

ORIGINAL ARTICLE

Factors Associated With Good Response in Methadone Therapy in a Malaysian District Hospital

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ABSTRACT

Introduction: Methadone maintenance treatment is effective in reducing opiate use, related crime and HIV risk behaviors. However, the number of patients dropping out of treatment or continue misusing drugs are significant. Primary screening of such patients could be useful in the development of guidelines targeted to prevent such incident. The aim of this study was to determine the prevalence of good treatment responders and whether socio-demographic factors and methadone dosage are associated with good responses. **Methods:** Respondents were studied from November 2009 until April 2010 and involved all patients that had undergone methadone therapy from November 2005 to November 2009. Data was obtained from medical and pharmacy records. Missing data was obtained directly from patients via direct interviewing. Patients were considered to have a good response if they stay in the programme and have negative urinalysis result within 6 months of enrolment. **Results:** 66 out of 104 patients have a good response in methadone therapy. There is an association between good response in methadone therapy and educational level ($p=0.045$) and district of origin ($p=0.041$). However, there were no associations with methadone dosage. **Conclusion:** Higher educational level of at least secondary school education was found to be a good predictor of good response to methadone therapy. Patients who originated from nearby areas have better outcomes. This could be due to the direct observation therapy which could have an effect on non-compliance of patients who lived far away. This suggests the need to provide methadone therapy in local areas for better accessibility and compliance.

Keywords: Methadone, Sociodemographic factors, Methadone dose, Predictor of compliance

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INTRODUCTION

Apart from Naltrexone and Buprenorphine, Methadone maintenance therapy is one of the most commonly used form of treatment in opiate addiction (1). The benefits of Methadone maintenance treatment in combating opiate use, related crime and HIV risk behaviours have been well researched (2, 3). Nonetheless, a significant number of patients will become non adherent to treatment and some may continue using opiates and other illicit drugs. Significant treatment drop-outs typically occur at the initial stage of treatment (4). Therefore, early screening of such patients is imperative to guide the development of treatment policy in order to prevent such incident. The methadone maintenance therapy is a drug substitution therapy conducted at national level with the aim of harm reduction. For the state of Pahang, Hospital Sultan Haji Ahmad Shah was selected as one of the first centre to conduct such therapy in 2005. Several studies had found that certain sociodemographic characteristics such as older age (5, 6) and being married (7) were

associated with good treatment response. Apart from that, Methadone dosage also played a major role in the retention of patients in the programme (8, 9). Retention in the programme and negative urinalysis result were used as indicators for treatment adherence. Those with 3 positive urinalysis results were terminated from the programme. This is a useful indicator of the effectiveness of a new or changed treatment guideline (10).

The aim of this study is threefold; to assess the prevalence of good responders in Methadone therapy, to identify the socio-demographic characteristics of good treatment responders and to determine whether methadone dosage is associated with good response in methadone therapy.

MATERIALS AND METHODS

The study was conducted at the methadone clinic of Hospital Sultan Haji Ahmad Shah. Hospital Sultan Haji Ahmad Shah is a government specialist hospital situated in Temerloh, Pahang. The Methadone programme provides a service to patients who come from Temerloh and Maran district. Its patient catchment area includes those living in Temerloh, Chenor, Sanggang, Mentakab and nearby Felda areas. Most of these patients were

male, young and employed. The Methadone programme was initiated in November 2005 as part of the national programme in harm reduction. The programme is voluntary, and treatment was publically funded. Patients received formal counselling as per the Methadone substitution counselling guideline.

Study design

This is a cross sectional study to determine whether socio-demographic factors and methadone dosage were associated with good response in Methadone therapy. Patients were recruited from the Hospital Sultan Haji Ahmad Shah’s Methadone treatment programme. Respondents were studied from November 2009 to April 2010. This involved all patients that had undergone methadone therapy from November 2005 until November 2009. Patients with co-morbid psychiatric illness and taking anti-retroviral therapy were not included in the study. Informed consents were acquired prior to the study.

Individual data on each patient’s socio-demographic characteristics such as their age, marital status, occupations, educations and district of origin were taken as independent variable. Induction and maintenance methadone dosing were also collected. Patients’ case notes were also reviewed.

Good response to treatment is defined as;

- 1) Retention in programme for 6 months after enrolment.
- 2) No positive result of any substance in urinalysis from seven urinalysis performed randomly within 6 months of enrolment.

Patients who did not fulfil the above criteria were deemed as poor treatment responders. Data that were not available or missing from medical records were obtained by direct interviewing. Psychometric test was not performed as the bulk of the data was obtained directly from patients’ medical records.

Data analysis

SPSS for windows 17.0 was used in the analysis of the data. Socio-demography of patients, methadone dosage and prevalence were analysed. Univariate analysis was carried out to assess the association between outcome (treatment response) and independent variables. Chi-square test and t-test were used. Fischer’s exact test was utilised if the assumption of chi-square test was not met. Significant level for all statistical analysis was set at 0.05.

RESULTS

A total of 152 participants out of 258 fulfilled the inclusion and exclusion criteria. Out of the 152, 29 of them unfortunately passed away. 19 were transferred to other centres, therefore leaving the final tally of 104 participants to be included in the study (Figure 1). Most patients were male (99.0%), Malay (97.1%),

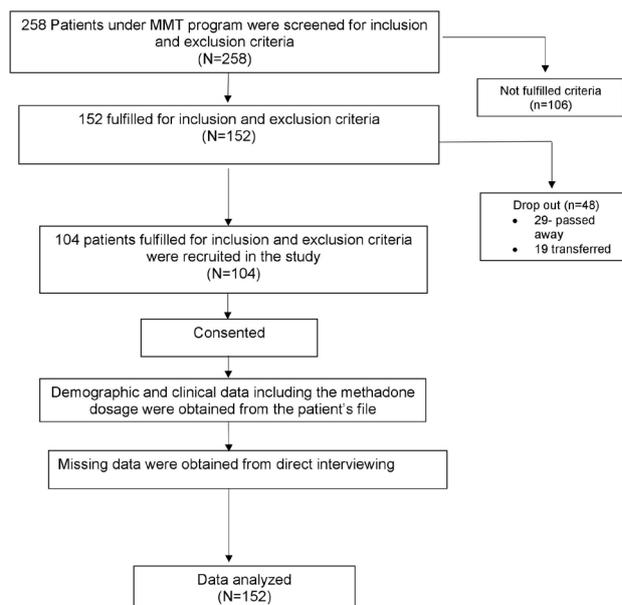


Figure 1: The flow of study process

self-employed (61.5 %) and single (51.9%). 85.6% of them obtained secondary school education and 67.3% resided in Temerloh. The average age of participants was 40.4 (± 7.9) years. The age ranged from 27 to 61. The mean induction dose was 20.4mg (± 2.1) while the mean maintenance dose was 29.4mg (± 6.2). In terms of outcome, 63.5% of patients showed good response to methadone therapy (Figure 2). This was broken down into fulfilling the criteria of having retention to therapy after 6 months of enrolment (87.5%) and negative urinalysis result (71.2%).

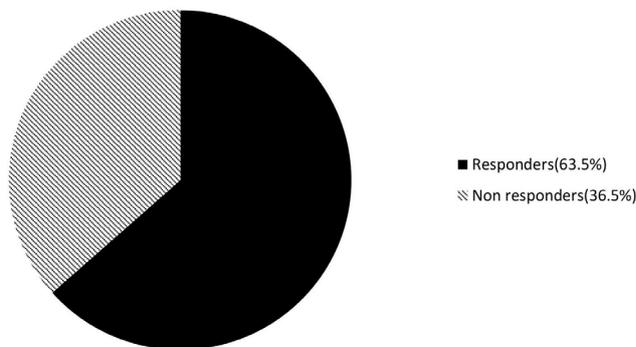


Figure 2: Pie chart depicting response outcome in subjects

Table I shows the univariate analysis of the relationship between the socio-demographic variables and treatment response. Educational status and district of origin are the only significant factors associated with good response (p < 0.05).

Table II shows the univariate analysis of the relationship between the methadone dosage and treatment response using t-test. There is no significant association.

DISCUSSION

In this study, 63.5% of respondents achieved a good treatment response. Good response to treatment was

Table I : Socio-demographic characteristics of good treatment responders and its association with treatment response

Socio-demographic characteristics		Good treatment responders		Poor treatment responders		Stat χ^2	df	p
		%	N	%	N			
		Age	40 years and less	33	60.0			
	> 40	33	67.3	16	32.7			
Marital status	Single	33	61.1	21	38.9	3.604	2	0.165
	Married	30	71.4	12	28.6			
	Divorced	3	37.5	5	62.5			
Occupation	Unemployed	12	63.2	7	36.8	0.001	1	0.976
	Employed	54	63.5	31	36.5			
Educational status	Primary and below	5	38.5	8	61.5	4.005	1	*0.045
	Secondary and above	61	67.0	30	33.0			
District of origin	Temerloh/Mentakab	55	68.8	25	31.2	4.181	1	*0.041
	Others	11	45.8	13	54.2			

Table II: Association between methadone dosage and treatment response

Methadone dose	Dosage	Good response		Poor treatment response		Stat χ^2	Df	p
		N	%	N	%			
		Induction	< 25mg	65	63.7			
	> 25mg	1	50	1	50			
Maintenance	< 30mg	43	61.4	27	38.6	0.382	1	0.537
	>30mg	23	67.6	11	32.4			

defined as retention to treatment and having negative urinalysis result within 6 months of enrolment. Adherence to these strict requirements could however be influenced by environmental factors and are prone to biased. Patients who are in full time employment would often have difficulties attending the Methadone centres; this is also true for patients who do not live in the local area. It is well known that in the initial stage of Methadone commencement, urine toxicology is performed quite frequently in these patients as opposed towards patients in the maintenance period. This could influence drop-out rates among these new patients as during this transition phase they could be more susceptible to cues that encourage relapse.

Retention of treatment is one of the best indicators of a methadone program's success. It is therefore an important indicator of the effectiveness of a new or changed treatment policy (10). Retention is crucial as drop-out from MMT is often subsequently followed by relapse and other negative consequences in opioid dependent patients (11). Treatment drop-out may result in overdoses, HIV and Hepatitis C infection or transmission, anti-social behaviour and early deaths (12). Therefore, all methadone programs should focus on treatment retention as gold standard (10).

This study found that 87.5% of participants adhered to therapy. This is much higher compared to other centres. This is however since the duration of other studies was different from ours. A local study conducted

in University of Malaya in 2007 for a duration of 18 weeks has a retention rate of 75% (4). A similar study that was conducted in Hospital Tengku Ampuan Afzan had a retention rate of 62%(13). Historically, those who entered treatment between 1993 to1996, retention rate was low (60%) 10. (10). In our research, the high retention rate could be due to the short duration of study. Perhaps, a longer period of study could lead to higher attrition rate.

According to a study conducted in Malaysia, subjects will most likely default in the initial stage of treatment. 6 out of 9 will do so within the first 4 weeks (4). About 1/4 to 1/2 of clients dropped out before stabilization (10). These studies do suggest that 6 months was an adequate duration for our research.

The higher retention rate in our study is most likely because our patients mostly hailed from Temerloh and Mentakab, making it convenient for them to attend. They were mostly self-employed (61.5 %), meaning that they were not bound to any tight working schedule. Another possibility is that methadone program was a voluntary program and free of cost. Therefore, the likelihood of drop-out was much less. Being in an employment is the sole predictor of Methadone therapy compliance in the study that was done in Hospital Tengku Ampuan Afzan (13). It is postulated that being in an employment reduced the harmful cues to opioid misuse and patients are more motivated to discontinue the habit. In some centres, takeaway Methadone was permitted to facilitate with employment and the ease of weekly transportation (12). Patients who were currently employed, married, on lower doses of methadone, and had been in methadone treatment for a longer duration were shown to exhibit greater improvement in quality of life (12).

In terms of urine toxicology, we found that 28.8% of all patients were found to have positive results. Many of them were within the first few weeks of therapy. This was rather unsurprising as during this period, methadone dosage was still being adjusted to reach a steady state. In total, the number of patients with a good response was found to be higher (63.5 %) compared to those who do not.

Patients with higher educational level (secondary education and above) and those who hailed from nearby Temerloh and Mentakab areas were found to have a significant positive association with treatment response. When socio-demographic variables are concerned, previous studies had shown heterogenous results.

Most patients were single, Malay (97.1%), male with at least secondary school education and most were self-employed. Being in an employment was found to be one of several predictors of opioid abstinence and treatment retention (12). This reflects the pattern of substance misuse in Malaysia, particularly Opioid

based. Gender was found to have no association with treatment response. This could be because of only one female sample available. Gender and ethnicity were not analysed statistically as there was uneven number of samples in both groups. The high rate of self-employment and not being in a relationship can be attributed to the disorganized and disruptive lifestyle of substance abusers.

Most of them did not progress beyond secondary school level. This could be the chaotic nature of the life of substance abusers during their formative years. Previous studies had shown that being older, married and being a parent predicts a better outcome in Methadone therapy. However, these factors were not statistically significant in our study.

Average age of patients in our study was 40.4 (S.D \pm 7.9). Although the age ranged from 27-61, the number in the older age group was slightly smaller. Being in an older age group (5) has been associated with a significant positive treatment response (48.39 \pm 9.40). This study found that younger patients (< 54 years) had a reduced retention rate of 22% compared to 59% of older patients. This shows that being in a particular age groups do play a role in predicting future response. Similar inference could be made about the marital status of participants as a proportion of patients who were married were only 40.4%. This smaller proportion could explain why marital status was found to have no significant association with treatment response in this study.

Roughly two third of participants (63.5 %) showed good treatment responses to methadone therapy. In terms of socio demography, having good educational status and being from a nearby district of origin predicted a good response to therapy. Those with higher educational level were shown to be more likely to adhere to treatment and abstained from drugs misuse. Participants who hailed from the areas of Temerloh and Mentakab responded better to therapy, owing probably to the ease of travelling to treatment centres.

There are two types of methadone dosage given to patients; methadone induction and maintenance dosing. The induction dose is the dose administered during the induction phase, which is the first 2 weeks of therapy. The maintenance phase usually commences after 2 weeks. An initial dose of 20-30 mg is usually safe and effective.

The mean induction dose was 20.38mg (S.D \pm 2.05) followed by a mean maintenance dose of 29.4mg (S.D \pm 6.2) in this study. This is lower in comparison to the studies done internationally. The average maintenance methadone doses usually documented in these studies ranged from 60-120mg per day (14,15). The Malaysian study done in University Malaya explained why the

local population requires lower dosing (4). The main reason is that the quality of heroin used in Malaysia only contains less than 10% heroin (4). This could be the reason why intravenous injection is the preferred method of choice to get the desired effects. The other possible reason is the different genetic make-up among Asians, as compared to the Caucasian population. Our findings on the lower dosing correlated with the study done in Universiti Malaya.

There were several other studies that suggest higher methadone dosing actually improved therapy retention (13,16). Higher methadone dosing of equal or more than 59 mg/day is one of the strongest indicator of retention at 12 month follow-up (5). In the last 3 decades, studies have consistently shown that Methadone dosing of 60 mg/day or greater is associated with greater retention and outcome (12,17-18). Dosages ranging from 60 to 100 mg/day have been shown to be more effective than lower dosages in increasing patients' retention and reducing heroin misuse during treatment (19). The risk of non-compliance in patients who received daily maximum dose of 60 mg or more was proportionately lower (70%) than for those taking less than 30 mg per day (8). Higher maintenance dosing is a prognosticator of reduced heroin use, with each subsequent milligram of prescribed methadone causing a 2% reduction in the probability of regular heroin abuse (20). In principal, most of the available data suggested a dosing of more than 60 mg daily. Statistically, the non-significant result of this study could be because lower mean maintenance dosing (29.4 mg \pm 6.2) was used in this study sample. Counselling is a mandatory requirement in Methadone maintenance therapy. It helps in the enhancement of patients' understanding of the illness, prevents relapses and reduces high risk behaviour associated with opioid misuse (21). There are evidences that Methadone maintenance therapy in adjunct with structured counselling resulted in more commitment to therapy and less frequent relapses among patients (22,23), this association could have bearings in this study.

Even though this study did not explore other psychological comorbidity associated with methadone treatment, it is worth briefly to highlight these issues. The rate of depression among patients on Methadone maintenance therapy was found to be 44.4% in a study that was done in Malaysia (24). The authors highlighted the under detection of depression and subsequent treatment among these group of patients. There were significant associations in Malay ethnicity, secondary education level and concurrent illicit cannabis. Another factor that might influenced compliance to Methadone maintenance therapy is Erectile Dysfunction as a possible side effect. Following multivariate analysis of patients undergoing Methadone maintenance therapy, being in an older age group was the sole predictor of developing Erectile Dysfunction among these cohorts (25). Methadone dosing and duration of treatment were

not significantly associated with Erectile Dysfunction.

CONCLUSION

A higher educational level (of at least secondary school education) was found to have a positive influence in good response to methadone therapy. This finding could be beneficial in terms of patient's selection into the programme. Nearby patients who hailed from Temerloh and Mentakab also have a better outcome in therapy. This is likely since direct observation therapy (DOT) given during the initial phase of treatment pose some compliance difficulties for people who lived far away, resulting in drop outs. This may suggest the need to provide methadone therapy in the local Klinik Kesihatan in each district for better accessibility.

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