ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 17, Issue 8, 2024

Online - 2455-3891
Print - 0974-2441

Research Article

METHADONE VERSUS BUPRENORPHINE: TO STUDY THE EPIDEMIOLOGY AND COMPARE THE TREATMENT OUTCOME AS IN RETENTION RATE BETWEEN METHADONE AND BUPRENORPHINE TAKING OPIOID DEPENDENT PATIENTS FROM OST CENTER

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Received: 12 April 2024, Revised and Accepted: 31 May 2024

ABSTRACT

Objectives: The objective is to study sociodemographic profile and compare retention rate between methadone and buprenorphine (BPN) taking opioid-dependent patients from opioid substitution therapy (OST) centers.

Methods: Two hundred patients, 100 each on methadone and BPN already taking treatment from OST center under the Department of Psychiatry, GMC Amritsar and Civil Hospital, Kapurthala, were studied. The precise aim of the interview and the nature of the study were explained to the enrolled patients and patients were reassured about the confidentiality of the information given. In this 1-year study, patients were followed up at 3, 6 and 9 months and compared to find the drug associated with higher patient retention on treatment. Hence, establishing which drug is more effective in treatment adherence.

Results: The majority of patients, that is, about 80% in the BPN group and 93% in the methadone group were below 40 years of age. In the BPN group, 70% of subjects were married persons (70%) compared to 74% in the methadone group. Most patients in both groups were educated up to 10th and 12th standards. Most of the patients in both groups had duration of substance dependence between 5 and 10 years. In the BPN group, 51% of participants had previously attempted some treatment for drug abuse while in the methadone group, 57% had attempted the same.

Conclusion: After comparing the retention between the two drug groups, no statistically significant difference was found.

Keywords: Opioid substitution therapy, Opioid dependence, BPN, Methadone, Retention rate.

 DOI: http://dx.doi.org/10.22159/ajpcr.2024v17i8.51106. Journal homepage: https://innovareacademics.in/journals/index.php/ajpcr

INTRODUCTION

Drug addiction, a complex illness, is identified by traits such as an intense craving for drugs which is usually uncontrollable. Addiction hits brain circuits which are involved in reward and motivation, cognition and memory, and inhibitory control over behavior. Even as a person chooses to take drugs voluntarily in the beginning, a protracted timeline of exposure to the functioning of the brain interferes with their ability to choose. However, addiction is not just a compulsive drug-abusing habit but also has devastating health and social ramifications [1].

"Opioid" is a complex soup which includes drugs containing natural opiates derived from the opium-bearing poppy plant, *Papaver somniferum* and a range of synthetic and semi-synthetic substances which induce a morphine-like effect [2]. Most natural and synthetic opioids come under the scope of the NDPS Act, and their production, sale and distribution are subject to regulations of the act. Citing the medical significance of a number of compounds, a 2014 amendment to the NDPS designated certain opioid compounds as "essential narcotic drugs" [3].

Pure heroin (diacetylmorphine), a white powder with a bitter taste, is abused for its euphoric effects and is roughly 2–3 times more potent than morphine [4]. It is usually injected, smoked, or snorted up the nose. It exhibits a euphoric rush, anti-anxiety, and pain-relieving properties. The users report feeling an increase of euphoria (the "rush") which is accompanied by a warm flushing of the skin, a dry mouth, and heavy extremities after injection [5]. Even novel combinations being explored for various diseases are at risk of being abused [6].

Drug dependence is a state of psychic or physical dependence or both, on a drug, in a person following the administration of that drug on a periodic or continuous basis [7]. Addiction treatment should not only help an individual in avoiding using drugs but also in maintaining a drug-free lifestyle, with a productive role in family, work, and society [1].

Opioid substitution therapy (OST) is a long-term intervention for the treatment of opioid dependence syndrome along with the prevention of HIV. The therapy works on the premise that an illegal substance such as heroin which is administered through a high-risk route (through injection) is substituted with legal medication whose potency and purity are predetermined. Both methadone and buprenorphine (BPN), the medicines for OST have been listed under the WHO model list of essential medicines [8].

Methadone, which was synthesized in Germany as a potent analgesic in the late 1930s, is a long-acting, synthetic, complete agonist of the μ opioid receptor. Methadone meets two important criteria for medication to be used for the treatment of drug dependence: High systemic bioavailability (>90%) with oral administration and long apparent half-life with long-term administration in humans. If the intake is chronic, methadone is stored and accumulates in the liver [9]. Methadone is preferred over BPN for patients who are at increased risk of dropouts, like intravenous drug users (IDU). Furthermore, Youth and pregnant women should receive methadone first if they use drugs intravenously [10].

FDA approved the usage of BPN alone and in combination with Naloxone in 2002 as an office-based sublingual treatment for heroin and opioid addiction. It is a synthetic opioid medication that acts as a partial agonist at opioid receptors. It does not produce the euphoria and sedation caused by heroin or other opioids but is able

to reduce or eliminate withdrawal symptoms associated with opioid dependence [11]. BPN has a low overdose risk due to its ceiling effect and hence is recommended to be used in the elderly, in patients taking benzodiazepines or other sedating drugs, alcohol users, patients with lower levels of opioid tolerance, and those at high risk of QT prolongation [10]. It is increasingly being used under OST and was also included in the 2005 WHO's Model List of Medicines [2]. Further abuse-deterrent sublingual film of BPN is being developed for the management of non-substance abuse-related patients [12].

According to a recent national survey done by AIIMS New Delhi, the Magnitude of Substance Use in India in 2019 was assessed which showed the extent, trends and pattern of drug use. The prevalence of current opioid use in our country is about 2.06% with heroin being the most commonly used opioid. Out of the estimated 77 lakh opioid problem users, more than half of the users are contributed by only a few states of India. Punjab is the second state, after Uttar Pradesh, with the largest number of opioid users in India [3].

The Punjab Opioid Dependence Survey shed light on the opioid dependence scenario in the state of Punjab. The survey, which was carried out in 10 districts of Punjab, showed that the most common opioid drug used was heroin (53%), followed by opium/doda/bhukki (33%) and pharmaceutical opioids (14%). About one-third used the intravenous route for taking opioids and almost 90% of the IDU injected heroin. About 80% reported that they have tried to quit using the drug but only 35% had received any kind of treatment. The national annual expenditure on opioids by dependent persons is about Rs 7,575 crore per year [13].

Enhancing treatment retention rates is crucial for improving treatment outcomes as it is an important indicator of favorable treatment outcomes [14]. The methadone and BPN maintenance treatments were conceived to prevent the illegal or harmful usage of opioids coupled with other problems associated with this addiction such as crime, disease, and death [15].

The focus of our study was to compare methadone and BPN, in terms of retention among the opioid users taking treatment from the OST center, Department of Psychiatry, GMC Amritsar and Civil Hospital Kapurthala.

Aims and objectives

The objectives of the study are as follows:

1. To study the sociodemographic profile of opioid-dependent patients taking treatment from OST Centre.
2. To find and compare the retention rate among opioid patients put on methadone and BPN maintenance treatment.

METHODS

Study setting

The present study was conducted at 2 OST centers, one under the Department of Psychiatry, GMC Amritsar and the second under CH Kapurthala. The study was conducted after approval from Institutional Ethics Committee Government Medical College, Amritsar and Civil Surgeon Office, Kapurthala and informed consent from patients to be enrolled in the study. In this study, 200 patients, 100 each on methadone and BPN maintenance treatment; diagnosed as cases of opioid dependence as per ICD 10 criteria were enrolled. The duration of the study was 1 year. The diagnosis was established by consultants.

The precise aim of the interview and the nature of the study were explained to the enrolled patients and patients were reassured about the confidentiality of the information given. The data were interpreted and were analyzed through standard statistical methods.

Inclusion criteria

The following criteria were included in the study:

a. Diagnosis of opioid dependence as per ICD 10 criteria.
b. Patients on methadone or BPN treatment for a period of at least 3 months.
c. Patients older than 18 years of age.
d. Patients who appeared mentally competent to give informed consent.
e. Patients who are willing to sign an informed consent document.

Exclusion criteria

The following criteria were excluded from the study:

a. If the patient is pregnant or lactating.
b. If the patient is suffering from any acute medical condition.
c. Patient is currently using anticonvulsive or antipsychotic medication.

Method of selection

One hundred patients taking methadone and 100 patients taking BPN from the OST centers under the Department of Psychiatry, GMC Amritsar and Civil Hospital, Kapurthala, diagnosed as cases of opioid dependence as per ICD 10 criteria were enrolled. Diagnosis was established by consultants. After getting informed consent from the patient, DAMS Pro forma containing sociodemographic details, details of drug use pattern, present history, history, family history of any substance abuse, high-risk behavior, and compelling needs were filled. The patients were assessed and followed up every 3 months (0, 3, 6, and 9) in 1 year of study to find the retention of patients.

OBSERVATIONS AND RESULTS

Age-wise distribution of participants is summarized in Table 1 and Fig. 1.

Marital status-wise distribution revealed that in the BPN group, married persons were 70%, never married were 24% and divorced accounted for 6%. In the methadone group, 74% were married, 19% were never married, and 7% were divorced. In education status-wise distribution, 5% of patients were illiterate, 9% had studied up to primary level (5th), 11% up to middle level (8th), 64% had studied up to 10th and 12th standard

Table 1: Age distribution within study groups

Age group	Group (%)	
	BPN	Methadone
≤20	9 (9.0)	5 (5.0)
21–30	46 (46.0)	56 (56.0)
31–40	25 (25.0)	32 (32.0)
41–50	16 (16.0)	7 (7.0)
51–60	3 (3.0)	0 (0.0)
>60	1 (1.0)	0 (0.0)
Total	100 (100.0)	100 (100.0)

p=0.062; d.f. 5

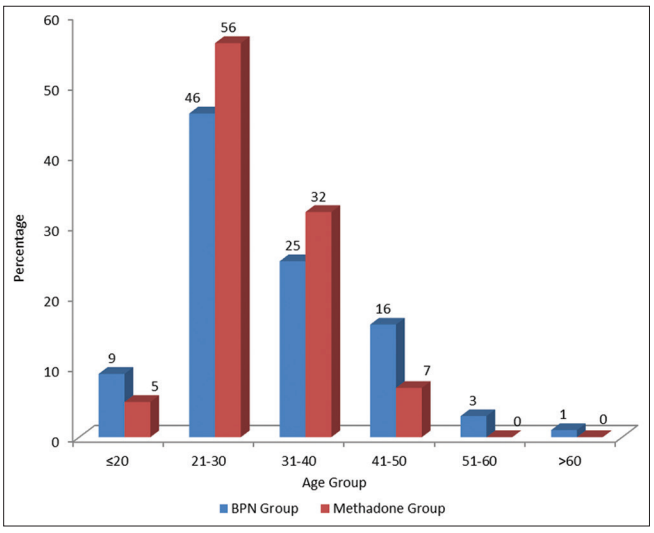

Fig. 1: Age distribution within study groups

and 10% had completed their graduation in BPN group. In the methadone group, 3% were illiterate, 4% could read and write, 2% had studied up to primary level (5th), 13% up to middle level (8th), 71% studied upto10th and 12th standard, and 7% had completed their graduation. In the employment status-wise comparison between the two groups, the BPN group had 58% self-employed, 18% fully employed, 1% part-time employee, 16% presently unemployed, and 3% never-employed. In the methadone group, 68% were self-employed, 13% were fully employed, 10% were presently unemployed, and 7% were never employed.

Regarding the living status-wise distribution, the BPN group had 57% from a nuclear family and almost a similar percentage was from the methadone group. In the BPN group, 43% were from a joint family and about 41% of the methadone group belonged to a joint family. The religion-wise comparison between the two groups indicated that in the BPN group, 77% were Sikhs and 23% were Hindus. In the methadone groups, 75% were Sikhs and 25% were Hindus.

Regarding age at initiation of opioid use, in the BPN group, 28% started at <20 years of age, 71% at 21–40 years of age and only 1% after 60 years of age. In the methadone group, 22% started at <20 years of age, and 77% at 21–40 years of age. The history of previous treatment of drug abuse among the groups indicates that in the BPN group, 51% had previously attempted the treatment of drug abuse while in the methadone group, 57% had attempted the same. About 48% of the BPN group had <5 years of substance dependence while 51% were between 5 and 10 years and only 1% had more than 10 years of dependence. Among the methadone group, 46% had <5 years of substance independence, 53% were between 5 and 10 years and only 1% had more than 10 years of dependence (Summarized in Table 2 and Fig. 2).

The retention rate for the BPN group at 3 months follow-up was 97% and for the methadone group was 98% with a p=0.651 (not significant). The 6-month retention rate for the BPN group was 93% and that of the methadone group was 94% with a p=0.774 (not significant). At 9-month follow-up, the retention rate in the BPN group further decreased to 90% and that for methadone group up to 93% with no statistically significant difference between the two groups (p=0.447). The retention rates in both groups are given in Table 3 and Fig. 3.

Table 2: Duration of opioid dependence within study groups

Duration	Group (%)	
	BPN	Methadone
<5 years	48 (48.0)	46 (46.0)
5–10 years	51 (51.0)	53 (53.0)
>10 years	1 (1.0)	1 (1.0)
Total	100 (100.0)	100 (100.0)

p=0.960; d.f. 2

Table 3: Retention rate within study groups

Retention	Group (%)	
	BPN	Methadone
At 3 months Follow up		
Left treatment	3 (3.0)	2 (2.0)
On treatment	97 (97.0)	98 (98.0)
Total	100 (100.0)	100 (100.0)
At 6 months follow up		
Left treatment	7 (7.0)	6 (6.0)
On treatment	93 (93.0)	94 (94.0)
Total	100 (100.0)	100 (100.0)
At 9 months follow up		
Left treatment	10 (10.0)	7 (7.0)
On treatment	90 (90.0)	93 (93.0)
Total	100 (100.0)	100 (100.0)

RESULT AND DISCUSSION

In our study, most patients belonged to the age group of 21–30 years in both groups. In the BPN group, 46% of patients were of 21–30 years and 25% in 31–40 years of age. In the methadone group, 56% were in 21–30 years of age and 32% in 31–40 years. The above results show that the majority of patients in both groups belong to early adulthood. Our findings are supported by Basu *et al*. as in their study mean age in three decades from 1978 to 2008 was 32.68±11.52 years, 30.83±9.94 years, and 28.33±8.37 years, respectively [16]. In another study done by Nigam *et al*., the mean age of substance abuse was 28.7±7.2 years [17].

In our study, there were two females in the BPN and nine in the methadone group. The majority of patients (more than 90%) in both groups were male. The results are similar to the study done by Lal and Singh who found only one female user in their study [18]. In another study done by Avasthi *et al*., 98.1% of the opioid users were males and only 1.86% were females [19].

Regarding marital status, the majority of the patients in our study from both groups were married. In the BPN group, 70% were married while in the methadone group, it was 74%. Our study findings are supported

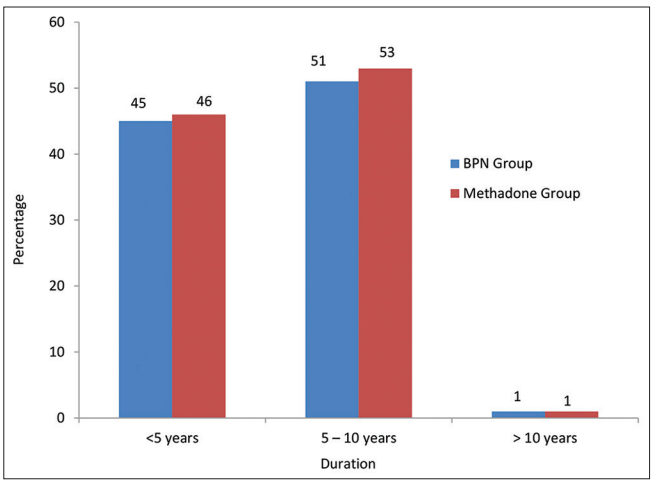

Fig. 2: Duration of opioid dependence within study groups

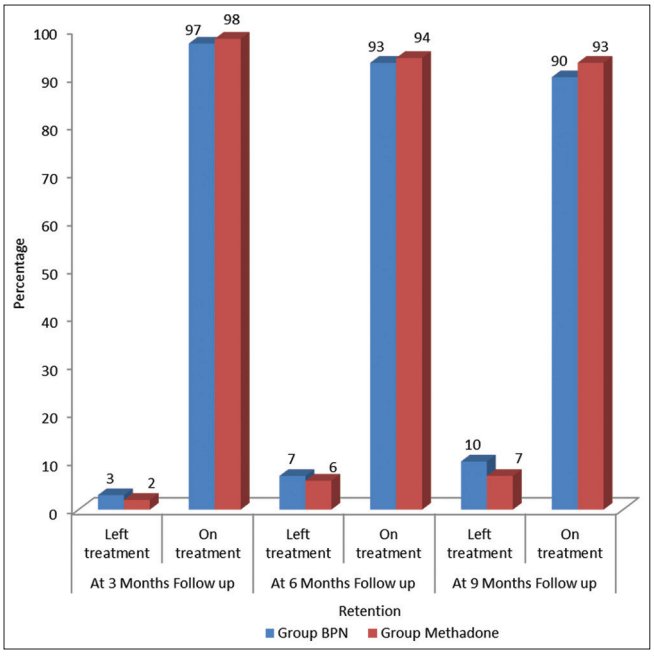

Fig. 3: Retention rate within study groups

by studies of Chavan *et al*. who reported 73.80% of their study sample was married [20]. Our study findings are in conformity with yet another study by Malik *et al*. who reported 95% married subjects [21].

Regarding the education status, most of the patients in both groups had studied until matric and +2 and the difference was not statistically significant. The percentage of patients falling in the majority is 64% for the BPN group and 71% for the methadone group in our study sample. Our study results are supported by Rather *et al*. in their study on the sociodemographic profile of drug abusers and reported 53.5% of abusers were educated up to the high school level [22].

Another study conducted by Mattoo *et al*. (2013) reported 55% of patients being educated above the high school level. Singh *et al*. also reported that 40% of their study subjects were educated up to a higher secondary level [23]. Singh also reported 40% of their study sample to be educated up to a higher secondary level [24].

Regarding employment status, most of the patients were employed in our study. It was 77% and 81% in the BPN and methadone groups, respectively. Unemployment among both groups was around 10%. In a study conducted by Vivek *et al*. on opioid-dependent patients, it was found that 83% of patients were employed [25].

In our study, majority of patients in both groups belonged to a nuclear family, which was 57% and 59% for the BPN and methadone groups, respectively. Both groups were comparable and had no significant difference in terms of family type. Our study is supported by Saluja *et al*., which concluded that 63.5% of dependents belonged to nuclear family [26].

In our study, 77% and 75% of subjects in the BPN and methadone groups, respectively, were Sikh. These findings result from the study being conducted in a Sikh-dominant area.

In our study, most patients had a duration of substance consumption of <10 years. Among both groups, about half of patients had <5 years of dependence. Margoob and Dutta also reported similar results. In their study, they concluded that 41.65% of the patients used substances for more than 5 years [27].

Another study that supported our finding is that of Farhat *et al*., which showed that the mean duration of opioid consumption was 5.75±3.12 years [28].

In our study, the age at initiation of the majority of patients in both groups falls between 21 and 40 years of age. It is 71% for the BPN group and 77% for the methadone group and no statistical difference is found between the two. Our results are supported by studies done by Kalra and Bansal *et al*., Farhat *et al*. and Nigam *et al*. which reported the mean age of initiation as 25.4±7.613 years, 27.64±4.60 years and 28.7±7.2 years, respectively [17,29,28].

About 51% and 57% of patients in the BPN and methadone groups, respectively, had at least one previous detoxification. Our findings are supported by a study done by Rapp *et al*. in which 74.7% of patients had already taken earlier treatment for substance abuse [30].

In our study, the retention rate at 9-month follow-up was 90% for the BPN group and 93% for the methadone group. However, the difference (10 vs. 7 participants) was not found to be statistically significant indicating that both drugs are equally effective in the maintenance treatment of opioid dependence.

Our findings are supported by Kosten *et al*., which reported statistically no significant difference between the retention rate of methadone and BPN groups. Results showed that the retention rate was 52%, 40%, and 35% for the M80, M30, and BPN groups, respectively, at the end of 26 weeks of treatment [31].

Another study conducted by Soyka *et al*. comparing methadone and BPN showed a favourable treatment outcome, with an overall retention rate of 52.1% and the difference between the two treatment groups was found to be not significant (55.3% methadone vs. 48.4% BPN) [32].

Limitations of study

1. The sample size was small.
2. Only opioid-dependent patients taking treatment from OST Centre were included in the study. Caution should be exercised while applying these findings to patients in other treatment settings.
3. No control group was taken in the study for comparison.
4. There were only a few female patients in our study, so caution should be exercised when applying these findings to female patients.

CONCLUSION

The majority of patients, that is, about 80% in the BPN group and 93% in the methadone group were below 40 years of age. This shows that the early adulthood age group is most frequently involved in opioid dependence and substance abuse. About 70% of patients were married in the BPN group and 74% in methadone group. The majority of the patients in the study were male in both groups. There were only two females in the BPN group and nine in the methadone group. Regarding the educational status, the majority of patients had studied up to matric and 10+2, that is, 64% and 71% in BPN and methadone groups, respectively. About 58% of the BPN group were self-employed as compared to 68% of the methadone group, although the difference between the two was not statistically significant. <20% of the patients in both groups were unemployed. About 57% of both groups belonged to a nuclear family. About 77% of the patients in the BPN group and 75% of the methadone group belonged to the Sikh religion. In the majority, the age of initiation among both groups was between 20 and 41 years age group. The majority of patients, about 80% in both the groups were poly-substance abuser. In the BPN group, 51% had previously taken treatment for opioid dependence while in the methadone group, 57% had attempted the same. After comparing the retention between the two drug groups, 90 patients were retained in the BPN group and 93 in the methadone group. No statistically significant difference was found between the two.

Institutional Ethics Committee approval Number: 40/TH/D-26/2018 Batch

CONSENT FOR PUBLICATION

Authors declare that informed written consent for publication of data was obtained from all participants.

ACKNOWLEDGEMENTS

None.

AUTHORS' CONTRIBUTIONS

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work. (1) Rajiv Arora: (a) Concept and design, (b) Supervision of study, (c) Critical review of the manuscript. (2) Shiny Dehal: (a) Concept and design, (b) Acquisition, analysis, or interpretation of data, (c) Drafting of the manuscript, (d) Critical review of the manuscript. (3) Neeru Bala: (a) Concept and design, (b) Supervision of study, (c) Critical review of the manuscript, (4) Khushbinder Singh: (a) Concept and design, (b) Supervision of study, (c) Critical review of the manuscript. (5) Harshpreet Singh: (a) Acquisition, analysis, or interpretation of data, (b) Critical review of the manuscript.

CONFLICTS OF INTERESTS

Authors have no conflicts of interest to declare.

FUNDING

All authors have declared that no financial support or grants were received from any organization for the submitted work.

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