

# Heroin-induced headache in female heroin addicts

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## Abstract

**Objective:** To investigate the manifestations and incidence of headaches caused by heroin in Chinese women.

**Methods:** This was a survey study conducted from 29 June to 3 July 2015 with women attending the Shanxi Drug Rehabilitation Centre for Women (China). All study subjects were newly admitted and had not begun their drug rehabilitation. Demographic characteristics, heroin usage and headache episodes within the previous 3 months were surveyed, especially the presence of a headache within 2 hours of heroin use. Details of the severity, location, premonitory symptoms and characteristics of headaches were recorded.

**Results:** Of the 90 heroin-dependent patients, 74 experienced headache attacks within 2 hours of heroin use, and the headaches subsided within 72 hours of discontinuation of heroin use. Most heroin-induced headaches were similar to migraines and manifested as pulsating pain in 54 patients (51/74, 68.9%); bilateral pain was reported by 46 patients (46/74, 62.2%). Approximately half of the patients with heroin-induced headaches also reported accompanying symptoms of nausea, vomiting, and light and sound sensitivity.

**Conclusions:** Heroin-induced headache may eventually be listed as a new class of headache in the International Classification of Headache Disorders.

## Keywords

Headache, heroin, women, migraine-like headache, heroin-induced headache, China

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## Introduction

Although the use of recreational drugs dates back to antiquity, the phenomenon of headaches caused by illicit drugs is a relatively recent phenomenon that was first described in the 1980s.<sup>1</sup> Headache is a common symptom following drug use, and has a very high incidence rate. For example,

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Fofi et al.<sup>2</sup> reported that the prevalence of headache among cocaine addicts was 90%. Substances known to cause headache include cocaine and methamphetamine.<sup>2-4</sup>

Opioid addiction is a global issue and is a complex chronic brain disease caused by long-term opioid abuse. Heroin is the most commonly used opioid and is often called the 'king of the opioids'. As many as 14 million to 21 million people worldwide use heroin,<sup>5</sup> and it is the most widely used illicit drug among drug users in China.<sup>6</sup> According to the 2015 China Anti-Drug Report, by the end of 2014, there were 2.098 million drug addicts in China and 1.272 million opioid users, most of whom (1.245 million) were heroin users.<sup>7</sup>

Many studies have been conducted on cocaine-induced headaches in European and American countries,<sup>2,8,9</sup> probably because of the large number of cocaine addicts in these countries. International studies on heroin-induced headaches are very rare. To the best of our knowledge, the only study on this topic was published by De Marinis et al.<sup>10</sup> in 1991. The authors recruited 40 opioid addicts (30 men, 10 women) and described their headache episodes. The overuse of opiates for the management of migraines leads to medication overuse headaches in many patients.<sup>11,12</sup> There are currently no studies on the incidence of headaches caused by heroin in China. Because heroin is the most widely used drug in China, there is a need for research on heroin-induced headaches to improve the management of these patients.

Generally, men account for a higher percentage of drug addicts than women.<sup>13</sup> However, the most common headache types, including migraine, tension-type headache and medication overuse-induced headache, are much more common in women than in men.<sup>14</sup> Therefore, the aim of the present study was to examine the characteristics of heroin-induced headaches in female heroin addicts.

## Materials and methods

### Study design and subjects

This was a survey study conducted with women attending a drug addiction rehabilitation centre in China. One centre was randomly selected from the 32 official drug rehabilitation centres in China: the Shanxi Drug Rehabilitation Centre for Women. After the World Drug Abuse Day on 26 June 2015, a number of new drug addicts were admitted to this drug addiction rehabilitation centre. The survey was conducted from 29 June to 3 July 2015. The study was approved by the ethics committee of the Chinese PLA General Hospital (#2014S00959). All participants provided written informed consent before inclusion in the study.

The inclusion criteria were 1) diagnosis of heroin addiction according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV);<sup>15</sup> 2) no history of methadone replacement therapy; 3) no history of withdrawal therapy; and 4) no use of addictive drugs other than heroin. The exclusion criteria were 1) other types of secondary headaches such as post-traumatic headache and history of migraines (at admission a neurologist carefully explained the clinical manifestations and diagnostic criteria of migraine to the women and asked them to carefully recall whether they had a history of migraine attacks before their first-ever use of heroin); 2) serious concomitant pain disorders (e.g. cancer pain or serious joint pain) and long-term oral administration of analgesics; 3) other serious systemic diseases or nervous diseases such as hypertension, cardiac disease, diabetes mellitus, liver and kidney dysfunctions, epilepsy, dementia or stroke; 4) positive for human immunodeficiency virus or syphilis (because acquired immunodeficiency syndrome and syphilis may cause brain lesions that can

lead to headache); or 5) incomplete medical records.

### Questionnaire

The questionnaire comprised three parts: 1) basic demographical data; 2) heroin usage; and 3) headache diagnosis (Supplementary Material). Parts 1 and 3 included questions selected from the headache questionnaire of the Lifting The Burden (LTB) campaign initiated by the World Health Organization.<sup>16</sup> The Chinese version of the LTB questionnaire has demonstrated reliability and validity for diagnosing headache in China. This questionnaire has been used in a national population-based epidemiological survey of headaches<sup>17</sup> and for special populations in China.<sup>18,19</sup> The demographic data recorded were age, educational level and annual income. Questions related to headache diagnosis focused on the quality, severity, concomitant symptoms and aggravating/alleviating factors of headaches. Details of headache episodes after heroin use were recorded and included headache onset, the length of time between heroin use and headache onset, degree of headache (measured by a visual analogue scale), the duration of the headache before its relief, and changes in the headache caused by heroin use during the headache episodes. Part 2 of the questionnaire focused on heroin usage and included details of the duration, methods, dose, monthly frequency over the past 3 months and whether other drugs were simultaneously used. Participants without headaches filled out only Parts 1 and 2; participants with headaches were required to complete the entire questionnaire.

The researchers who conducted the survey were neurologists familiar with the content of the questionnaire and the protocols for headache diagnosis and treatment. The same researchers administered a face-to-face questionnaire with heroin-dependent

patients. The doctors explained the purpose and method of the research to each potential research subject in a private room and administered the questionnaire. Thirty surveys were completed on a working day, and the survey was conducted for 4 days.

### Diagnostic criteria

The 3rd edition (beta version) of the International Classification of Headache Disorders (ICHD-3 beta) by the Headache Classification Committee of the International Headache Society (2013) was used for headache diagnosis.<sup>20,21</sup>

### Statistical analysis

SPSS version 17.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. The Kolmogorov–Smirnov normality test was performed to determine the distribution of continuous data. Data following the normal distribution were expressed as means  $\pm$  standard deviations and analysed using analysis of variance and the Student–Newman–Keuls *q* post hoc test. Continuous data that did not follow the normal distribution were described as medians (25th and 75th percentiles) and analysed using the Kruskal–Wallis *H* test. Categorical data were expressed as frequencies (percentages) and were analysed using the chi-square test. *P*-values  $<0.05$  indicated a statistically significant difference.

## Results

### Demographic data

The survey was conducted with 101 patients from 29 June to 3 July 2015. After the exclusion of nine patients who declined to participate in the study and two patients whose questionnaires were incomplete, data for 90 heroin-dependent women were included in the analysis, a participation rate of 89.1%. Table 1 presents the demographic

**Table 1.** Demographic characteristics of the 90 female heroin-dependent patients.

Characteristics	Female heroin-dependent patients
Age (years)	32.4 ± 10.6
Educational level, n (%)	
Middle school and below	57 (63.3)
High school or vocational-technical school	26 (28.9)
College and above	7 (7.8)
Annual income, n (%)	
CNY <15,000	39 (43.3)
CNY 15,000–30,000	17 (18.2)
CNY >30,000	34 (37.8)

Data are means ± standard deviations unless otherwise stated.

characteristics of the patients. The educational level and income of the 90 heroin-dependent patients was relatively low.

#### *Demographic and heroin usage data for patients with/without headaches after heroin use*

Of the 90 patients, 74 had headache attacks occurring within 2 hours of heroin use and subsiding within 72 hours of discontinuation of heroin use. The two groups of patients (with vs. without headaches after acute heroin use) did not show any significant differences in demographic characteristics. No patients had had migraines prior to their first use of heroin. In addition, the groups did not significantly differ in the age at first drug use, duration of heroin use history and method of heroin use. Patients who had headaches after heroin use used heroin significantly more frequently than patients without headaches after heroin use (median, 8 vs. 5,  $P = 0.02$ ) (Table 2).

#### *Clinical characteristics of headache attacks after acute heroin use*

Headaches caused by heroin use were reported to be similar to migraines and manifested as pulsating pain in 54 patients

(51/74, 68.9%). Approximately half of the patients with headaches also had other symptoms of vomiting, nausea and light/sound sensitivity (Table 3). Bilateral pain was reported by 46 patients (46/74, 62.2%). Of the 74 patients who experienced heroin-induced headaches, 45 took heroin again during the headache episodes, but retaking heroin aggravated rather than alleviated the existing headache. Indeed, of the 56 patients who took heroin again when the heroin-induced headache occurred, 40 (40/56, 71.4%) experienced deterioration of the headache and only 2 patients (2/45, 4.4%) experienced headache relief.

## **Discussion**

Opioid addiction is a global issue, and heroin is the most widely used opioid in China.<sup>6,7</sup> There are no studies on headaches in heroin-dependent women. This study aimed to investigate the manifestations and incidence of headaches caused by heroin in Chinese women and to examine the possible mechanisms. The results suggest a very high incidence rate of headache within 2 hours of heroin use. Heroin-induced headache may eventually be listed as a new class of headache in the ICHD-3.

**Table 2.** Comparison of general characteristics and heroin usage between patients with/without headaches after acute heroin use.

Characteristics	Patients with headaches after heroin use (n = 74)	Patients without headaches after heroin use (n = 16)	P
Age (years)	30.6 ± 10.2	29.63 ± 9.8	0.751
Age at first drug use (years)	27.5 ± 9.4	24.6 ± 7.6	0.064
Frequency of heroin use (number of times per month)	8 (5, 16)	5 (3, 13)	0.015
Duration of heroin use history (years)	6.3 ± 2.5	5.9 ± 1.7	0.083
Amount of heroin used per month (g)	68.5 ± 13.6	65.3 ± 9.3	0.074
Method of heroin use, n (%)			
Oral use or snorting	50 (67.6)	11 (68.8)	0.830
Intravenous injection	22 (29.7)	84 (25)	
Other	2 (2.7)	1 (6.3)	

Data are means ± standard deviations unless otherwise stated.

**Table 3.** Characteristics of headaches after acute heroin use.

Characteristics	Patients (n = 74)
Family history of headache of any type, n (%)	20 (27.0)
Years of headache history	5.7 ± 3.1
Frequency of headache attacks (times per month)	10 (3, 18)
Degree of headache (visual analogue scale)	7.1 ± 2.2
Whether used heroin during a headache attack, n (%)	
Yes	56 (61.5)
No	35 (38.5)
Duration from heroin use to the onset of headache, n (%)	
<2 hours	3 (4.1)
2–4 hours	13 (17.6)
>4 hours	58 (78.4)
<72 hours	74 (100)
Characteristics of headache, n (%)	
Pulsating pain	51 (68.9)
Swelling pain	13 (17.6)
Others	10 (13.5)
Location of headache, n (%)	
Bilateral	46 (62.2)
Unilateral	28 (37.8)
Concomitant symptoms, n (%)	
Vomiting/nausea	36 (48.6)
Photophobia/phonophobia	39 (50.7)

Data are means ± standard deviations unless otherwise stated.

The educational level of the 90 heroin-dependent patients was considerably lower than that of the general Chinese female population.<sup>22</sup> Overall, heroin-dependent patients had a relatively low income; 61.5% estimated their annual income at CNY 30,000 or below, whereas the gross national income per capita of China is CNY 39,351, according to the World Bank database.<sup>23</sup>

This study primarily investigated the frequency, type and characteristics of headaches induced by acute heroin use in female heroin-dependent patients. The results revealed a high incidence of acute headache after heroin use in these patients (74/90, 82.2%), which is remarkably higher than the incidence of headache among the general female population.<sup>17</sup> However, there are no other studies on the incidence of headaches caused by heroin. Fofi et al.<sup>2</sup> reported that the prevalence of headache among cocaine addicts was 90%, but the mechanisms underlying heroin and cocaine action are different.<sup>24-26</sup> The few studies that have focused on headaches in patients addicted to other drugs have shown that headaches often occur in patients addicted to drugs such as cocaine, methamphetamine and 3,4-methylenedioxymethamphetamine ('Ecstasy').<sup>2-4,9</sup> Fofi et al.<sup>2</sup> conducted a study of 80 cocaine-dependent patients and found that 72 patients (13 men and 59 women) experienced headaches after cocaine use. The present study showed that the headaches induced by heroin use in female heroin-dependent patients were similar to migraine and were rarely accompanied by premonitory signs. This type of headache manifested mainly as pulsating pain accompanied by other symptoms such as vomiting, nausea and light/sound sensitivity. Most patients reported moderate to severe heroin-induced headaches that were aggravated by physical activity. These characteristics are similar to those of migraine headaches. However, 62.2%

of patients reported bilateral pain, whereas migraines are usually unilateral.<sup>20,21</sup> The mechanisms involved in opioid-induced pain are still poorly understood.<sup>11,27,28</sup>

In this study, headaches occurred within 2 hours of heroin use and subsided within 72 hours of acute use in 74 of the 90 heroin-dependent patients. Because the study subjects had not yet received any drug rehabilitation, their headaches could not be categorised as heroin-withdrawal headaches and did not belong to any existing categories listed in the ICHD-3. Therefore, we named this condition a heroin-induced headache. The heroin-induced headache identified in this study is not specifically classified in the ICHD-3. The two subtypes that are closest are '8.1.13: Headache attributed to the use of or exposure to other substances' and '8.2.4: Opioid-overuse headache'. Therefore, we suggest the inclusion of a subtype of headache named 'heroin-induced headache' in ICHD-3, similar to '8.1.6: Cocaine-induced headache'. Of the headache episodes in the heroin-dependent patients in this study, 98% met the diagnostic criteria of '8.1.13: Headache attributed to the use of or exposure to other substances'. For example, the headache attacks after heroin use in heroin-dependent patients mostly occurred within 12 hours of heroin use and subsided within 72 hours of discontinuation of heroin use. Nevertheless, additional studies are needed to more fully describe and understand this type of headache.

In ICHD-3, the subtypes '8.1.1-8.1.12' under '8.1: Headache attributed to use of or exposure to a substance' include headache induced by a specified substance (e.g. '8.1.1: Nitric oxide (NO) donor-induced headache', '8.1.2: Phosphodiesterase (PDE) inhibitor-induced headache', and '8.1.6: Cocaine-induced headache'). Apart from the above-mentioned substances, headaches induced by other substances are all classified as '8.1.13: Headache attributed to the use of

or exposure to other substances'. Therefore, the subtype '8.1.13' is almost clinically meaningless because it includes headache types induced by any substance except for the substances mentioned above. A broad range of substances can induce headaches, including traditional Chinese medicine and other plant and animal substances. Many substances that can induce headaches are not specified in the ICHD-3; instead, their induced headaches are all included in one subtype ('8.1.13') with relatively general diagnostic criteria. Owing to a lack of specific diagnostic criteria, this classification system is of little use in future research on heroin-induced headaches.

The subtype '8.2.4: Opioid-overuse headache' is under '8.2: Medication-overuse headache'. However, although heroin is a type of opioid, only a very small portion of headache attacks in heroin-dependent patients meet the diagnostic criteria of this headache subtype (7.8%). The diagnostic criteria for '8.2.4: Opioid-overuse headache' include all of the following: 1) a previous headache history; 2) current headache frequency  $\geq 15$  days per month; and 3) regular intake of one or more opioids on  $\geq 10$  days per month for  $>3$  months. In this study, only 23% of the heroin-dependent patients had a headache history. In addition, the heroin use frequency of the patients was irregular owing to a variety of influencing factors, and very few patients used heroin on  $\geq 10$  days per month for more than 3 consecutive months. Therefore, very few patients met the diagnostic criteria for '8.2.4: Opioid-overuse headache'.

There are some limitations to this study. The sample size was small, and the subjects were from only one detoxification centre in China. Whether the results of this study can be applied to other regions in China or other countries remains unknown. In addition, headache changes after the onset of heroin-withdrawal therapy were not followed and observed after the study.

Finally, the treatments taken by the women to manage the headaches were not recorded.

Considering the very high incidence rate and unique characteristics of headache after acute heroin use, the further understanding of headaches in heroin-dependent patients, and the development of an effective treatment approach, have great social significance. Therefore, we hope that more attention will be paid to this topic and recommend that 'heroin-induced headache' be listed as a separate type with specific diagnostic criteria in the final official version of the ICHD-3. We believe this topic is of great importance for both basic and clinical research on heroin dependency and heroin-induced headaches.

### Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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### Supplemental material

Supplemental material for this article is available online.

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