Original Article

Monthly Take-Home Methadone Maintenance Regime for Elderly Opium-Dependent Users in Singapore

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Abstract

Introduction: Research suggests that methadone maintenance treatment (MMT) effectively reduces opiate dependence and related health and social problems. However, few studies have examined its effectiveness among the elderly. This study examined a monthly MMT regime for elderly opium addicts attending the National Addictions Management Service, Singapore. Materials and Methods: This study used a cross-sectional design and comprised 40 patients attending the addiction service and 40 caregivers who monitored methadone consumption (mostly patients' sons and daughters). Participants completed a semi-structured interview comprising measures of opiate craving and withdrawal, physical and psychological health. Objective measures were urine drug screens and blood tests. Results: Participants who averaged 74.8 years old had been using opium for around 44 years and had been in MMT for an average of 35 months. The maintenance dose of methadone was 9.2 mg/day. At interview, no opiate usage (other than methadone) was detected in urine screens; however, clinical records indicated that 6 had tested positive during the previous 6 months of MMT. No major withdrawal symptoms, side effects, or incidents of diversion were reported. Quality-of-life scores were in the normal range and satisfaction with the treatment regime was expressed by caregivers. Conclusion: Whilst MMT is the predominant pharmacotherapy for opiate dependence for users of all ages elsewhere, our study group constitutes a unique population that differs markedly from younger opiate users who will eventually grow old. In Singapore, MMT appears to be an effective treatment for stable, elderly opium-dependent patients where families are fully engaged in the treatment regime.

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Introduction

The misuse of illicit opiates remains a global problem, placing a heavy burden on society.[1,2] Literature on the effectiveness of opiate substitution pharmacotherapies in reducing consumption of illegal drug use, criminal activities, injecting and sharing behaviours, the spread of blood-borne diseases and mortality, now spans several decades and countries.[3-10] In most countries, the most widely used pharmacotherapy for the treatment of opiate dependence continues to be methadone maintenance treatment (MMT).[11-14]

Little is known, however, about how well methadone treatment works with elderly opium-dependent individuals. It has been estimated that about 10% of patients in some methadone programmes are over the age of 50.[15] A US study found that elderly MMT patients had significantly longer periods of treatment, more liberal take-home schedules and were less likely to report current heroin use or drug use than younger MMT patients.[16] Another study found that older patients engaged well in addiction treatment, showed a similar response to treatment experiences and programme factors and achieved comparable outcomes to those of younger adults in age-integrated community-based treatment programmes.[17]

In Singapore, there is zero-tolerance for all illicit drug use. However, there remains a small population of elderly opium-dependent patients, many of whom were once labourers working from a young age and using opium as a means of coping with harsh working conditions. They are considered to be distinct and with different needs to those of

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young heroin dependent users. The main differences are that their families (usually their children) accept their parents' opium use, often offering financial support for continued use, despite the user having undergone detoxification many times and failing to abstain from opium. In contrast to the younger opiate-dependent patients (largely heroin), they are rarely engaged in criminal activity to sustain their opiate use. Methadone treatment has been used with elderly opium-dependent patients at National Addictions Management Service (NAMS) since 2004. This study set out to examine the characteristics of elderly opiate-dependent patients undergoing MMT, to assess its impact on illicit opiate use, psychological and social functioning and to examine the feasibility of caregiver involvement supporting a monthly take-home regime. The literature defines the strengths and pitfalls of MMT; however, it is not known whether an opium-addicted population in Singapore, or indeed an elderly population poses the same challenges with MMT. Should these challenges exist, it may be necessary to implement strategies such as more frequent dispensing and routine testing of blood-borne diseases to further enhance patient safety and prevent diversion and accidental overdose.

Materials and Methods

This study used a cross-sectional design and was conducted on opium-dependent elderly patients receiving methadone as part of their treatment at NAMS as well as their caregivers. Most (n = 33) patients attended the clinic on a monthly basis, 6 patients attended less than monthly and one fortnightly. All patients attended the clinic with a caregiver. For 22 (55%), the caregiver was their son or daughter (or in-laws); for 8 (20%), it was their partner; and for 10 (25%), it was another relative. The sample comprised 40 patients using opiates who met DSM-IV criteria for opiate dependence, aged 60 years or above. Patients using opiates for pain-related conditions without a history of opium abuse were excluded. The study was approved by the Institution Review Board and written informed consent was taken from all patients expressing a willingness to take part. Recruitment to the study took place between May 2007 and October 2007.

The research interview used a semi-structured questionnaire to elicit information on the patient's demographic profile, socio-economic status, history of opiate and other illicit drug and/or alcohol use, legal problems, methadone dosage and side effects, severity of withdrawal symptoms [measured by the subjective opiate withdrawal scale (SOWS)],[18] quality of life [measured by the SF-36],[19] craving for drugs [measured by visual analogue scale], mood [measured by the hospital anxiety and depression scale (HADS)][20] and associated psychiatric diagnoses. A separate 5-item questionnaire assessed family satisfaction and perceived effectiveness of MMT. Objective measures included a urine drug screen test (to detect morphine, amphetamine, buprenorphine, methadone and marijuana) and a blood test to determine full blood count and liver function (to monitor the side effects of methadone). All collected data were analysed using SPSS version 17.

Results

Social Demographic Characteristics of the Sample

Most (80%) of the participants were male. With the exception of 1 Indian participant, the majority (97.5%) of the participants were Chinese. The mean age was 74.8 (± 8.8) years (range, 61 to 100). Three-quarters were married and most (88%, n = 35) lived with their spouse or their children. The majority (58%, n = 23) had no formal education and were now retired, with 9 participants working "odd jobs" and 8 receiving allowances for looking after grandchildren. Financially, half were dependent on their children, one third reported an income of less than $500 a month, and only 4 earned more than $500 a month (Table 1). Despite this, only 1 participant reported being in debt.

History of Illicit Drug Use and Current Substance Use

The mean age of onset of opium use was 31.4 years (± 12.3), which meant they had been using for an average of 44 years. The majority (60%) reported that opium was the first substance they had experimented with. Slightly more than half (n = 22) ingested opium orally, 17 through smoking and 1 patient had previously injected opium. Only 4 reported ever injecting opium or other opiates. Twenty-one reported initiating opium use for its medical benefits. The average amount spent per month when using opium was $574 a month (range, $6 to $3000). Opium had been used alongside other substances by 22 participants; cigarettes (n = 12), alcohol (n = 5), heroin (n = 2) and other drugs (n = 3). Regarding current substance use, 22 (55%) were smokers, although 17 reported reducing their consumption since commencing MMT. Only 5 participants reported consuming alcohol and this was reported to be only occasional use.

Past and Current Treatment

One-quarter of the sample (n = 10) had been sent to a drug rehabilitation centre, 7 on more than one occasion with treatment episodes ranging from 1 to 6 years. Only 9 participants had served a prison sentence, of which 4 were drug-related offences. Interviews were conducted when the patient had been on methadone treatment for an average of 3 years (mean, 35 ± 22.4 months; range, 8 to 156 months). The mean methadone dose was 9.2 mg at the time of interview (Table 2). Methadone consumption was closely supervised by the caregiver in accordance with a contract signed by the patient, caregiver and case manager. In addition to methadone, just over one-

Table 1. Social Demographic Characteristics

Variable	n (%)
Gender	
Female	8 (20)
Male	32 (80)
Race	
Chinese	39 (97.5)
Indian	1 (2.5)
Marital status	
Married	30 (75)
Divorced, Separated	2 (5)
Widowed	8 (20)
Education	
No education	23 (57.5)
Primary school	15 (37.5)
Secondary school	2 (5)
Financial situation	
Income below $500/month	13 (32.5)
Income higher than $500/month	4 (10)
Depends on compensation	1 (2.5)
Depends on child	20 (50)
Others	2 (5)
Accommodation	
Alone	4 (10)
Husband/wife(+/-children)	22 (55)
Children	13 (32.5)
Others	1 (2.5)

quarter of participants were prescribed other medications, mainly antihistamine (n = 21), diazepam (n = 11) or antidepressants (n = 5) (Table 2). The mean total cost of treatment to the patient for prescribed medications, consultation and urine screens (excluding travel to each appointment) was $79 a month (range, $56 to $106).

Changes in Opiate Use

On the day the interview was conducted, 39 patients provided a urine sample to detect prescribed and illicit drug use. Thirty-nine (97.5%) were positive for methadone (1 was negative but tested positive on all subsequent visits) and 7 were positive for benzodiazepines. This verified consumption of their prescribed medications and is consistent with reports of no diversion of methadone to others. One urine sample was positive for cannabis and another for amphetamines. However, as part of treatment, patients provided a urine sample at each visit. Six months prior to interview, 6 (15%) patients had tested positive for the presence of morphine indicating use of other non-prescribed opiates. Five patients attributed this to the use of codeine-based cough medicines and 1 to the use of opium. Four had complained that during this time they were experiencing withdrawal symptoms or that the methadone dose was too low. Following counselling in relation to the positive urine screens, all subsequent urine screens were negative.

Craving and Withdrawal

Patients were asked to rate their craving for opium using a visual analogue scale ranging from 0 (representing no craving) through to 10 (representing more craving than ever). Just under three-quarters of the sample (29/40) reported experiencing at least some craving, although for the majority (n = 13) it was mild (a score of 1 to 3), for 9 it was moderate (a score of 4 to 7), and for 7 it was severe (a score of 8 to 10) in nature. The mean score on the SOWS was 0.67

Table 2. Methadone Treatment

	Minimum	Maximum	Mean	SD
Treatment duration (months)	8	156	35	22.4
Current dose (mg)	2.5	15	9.2	3.5
Other prescribed medications	Diazepam	Hydroxyzine	Lactulose	Fluvoxamine
n (%)	11 (27.5)	21 (52.5)	1 (2.5)	5 (12.5)
Results of urine analysis (n/%)			Positive	Negative
Urine test for methadone			39 (97.5)	1 (2.5)
Urine test for THC			1 (2.5)	37 (92.5)
Urine test for amphetamine			1 (2.5)	38 (95)
Urine test for benzodiazepine			7 (17.5)	32 (80)
Urine test for morphine			0 (0)	39 (97.5)

(±0.93) (range, 0 to 3) which is indicative of withdrawal symptoms being less than mild. Around three-quarters (n = 31) had a mean score of less than 1, 4 (10%) had a mean score of 1 to 2 indicating "mild withdrawal", 2 had a mean score of 2 indicating "moderate withdrawal" symptoms, and 3 had a mean score of 3 indicating "severe withdrawal". Pearson's correlation indicated there was no correlation between SOWS score and dose of methadone ($r = -0.01$, $P = 0.94$). Responses to individual items indicated that the most common withdrawal symptoms experienced were aches and pains (40%) and feeling sick (37.5%); however, yawning, insomnia and runny eyes were rated as the most severe symptoms among those experiencing them.

Medical Comorbidity and Side Effects of MMT

Eight patients reported suffering from hypertension, 8 from ischaemic heart disease, 4 from diabetes and 4 from asthma, all of which were well-controlled. There were few reports of side effects from taking methadone, such as dry mouth (n = 1), drowsiness (n = 2) and constipation (n = 1) and all were reported to be mild in severity. Most participants (57.5%) had a normal full blood test result and a normal liver function test result (55%).

Quality of Life (Psychological and Social Functioning)

On the Social Functioning Scale (SF36), the mean score on the physical component was 51.4 (±14.8), which is just above the normative value (50); and the mean score on the mental component was 63.5 (±19.0), also above the normative value (50). On the item concerning how their health was rated in general, 14 (35%) rated it as "poor" or "fair", 14 (35%) as "good", 10 (25%) as "very good" and 2 as "excellent". The mean scores on the HADS were 4.5 (±4.1) for anxiety, which is in the normal range and suggests an absence of anxiety and 5.2 (±4.6) for depression, which is in the normal range and suggests an absence of depression. Only 5 (12.5%) patients were borderline abnormal for anxiety and 6 (15%) borderline abnormal for depression. Four (10%) patients achieved an abnormal score indicating probable presence ("case") of anxiety and 7 (17.5%) patients achieved an abnormal score indicating probable presence ("case") of depression.

Caregiver's Experiences

The responses of caregivers to the items below indicate an overall satisfaction with the impact that the treatment had on the patients. The majority (82.5% to 95%) either "agreed" or "totally agreed" with each item, indicating that the treatment had had a positive impact on the patients' condition, their interpersonal relationships and had reduced both the burden to the family and the patients' drug seeking behaviour (Table 3).

Discussion

The study set out to determine the characteristics of elderly opiate-dependent patients undergoing MMT, to assess the impact of MMT on illicit opiate use and examine the feasibility of caregiver involvement in a monthly take-home regime for this group of people. The results of the study suggest that MMT is an effective means of eliminating the use of illicit opiates among elderly opium users. All patients had tested positive for morphine on entry to treatment and none reported using opiates when interviewed on average 3 years into treatment (corroborated by urine analysis on the day of interview). However, 6 patients reported that they had tested positive for opiates at some point in the previous 6 months and this was confirmed by urine analysis reports in medical records. This was attributed to the use of cough medicine in some instances, although complaints of insufficient dose to prevent withdrawal symptoms accompanied 4 of the 6 cases. The proportion of MMT patients using illicit opiates (15%) is considerably lower than reported in other studies. Among a UK sample of MMT patients, 53% tested positive for non-prescribed opiates[21] and among a Canadian sample, 46% tested positive for illicit opiates, with only 7% abstaining from all illicit

Table 3. Treatment Satisfaction Expressed by Caregiver of Patients

Relative to when the patient was using illicit drugs, there has been…	**Totally disagree n (%)**	**Somewhat Disagree n (%)**	**Neither Agree/Disagree n (%)**	**Somewhat Agree n (%)**	**Totally Agree n (%)**
a significant improvement in patients general conditions	1 (2.5%)	0	3 (7.5%)	13 (32.5%)	23 (57.5%)
a reduction of burden to family	1 (2.5%)	0	2 (5%)	15 (37.5%)	22 (55%)
a reduction in patient's drug seeking behaviour	0	0	2 (5%)	13 (32.5%)	25 (62.5%)
an improvement in interpersonal family relationship	1 (2.5%)	1 (2.5%)	5 (12.5%)	12 (30%)	21 (52.5%)
satisfactory treatment for your family member	0	0	3 (7.5%)	17 (42.5%)	20 (50%)

drugs throughout the study period.[22] It is encouraging that the positive screens appeared to have been a one-time occurrence and that following counselling, all subsequent urine tests for the presence of illicit opiates were negative.

The dose of methadone for the treatment of heroin dependence is typically in the range of 60 to 120 mg.[23] In consideration of patient safety, the dose for this group of elderly opium users was low (a mean of 9 mg). With this dose regime, there were few reports of side effects or related physical health conditions. Average scores on measures assessing quality of life, physical and psychological health (mood), and social functioning scores indicated that they were functioning at a normal level. Whilst three-quarters of the sample reported at least "mild" craving, with 40% reporting moderate or severe craving, only one-quarter reported any symptoms of withdrawal. In a longitudinal cohort study of patients receiving opiate substitution medication in developing and transitional countries, it was found that Asian countries (China, Thailand and Indonesia) administered lower doses, yet achieved similar outcomes and retention rates compared to countries in the Middle East, Eastern Europe and Australia.[10] Interestingly, Chinese participants were found to be more likely to have dropped out of treatment if they had received higher, not lower doses of methadone.

In countries where methadone diversion is a concern, prescribing guidelines encourage the dispensing of prescriptions in multiple and regular instalments, and for consumption to be supervised by medical or dispensing staff. However, it is both difficult and impractical for the elderly to visit the clinic daily and thus the monthly take-home regime was designed specifically for this population once stability had been achieved. The presence of methadone derivatives in urine suggests that the patients were taking their methadone which corroborates denial of any acts of diversion to others. The fact that no patient reported experiencing an overdose suggests that the monthly-take instalment offers a safe and feasible treatment regime with this population.

International policy and guidance acknowledges how families and caregivers have a unique and vital role in the treatment of addiction.[1,23,24] There is recognition that their involvement can increase the chances of the user entering and engaging in treatment, reducing or ceasing drug misuse, successfully completing treatment and reduces the chances of major relapse.[25] In Singapore, government policy encourages children to live with their parents, and to maintain the traditional family relationship. This is often achieved by means of housing allocation and subsidies. Usually the elderly live with, or close by to at least one of their children. The disadvantage of this set up is that the whole family are exposed to the negative impact of the opium-using member. The advantage is that the whole family is available to support and encourage the user and can be actively involved in their treatment process – accompanying them to hospital visits and administering prescribed medications. This unique situation enables psychiatrists to prescribe a "take-home" methadone regime with monthly reviews which serves to preserve hospital resources. On the whole, caregivers also expressed satisfaction with MMT, reporting that it had made a positive impact on the lives of the patients for whom they were caring; in particular, 85% reported a reduction in the burden on the family. Although detoxification is one treatment option to achieve abstinence, most of the patients had failed previous attempts to cease opium use on numerous occasions. In the later stages of life, minimising discomfort and maximising quality of life is of paramount importance. Family members were happy to escort the patient to hospital visits and to take on the responsibility of monitoring and supervising medication.

MMT is recognised as a cost-effective treatment for opiate dependence.[26-28] The data from the current study indicate that the average cost of MMT to the patient was $79 a month. For the patient, this compares favourably to monies spent (averaging $574) per month on opium prior to treatment and possibly contributed positively to the strict adherence to the programme. In addition to alleviating financial constraints on the family, being in MMT is likely to reduce the emotional burden on the primary caregiver, enabling the caregiver to be more productive. The greatest savings may be in its burden on society, since being in MMT is likely to diminish demands of the illicit opiate market which will ultimately reduce its supply.

The results of the current study support those of others reporting on the effectiveness of MMT with elderly addicted populations.[16,17] However, there are some limitations of the current study that are worthy of consideration. The study used a cross-sectional design, examining clinical characteristics at a single point in time. Since no baseline measures were taken, it is not possible to determine whether or not there have been significant or clinically meaningful improvements in physical, psychological or social functioning resulting from MMT. Similarly it cannot be assumed that patients were functioning at an impaired level, prior to or upon entry to treatment, or that any improvements were due to MMT and not other factors.

Nonetheless, the implications for the treatment of this unique clinical population for whom MMT is available, is that it appears to be a successful treatment regime. However, the context of that regime is one of strict control and monitoring of methadone prescribing, strict adherence to guidelines, a multidisciplinary team to engage the family, counselling for alternatives to anxiety and pain management and highly skilled and experienced addiction psychiatrists.

The well-retained family support structure is likely to have facilitated the successful monthly home-dose arrangement. Whilst there are encouraging findings, it is important to recognise that elderly opium addicts are a dying breed in Singapore and differ markedly from younger opiate users who will eventually grow old.

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REFERENCES

1. HM Government. Drugs: Protecting Families and Communities. The 2008 drug strategy.
2. Daley DC, National Institute on Drug Abuse. Approaches to drug abuse counselling. 2000. Available at: http:///www.drug.abuse.gov/ADAC/ADAC3.html. Accessed 20 October 2009.
3. Gossop M. A review of the evidence for methadone maintenance as a treatment for narcotic addiction. Lancet 1978;1:812-5.
4. Senay EC. Methadone maintenance treatment. Int J Addict 1985;20: 803-21.
5. Avants SK, Margolin A, Sindelar JL, Rounsaville BJ, Schottenfeld R, Stine S. Day treatment versus enhanced standard methadone services for opioid-dependent patients: a comparison of clinical efficacy and cost. Am J Psychiatry 1999;156:27-33.
6. Preston KL, Umbricht A, Epstein DH. Methadone dose increase and abstinence reinforcement for treatment of continued heroin use during methadone maintenance. Arch Gen Psychiatry 2000;57:395-404.
7. Darke S, Ross J, Teesson M. The Australian Treatment Outcome Study (ATOS): what have we learnt about treatment for heroin dependence? Drug Alcohol Rev 2007;26:49-54.
8. Gossop M, Marsden J, Stewart D, Treacy S. Outcomes after methadone maintenance and methadone reduction treatments: two year follow-up results from the National Treatment Outcome Research Study. Drug Alcohol Depend 2001;62:255-64.
9. Connock M, Juarez-Garcia A, Jowett S, Frew E, Liu Z, Taylor RJ, et al. Methadone and buprenorphine for the management of opioid dependence: a systematic review and economic evaluation. Health Technol Assess 2007;11:1-171.
10. Lawrinson P, Ali R, Buavirat A, Chiamwongpaet S, Dvoryak S, Habrat B, et al. Key findings from the WHO collaborative study on substitution therapy for opioid dependence and HIV/AIDS. Addiction 2008;103: 1484-92.
11. Gossop M. Maintenance treatments across countries. Addiction 2008; 103:1493-4.
12. Strang J, Manning V, Mayet S, Ridge G, Best D, Sheridan J. Does prescribing for opiate addiction change after national guidelines? Methadone and buprenorphine prescribing to opiate addicts by general practitioners and hospital doctors in England, 1995-2005. Addiction 2008;102:761-70.
13. Burns L, Randall D, Hall WD, Law M, Butler T, Bell J, et al. Opioid agonist pharmacotherapy in New SouthWales from 1985 to 2006: patient characteristics and patterns and predictors of treatment retention. Addiction 2009;104:1363-72.
14. Banta-Green CJ, Maynard C, Koepsell TD, Wells EA, Donovan DM. Retention in methadone maintenance drug treatment for prescription-type opioid primary users compared to heroin users. Addiction 2009;104: 775-83.
15. Gossop M, Moos R. Substance misuse among older adults: a neglected but treatable problem. Addiction 2008;103:347-8.
16. Rajaratnam R, Sivesind D, Todman M, Roane D, Seewald R. The aging methadone maintenance patient: treatment adjustment, long-term success, and quality of life. J Opioid Manag 2009;5:27-37.
17. Lemke S, Moos RH. Treatment and outcomes of older patients with alcohol use disorders in community residential programs. J Stud Alcohol 2003;64:219-26.
18. Gossop M. The development of a Short Opiate Withdrawal Scale (SOWS). Addict Behav 1990;15:487-90.
19. Ware JE, Sherbourne CD. The MOS 36-Item Short-Form Health Survey (SF-36®): conceptual framework and item selection. Med Care 1992;30:473-83.
20. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand 1983;67:361-70.
21. Dunn J. A survey of methadone prescribing at an inner-city drug service and a comparison with national data. Psychiatric Bull 2003;27:167-70.
22. Raffa JD, Grebely J, Tossonian H, Wong T, Viljoen M, Khara M, et al. The impact of ongoing illicit drug use on methadone adherence in illicit drug users receiving treatment for HIV in a directly observed therapy program. Drug Alcohol Depend 2007;89:306-9.
23. Department of Health (England) and the devolved administrations. Drug Misuse and Dependence: UK Guidelines on Clinical Management. DH London. 2007. Available at: http://www.nta.nhs.uk/publications/documents/clinical_guidelines_2007.pdf. Accessed 21 May 2010.
24. Department of Health. Carers at the Heart of 21st Century Families and Communities: A Caring System On Your Side, A Life Of Your Own. DH London. 2008. Available at: http://www.dh.gov.uk/en/publicationsandstatistics/publications/publicationspolicyandguidance/DH_085345. Accessed 21 May 2010.
25. National Treatment Agency for Substance Misuse. Supporting and involving carers. 2008 September. Available at: http://www.nta.nhs.uk/areas/users_and_carers/supporting_and_involving_carers.aspx. Accessed 21 May 2010.
26. Mattick RP, Breen C, Kimber J, Davoli M. Methadone maintenance therapy versus no opioid replacement therapy for opioid dependence. Cochrane Database Syst Rev 2003;(2):CD002209.
27. Schilling RF, Dornig K, Lundgren L. Treatment of heroin dependence: Effectiveness, costs, and benefits of methadone maintenance. Research on Social Work Practice 2006;16:48-56.
28. Moore TJ, Ritter A, Caulkins JP. The costs and consequences of three policy options for reducing heroin Dependency. Drug Alcohol Rev 2007;26:369-78.