Sexual Dysfunction in Males Receiving Buprenorphine-naloxone-based Opioid Substitution Therapy

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ABSTRACT

Background: Benefits of buprenorphine-based opioid substitution therapy (OST) may be offset by its adverse effects on sexual functioning.

Aim and objective: The aim of the article was to assess the prevalence and degrees of sexual dysfunction in sexually active males on buprenorphine-based OST for 6 months or longer.

Materials and methods: Study participants were recruited from among the clients using the services at the Opioid Substitution Therapy Centre inside the premises of Silchar Medical College and Hospital. A semistructured questionnaire was used to collect sociodemographic data and to rule out the presence of symptoms of sexual dysfunction prior to initiation of OST. Two instruments, namely Arizona Sexual Experience Scale (ASEX) and International Index of Erectile Function (IIEF-15), were administered to evaluate the presence and degree of sexual dysfunction.

Results: Fifty participants were enrolled in the test group and another 50 in the age-matched control group. Among the test participants, 52% had sexual dysfunction as per ASEX scale. As per IIEF-15, all but one of the test participants had some degree of erectile dysfunction (ED), with 6% having mild, 46% mild to moderate, 34% moderate, and 12% severe ED. None in the control group had sexual dysfunction as assessed by ASEX, while one among them had mild ED and the rest had no ED as per IIEF-15 scores. The test group showed significantly higher levels of dysfunction in all domains of sexual functioning measured by both the scales. No significant effect of age, current dose of buprenorphine, and duration of therapy was found on the prevalence or degree of sexual dysfunction.

Conclusion: Different degrees of sexual dysfunction were highly prevalent in the participants making it imperative to routinely assess sexual functioning of the clients on buprenorphine-based OST and provide them with psychosexual counseling and necessary interventions whenever necessary.

Keywords: Buprenorphine-naloxone, Harm reduction, Intravenous drug abuse, Opioid substitution therapy, Sexual dysfunction.

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INTRODUCTION

Abuse of opioids has exerted a tremendous economic, social, legal impact apart from its dire consequences on the individual user’s health. Heroin is a quite common illicit opioid and has a wide client base. The abuser self-administers heroin by two common methods, namely chasing and intravenous injection. Intravenous administration is associated with high risks of contracting parenterally transmitted infections like hepatitis B, hepatitis C, HIV, as well as infective endocarditis, and thrombophlebitis. The unsafe injecting practices include sharing of needles, syringes, and other paraphernalia. The National AIDS Control Programme, currently in its fourth phase (NACP-IV), makes provisions for strategies known as “harm reduction” to prevent transmission of HIV among intravenous drug users. The harm reduction strategies include needle and syringe exchange program (NSEP), behavior change communication (BCC), community outreach, condom distribution, and opioid substitution therapy (OST).¹

In OST, the drug user’s primary drug of abuse (opioid) is replaced with a medically safer alternative drug or the same opioid in a safer mode of administration under medical supervision.² The replacement drug is a medication that is long acting and safer and administered through oral/sublingual route. Buprenorphine is a commonly used opioid medication for OST. It is often used in combination with naloxone. Buprenorphine-naloxone is a 4:1 combination of buprenorphine, a partial µ-receptor agonist, and naloxone, an opioid antagonist. It has been found that opioid maintenance treatment is effective in reducing mortality, criminal activities, as well as in improving psychosocial functions.³ Buprenorphine-naloxone maintenance treatment was showed to be associated with good treatment retention and significantly reduced opioid use.⁴,⁵

Buprenorphine is a semisynthetic opioid and is a partial µ-receptor agonist with potent antagonistic action at κ-receptor. Buprenorphine being a partial agonist decreases the side effects of opioid substitution like risk of respiratory depression with overdose. Naloxone is added in the combination so as to prevent the intravenous abuse potential of buprenorphine given alone. As an opioid antagonist, it nullifies the effects of buprenorphine if any user attempts to use the combination drug intravenously, thereby precluding the abuse potential of the drug.
Despite their great utility, such substitution drugs come with their own side effect profile that includes sexual dysfunction. Sexual dysfunction is a complex phenomenon where various hormonal, neurobiological, and psychosocial factors are at play. It is a condition that may manifest as reduced sexual interest, problems with sexual arousal and ejaculation, and orgasmic dysfunction. Drugs used in OST influence the hormonal axes involved in sexual functioning. They may act via (1) acting on hypothalamic-pituitary-gonadal axis (affecting luteinizing hormone (LH), follicle-stimulating hormone (FSH), gonadotropin-releasing hormone (GnRH)), (2) elevation of serum prolactin, and (3) suppressing testosterone production with direct action on the testes. Such side effects associated with long-term use of opioid antagonists or agonists could result in abandoning the substitution therapy. Matto et al. demonstrated intercourse dissatisfaction (95%) and hypoactive sexual desire (92.5%) as almost universal, while 77.5% of the participants reported erectile dysfunction (ED) among men who received buprenorphine-naloxone combination for more than 6 months.

Under Assam State AIDS Control Society (ASACS), opioid substitution therapy centers (OSTCs) have been functionalized in the state. One such center was functionalized within the premises of Silchar Medical College and Hospital, Silchar, in June 2019. There has been a satisfactory level of utilization of its services by clients from different parts of the Barak Valley. However, possible sexual dysfunction reduces quality of life in patients on OST, which may contribute to treatment nonadherence. Taking into account the limited number of studies regarding OST and sexual dysfunctions as a side effect of this therapy in men, the present study puts its focus on the presence of sexual dysfunctions in Indian male patients treated for opioid dependence with buprenorphine and naloxone in a specialized outpatient center. The authors hypothesize that OST impacts the sexual health of opioid-dependent subjects.

**Materials and Methods**

**Participants and Data Collection**

It was a hospital-based observational study. Participants for our study were recruited from patients attending the OSTC at Silchar Medical College and Hospital. It was approved by the Institutional Ethics Committee (IEC). Fifty consecutive patients undergoing OST were selected as the test group. A similar number of participants were chosen for the control group. The control group participants were recruited from among the attendants, either family members or relatives or friends, who were matched for age.

*For study group:* The study sample consisted of men seeking treatment at OSTC for opioid dependence. The study group was selected by purposive random sampling. The inclusion criteria were married/sexually active males who are on buprenorphine-based OST for a period of 6 months or longer, patients in the age group 18–60 years, and patients providing informed consent. Exclusion criteria were patients who reported sexual dysfunction prior to initiation of buprenorphine-based OST, patients having medical or surgical conditions known to contribute to sexual dysfunction (e.g., diabetes mellitus, hyperlipidemia, thyroid dysfunction, and lower spinal cord injury), and patients with significant psychiatric comorbidities.

*For control group:* The subjects of this group were relatives and caregivers of the patients attending the OSTC. Inclusion criteria were age-matched married/sexually active males and the exclusion criteria were diagnosed cases of sexual dysfunction and substance abuse.

The study group participants were on sublingual buprenorphine therapy with current maintenance doses of buprenorphine ranging from 2 to 6 mg sublingually per day.

**ASEX and IIEF-15**

After getting informed consent, the participants were administered two scales for the assessment of sexual functioning: Arizona Sexual Experience Scale (ASEX) and International Index of Erectile Function (IIEF-15).

The ASEX is a questionnaire with five questions the responses to which are scored in a Likert-type style with scores ranging from 1 to 6 for each, a minimum total score of 5 and maximum total score of 30. The questions address issues of sex drive, arousal, penile tumescence and vaginal lubrication, ability to reach orgasm, and satisfaction from orgasm over a period of 1 week including the day of interview. A total score of 19 or more, or a score of 5 in one or more questions, or scores of 4 in three or more questions indicate the presence of sexual dysfunction. It is a widely used reliable and validated instrument for assessment of sexual functioning.

In the present study, the Hindi-translated version that is available was used.

The IIEF-15 is a 15-question self-reporting instrument with Likert-type scoring. It is a validated diagnostic tool for identifying and grading the degrees of ED in males. The scale is subdivided into five domains to assess various aspects of sexual functioning: erectile function (questions 1, 2, 3, 4, 5, and 15), orgasmic function (questions 9 and 10), sexual desire (questions 11 and 12), intercourse satisfaction (questions 6, 7, and 8), and overall satisfaction (questions 13 and 14). The questions address these domains of the sexual functioning of the respondent over a period of 1 month. A higher score indicates better sexual functioning. In the erectile function domain, a score of 26–30 is considered as normal functioning. While scores less than 26 are taken to be indicative of various degrees of ED: mild dysfunction (22–25), mild to moderate dysfunction (17–21), moderate dysfunction (11–16), and severe dysfunction (6–10). There is no consensus regarding the interpretation of the scores in the other domains. In the present study, the Hindi-translated version which is available was used.

**Statistical Analysis**

Collected data were analyzed using the IBM Statistical Package for the Social Sciences (SPSS), version 21. Chi-squared or Fisher’s exact test was used to compare categorical variables between groups. Independent sample t-test and analysis of variance (ANOVA) were employed to compare means between and among groups, while Pearson’s correlation was used to find linear relationship between different quantitative variables.

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Scores for each component, as shown in Table 3, were found to be significantly higher in the test group than in the control group. IIEF-15 scorings showed a total mean score of 41.12 ± 8.97 (range 15–61) in the test group and 66.94 ± 4.27 (range 25–30) in the control group. This difference was highly statistically significant. In the erectile function domain, the test group scores ranged from 7 to 26 with a mean of 16.76 ± 4.20, while the control group scored a mean of 28.10 ± 1.36, which was significantly higher than the test group score. As shown in Table 4, a major proportion of the participants had mild or mild to moderate ED (52%) followed by moderate to severe dysfunction (46%) and 2% had no ED. On the contrary, except one participant in control group, none had ED. As

| Variable                      | Study group frequency (%) | Control group frequency (%) | Significance |
|-------------------------------|---------------------------|----------------------------|-------------|
| Age group                     |                           |                            |             |
| 20–29 years                   | 8 (16)                    | 5 (10)                     | Fisher's exact value = 1.179 |
| 30–39 years                   | 29 (58)                   | 29 (58)                    | p = 0.780   |
| 40–49 years                   | 11 (22)                   | 14 (28)                    |             |
| 50–59 years                   | 2 (4)                     | 2 (4)                      |             |
| Religion                      |                           |                            |             |
| Islam                         | 30 (60)                   | 30 (60)                    |             |
| Hinduism                      | 20 (40)                   | 20 (40)                    |             |
| Residence                     |                           |                            |             |
| Rural                         | 21 (42)                   | 18 (36)                    | Fisher's exact value = 2.509 |
| Semiurban                     | 26 (52)                   | 24 (48)                    | p = 0.331   |
| Urban                         | 3 (6)                     | 8 (16)                     |             |
| Type of family                |                           |                            |             |
| Nuclear                       | 23 (46)                   | 32 (64)                    | Pearson's Chi-squared = 4.675 |
| Joint                         | 6 (12)                    | 7 (14)                     | p = 0.097   |
| Extended                      | 21 (42)                   | 11 (22)                    |             |
| Educational status            |                           |                            |             |
| Till middle schooling         | 40 (80)                   | 39 (78)                    | Pearson's Chi-squared = 0.060 |
| High school and above         | 10 (20)                   | 11 (22)                    | p = 0.806   |
| Occupation                    |                           |                            |             |
| Unemployed                    | 7 (14)                    | 3 (6)                      | Fisher's exact value = 4.327 |
| Daily-wage earner/ farmer     | 11 (22)                   | 15 (30)                    | p = 0.238   |
| Self-employed (drivers)       | 30 (60)                   | 26 (52%)                   |             |
| Salaried person               | 2 (4)                     | 6 (12%)                    |             |
| Socioeconomic status          |                           |                            |             |
| Lower                         | 9 (18)                    | 10 (20%)                   | Fisher's exact value = 0.935 |
| Upper lower                   | 33 (66)                   | 30 (60%)                   | p = 0.965   |
| Middle                        | 5 (10)                    | 7 (14%)                    |             |
| Upper middle                  | 2 (4)                     | 2 (4%)                     |             |
| Upper                         | 1 (2)                     | 1 (2%)                     |             |

**RESULTS**

**Sociodemographic Characteristics**

The participants ranged in age from 23 to 56 years with a mean age of 35.70 ± 7.305 years. Most (58%) were in the third decade of their lives and were Muslims by religion (60%), from a rural or semiurban background (94%). Maximum were educated up to middle (80%) level of schooling. By occupation, a major (60%) proportion were self-employed (drivers of trucks), while 22% were daily-wage laborers, and another 14% were unemployed. Maximum (66%) participants belonged to upper lower socioeconomic class. The control group did not differ significantly than the test group in age as well as other sociodemographic parameters as shown in Table 1.

**Drug Use and Treatment-related Variables**

It was found that the duration of opioid use ranged from 1 to 25 years, with 34% having 5 years or less, 36% having 6–10 years, and 30% having more than 10 years of usage. Most of the participants were interviewed after the completion of 6 months (52%) and 7 months (40%). The dose of sublingual buprenorphine ranged from 2 mg/day (30%) through 4 mg/day (46%) to 6 mg/day (24%) (Table 2).

**Sexual Functioning**

As assessed by ASEX scale, 26 (52%) test group participants were found to be having sexual dysfunction, while none of the control group was found to have sexual dysfunction. Individual mean scores for each component, as shown in Table 3, were found to be significantly higher in the test group than in the control group. IIEF-15 scorings showed a total mean score of 41.12 ± 8.97 (range 15–61) in the test group and 66.94 ± 4.27 (range 25–30) in the control group. This difference was highly statistically significant. In the erectile function domain, the test group scores ranged from 7 to 26 with a mean of 16.76 ± 4.20, while the control group scored a mean of 28.10 ± 1.36, which was significantly higher than the test group score. As shown in Table 4, a major proportion of the participants had mild or mild to moderate ED (52%) followed by moderate to severe dysfunction (46%) and 2% had no ED. On the contrary, except one participant in control group, none had ED. As
Table 3: Mean scores of ASEX and IIEF domains and prevalence of sexual dysfunction and severity of ED

| Variables                  | Study group | Control group | t   | p value |
|----------------------------|-------------|---------------|-----|---------|
| **ASEX component**         |             |               |     |         |
| Sexual drive               | 3.48 ± 0.74 | 2.24 ± 0.74   | −8.383 | <0.001  |
| Psychological arousal      | 3.58 ± 0.67 | 1.86 ± 0.57   | −13.775 | <0.001  |
| Erection                   | 3.62 ± 0.80 | 1.64 ± 0.60   | −13.958 | <0.001  |
| Ease of orgasm             | 3.54 ± 0.79 | 1.56 ± 0.58   | −14.335 | <0.001  |
| Orgasm satisfaction        | 3.56 ± 0.70 | 1.72 ± 0.67   | −13.370 | <0.001  |
| ASEX total                 | 17.58 ± 2.86| 9.00 ± 2.67   | −15.485 | <0.001  |
| **IIEF domains**           |             |               |     |         |
| Erection function          | 16.76 ± 4.20| 28.10 ± 1.36  | 18.176  | <0.001  |
| Orgasmic function          | 6.10 ± 1.40 | 8.84 ± 0.79   | 12.024  | <0.001  |
| Sexual desire              | 5.38 ± 1.23 | 7.76 ± 0.85   | 11.289  | <0.001  |
| Intercourse satisfaction   | 7.38 ± 2.33 | 13.08 ± 1.05  | 15.785  | <0.001  |
| Overall satisfaction       | 6.04 ± 1.40 | 9.16 ± 1.18   | 12.036  | <0.001  |
| IIEF total                 | 41.12 ± 8.97| 66.94 ± 4.27  | 18.378  | <0.001  |

Table 4: Prevalence of sexual dysfunction and severity of ED

| Frequency (%) | Study group | Control group | Fisher’s exact value | p value |
|---------------|-------------|---------------|----------------------|---------|
| ASEX          |             |               |                      |         |
| Sexual dysfunction | 26 (52) | 0 (0)          | 112.511              | <0.001  |
| None          | 1 (2)       | 49 (98)       |                      |         |
| Mild or mild to moderate ED | 26 (52) | 1 (2)          |                      |         |
| Moderate or severe ED | 23 (46) | 0 (0)          |                      |         |

shown in Table 3, the test group scored significantly lower than the control group in each of the domains of IIEF-15.

On further analysis, statistically significant negative correlations were seen between analogous components of the two scales. For example, as shown in Table 5, significant negative correlations were seen between ASEX question 1 (sexual drive) score and IIEF-15 sexual desire domain score and between ASEX question 3 (erection) score and IIEF-15 erection function score. Hence, despite the two scales measuring a different prevalence of sexual dysfunctions, the levels of dysfunction as assessed by the two scales had significant linear relationships, i.e., the findings elicited by the two different scales were not inconsistent.

**Discussion**

The combination of buprenorphine and naloxone is a commonly used drug in OST; the side effect profile includes sexual dysfunction. As sexual dysfunction due to medication use may lead to treatment nonadherence, it is essential to assess the prevalence and intensity of sexual dysfunction among the clients receiving such opioid substitution drugs.

The current study employed two widely used and validated instruments, namely ASEX and IIEF-15, in an attempt to assess the prevalence and extent of sexual dysfunction, among individuals receiving buprenorphine for a duration longer than 6 months.

As was evident in our results that the prevalence of sexual dysfunction, as measured by both ASEX and IIEF-15 scales, was significantly higher in the test group than in the control group individuals. Ramdurg et al., in a study conducted in the Delhi NCR region using the Brief Male Sexual Functioning Inventory (BMSFI), reported experience of at least one sexual dysfunction symptom in 83% of the opioid using subjects treated with buprenorphine therapy. On the contrary, Mattoo et al., in a study recruiting 40 male patients on buprenorphine-naloxone-based substitution therapy, found the prevalence of sexual dysfunction to be 40% using the ASEX scale. The current study, while employing the ASEX scale, found sexual dysfunction in 52% of the subjects.

Baykara and Albano conducted a similar study on subjects on buprenorphine-naloxone maintenance therapy for 4 months. The mean scores for the individual components and mean total score in their study, respectively, were 3.01 ± 1.56, 3.11 ± 1.44, 3.03 ± 1.44, 2.93 ± 1.39, 2.95 ± 1.59, and 15.03 ± 6.61. These scores were more or less comparable to the findings in our study: 3.48 ± 0.735, 3.58 ± 0.673, 3.62 ± 0.805, 3.54 ± 0.788, 3.56 ± 0.705, and 17.58 ± 2.865, respectively. Hence, a comparable level of dysfunction in sexual desire, arousal, erection, orgasm, and orgasmic satisfaction was found in our study participants.

When we assessed sexual functioning using the IIEF-15, ED of any degree was found in all 98% of the individuals on buprenorphine-naloxone-based treatment. In the study by Baykara and Albano, the same rate was found to be 64.2%. In the study by Quaglio and Lugoboni, among 201 male patients on maintenance therapy (42% on methadone; 58% on buprenorphine), only 36.3% of the subjects on buprenorphine-based therapy were found to be having ED as assessed by IIEF-15. Among the participants, 12.9% had mild ED, 3.5% mild to moderate ED, 1.8% moderate ED, and 18.1% severe ED. In contrast, the current study found mild or mild to moderate ED (52%) followed by moderate to severe dysfunction (46%) and 2% had no ED. Response bias cannot be ruled out to be accounting for such a higher prevalence. This bias might be rooted in prevalent cultural beliefs regarding virility, perceived “penile strength,” etc. However, this possible cultural artifact needs further systematic investigation. Another possible contributing factor for this high prevalence of ED as assessed by IIEF-15 might be low levels of marital satisfaction or interpersonal issues of the conjugal lives of the individuals with a history of opioid abuse. Notwithstanding such possible confounding factors, the distress due to perceived erectile problems was high among the participants. This necessitates
the role of proper psychosexual counseling for all the patients undergoing OST.

The current study identified some important sociodemographic patterns to opioid use. In our study sample, a typical opioid abuser tended to be of lower socioeconomic strata with lower level of education and engaged in a poorly remunerated occupation. A certain demographic section among the participants was engaged in driving (goods-carrying vehicles or trucks). This finding points toward the need of targeted intervention in curbing opioid abuse in the population.

**Limitations**

Several limitations need mention in the current study. First, the study was a cross-sectional one, and comparison of pretreatment and posttreatment sexual dysfunction status could not be done. The pre-OST sexual dysfunction was assessed only by means of retrospective data obtained with the help of a semistructured interview, which is prone to recall bias. Again, response bias might be in play that might possibly be rooted in cultural beliefs as we have mentioned earlier. Thirdly, the number of participants was a relatively small one (50 only in the test group). Further, due to a resource-limited setting, we could not do hormonal measurements to complement our study findings.

The strength of our study lies in its being one of the first to assess sexual dysfunction in long-term buprenorphine-naloxone-based OST in this particular population.

**Conclusion**

Opioid substitution therapy has become an established harm reduction method in preventing illicit opioid use and subsequent adverse events. The OSTCs have been functionalized under government agencies like ASACS which have seen a satisfactory level of utilization by the population. The possible adverse effects of the buprenorphine-based therapy provided in these centers, however, can potentially mar the benefits. As sexual dysfunction is one of such adverse effects, it becomes imperative to assess the prevalence and degrees of sexual dysfunction among the clients, particularly after a long duration of therapy. The current study employed two widely used and validated instruments, namely ASEX and IIEF-15. ASEX scorings showed 52% prevalence of sexual dysfunction among the participants. Further, IIEF-15 scorings showed some degrees of ED among all the participants except one. A total of 98% of the ED was of mild to moderate and moderate severity. Such a high prevalence of ED may be attributed apart from treatment-related factors to response bias rooted in cultural beliefs regarding virility and sexual performance or interpersonal conflicts in conjugal life. On further analysis, no significant effects of age, current dose of buprenorphine, and duration of therapy on the prevalence and degree of sexual dysfunction were found. The study also revealed important sociodemographic correlates of opioid use. These findings suggest the need for evaluation of sexual functioning in all the clients of OST, the need of psychosexual counseling, and timely medical or psychological interventions.

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