengths of the study

This study was conducted in Sikkim, where for the past one decade opioid use and dependency have assumed an alarming proportion. This study tried to throw an insight into the comorbid mood and anxiety disorders present in this population. This study will help in generating some baseline data on which further study could be designed in future.

Limitations of the study

The present study was a cross-sectional study and did not include those cases who might have been asymptomatic at the time of the interview but may have had episodes of depression or mania in the past. This is a hospital and deaddiction centre-based study where usually patients who can afford and bear the costs of healthcare delivery are represented. Hence, the finding cannot be generalised to the community. Personality assessment, social and situational factors like family dysfunction, environmental factors, and other stressors which could act as causative and aggravating factors for opioid dependence and mood disorders were not assessed. Separate assessment of specific anxiety disorders such as generalized anxiety disorder, panic disorder, obsessive-compulsive disorder, posttraumatic stress disorder was not done and only the severity of anxiety was measured with the help of HAM-A. The study included cases from long-stay rehabilitation centres in Sikkim. As those patients were staying away from their families and were made to adjust to new surroundings

and living conditions, there could be a false increase in the severity of depression as graded on HAM-D. This study did not take into account the age of onset of initiation of opioid use and also severity of opioid use was not assessed, both of which have an established correlation with lifetime risk of opioid dependence.

Conclusion

There is a high prevalence of coexisting mood and anxiety disorders associated with opioid dependence. Hence, the treatment of opioid dependence should not be limited to de-addiction, but should also include the treatment of coexisting psychopathology. Secondly, the sociodemographic patterns seem to influence opioids use. Understanding this pattern will help us in framing guidelines for educating the public and in the menace of opioid dependence at a primary stage.

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Table 1:

Sociodemographic variables of the participants

Sociodemographic variables		N	%
Age (years)	<20	8	8.0%
	21–40	86	86.0%
	41–60	6	6.0%
Gender	Male	96	96.0%
	Female	4	4.0%
Religion	Hinduism	51	51.0%
	Buddhism	34	34.0%
	Christianity	14	14.0%
	Others	1	1.0%
Education	Illiterate	3	3.0%
	Primary	22	22.0%
	Secondary	48	48.0%
	Graduate	27	27.0%
Occupation	Unemployed	31	31.0%
	Self-employed	18	18.0%
	Govt. Employee	16	16.0%
	Private enterprise employee	25	25.0%
	Student	10	10.0%
Marital status	Single	54	54.0%
	Married	38	38.0%
	Divorced/separated	8	8.0%
Family type	Nuclear	66	66.0%
	Joint	34	34.0%
Residence	Urban	84	84.0%
	Rural	5	5.0%
Socioeconomic status[a]	Class I	74	74.0%
	Class II	17	17.0%
	Class III	5	5.0%
	Class IV	3	3.0%
	Class V	1	1.0%

[a]BG Prasad's Socioeconomic Scale (May 2014)

Table 2:

Type of opioids used by the participants

Gender	Type of opioids used						
	Codiene containing cough syrup	Dextropropoxyphene containing pain killers	Heroin	IVDU (Morphine,Pentazocine)	Others	Multiple opiate use	Total
Male	6	33	1	1	0	55	96
	6.3%	34.4%	1.0%	1.0%	0.0%	57.3%	100.0%
Female	0	1	0	0	1	2	4
	0.0%	25.0%	0.0%	0.0%	25.0%	50.0%	100.0%
Total	6	34	1	1	1	57	100
	6.0%	34.0%	1.0%	1.0%	1.0%	57.0%	100.0%

IVDU=Intravenous drug users

Table 3:

Distribution of participants according to severity in HAM-D score

HAM-D	N	%
Normal	18	18.0
Mild depression	21	21.0
Moderate depression	48	48.0
Severe depression	13	13.0
Total	100	100.0

HAM-D=Hamilton Depression Rating Scale

Table 4:

Distribution of participants according to severity in HAM-A score

HAM-A	N	%
Normal	44	44.0
Mild anxiety	36	36.0
Moderate anxiety	20	20.0
Total	100	100.0

HAM-A=Hamilton Anxiety Rating Scale

Table 5:

Distribution of participants with YMRS>12

Ethnicity	YMRS>12		
	Yes	**No**	**Total**
Nepali	5	85	90
	5.6%	94.4%	100.0%
Hindi	1	0	1
	100.0%	0.0%	100.0%
Lepcha	0	1	1
	0.0%	100.0%	100.0%
Bhutia	0	2	2
	0.0%	100.0%	100.0%
Others	0	6	6
	0.0%	100.0%	100.0%
Total	6	94	100
	6.0%	94.0%	100.0%

YMRS=Young Mania Rating Scale