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Quality of Life and Substance Use over 1-year among Buprenorphine-treated Heroin Use Disorder Patients in Taiwan

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Abstract

Objective: Owing to the higher cost of Buprenorphine Maintenance Treatment (BMT) and harm reduction policy in Taiwan, the percentage of Heroin Use Disorder (HUD) patients receiving BMT is much lower than that of receiving methadone maintenance treatment in Taiwan despite the lower addictive, milder withdrawal symptoms and safer characteristics of BMT. As a consequence, the study on treatment outcomes of BMT in Taiwanese HUD patients is relatively limited. The purpose of this prospective, 1-year observational study was to investigate the effects of BMT on the quality of life, self-efficacy, substance use, and retention rate among HUD patients in Taiwan.

Methods: Forty-two HUD patients aged between 20 and 60 years old without serious psychiatric illness were recruited from five medical centers and were given BMT for 12 months. Efficacy assessments using the Taiwan version of Brief Version of World Health Organization Quality of Life Instrument (WHOQoL-BREF-TW) and 8-item Drug-Taking Confidence Questionnaire (DTCQ-8), as well as urine drug test were performed at baseline and every 3 months thereafter.

Results: Of the 25 subjects who comprised the Intent-To-Treat (ITT) population for efficacy analyses, significant improvements were seen in the psychological and social relation domains of the WHOQoL-BREF at 9 months. Significant improvements also observed in the DTCQ score under both pleasant and unpleasant emotions, testing self-control, and friend's incitement circumstances throughout the study period. The 12 months retention rate was 36%. The positive rates of urine morphine maintained low during the study.

Conclusion: This study indicated the long-term efficacy of BMT on the quality of life, self-efficacy, and reduction of illicit drug use in Taiwanese heroin use disorder patients who maintained in the BMT treatment.

Keywords: Heroin use disorder; Buprenorphine maintenance treatment; Quality of life; Self-efficacy; Retention rate; Urinary drug screening

Background

Heroin Use Disorder (HUD) is a chronic and relapsing disease that not only impairs one's life in terms of physical health, mental health, social relations, and abilities to work but also impacts public safety and public health due to criminality and morbidity [1]. All of these negative impacts result in a huge socioeconomic burden. HUD is estimated at a total economic cost of US$18,310 per person-year, in which 64% of the total cost was the direct cost used in purchasing illegal drugs and the remaining 36% of the total cost was the indirect cost accounted by the loss of productivity [2]. The Years of Potential Life Lost (YPLL) was estimated to be 18.4 years among Taiwanese HUD patients [3].

Besides the widely-used Methadone Maintenance Treatment (MMT), Buprenorphine Maintenance Treatment (BMT) is another option for the treatment of HUD in Taiwan. BMT is characterized by lower overdose risk, milder withdrawal discomforts, lower risk of respiratory depression, and less QT interval prolongation [4,5]. This also allows unsupervised administration and convenience in dispensing compared to MMT. The efficacy and safety of BMT had been demonstrated in numerous studies conducted worldwide [6-12]. Being non-inferior to MMT, BMT had a 12 month retention rate of 56.9%-78.3%. It also improved the quality of life, illicit opiate drug use, craving for opiates, and opiate withdrawal symptoms in HUD patients [6-12].

However, the higher cost of BMT affects the patients' willingness in receiving BMT. As the percentage of patients receiving BMT is much lower, the study on BMT in Taiwan population is very limited in comparison to MMT which was well-researched in Taiwan in terms of efficacy as well as cost-effectiveness [13-19]. Therefore, the objective of this study was to evaluate the change in the quality of life, self-efficacy, and illicit drug use in Taiwanese HUD patients during the course of BMT and hope to provide clinical evidence in real world clinical practice to physicians and policy makers.

Methods

Trial design

This was a prospective, multicentre, 12 month observational study designed to investigate the treatment outcomes of buprenorphine in heroin use disorder patients who had used heroin for at least a year. This study was conducted in five medical centers in Taiwan between August 2014 and August 2016. The dosage of buprenorphine for induction and maintenance period were adjusted based on the subject's status and physician's judgment in accordance with the clinical guidelines for opiate addiction replacement therapy and routine clinical practices in Taiwan. Generally, the initial dose of buprenorphine was 4-8 mg and the maintenance dose was in the range of 4-16 mg daily. In most cases, the dose of buprenorphine was maintained at 4-8 mg throughout the study. Four visits at three months interval were scheduled after baseline visit for treatment evaluation. This study was conducted in compliance with the ethical principles of the Declaration of Helsinki and was consistent with the International Conference on Harmonization Good Clinical Practice guidelines. The ethics committee had approved the study at each study site. All subjects gave their informed consent for the study participation.

Participants

All patients were screened by psychiatrists at outpatient visits. Patients who fulfilled all of the following criteria were included: (1) have used heroin for at least one year and was opioid dependent diagnosed by criteria of the Diagnostic and Statistical Manual of Mental Disorders fourth edition (DSM-IV), (2) aged 20 to 60 years old, (3) willing to adhere to the treatment plan and agree with the follow-up schedules, urine and blood test, and (4) signed informed consent. Patients were excluded from the trial if they met any of the following conditions: with serious psychiatric illness, convicted for being involved in drug trafficking or manufacturing, or demonstrated a previous hypersensitivity to buprenorphine. Additional exclusion criteria included pregnancy, lactation or breastfeeding.

Outcome evaluation

Quality of life: The Taiwan version of the Brief Version of the World Health Organization Quality of Life Instrument (WHOQoL-BREF) is a validated self-administered questionnaire contains 28 items assessing the overall Quality of Life (QoL), overall health and four domains in life, i.e. physical, psychological, social relation, and environmental. Each item is rated on a 5-point Likert scale. The scores for each domain ranged from 4 to 20 (mean score for all items in each domain multiply by four). The higher the score, the better the QoL [20].

Self-efficacy: The 8 item Drug-Taking Confidence Questionnaire (DTCQ-8) is a brief and validated instrument measures one's confidence to abstain from illicit drug use in eight high-risk situations. The DTCQ-8 score ranged from 0-100, a higher score indicates greater confidence or self-efficacy to abstain from drug use. A score of<20% is considered low self-efficacy, between 20% and 80% is considered moderate self-efficacy, and>80% is considered high self-efficacy [21].

Retention rate and urine drug screen: Retention rate and urine analyses to screen for concurrent use of heroin were performed at 3 months interval.

Statistical analyses

Efficacy analyses were performed in the Intention-To-Treat (ITT) population comprising all subjects who took at least one dose of study medication and had at least one post-baseline assessment. Changes in DTCQ-8 and WHOQoL-BREF were analyzed by paired T-test. All statistical assessments were tested at the two-tailed significance level of 0.05 using SAS 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

Forty-two subjects were recruited to the study. Among the 42 subjects, 17 dropped out of the study before the first scheduled treatment evaluation at Month 3 with the reasons of lost to follow-up (4,23.5%), imprisoned (3,17.6%), withdrew consent (4,23.5%), protocol violation (2,11.8%), self-perceived abstinence (2,11.8%), and unspecified (2,11.8%). The remaining 25 subjects who had completed the first 3-month treatment composed the ITT population with the majority of them being male (80.0%) and having detoxification experiences (84.0%); half of them (52.0%) were single or divorced, hepatitis C carrier and with severe substance use disorder. The detailed baseline demographic and clinical characteristics are shown in Table 1.

Characteristics	All (n=42)	ITT population (n=25)
Age, years	43.5 (7.39)	44.0 (7.19)
Male	35 (83.3%)	20 (80.0%)
Education level		
Elementary	5 (11.9%)	2 (8.0%)
Junior high	18 (42.9%)	10 (40.0%)
Senior high	19 (45.2%)	13 (52.0%)
Marital status		
Married	14 (33.3%)	11 (44.0%)
Single or divorced	27 (64.3%)	13 (52.0%)
NA	1 (2.4%)	1 (4.0%)
Substance use disorder severity		
Mild	8 (19.0%)	5 (20.0%)
Moderate	7 (16.7%)	6 (24.0%)
Severe	26 (61.9%)	13 (52.0%)
NA	1 (2.4%)	1 (4.0%)
Syphilis-positive	4 (9.5%)	2 (8.0%)
Hepatitis B carrier	7 (16.7%)	4 (16.0%)
Hepatitis C carrier	26 (61.9%)	13 (52.0%)
Had detoxification experience	35 (83.3%)	21 (84.0%)

Table 1: Demographic and clinical characteristics; the data are expressed in N (%) or mean (SD); ITT: Intent-To-Treat; n, number; NA: Not Available; SD: Standard Deviation.

WHOQoL-BREF

As summarized in Table 2, improvement from baseline in the quality of life assessed by Taiwan version of WHOQoL-BREF was observed in all domains during the study. The mean changes from baseline were statistically significant in the psychological domain (1.6 ± 2.47, p=0.02) and social relation domain (1.8 ± 2.88, p=0.02) at Month 9.

	WHOQoL-BREF-TW, mean (SD)				
	Overall	**Physical**	**Psychological**	**Environmental**	**Social relation**
Baseline (n=25)	13.6 (2.83)	14.2 (2.45)	13.3 (2.14)	14.3 (2.20)	14.2 (3.03)
Month 3 (n=25)	13.6 (2.31)	14.1 (2.26)	13.6 (1.96)	14.0 (2.02)	14.3 (1.84)
Month 6 (n=21)	14.3 (3.70)	14.9 (2.43)	14.3 (2.44)	14.9 (2.37)	14.7 (2.50)
Month 9 (n=16)	15.5 (2.48)	15.6 (2.06)	15.2 (1.59)	15.0 (1.84)	16.0 (2.13)
Month 12 (n=15)	13.9 (3.66)	15.3 (2.83)	14.4 (2.33)	14.8 (2.45)	15.1 (3.71)
Change baseline *vs.* Month 3	0.0 (2.83)	-0.1 (2.19)	0.3 (2.70)	-0.3 (2.38)	0.1 (3.12)
Change baseline *vs.* Month 6	0.6 (4.61)	0.5 (2.33)	0.8 (2.95)	0.7 (2.88)	0.3 (3.85)
Change baseline *vs.* Month 9	1.3 (3.49)	1.0 (2.14)	1.6 (2.47)*	0.8 (2.01)	1.8 (2.88)*
Change baseline *vs.* Month 12	-0.3 (3.53)	0.6 (1.52)	1.0 (1.92)	0.7 (1.71)	0.7 (2.61)

Table 2: Results of the WHOQoL-BREF-TW score in the ITT population (n=25); *p<0.05; SD: Standard Deviation; WHOQoL-BREF-TW: Taiwan version of the Brief Version of the World Health Organization Quality of Life Instrument.

DTCQ-8

The levels of and changes in DTCQ-8 during the study are presented in Table 3. Among the eight high-risk situations, significant improvement were observed under the situation of unpleasant emotions (18.1 ± 36.28, p=0.03 at Month 6; 20.0 ± 26.33, p=0.008 at Month 9), remembering pleasant times (15.2 ± 32.81, p<0.05 at Month 6; 20.0 ± 26.19, p=0.01 at Month 12), self-control testing (19.2 ± 36.28, p=0.01 at Month 3; 17.5 ± 29.10, p=0.03 at Month 9), friend's incitement (16.0 ± 36.51, p=0.04 at Month 3; 24.8 ± 32.81, p=0.003 at Month 6; 25.0 ± 23.66, p<0.001 at Month 9; 22.7 ± 21.20, p=0.001 at Month 12), and pleasant time with friends (8.0 ± 12.65, p=0.03 at Month 12).

	DTCQ-8 scores, mean (SD)							
	Unpleasant emotions	**Sleep problems**	**Pleasant emotions**	**Testing self-control**	**Found heroin**	**Conflict with others**	**Friend's incitement**	**Pleasant time with friends**
Baseline (n=25)	60.8 (31.35)	71.2 (33.21)	68.0 (31.62)	60.0 (33.17)	69.6 (32.21)	73.6 (31.47)	56.8 (33.51)	73.6 (32.52)
Month 3 (n=25)	72.8 (31.03)	76.0 (32.15)	83.2 (25.61)	79.2 (24.14)	78.4 (28.82)	82.4 (27.88)	72.8 (29.37)	80.0 (28.28)
Month 6 (n=21)	81.0 (30.64)	79.0 (27.19)	83.8 (22.47)	77.1 (37.03)	76.2 (34.42)	82.9 (29.18)	83.8 (27.29)	87.6 (22.34)
Month 9 (n=16)	86.3 (26.04)	87.5 (22.95)	86.3 (26.04)	82.5 (33.37)	85.0 (26.83)	87.5 (26.20)	88.8 (26.30)	91.3 (25.27)
Month 12 (n=15)	76.0 (34.81)	80.0 (27.26)	88.0 (14.74)	74.7 (35.83)	NA	82.7 (26.04)	82.7 (26.04)	84.0 (24.14)
Change baseline *vs.* Month 3	12.0 (42.82)	4.8 (44.08)	15.2 (39.70)	19.2 (36.28)*	8.8 (40.86)	8.8 (41.26)	16.0 (36.51)*	5.0 (32.44)
Change baseline *vs.* Month 6	18.1 (36.28)*	5.7 (33.55)	15.2 (32.81)*	16.2 (46.31)	4.8 (37.90)	3.8 (29.41)	24.8 (32.81)**	7.6 (23.22)
Change baseline *vs.* Month 9	20.0 (26.33)**	10.0 (20.66)	13.8 (28.02)	17.5 (29.10)*	7.5 (25.17)	5.0 (20.00)	25.0 (23.66)**	10.0 (20.66)

Change baseline *vs.* Month 12	14.7 (28.75)	5.3 (19.22)	20.0 (26.19)*	14.7 (27.74)	NA	2.7 (16.68)	22.7 (21.20)**	8.0 (12.65)*

Table 3: Results of the DTCQ-8 score in the ITT population (n=25); *p<0.05; **p<0.01; DTCQ: Drug Taking Confidence Questionnaire; NA: Not Available; SD: Standard Deviation.

Urine drug test

As presented in Table 4, the percentage of subjects using heroin before treatment was 24.0%. After treatment, its percentage reduced to 20.0% at Month 3, 19.0% at Month 6, and 6.3% at Month 9, and 13.3% at Month 12 in the ITT population.

	Urine-Morphine positive
Baseline (n=25)	6 (24.0%)
Month 3 (n=25)	5 (20.0%)
Month 6 (n=21)	4 (19.0%)
Month 9 (n=16)	1 (6.3%)
Month 12 (n=15)	2 (13.3%)

Table 4: Urine drug test positive rate in the ITT population (n=25).

Retention rate

The result of retention rate was analyzed using the full analysis set and is presented in Table 5. Out of the 42 subjects, 25 (59.5%), 21 (50.0%), 16 (38.1%), and 15 (35.7%) subjects remained in the study at Month 3, 6, 9, and 12, respectively. The documented reasons for discontinuation were lost to follow-up (5/18.5%), switch to other medication (2/7.4%), lack of motivation (1/3.7%), self-perceived abstinence (5/18.5%), protocol violation (3/11.1%), withdrew consent (6/22.2%), imprisoned (3/11.1%), and unspecified (2/7.4%).

	Retention rate
Baseline	42 (100.0%)
Month 3	25 (59.5%)
Month 6	21 (50.0%)
Month 9	16 (38.1%)
Month 12	15 (35.7%)

Table 5: Retention rate in the full analysis set (n=42).

Discussion

This study examined the efficacy of BMT in Taiwanese HUD patients in terms of quality of life, illicit drugs use, and retention rate over 1 year. We found that continuing BMT improved or maintained the QoL of HUD patients in all domains (especially psychological and social relation domains, p<0.05) as well as their self-efficacy in resisting illicit drug use in high-risk situations (especially pleasant and unpleasant emotions, testing self-control, friend's incitement, and pleasant time with friends, p<0.05). These outcomes are positive and encouraging as improvement in QoL and self-efficacy are more likely to motivate HUD patients to remain abstinent and retain in the treatment and which in turn further improves their QoL and self-efficacy [22]. To verify objectively, urine drug test was conducted and the reduction in the positive rate of morphine was in line with the improvement in QoL and self-efficacy in the study. This is further evidence that BMT is effective in reducing illicit drug use, hence fulfilling the objective of Opioid Maintenance Treatment (OMT).

In addition, we found that the HUD patients in our study had a better baseline QoL score ranged 13.3-14.2 than those previously reported [2,18,23] which ranged 11.6-13.5. A possible reason for this phenomenon may be the difference in patient selection as our study ruled out the patients with psychiatric comorbidity which is found to be prevalent in HUD patients and can lower the QoL [24-26].

HUD is a chronic disease characterized by drug seeking that is hard to control. Even with the help of medication, sometimes patients still fail the temptation. From our findings, a drop in QoL (overall QoL, psychological domain, and social relation domain) and self-efficacy score (unpleasant emotions, sleep problems, testing self-control, conflicts with others, friend's incitements, and pleasant time with friends) seems to be in tune with the increase in urine toxicology positive rate from Month 9 to Month 12. These results indicate that failure in remain abstinence would discourage the HUD patients and they are more vulnerable to psychological problems (unpleasant emotions, sleep problems, testing self-control) and social relation problems (conflicts with others, friend's incitements, and pleasant time with friends). Nonetheless, dealing with HUD is a process. The relapse rate for HUD is alike to other chronic diseases such as diabetes and hypertension, which occasional relapse does not mean a treatment failure but rather an adjustment and understanding of the patient's reason for his or her relapse is needed [27].

Research had found that remaining in the OMT is critical, directly related to improvement in treatment outcomes [28], and a minimum of 3 months is predicted to be necessary to gain positive treatment outcomes [29]. In our study, 17 out of 42 enrolled patients (40.5%) left the study within the first three months. This high rate of dropout within first 3 months of the treatment reflects the real world situation [30,31]. Every effort should be made and assistance should be provided in helping patients to retain in the treatment. In addition, our 12-month retention rate of 36% is moderate compared with that of MMT ranging 26% to 55% in Taiwan [14,16-19].

In the real world, travel distance and time spent for daily visit to the clinics for MMT are factors that affect the patient's retention rate [32,33]. Moreover, the patients may have to adjust their work schedules to match with the specified clinic visit time for methadone prescription and these would be another hurdle for HUD patients to stay in treatment. On the contrary, as buprenorphine allows take-home prescription, the patients receiving BMT could avoid the difficulties in asking for leave and arranging a time for clinic visit during the specified period that may affect their works. This would enhance and enable the patients' ability to reintegrate into social and occupational life and the patients do not have to deal with self-esteem and other emotional and psychological issues associated with visiting a clinic.

There were some limitations of our study. First, the results of WHOQoL-BREF and DTCQ-8 were based upon patients' self-reporting, thus different patient composition might influence the obtained results. Second, the sample size of this study was relatively small due to the difficulty in recruitment and the unpredictive circumstances in these patients. Third, there was some missing data in this study. However, despite these limitations, this study was the first to examine the treatment outcome of BMT in HUD patients in Taiwan. The same generic scale, WHOQoL-BREF was used in this study, thus results of this study can be comparable with those other studies conducted in Taiwan. Another advantage of this study is that it evaluated the patient's self-efficacy that other MMT studies in Taiwan did not.

Conclusion

In conclusion, this longitudinal observational study found that BMT improved QoL and self-efficacy, reduced illicit drug use among Taiwanese heroin use disorder patients and had an overall 12 month retention rate of 36%. Despite its expensiveness, the lower abuse potential, safer profile and convenience from not needing to go to the specialized clinic for daily medication make buprenorphine a fairly good medication for OMT.

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Conflict of Interest

None of the authors has any conflict of interest to disclose.

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