Introduction

Heroin use, particularly heroin injection, is a major public health concern. Heroin is a highly addictive drug. It induces euphoric, anxiolytic, and analgesic central nervous system effects that may result in drug dependence and global functional loss [1]. The social costs of heroin-associated crime significantly exceed those of most of other illicit drugs [2]. Heroin use is associated with the spread of various infectious diseases, such as HIV, syphilis, and viral hepatitis, and the death rate of users is 13-17 times higher than that of their age-matched peers, primarily because of overdosing, traumatic accidents, and suicide [3,4]. The negative effects of heroin use involve significant loss of life years and life quality [5,6].

Methadone Maintenance Treatment (MMT) is the most widely used and extensively researched treatment for opioid dependence. MMT has been shown to reduce illicit heroin use, mortality, and the incidence of infectious diseases as well as to improve the life quality of opioid users [7]. Buprenorphine–naloxone treatment (Suboxone®), another treatment option for opioid dependence, has also been shown to be effective in reducing opioid use and craving for opioids [8].

In an effort to identify safe and effective treatments for opioid dependence, Traditional Chinese medicine (TCM) is being considered a new approach to the treatment of opioid dependence. Past reports have shown that TCM is effective in the treatment of the acute withdrawal symptoms of methadone when used for treating patients with opioid dependence [9,10]. However, few studies have reported the effects of TCM treatments during a drug switch from methadone to buprenorphine.

Case Report

This case involved a 46-year-old single man with a 24-year history of heroin dependence. He has used illicit substances since aged 16 years. While working as a printing factory laborer, he used amphetamine to stay alert during work. Heavy amphetamine use in the following 6 years resulted in persistent restlessness, irritability, and insomnia. He started using heroin at the age of 22 years initiated into its use by his friends. Heroin also provided him with comfort and euphoria. Full heroin dependence symptoms were noted the following years. He was infected with hepatitis C because of needle sharing. The high cost of heroin caused him immense financial stress. He was repeatedly incarcerated, and during his fifth jail term, his father passed away, causing him to miss his father’s funeral and motivated him to quit heroin.

The patient undertook his first methadone clinic visit in 2008. He initially received 20 mg of methadone per day. In June 2011, he showed persistently active heroin use. The methadone dosage was then raised to the maximum dose of 70 mg per day. His adherence and insight
improved during the long-term follow-up, for which he exhibited good participation. In 2013, his heroin craving was more effectively controlled and the methadone dosage was decreased to 10-20 mg per day.

The patient maintained low dose methadone with good adherence; however, he found daily visits for MMT inconvenient because of his work. Buprenorphine-naloxone was introduced by the methadone clinic, but the patient refused because he was worried about methadone withdrawal during the drug switch and was doubtful of the effectiveness of buprenorphine-naloxone for relieving opioid craving symptoms. Under facilitated TCM treatments, he decided to start the drug switch.

In April 2016, he attempted to stop the use of 10 mg of methadone per day and switch to 2 mg of buprenorphine every 2 days with TCM herbal treatments after a TCM diagnosis. The TCM physical inspection revealed dark-red tongue with bilateral tooth marks and thin-yellow fur while the pulse examination revealed bilateral wiry pulse. Therefore, the TCM constitutional diagnosis involved liver Qi stagnation and blood stasis. Regarding the diagnosis, we prescribed herbal synergic regimen of Xue-Fu-Zhu-Yu decoction (XFZYD), Suanzaoen decoction (SZRD), Chaihu-Shugan-San (CSS), and Chin-Gin-Kuan-Ming tablets (CGKM) (Table 1).

Initially, he experienced methadone withdrawal symptoms such as sleeplessness, sneezing, running nose, mild tremors, itchy skin, and appetite loss. The acute methadone withdrawal symptoms improved gradually, while the staff provided support and affirmation. He maintained at 2 mg of buprenorphine every 2 days. Four months later, he attempted to reduce this dosage. Eventually, he stopped buprenorphine in September and maintained abstinence from heroin, methadone, and buprenorphine. The XFZYD, SZRD, CSS, and CGKM regimen was continued. Within the 5-month period from April to September, unscheduled urine drug screenings were performed five times and indicators of heroin and amphetamine use were all negative.

Discussion

We report a case of TCM-facilitated drug switch from methadone to buprenorphine-naloxone treatment. To our knowledge, this is the first case to report TCM use during a drug switch from methadone to buprenorphine-naloxone.

Opioid dependence is a chronic illness that may result in considerable physical and psychological functional disturbances [11]. Opioid agonist therapies, such as methadone treatment and buprenorphine-naloxone maintenance treatments, have revealed significant clinical effects [12]. MMT was launched in Taiwan in 2006 following an HIV/AIDS outbreak among intravenous drug users, and the treatment programs are being continuously developed [13,14]. In Taiwan, MMT has effectively controlled drug craving, facilitated lifestyle remodeling, prevented the spread of infectious diseases, and reduced criminal activity associated with heroin use [15]. However, because take-home methadone programs are not available in Taiwan in the current practice system, daily MMT may considerably inconvenience patients. Traffic congestion, the service hours of the methadone clinic, and weather disturbances, such as the frequent typhoons Taiwan experiences in summer, may inconvenience the patients. Consequently, poor methadone adherence and active heroin use are common. Therefore, buprenorphine-naloxone use can be considered a treatment of choice.

Several obstacles and challenges remain in the switch from methadone to buprenorphine, for instance, the discomfort of discontinuing methadone, precipitated withdrawal symptoms, and poor psychosocial adjustments such as anticipatory anxiety regarding severe opioid withdrawal [16]. Tapering high methadone doses before switching to buprenorphine involves discomfort and a high risk of relapse [17].

<table>
<thead>
<tr>
<th>TCM treatment</th>
<th>Major herbal ingredients</th>
<th>Treatment effects under TCM theory</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suanzaoen decoction (SZRD)</td>
<td>Sm. Zizyphi Spinosae, Poria, Rx. Anemarrhenae, Rx. Ligustici, Rx. Glycyrrhizae</td>
<td>To provide central nervous system tranquilizing effect and to improve sleep quality</td>
</tr>
<tr>
<td>Chaihu-Shugan-San (CSS)</td>
<td>Per. Citri Reticulatae, Rx. Bupleuri, Rx. Chuanxiong, Fr. Auranitl, Rx. Paeoniea Alba, Fried Rx. Glycyrrhizae, Rz. Cyperei</td>
<td>To improve the flow of systemic Qi, to relieve the stagnation of liver Qi, to relieve depression, and to provide analgesic effects</td>
</tr>
<tr>
<td>Chin-Gin-Kuan-Ming tablets</td>
<td>Chai-Hu-Jia-Long-Gu-Mu-Li-Tang, Xiao-Chaihu-Tang, and Wen-Dan-Tang</td>
<td>To promote Qi movement and to sedate and calm the spirit</td>
</tr>
</tbody>
</table>

Table 1: Major herbal ingredients and its treatment targets based on TCM theory.

The experiences of precipitated withdrawal, or the effect of buprenorphine-naloxone-induced acute opioid withdrawal symptoms, can be very traumatic for a patient seeking help, and the symptoms may be one of the leading causes of people discontinuing buprenorphine-naloxone. Sufficient counseling services in this regard should be provided [16,18,19]. Although a past study revealed that providing non-TCM ancillary medication during buprenorphine detoxification does not improve treatment outcomes [20], TCM was provided to our case. We hypothesized that successfully switching from methadone to buprenorphine will enhance the patient's perceived...
control and psychological resilience as well as improve their quality of life [21].

Some herbal regimens have been proven to be effective in relieving the withdrawal symptoms of opioid use [22]. TCM treatments can deliver pain relief and can treat comorbidities, such as hepatitis, constipation, and pain, in heroin users, as well as provide a collaborative and holistic care model that is based on TCM healthcare theory. The Han ethnic group is noted for having an aversion to the long-term use of Western medication. Moreover, methadone is often highly stigmatized and incorrectly considered a hepatic and renal toxin. In addition to relevant knowledge of MMT, adjunctive TCM treatments may offer heroin users new and culturally appropriate approaches with higher motivational enhancement and psychological acceptability.

In this case, we applied TCM for the following reasons: enhancement of methadone metabolism and detoxification, analgesic effects, and anxiolytic and hypnotic effects during the drug switch. XFZYD was prescribed for reducing the concentration of methadone and expelling the remaining methadone from the body to prevent precipitated withdrawal. SZRD was prescribed to relieve anxiety and improve sleep quality. Because the patient was often depressed and irradiated, CSS and CKGM were prescribed to relieve anxiety, depression, and pain symptoms.

Animal models and in vitro studies have provided hypotheses for the mechanisms underlying TCM treatment. Past studies have revealed that XFZYD potentiated r-tPA-mediated neuroprotection against thromboembolic stroke in rats. This neuroprotection is probably mediated by the inhibition of HIF-1 α and TNF-α, followed by the inhibition of inflammatory responses (i.e., iNOS) and apoptosis (active caspase-3) [23]. SZRD increases sleep activity and exhibits binding affinity for serotonin receptors [24]. An aqueous extract of CSS has antidepressant-like effects in animal models and its antidepressant mechanisms are mediated by reversing the stress-induced disruption of ERK5 activity [25]. CGKM tablets were composed of ingredients including Chai-Hu-Jia-Long-Gu-Mu-Li-Tang, Xiao-Chaihu-Tang, and Wen-Dan-Tang. Chai-Hu-Jia-Long-Gu-Mu-Li-Tang may also protect against hypercholesterolemia and atheromatous lesions by affecting apoE and LDL receptor mRNA expression in the liver [26]. Xiao-Chaihu-Tang exhibited therapeutic effects in animal models of depression through enhancing the serotoninergic system in the prefrontal cortex and hippocampus [27] Wen-Dan-Tang treatment may regulate negative emotions induced by sleep deprivation through regulation of orexin-A and leptin expression [28].

In conclusion, in our study, TCM medications were demonstrated to be effective in alleviating discomfort during the initial methadone withdrawal period and reducing the occurrence of precipitated withdrawal induced by buprenorphine-naloxone treatment. The medications also produced a holistic and multidisciplinary treatment effect that improved the patient's psychological resilience. A TCM-facilitated drug switch from methadone to buprenorphine has potential as an optimal treatment model. Further studies should address TCM treatment for heroin-dependent individuals during the period of switching from methadone to buprenorphine-naloxone.

References

26. Yoshie F (2001) Protective effects of Saiko-ka-ryukotsu-borei-to (Chai-Hu-Jia-Long-Gu-Mu-Li-Tang) against atherosclerosis in Karasawa and...
