

ORIGINAL ARTICLE

**ASSESSMENT EFFECTS OF MAINTENANCE THERAPY
ON QUALITY OF LIFE OF OPIATE ABUSERS**

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Abstract

Objective: This study was conducted to assess the effects of Methadone Maintenance Therapy (MMT) and buprenorphine-naloxone Maintenance Therapy (BNX) on the Quality of life (QoL) of opiate abusers. **Methods:** The QoL status of opioid-dependent patients was assessed using the WHOQOL-BREF questionnaire. It is a cross-sectional study involving a total of 108 patients who received MMT or BNX therapy in Malaysia from May 2011 to September 2011. **Results:** A statistically significant difference in the overall QoL and psychological aspect among patients on MMT was observed. On the contrary, the scores of overall QoL and quality of social relationship for BNX group were higher in patients with lower dosage. **Conclusion:** The comparison between patients on high dose MMT and high dose BNX exhibited significant difference in the overall QoL especially in psychological, social relationship and environment domains, with the high dose MMT group having better mean score. *ASEAN Journal of Psychiatry, Vol. 15 (2): July – December 2014: 131-139.*

Keywords: Buprenorphine-Naloxone (BNX), Maintenance Treatment, Malaysia, Methadone, Opiate Abusers, Quality of Life

Introduction

Substance abuse has always been a major concern and given a negative impact on the mental and physical health of individuals, families and communities worldwide. According to global estimations, there were 185 million illegal drug users in the year 2002 with more reported psychoactive substance abuse cases in developed countries than in developing countries [1]. Drug abuse in Malaysia, began as early as the 8th century and increased during the British colonial era [2]. In the year 2007, it was estimated that there were 400,000 to 800,000 drug users in Malaysia [3]. Based on the information provided by the National Anti-Drugs Agency Malaysia, heroin, morphine, methamphetamine, and cannabis are the most common illegal drugs, with heroin being the

most common while cannabis the least common [4]. MMT was first developed as a treatment for heroin addiction in the mid-1960s [5] and has been widely known for its pharmacological treatment property for opioid dependence which decreases heroin addiction [6]. It can be used as a single dose daily due to its pharmacological mechanism and documented as an effective and safe mode of treatment [7, 8]. The first pilot MMT project in Malaysia commenced in 17 centres in nine states in 2005 proved its efficacy which was later supported by National Task Force on Harm Reduction (NTFHR) [9]. BNX was introduced two years later after methadone when it was proven to have the ability to reduce potential problems with diversion and abuse. It is a combination of buprenorphine with naloxone at a 4:1 ratio in order to reduce buprenorphine abuse. Naloxone is an opioid

antagonist. BNX produces minimal withdrawal symptoms when discontinued, has a low potential for overdose, a long duration of action, and the ability to block heroin effects making it suitable for drug substitution therapy [10]. Even though studies have shown that methadone has a higher treatment retention rate compared to buprenorphine, the main advantage of using buprenorphine is that it has a lower risk of overdose compared to methadone [11]. Thus, the aim of this study is to compare the effects of 2 different substitution therapies i.e. MMT and BNX on the QoL of opiate abusers and to analyze the possible factors that may affect their efficacy. It intends to contribute in providing vital practical 'on-the-ground reflections' for future revision of the national substance programme guidelines.

Methods

This is a cross-sectional study involving a total of 54 patients from the MMT programme of a tertiary hospital (Hospital Tuanku Jaafar) in Negeri Sembilan, Malaysia and another 54 from BNX programme in a polyclinic (Poliklinik Damai 24 Jam) in Selangor, Malaysia from May to September 2011. All patients from the tertiary hospital received MMT while all patients from the polyclinic received BNX. The patients were consented and enrolled into the study according to the following inclusion criteria: (i) Patients who have been receiving drug maintenance therapy either MMT or BNX for more than four months and without other underlying medical illnesses, (ii) ICD-10 diagnosis of opioid dependence (F11), (iii) The patients must be 18 years old or older, (iv) No contraindications with methadone or BNX. The term stability of treatment used in this research is defined as the period where patient is able to sustain the same dose of therapy. High dose methadone is defined as 50mg or higher, while low dose methadone is defined as less than 50mg. On the other hand high dose BNX is defined as 8mg or more while low dose BNX is defined as less than 8mg [12]. An adapted version of the WHOQOL-BREF questionnaire [13] (English and Malay translated version) was used and its administration adhered to the WHO criteria.

Instrument

The WHOQOL-BREF is a self-administered questionnaire. If necessary it can be interviewer-assisted or interview-administered. There are a total of 26 questions in the questionnaire which is grouped into four domains (physical, psychological, social relationships and environment) and two items from overall QoL and general health facets. The four domain scores denote an individual's perception of QoL in each particular domain. Interviewers were trained by an experienced researcher prior to the commencement of the study.

Data Analysis

Software package for statistical analysis (SPSS) version 19 was used for statistical analysis. If more than 20% of data were missing from an assessment, the assessment was discarded. If there were up to two items missing, the mean of other items in the domain was used as a substitute. If there were more than two items missing from the domain, the domain score was not calculated (with the exception of domain 3, where the domain was only calculated if < 1 item is missing). The score for each domain was converted to make it comparable with WHOQOL-100 scores using the table provided in the WHOQOL-BREF Instructions, Administration Guidelines. WHOQOL-100 is a instrument used to measure QoL. It consists of six broad domains of QoL and twenty four facets. Each facet has four items. It also consists of four general items covering subjective overall QoL and health which make up a total of 100 items. All items are rated from 1-5. It is possible to derive six domain scores, 24 specific facet scores, and one general facet score that measures overall QoL and general health. Domain scores and facet scores are from 4-20. Higher scores denote higher QoL.

Chi-square or Fisher exact test (for small samples) was used for the comparison of socio-demographic characteristics and addiction history whereas independent t-test was used for the comparison of QoL of patients. Statistical significance was set at $p < 0.05$. If $p < 0.05$, the null hypothesis was rejected. Logistic regression was used to

estimate the predictive power of key independent variables (types of treatment, dosage of medication etc) on the overall QoL.

Results

Socio-demographic characteristics

Out of 112 opioid-dependent patients from both MMT and BNX clinic who were selected to participate in this study, only 108 participants completed the WHO-QOL BREF questionnaire appropriately. The

characteristics of these patients were compared between both groups. The socio-demographic characteristics were quite similar in both groups. Most were older than 40, men, Malay, smoked cigarettes and achieved secondary education. About half of them were married. There was no significant difference in all the above for both groups. However, there was a statistically significant difference in the working status ($p=0.038$) and monthly income ($p=0.002$). Table 1 shows the characteristics of patients involved.

Table 1. Comparison of the socio-demographic characteristics of the respondents

	MMT		BNX		<i>p</i> -value
	N	%	N	%	
Age (years)					0.129
<40	36	66.7	43	79.6	
≥40	18	33.3	11	20.4	
Sex					0.243
Male	51	94.4	54	100	
Female	3	5.6	0	0	
Ethnicity					0.540
Malay	47	87.0	49	90.7	
Non-Malay	7	13.0	5	9.3	
Marital status					0.847
Married	29	53.7	28	51.9	
Single/Divorced/ Widowed	25	46.3	26	48.1	
Religion					0.540
Muslim	47	87	49	90.7	
Non- muslim	7	13	5	9.3	
Working status					0.038*
Yes	44	81.5	51	94.4	
No	10	18.5	3	5.6	
Years of Working					<0.001*
0.1-5	33	75.0	20	39.2	
>5	11	25.0	31	60.8	
Monthly income					0.002*
≤1000	30	55.6	14	25.9	
>1000	24	44.4	40	74.1	

* $p < 0.05$; BNX = buprenorphine-naloxone Maintenance Therapy; MMT = Methadone Maintenance Therapy

Substitution Therapy and Drugs Abused

There was no difference in the duration of treatment. Majority of patients on MMT were taking high dose (68.5%) compared to BNX where majority of patients were on low dose BNX (55.6%). There was a clear difference in stability of drug treatment between the groups as 52 (96.3%) of MMT patients had the dosage

of drug adjusted while majority of BNX patients maintained a stable dose for a longer period. Comparison between the type of drugs abused before therapy shows that there was no significant difference for heroin ($p=0.153$) though it was significantly more for ganja and amphetamine-type stimulants (ATS) in the BNX group. See Table 2.

Table 2. Comparison of the duration of treatment, the latest dosage, stability of treatment and the association between different type of additional drugs abused for the two groups (MMT and BNX)

	Methadone		BNX		p-value
	N	%	N	%	
Duration of treatment (months)					
≤24	30	55.6	20	37.0	0.054
>24	24	44.4	34	63.0	
Latest dosage					
Low dose	17	31.5	30	55.6	0.012*
High dose	37	68.5	24	44.4	
Stability of treatment dosage (months)					
≤12	52	96.3	11	20.4	<0.001*
>12	2	3.7	43	79.6	
Drug Abused					
Heroin	54	100	52	96.3	0.153
Ganja	30	55.6	49	90.7	<0.001*
ATS	26	48.1	41	75.9	0.003*

(* $p < 0.05$; BNX = buprenorphine-naloxone Maintenance Therapy; MMT = Methadone Maintenance Therapy)

Assessment of QoL

The results showed significantly improved overall QoL especially in the psychological aspects of patients on MMT compared to BNX. There was no significant difference in other aspects ie; overall health, physical, social relationship, and environment for both groups (Table 3). Our result also shows that dosage

of drug also affects the QoL of these patients. There was a significant difference in the overall QoL where higher scores were attained in the patients with high dose MMT but low dose BNX. The social relationship aspect seems to be better in BNX patients with low dosage whereas no difference was detected among patients in MMT group. The difference of effect is shown in Table 4 and 5.

Table 3. Independent t-test comparison of all 6 aspects in QoL assessment in MMT and BNX groups

Domain	Range	Mean	SD	p	95% CI
Overall QoL				0.011	0.07 - 0.52
Methadone	3-5	3.91	0.62		
BNX	3-5	3.61	0.56		
Overall health				0.563	-0.41 - 0.22
Methadone	1-5	3.69	0.87		
BNX	2-5	3.78	0.79		
Physical				0.932	-0.83 - 0.90
Methadone	9-18	14.44	2.20		
BNX	10-19	14.41	2.34		
Psychological				0.024	0.14 -1.93
Methadone	8-20	14.96	2.54		
BNX	10-18	14.30	2.14		
Social relationships				0.144	-0.29 -2.00
Methadone	8-20	14.30	3.22		
BNX	8-20	13.44	2.77		
Environment				0.132	-0.20 -1.54
Methadone	10-20	14.96	2.24		
BNX	10-20	14.30	2.32		

(SD = Standard deviation; CI= Confidence interval, BNX = buprenorphine-naloxone , MMT = Methadone Maintenance Therapy)

Table 4. Independent t-test comparison of the outcomes in QoL of MMT and BNX patients when comparison is made between the different dosages

	Low dose (mean)	High dose (mean)	p- value	95% CI
MMT				
Overall QoL	3.65	4.03	0.036*	-0.73 to -0.03
Overall Health	3.35	3.84	0.112	-1.09 to 0.12
Physical	14.24	14.54	0.688	-1.86 to 1.25
Psychological	13.94	15.57	0.092	-3.54 to 0.29
Social relationship	13.94	14.46	0.637	-2.76 to 1.72
Environment	14.47	15.19	0.373	-2.36 to 0.92
BNX				
Overall QoL	3.83	3.33	0.001*	0.22 to 0.78
Overall Health	3.97	3.54	0.054	-0.01 to 0.86
Physical	14.70	14.04	0.308	-0.62 to 1.94
Psychological	14.30	13.67	0.284	-0.54 to 1.81
Social relationship	14.23	12.46	0.014*	0.38 to 3.17
Environment	14.73	13.75	0.123	-0.27 to 2.24

(*p < 0.05, SD = Standard deviation; CI= Confidence interval, BNX = buprenorphine-naloxone , MMT = Methadone Maintenance Therapy)

Table 5. Independent t-test comparison between high dose methadone and high dose BNX in all aspects of QoL

High dose	Methadone	BNX	p value	95% Confidence interval
Overall QoL	4.03	3.33	<0.001*	0.40 to 0.99
Overall Health	3.84	3.54	0.136	-0.10 to 0.69
Physical	14.54	14.04	0.381	-0.63 to 1.63
Psychological	15.57	13.67	0.001*	0.86 to 2.94
Social relationship	14.46	12.46	0.004*	0.67 to 3.34
Environment	15.19	13.75	0.009*	0.37 to 2.51

(*p < 0.05, SD = Standard deviation; CI= Confidence interval, BNX = buprenorphine-naloxone , MMT = Methadone Maintenance Therapy)

Comparisons between the MMT and BNX groups of similar dosage do not show any significant difference in those of low dosage. However, marked differences were appreciated between the 2 groups with high dose in the overall quality of

lifeQoL ($p < 0.001$), psychological ($p = 0.001$), social relationships ($p = 0.004$) and environment ($p = 0.009$) with the methadone group having better mean scores compared to BNX.

Table 6. Logistic Regression on Overall QoL as the Dependent Variable

Predictor variable	Odds Ratio (95%CI)	P-value
Types of treatment	2.85(1.09-7.47)	0.03*
Monthly income	1.07(0.38-3.04)	0.90
Duration of treatment (months)	1.75(0.70-4.37)	0.23
Age (years)	0.99(0.35-2.79)	0.98
Latest dosage	1.77(0.72-4.36)	0.21
Working status	2.64(0.61-11.38)	0.19
Marital status	0.48(0.19-1.24)	0.13

* $p < 0.05$

Logistic regression was used to evaluate the effect of selected predictor variables on the probability of being classified as good overall QoL (ie, overall QoL ≥ 4). Only types of treatment was significantly associated with overall QoL (odds ratio 2.85, 95%CI:1.09-7.47, $p = 0.03$). Methadone was associated with better general QoL compare to use of suboxone. Other variables were not significantly related to overall QoL.

Discussion

Drug abuse has always been known as a chronic relapsing disorder which explains the need of substitution therapy for a prolonged period of time. Our study revealed that no age group was spared as the youngest patient was 20 years old while the oldest was 56 years old. Most of them began abusing drugs as early as when they were 12 years old. A few possible explanations on reasons of abuse include poor upbringing and strong influence by older family members or peers. QoL is defined by World Health Organization (WHO) as individuals' perception of their position of life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. It is a broad ranging concept affected in a complex way by the person's physical health, psychological state, level of independence, social relationships, personal beliefs and their relationship to salient features of their environment [15]. Abuse of drugs is a global

issue where its impact on the economy, health and wellbeing of a society influences the productivity and civilization of a nation or country.

This study was designed to assess if there is any difference in the QoL among patients treated for 4 months or more with methadone maintenance therapy (MMT) or buprenorphine-naloxone (BNX). There have not been many similar researches on the particular areas locally or elsewhere. The characteristic socio-demographic profile of our sample corresponds to the demographic profile of Malaysian drug users based on the report by National Drug Agency of Malaysia in December 2010 which is mostly men, Malay and achieved secondary education [14]. However, we found that there was a statistical difference in the occupation status of methadone and BNX patients. There was a higher percentage of employment among BNX patients compared to those on MMT. This may be due to the difference in the setting of treatment centres where BNX is often available in private health care centres in Malaysia whereas MMT is of free prescription in government health care centres. In addition, employed patients may be seeking for flexibility in terms of treatment hours and easy accessibility to the prescription. There is also a significant difference ($p = 0.002$) in terms of the total income as majority of BNX patients are above the poverty level as compared to MMT patients. In Malaysia, the commonest drugs

abused are heroin, ganja and amphetamine type stimulants (ATS) [16]. This is consistent with our findings. However, we found that those who abused ganja and amphetamine type stimulants tend to choose BNX as their choice of treatment.

A study by I. Maremmani et al. [17] quoted that patients who enrolled in long term methadone or buprenorphine treatment showed improved status control over substance use, psychiatric status, social adjustment and general QoL [17]. In another study by Giacomuzzi et al. [18] it was discovered that the QoL after 6 months of treatment of buprenorphine showed significantly higher satisfaction score in terms of job, family and total score of physical symptoms compared to those who quit the treatment program before 6 months. On contrary, our study showed that patients on MMT seemed to have better impact on the QoL and psychological aspect than those on BNX. This is also proven in the logistic regression model (odds ratio 2.85, 95%CI:1.09-7.47, $p = 0.03$) where MMT is a significant predictor of better overall QoL. This could probably be due to additional psychosocial intervention included in the programme provided by the government health centres.

The effectiveness of therapy is also said to be dependent on the dosage of drug [19]. Our patients seemed to improve better with high dose of methadone which is comparable to other studies which also showed that methadone doses of above 50mg are more effective than doses below 50mg in reducing heroin use and retaining patients in treatment [12]. This is consistent with New South Wales Clinical guidelines of Opioid dependence, where studies of methadone show that better treatment outcomes are associated with higher doses [20]. Nevertheless, our study also found that the patients on low dose BNX performed better in all aspects of life especially overall QoL and social relationship to the MMT group but there is no statistical significance in other aspects. On contrary, comparing between high dose of MMT and BNX, the MMT group showed better mean scores in all aspects and statistical significance was clearly seen in the psychological domain.

The limitations in this study include a small sample size and design of the study where a randomized and double blind trial would give a higher value of analysis. Another limitation is the cost for treatment was not considered during this research. A follow up of this study is required to obtain more information about the effectiveness of the two drugs.

Conclusion

This study suggests that methadone improves the QoL especially among those treated with high dosage. The dose of drugs and its duration may play a role in the success of therapy. The factors that seem to affect this outcome include cost of therapy, good family support and background, positive influence of peers and stable working status. Given the limitations, the results of this study should be regarded as preliminary thus indicating the need for further studies in the future. Studies with a larger sample and higher level of design need to be conducted to determine the benefits of different types of maintenance therapy for drug abusers.

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