Short Communication

The effectiveness comparison of Jitai tablets versus methadone in community-based drug treatment: A 1-year follow-up study

Shen-Qiang Hao a,⁎,1, Min Zhao b,1, Rui-Wen Zhang c,1, Jian-Chen Zhang d,1, Jing Zhang e,1, Xue-Shan Feng a,1

a School of Public Health, Fudan University, Shanghai, China
b Shanghai Mental Health Center, Shanghai, China
c Technological and Industrial Promotion Center of Traditional Chinese Medicine, Shanghai, China
d Drug Control Office, Shanghai, China
e The Council of Shanghai Ziqiang Social Services, Shanghai, China

HIGHLIGHTS

• This is the first post-marketing effectiveness study of Jitai tablets.
• We carried out a cohort study with one year follow-up.
• Both methadone and JTT gained effective relapse prevention.
• JTT can be recommended to clinical doctors and drug addicts.

ARTICLE INFO

Keywords:
Community-based drug treatment
Chinese medicine
Jitai tablet
Methadone
Retention rate
Relapse prevention

ABSTRACT

Objective: The aim of the study was to compare the effectiveness of Jitai tablets (JTT) versus methadone in a community drug treatment program.

Methods: A cohort study was conducted with 386 eligible subjects from 7 districts to 65 communities in Shanghai. The subjects were placed into the JTT group (n = 206) or the methadone group (n = 180). The data were collected at 8-, 26- and 52-week follow-ups.

Results: The retention rates of the methadone group at the 8-, 26- and 52-week follow-ups were 97.78%, 91.67%, and 85.00%, respectively. The retention rates of the JTT group at these follow-ups were 90.78%, 83.50%, and 74.27%, respectively. A Chi-square test indicated a significant difference, and the P values were 0.0037, 0.0161, and 0.0095 for each follow-up. The relapse rates for the JTT group were 3.88%, 6.31% and 11.17% for each follow-up, and those for the methadone group were 1.11%, 2.78%, and 7.78% for each follow-up. The Chi-square test indicated no significance, and the P values were 0.1128, 0.1005 and 0.2594. A survival analysis indicated that the relapse survival curve had no significant difference between the two groups (log-rank test, P = 0.188).

Conclusion: Methadone and JTT combined with psychological intervention and social support provided effective maintenance treatment and relapse prevention in a community drug treatment program. The retention rate in the methadone group was higher, but the JTT group had the same relapse prevention as the methadone group. JTT can be recommended to clinical doctors and drug addicts.

© 2013 The Authors. Published by Elsevier Ltd.

1. Introduction

Modern science has confirmed that heroin addiction is a chronic recurrent brain disease (Friedman & David, 2009; O'Brien & McLellan, 1996). Detoxification alone has little benefit and high rates of relapse. Drug therapy combined with psychological rehabilitation and social intervention measures is more effective in the treatment of heroin addiction (Leshner, 1997; McLellan, Arndt, Metzger, et al., 1993; McLellan, Lewis, O'Brien, et al., 2000; Woody, McLellan, Luborsky, et al., 1995). With the implementation of a new anti-drug law on June 1, 2008, China's existing drug treatment strategy is centered on community drug treatment and mobilizes social services to help drug abusers return to society. The previous drug abuse policies based on required labor and compulsory treatment have been incorporated into the required isolation from society treatment model. As the number of
drug abusers increases, using community resources to develop a community-based drug-abuse recovery model has been a growing trend in relapse prevention and successful detoxification.

Jitai (JTT), which has been approved for the treatment of opiate addiction by the Chinese State Food and Drug Administration (SFDA), consists of 15 drugs, including Rhizoma corydalis, Radix salviae miltiorrhizae, Radix angeliacae sinensis, Ligusticum Chuanxiong, and Flos Daturae. Animal experiments have shown that JTT provides a positive effect equivalent to clonidine in detoxification treatment in morphine-addicted animals, with less harmful side effects (Lu, Pan, Fang, et al., 1998). Clinical research findings have shown that JTT can not only effectively control withdrawal symptoms in heroin addicts but can also relieve protracted withdrawal symptoms after a specific period of detoxification and consolidate the detoxification curative effects. JTT has no dependence potential and no obvious adverse effects (Dong, Wang, & Zhou, 2002; Xiong, Xiao, Li, et al., 2001; Xu, Duan, Wang, et al., 2000). There have been no reports of a post-marketing evaluation of JTT, such as effect evaluation and the surveillance of drug-adverse reactions in large populations. This study aims to explore the effectiveness of JTT combined with psychosocial intervention in community drug treatment and uses methadone, which is recognized worldwide for its effectiveness, as a control drug.

2. Materials and methods

2.1. Design and interventions

A cohort study with controls was designed with the research groups and intervention measures as follows.

Methadone group: We implemented methadone combined with psychological intervention and social supports according to the current community methadone maintenance treatment plan, with a treatment period of 1 year, including baseline screening and 8-, 26-, and 52-week follow-ups.

JTT group: We implemented JTT medication treatment combined with psychological intervention and social supports, with a treatment period of 1 year, including baseline screening and 8-, 26-, and 52-week follow-ups. The psychological intervention consisted of group psychological intervention and individual counseling.

The group psychology interventions consisted of 12 sessions over a 6-month period, with 1 session every two weeks, and were conducted by social workers who had been trained by qualified specialist physicians of the Shanghai mental health center. Each session had a theme, referred to as a group discussion, on topics including the following: role cognition; scene training; changing false understandings of family, social and personal behavior; providing help; and emergency measures. These sessions were scheduled for 1.5 h. Individual counseling was conducted by setting up a psychological consultation telephone hotline for actively seeking psychological support. The social support systems included providing subsidies, recommending employment, vocational training, medical fee reduction, conflict mediation, and family counseling, among others. Social workers are advocates for the participants and help the relevant agencies address the needs of the program participants.

Medication in treatment: JTT is dispensed in tablets of 0.4 g each. It can be taken at home under the supervision of family members. The participants receive a follow-up supply of the tablets according to a community doctor’s prescription, and the residual tablets are returned at the next stage. The specific medication directions for taking JTT are as follows: 3 tablets 2 × per day for 8 weeks, 2 tablets 2 × per day for 8–26 weeks, and then 1 tablet 2 × per day for 16–52 weeks. Methadone is an oral liquid, given flexibly according to the individual situation by doctors in doses of 15 ml to 120 ml everyday.

2.2. Setting and participants

The research sites covered 65 streets in the following seven districts of Shanghai: Yangpu, Pudong, Baoshan, Zhabei, Changning, Putuo, and Hongkou. The participants were recruited from June 2010 to September 2010. All of the participants who were opiate dependent (based on a clinical assessment), had not been prescribed either study drug for the preceding month, and were requesting maintenance treatment (for whom it was appropriate) were invited to participate. To be included, the patients were required to meet all of the following inclusion criteria: (1) between 18 and 65 years old; (2) completed the acute detoxification treatment; (3) meet the Diagnostic and Statistical Manual for Mental Disorders (4th ed., DSM-IV, American Psychiatric Association, 1994) criteria for opiate dependence; (4) patients (with a legal guardian) signed informed consent, agreed to comply with medication regime and completed the relevant information records for the duration of the study-based treatment; and (5) accept the authority of police and anti-drug social workers.

The patients were excluded if they had any of following exclusion criteria: (1) the presence of comorbid severe mental illness (schizophrenia, manic episodes, mental retardation); (2) a recent (in the last 3 months) serious organic disease; (3) pregnancy or lactation; or (4) ongoing medication treatment.

2.3. Measures

2.3.1. Treatment retention

Retention rate = (the number of participants retained in treatment /all of the participants) × 100%

Retained time was defined as the length of maintenance therapy from the initial prescription until lost to follow-up or the end of research. The subjects were considered to be “not retained” in the trial if they met one of the following standards: (1) canceled the informed consent; (2) lost to follow-up; (3) poor compliance; (4) adverse or serious adverse events occurred that could not be overcome; (5) appearance of suicide ideation, self-injury or impulsive action during the trial; (6) pregnancy; (7) violation of the experiment design; or (8) other reasons that the researchers considered unfavorable to continue medication.

2.3.2. Illicit drug use

Illicit drug use is reflected as a relapse rate. Relapse was defined as participants who failed a urine toxicology test for illicit drugs or were arrested by police and subject to compulsory isolation treatment during the follow-up period. The frequency of urine sample testing was a flexible schedule based on the level of engagement and on suspected or reported illicit drug use.

2.3.3. Safety indicators

The incidence rate and clinical manifestations of adverse events and side effect were monitored.

2.4. Data processing and statistical analysis

We used the EpiData version 3.02 to set up the data. All analyses were performed using SAS version 9.1. All of the statistical tests that we reported were two sided, and statistical significance was implied at \( P \leq 0.05 \). The continuous data, expressed as the means and standard deviations, were analyzed using a t-test, and the frequencies or proportions of the categorical data were analyzed using Chi-square test or Fisher’s exact test to compare the baseline characteristics and medical outcomes between the treatment projects. Kaplan–
Meier (K−M) survival analyses were conducted to identify relapse differences between the two groups.

2.5. Ethical approval

Ethical approval for this study was obtained from the Ethics Committee of Shanghai Mental Health Center. Informed consent was obtained from all participants.

3. Results

3.1. Baseline comparison

The data on the baseline characteristics of the participants of the two groups are shown in Table 1. The overall statistical tests (t-test or Chi-square tests) showed no significant differences between the two groups in terms of gender, age, age at first use of the drug, marriage, education, and smoking or non-smoking (amount and time). There were statistically significant differences in terms of employment status (in the last three years), previous medication, years of drug use and number of previous detoxifications. The participants in the methadone group were likely to have a higher proportion of previous medication treatment, more years of drug use, and more previous detoxifications. The participants in the JTT group were more likely to be from a free-limited environment.

3.2. Treatment retention

The retention rates of the methadone group at the 8-, 26-, and 52-week follow-ups were 97.78%, 91.67%, and 85.00%, respectively; the retention rates of the JTT group were 90.78%, 83.50%, and 74.27%, respectively. Chi-square of independence analyses showed statistical differences at the three follow-ups, and the P values were 0.0037, 0.0161, and 0.0095, respectively. The days retained averaged 334.7 ± 6.10 in the methadone group and 308.4 ± 7.87 in the JTT group, and the statistical difference was achieved between the two groups (t = 2.64, P = 0.0086).

The main reason for non-completion in both groups was being arrested and jailed for illegal drug use, which occurred in 51.85% in the methadone group and 39.62% in the JTT group.

3.3. Illicit drug use

3.3.1. Relapse rate

The relapse rates of the methadone group at the 8-, 26-, and 52-week follow-ups were 1.11%, 2.78%, and 7.78%, respectively, and the relapse rates of the JTT group were 3.88%, 6.31%, and 11.17%, respectively. The Chi-square test showed no statistical differences at any follow-up.

3.3.2. Survival analysis for relapse

A survival analysis of the 52-week follow-up demonstrated the difference in relapse rates (Fig. 1). A log-rank test comparing JTT to methadone indicated no statistically significant difference (P = 0.188).

3.4. Side effects and adverse event

Those receiving JTT complained of side effects more than those in the methadone group (7.28% vs. 0.56%, P = 0.001). The most common side effects in the JTT group were xerostomia (3.88%), somnolence (1.94%), gastrointestinal discomfort (1.94%), appetite suppression (1.94%), blurred vision (1.94%), dizziness (0.97%), and sweating (0.97%). These side effects were mild and primarily occurred in the early stage of medication. Two participants in the methadone group were injured in accidents, and one was hospitalized for another disease. One participant in the JTT group became pregnant during the treatment.

4. Discussion

4.1. High retention rate and low relapse rate in community-based drug treatment

We conducted a preliminary effectiveness evaluation of JTT versus methadone in a community drug treatment program in terms of...
efficacy and safety. Treatment retention is an important index for judging the maintenance status of the participants. In this study, the 12-month retention rates of the two groups were above 70%, and the methadone group achieved 85%. Compared with domestic studies, the results in our study were higher than those in other study reports, which ranged from 30.1% to 63.7% in other provinces that had no psychological intervention or social supports in drug treatment programs (Chen, Xia, Chen, et al., 2009; Li, Tan, Sun, et al., 2009; Liang, Liu, Zhong, et al., 2009; Yang, Duan, Xiang, et al., 2011). The results were similar in Jiangsu province, which provided psychological intervention and social support to the study subjects (Xu, Chen, & Li, 2009).

Relapse rates are related to the definitions of relapse (Ciesla, 2010; McKay, Alterman, Koppenhaver, et al., 2001; Saunders & Allsop, 1987). Although there is no consensual operational definition of the term, the definitions of “relapse rate” generally range from a strict standard to a loose standard as follows: a single drug use one time after a period of abstinence; a positive drug test after a period of abstinence; drug use with serious consequences after a period of abstinence; and not maintaining withdrawal after a period of abstinence (three months or one-half of a year) (Fareed, Vayalapalli, Stout, et al., 2011). High relapse rates have been generally observed in other studies, and evidence suggests that the twelve-month relapse rate following various classes of substance use ranges from 80 to 95% (Brandon, Vidrine, & Litvin, 2007; Kirshenbaum, Olsen, & Bickel, 2009). The relapse rates in the JTT and methadone groups in this study were below 15%, which is significantly lower than the results obtained in other national and international studies (Bao & Zhang, 2007; Brandon et al., 2007; Kirshenbaum et al., 2009; Lu, Gao, & Ni, 2010; Sun, Ve, & Qin, 2001), according to the strict definition of relapse used in our study.

4.2. Analysis of advantages and disadvantages of JTT in community drug treatment

Methadone is recommended by the World Health Organization for use as a drug substitute in community drug treatment programs. The efficacy of methadone has been confirmed by many studies during the drug’s nearly 50 years of development (Dole & Nyswander, 1965; Marsch, 1998; Mattick, Kimber, Breen, & Davoli, 2008). Some research indicated that (Kayman, Goldstein, Deren, et al., 2006; Schwartz, Kelly, O’Grady, et al., 2008) methadone may cause addiction, and withdrawal from methadone is thought to be worse than heroin withdrawal. In this study, we found that JTT displayed an equivalent effect in relapse prevention and has advantages over methadone. JTT is a Chinese compound formula tablet with no illegal composition, and it does not cause addiction. Doctors can directly prescribe JTT for patients, and it is convenient and helpful to protect privacy and avoid social discrimination. JTT is a prospective medication for use in community drug treatment because of its low cost of development and utilization and because we have valuable Chinese herbal medicine resources. It was found that the side effect rate was higher in the JTT group than in the methadone group, but these side effects have been noted in patient information instruction booklets about JTT. It is suggested that a clinical doctor prescribes a suitable dose and that research and development scientists improve the compatibility of the medicines.

The limitations of the study must be acknowledged. This study was nonrandomized, and selection bias therefore existed. Most participants in the methadone group had taken methadone before entering the study, which may have produced adaptability and led to a lower side effect rate than observed in the Jitai group. The preliminary evaluation of efficacy and safety in the study was a comprehensive result of JTT treatment versus methadone treatment combined with psychological intervention and social support; the results were not identified as the result of a single medication intervention.

5. Conclusions

Methadone and JTT combined with psychological intervention and social support showed effectiveness in promoting retention and relapse prevention in community-based heroin addiction treatment. Although the retention rate in the methadone group was higher, the JTT group had the same results for relapse prevention as the methadone group. JTT can be recommended to clinical doctors and drug addicts.

Role of funding source

The study of community drug treatment was funded by National Key Technology R&D Program for the 11th five-year plan (number: 2008BA149B00).

Contributors

Min Zhao, Rui-Wen Zhang, and Jian-Chen Zhang designed the present study. Shen-Qiang Hao and Jing Zhang assisted in the literature reviews. The data analysis was conducted by Shen-Qiang Hao and Xue-Shan Feng. All authors contributed to and have approved the final manuscript.

Conflict of interest

The authors report no conflict of interest regarding this study.

Acknowledgments

The authors gratefully acknowledge community doctors and social workers in seven districts of Yangpu, Pudong, Baoshan, Zhaabei, Changning, Putuo, and Hongkou in Shanghai for their great support in field intervention.

References


