Maintenance Treatment with Opium Tincture: A Preliminary Qualitative Study of the Factors Related to Treatment entry

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Introduction

Opium smoking has a long history in Iran while heroin has been introduced in recent decades (1). Despite the nationwide implementation of methadone maintenance treatment (MMT), buprenorphine maintenance treatment (BMT) and harm reduction services (2, 3), opiate use is still a major health concern in Iran (4). Therefore, as a culturally-accepted medicine, opium tincture (OT) (i.e., a liquid form of opium prepared in an alcohol-based solution) has been recently pilot tested as a treatment for opiate users in Tehran. In the first pilot study of the clinical effectiveness of OT at Iranian National Center for Addiction Studies, of 144 patients treated with OT, 91 patients remained abstinent from using opiates six months following the initiation of the treatment (5).
was a high retention rate in treatment compared with similar studies in other Asian countries such as Thailand (6, 7).

OT is used for the management of opiate withdrawal and detoxification in some Asian countries such as Thailand (6). Globally, there is a paucity of research of the clinical effectiveness of OT because it is more culturally accepted. A study of the clinical effectiveness of OT among 30 heroin and opium-dependent patients in Thailand showed that withdrawal symptoms were more severe in patients receiving OT than methadone, indicating less withdrawal management (6).

In contrast, a pilot study of 18 opiate-dependent patients showed the clinical effectiveness of OT in managing opiate dependence, withdrawal, improving physical and psychological health, and socio-economic status (7).

In order to evaluate the clinical effectiveness of OT in the management of opioid withdrawal in a group of Thai patients, 45 opium-dependent subjects were allocated to three dosing groups (6.66, 13.3 and 20 mg morphine equivalents, twice daily). On day 5 of dosing, subjects underwent an inter-dosing interval study. Blood specimens were collected. Withdrawal scores, heart rate and blood pressure (BP) were measured at 0, 1, 3 and 8 hours after initial treatment. Thirty two subjects completed the study. Withdrawal scores were low for all subjects (in a range from 9% to 23%). The study results showed that opioid withdrawal was treated by flexible dosing of OT (8).

In 2010, Iranian health authorities approved OT as a maintenance treatment for opiate users (5). There is a dearth of information about the OT experiences in Iran, we used qualitative methodology to guide the investigation and explore the self-perceived factors associated with treatment entry. These methods allow for a deeper, richer understanding of the participant experience via open dialogues between researchers and target population. Qualitative methods can enhance research by identifying additional relevant variables, generating new hypotheses, and by strengthening conceptual validity (10, 11).

This study was a preliminary study on the reasons associated with entry into maintenance treatment with OT among a sample of opiate-dependent patients in Tehran. The study settings included six outpatient centers that provided OT at the time of conducting the study in 2010.

**Methods**

**Design and Settings**

Due to the dearth of information about the OT experiences in Iran, we used qualitative methodology to guide the investigation and explore the self-perceived factors associated with treatment entry. These methods allow for a deeper, richer understanding of the participant experience via open dialogues between researchers and target population. Qualitative methods can enhance research by identifying additional relevant variables, generating new hypotheses, and by strengthening conceptual validity (10, 11).

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**Participants**

**Focus Group Interviews with Patients**

Patients were recruited through convenience sampling. Eligible patients were directly approached and recruited by the manager of each center but the research team directly supervised the screening of eligible respondents. Patients included 52 participants.

They participated in focus groups interviews. The focus group interviews provide a facilitative non-threatening group environment in which to explore the perceptions and personal experiences regarding a specified issue or topic.
The Key Informant Interviews with Health Professionals
A group of 4 physicians, 2 psychologists, 2 social workers and 2 nurses who worked as OT teams at the centers were also directly interviewed.

Inclusion and Exclusion Criteria
Patients receiving maintenance treatment with OT were eligible for enrollment if they were 1) ≥18 yr old, 2) reported opiate dependence based on DSM.IV-TR criteria prior to treatment entry, 3) agreed with signing consent form for study participation, and 4) were living in Tehran at the time of study. Exclusion criteria included 1) reporting severe craving and withdrawal symptoms which were likely to interfere with interviewing, and 2) disagreement with signing the consent form. Key informants were required to be OT treatment teams for at least 9 months and sign consent forms.

Study Procedure
A semi-structured, open-ended interview was developed to explore demographics, details of drug use and the self-perceived reasons associated with entry into treatment with OT among patients. Focus group interviews were held with patients. Focus group size ranged from 4 to 8 patients. Detailed narrative data was collected. The purpose of the focus groups for this study was to obtain information from participants who were in treatment and to further explore the issues identified in the key informant interviews. Groups discussed attitudes, beliefs and knowledge about treatment entry. They were encouraged to respond to all the issues raised by the facilitators, but were informed that they had the right not to respond to any issue. Patients sat in a circle to encourage participation and foster openness.

A semi-structured interview was also conducted with key informants to explore this issue further. The purpose of the key informant interviews was to gather and compare information about the reasons of treatment entry from a knowledgeable professional view. A Detailed summary of each audio-taped interview was conducted and selected quotations were transcribed verbatim.

The semi-structured interviews were conducted by 3 ethnographers (e.g. facilitators) with at least 5 years of opiate-related research experience, and professional training in qualitative methodology. Interviews were conducted in a quiet interview room at each center, other locations in participants’ neighborhood or at a research center site in order to enhance the comfort and convenience of the participants. Each in-depth face-to face interview took between 70 and 90 minutes, were audio-taped, and covered the perspectives of patients and key informants on the reasons of treatment entry.

The interview period was limited to the months between February 2010 and July 2010 because qualitative analysis of the interviews demonstrated that we had reached data saturation (12) and no new themes were emerging from continued interviews.

Data analysis
The transcribed interviews were reviewed for accuracy and completeness, and entered into the qualitative software. Results from the key informant and focus group interviews were discussed separately to fully present the information. For each of the interviews, the participants’ reasons for treatment entry were categorized by two members of the ethnographic research team (ZAM and RD). The initial process was evolving and the number of categorization expanded and contracted as additional detailed interviews were conducted and analyzed.

After the initial phase of categorization was completed, each transcript was read and coded in detail by two different research team members who met, discussed, and reached consensus concerning content coding. Transcripts were coded using a modified grounded theory of Strauss and Corbin (13), initially limiting the content analysis to a dictionary of prescribed codes developed for the project and then allowing for emergent themes from the participants’ narratives. The two team members who completed the consensus content analysis coding also discussed a participant’s primary categorization. If they questioned the original categorization of a participant, they brought the case
to the full ethnographic team for final consensus on the participant’s categorization. Demographic data and details of drug use were analyzed by performing frequency, percentage, mean and standard deviation in SPSS.v.18. Qualitative data analysis began after the first interview was completed in order to refine the research questions using the constant comparative method (14). The analysis of this qualitative study was based on constructing a thematic framework (15), which was used to classify and organize data according to key themes: concepts and emergent categories. The process of interpretation was affected by the original research objectives, as well as by the themes that emerged from the data. Qualitative data was analyzed by using Atlas-ti software.

**Ethical considerations**
The study protocol was approved by the Ethics Committee of Tehran University of Medical Sciences. Participation was voluntary and confidential. Before initiating the study, participants were informed that non-participation in the study would not impact their treatment or relationships with the staff at each center. All participants provided informed written consent at the time of their initial recruitment into the study. All conducted transcripts and audio-taped information were anonymous. Patients were given retail vouchers for study participation at the end of the interviews.

**Results**

**Demographic and Drug-Related Characteristics**
Forty five patients were male and 7 patients were female. Three patients were heroin injectors and the remaining patients were heroin smokers (67.3%) and opium smokers (32.7%). The median age of patients was 39 years. The duration of the current treatment ranged from 6 to 12 months, with an average treatment duration of 232 days. The patients had a mean number of 7.8 life time drug use treatment episodes. 84.6% reported lifetime positive experience with MMT (Table1).

| Variable                        | Number of participants (%) |
|--------------------------------|---------------------------|
| Gender                         |                           |
| Male                           | 45 (86.5%)                |
| Female                         | 7 (13.5%)                 |
| Median age (yr)                | 39                        |
| Median Education (yr)          | 9                         |
| Living status                  |                           |
| With family                    | 48 (92.3%)                |
| Unstable living                | 4 (7.7%)                  |
| Employment status              |                           |
| Currently employed             | 38 (73%)                  |
| Currently jobless              | 14 (27%)                  |
| Type of opiate use             |                           |
| Heroin                         | 35 (67.3%)                |
| Opium                          | 17 (32.7%)                |
| Route of opiate use            |                           |
| Smoking                        | 47 (90.4%)                |
| Injection                      | 5 (9.6%)                  |
| Initial age of opiate use (Years) | 19 (SD=8.9)            |
| Duration of opiate dependence (Years) | 14 (SD=12.4)         |
| Lifetime drug use treatment    | 52 (100%)                 |
| MMT                            | 44 (84.6%)                |
| Other drug use treatments      | 8 (15.4%)                 |
| Life time drug use treatment episodes | 7.8 (SD=6.6)      |

**Reasons Associated with Treatment Entry Methadone Misconceptions**
Dissatisfaction with MMT program is a category that covers common methadone misconceptions in the Iranian community including taking methadone as a chemical medication, methadone dependence, and long duration of MMT. This category describes the plurality of patients who left methadone treatment (n=44; 84.6%) and entered OT. Misconceptions on MMT program that led to leaving MMT generally developed over time with one frustration building on top of another. On average, patients remained in MMT for 259 days.
The subcategories below provide more details about what constitutes this category.

**Dissatisfaction with Taking Methadone as a Chemical Medication**
Among participants who reported dissatisfaction with MMT, some reported dissatisfaction with taking methadone because they believed that methadone is a chemically-made medication. They believed that chemical ingredients of methadone were associated with poor health. This issue resulted in a strong motivation among some of them to leave MMT and enter OTT.

A 26 year old man who was a tailor and was taking OT for 6 months quoted as follow:
"...I took methadone at a clinic near my work place for 10 months last year. I had too many problems with that (e.g. methadone). You know it (e.g. methadone) isn't herbal. Methadone is chemical so it wasn't good to my health... so I decided to come here (e.g. OT center) and take the medication (e.g. OT)...." (Code-21)

A doctor who prescribed OT for patients quoted as follow:
"...more than 90% of my OT patients have methadone misconceptions. They think methadone is a chemical medication with lots of side effects. They think they are addicted to methadone. They refer to OT because they think it is not addictive...I think we need more methadone education ...." (Code-28)

**Methadone Dependence**
Among patients who reported methadone misconceptions, some reported dissatisfaction with taking methadone because of physical and mental dependence. They believed that methadone was a narcotic drug and it was addictive in long-term use. This issue resulted in a strong motivation among them to stop MMT and enter OTT.

A 42 year old jobless woman who was a heroin smoker and was taking OT for 6 months quoted as follow:
"...It (e.g. MMT) was too long and my doctor had no plan to finish it (e.g. MMT).... I begged my doctor to stop methadone and let me go but he was too persistent with continuing methadone treatment....I was tired.... I was there (e.g. in MMT) for 12 months... I just left...." (Code-28)

A doctor who prescribed OT for participants quoted as follow:
"...Most of our patients like to quit addiction in a very short period of time. They don’t like to be in MMT for a long time so they frequently leave methadone treatment and refer to different treatments such as OT... I believe we need more methadone education"

**Long Duration of MMT**
Among patients who reported methadone misconceptions, some reported dissatisfaction with taking methadone because they believed that the duration of treatment was long. This issue led to a strong barrier against continued treatment and motivated them to leave MMT and enter OTT.

A 42 year old jobless woman who was a heroin smoker and was taking OT for 6 months quoted as follow:
"...most of our patients are scared of methadone. They think methadone is addictive. They come to my room and tell me methadone is addictive. They refer to OT because some of them think it is not addictive. I think OT is more culturally-accepted compared with methadone among our patients in Iran...."

**Recommendation of Other People in Treatment**
Some patients reported that they had some friends, colleagues, neighbors, relatives or family members who were in maintenance treatment with OT and their recommendations encouraged them to enter treatment. They reported that they relied on such recommendations and accepted OT as an appropriate treatment strategy for quitting opiate dependence.

A 43 year-old man who was a heroin smoker and was in treatment for 9 months quoted as follow:
"...My older brother, one of my neighbors and one of my cousins take OT here (e.g. OT clinic). For months, I told them they were taking opium. I told them it (e.g. OT)
wasn’t medicine for addiction. They encouraged me to come here (e.g. OT center). They told me OT is a real medicine… They were persistent so I decided to come here (e.g. OT center) and take it (e.g. OT)...I had no knowledge about OT” (Code-13)

A social worker who provided social work services for patients quoted as follow:

”...We know OT comes from opium so many patients can’t rely on it but when they see their friends or relatives are successful in OT, they come for the treatment…”

**OT-Related Characteristics**

OT-related characteristics are a category that reflects the patients’ expectations about OT including the herbal compound of OT, treating opiate craving and withdrawal symptoms and improving general health respectively. Some of participants reported this category was a strong motivation for them to enter treatment.

**Herbal Compound of OT**

The herbal compound of OT was a strong motivation for some of patients to enter treatment. Some patients reported that they desired for an herbal medication to quit opiate addiction because they believed that herbal medications have lower side effects compared with chemical medications such as methadone.

A 41 year-old man who was a taxi driver and was in treatment for 10 months quoted as follow:

"...It (e.g. OT) isn’t chemical like methadone. It’s herbal (e.g. OT). That’s why I’m here (e.g. OT center). ... OT is extracted from opium so it is healthy…” (Code-1)

A psychologist who provided psychological services for patients quoted as follow:

"...The herbal ingredients of OT are very serious issues for our patients at treatment initiation. I believe it is the most important feature of OT that our patients consider at initiation. They believe it is healthy to take a herbal medication... This is because of our culture which considers opium as a traditional medicine"

**Treating Opiate Craving and Withdrawal Symptoms**

A strong belief among some patients that OT use can treat craving and withdrawal symptoms was a strong motivation for some of participants to enter treatment. The quotations below explain this issue better:

A 38 year-old man who was a waiter at a restaurant and was in treatment for 6 months quoted as follow:

"...My legs still have pain but that’s OK. It’s because of long years of opium and heroin use. OT has relieved my body pain. I have no heroin craving for 4 months... I expected so before treatment…” (Code-25)

A nurse who provided OT for patients quoted as follow:

"...Some of our patients believe OT can treat opiate craving and withdrawal symptoms such as physical pain. I believe because OT substitutes opiate use in them. I believe they considered OT as a medication for treating physical pain and opiate craving before treatment entry…”

**Improving General Health**

Expecting that OT improved general health was a strong motivation for some of patients to enter treatment. Some patients reported that they had heard from people in treatment that OT was effective in improving general health. This issue was a strong motivation for some of them to enter treatment.

A 39 year-old man who was a heroin injector before treatment entry and was in treatment for 6 months quoted as follow:

"...I heard from other people OT was good in getting physical and psychological health improved. I wasn’t healthy because of heroin injection so I decided to enter treatment with OT…” (Code-27)

A nurse who provided OT for patients quoted as follow:

"...Patients come to our center and are interviewed by me. Before treatment, they expected OT improved their general health. Most of them have a poor quality of life and health before treatment entry. This is a strong motivation for them to enter treatment with OT…”

**Discussion**

OT is a newly approved treatment for opiate-dependent people in Iran. After MMT and BMT, it is the most widely used maintenance treatment for opiate users in Iran (5). Best to our knowledge, this is the first study that has provided a rare
glimpse into patient perspectives on reasons for entry into maintenance treatment with OT. Methadone misconceptions were strong motivations for most of the patients to enter treatment. In this category, dissatisfaction with the chemical compound of methadone, misconceptions about methadone dependence and long duration of MMT were their motivations to leave MMT and enter treatment with OT. Methadone misconceptions were likely to be the results of unsuccessful previous treatment attempts, inappropriate prescribing methadone dose and the lack of methadone education. Patients were likely to have a low level of knowledge on positive treatment effects of methadone and did not remain in MMT to experience improved health. This issue has important treatment and clinical implications and should be specifically considered by clinicians during implementing MMT. In addition, this study finding suggests that it would be worthwhile for MMT staff to assess client attitudes toward the treatment during methadone intake, and perhaps at subsequent reviews of client progress to prevent premature discharge from MMT.

Some of patients left MMT because the program was not meeting their expectations and concerns. Those who held misconceptions about methadone should be regarded as being at risk for premature termination. A consistent, thorough, and evidence-based patient education program may be of use in dealing with this pervasive issue in Iran. Bell and colleagues (2006) found that nearly two thirds of methadone clients dropped out within the first year (16). A study showed that 50% of methadone clients dropped out without completing treatment within the first year of treatment (17). Because good patient outcomes have been shown to be related to longer treatment retention (18), it is essential to conduct more studies on this issue in Iran.

Participants reported that they relied on those individuals who were in OT and reported positive experience with maintenance treatment with OT. Having an encouraging social network that encourages people to enter treatment for opiate use may be a strong motivation at initiation. Supportive living environments may facilitate entry into treatment and may be helpful in devising appropriate and targeted interventions to encourage drug treatment entry. More information should be provided about the treatment effects of OT for those individuals who desire for treatment with OT. A study on 245 drug injectors attending the Baltimore Needle Exchange Program in the US showed that those patients who were living with families and friends were more likely to enter drug treatment compared to individuals who lived alone (19).

Some OT-related characteristics and expectations such as the herbal compound of OT, treating opiate craving and withdrawal and improving general health were strong motivations for some participants to enter treatment. Best to our knowledge, no study has been conducted on OT-related characteristics and expectations and their positive roles in encouraging opiate-dependent patients to enter treatment. Therefore, this is a new study finding. Social observations that some of these patients had from the clinical effectiveness of OT among other opiate-dependent people were likely to motivate them to refer to OT. A study showed that family relationship and social functioning were improved among 22 male opium-dependent patients after six months of receiving OT (20).

Most people who develop opiate dependence require a combination of medication and psychotherapeutic services in order to optimize their treatment entry and outcomes. Like those who abuse other substances, people who are dependent on opiates should be provided adequate information in selecting a treatment such as OT. Like many others who have chronic illnesses, most people who abuse opiates find medication to be an important tool for the management of their condition.

In addition, many also need adjunct services such as individual psychotherapy; family therapy and supports (20). Though, some opiate-dependent patients eventually may be able to discontinue one treatment, most find that they cannot stop abusing opiates except by remaining in other treatments such as OT. Support for enrolling in drug use treatment and for adhering to the medication
regime is, therefore, essential for people with opiate dependence. This study offers important contributions to the literature, however there are important limitations that affect external validity and generalizability including (1) the small sample size and (2) the site of study which was only Tehran.

Conclusion

Positive treatment aspects of OT which were reported by our participants still need extensive studies in Iran. There is a gap in our knowledge about factors especially medical ones influencing some Iranian opiate-dependent patients who refer to OT for treatment. Better understanding of such factors could help to investigate positive aspects of OT use compared with highly approved MMT and BMT. Understanding the influential factors and comparing the pharmacological effects of OT in comparison with methadone and buprenorphine may also help to design programs to evaluate the feasibility and clinical effectiveness of OT.

Ethical notes

Ethical issues (Including plagiarism, Informed Consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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