Drug and Alcohol Dependence 194 (2019) 302–309

Contents lists available at ScienceDirect

Drug and Alcohol Dependence

journal homepage: www.elsevier.com/locate/drugalcdep

Full length article

Reduction in methamphetamine consumption trends from 2015 to 2018 detected by wastewater-based epidemiology in Dalian, China

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ARTICLE INFO

Keywords:
Methamphetamine
Wastewater-based epidemiology
Long-term monitoring
Reduction trend

ABSTRACT

Background: Wastewater-based epidemiology (WBE) has become a useful tool in long-term or short-term continuous monitoring of illicit drugs consumption over the world.
Methods: We investigated the trend of methamphetamine (METH) use between 2015 and 2018 through WBE in Dalian, a typical Chinese city. Samples were collected in 11 municipal wastewater treatment plants (WWTPs). An analytical method, solid-phase extraction combined with trifluoroacetic anhydride derivatization prior to gas chromatography–mass spectrometry (GC–MS) analysis was applied to detect METH concentrations.
Results: During the sampling period, the METH concentrations increased slowly from 315 ± 243 ng/L in 2015 to 523 ± 549 ng/L in 2016, followed by a significant decrease with the concentrations 188 ± 187 ng/L in 2017 and 54.6 ± 42.9 ng/L in 2018. Ammonium nitrogen (NH_4-N) was applied to estimate population size. The average coefficient of variation for population in 11 WWTPs was 35.3 ± 8.9%, reflecting the dynamic variations of population effectively. For METH consumption, there was a gradual increase from 2015 (231 mg/day/1000 people) to 2016 (414 mg/day/1000 people) and a significant linear decrease to 2017 (206 mg/day/1000 people) and 2018 (53.9 mg/day/1000 people). The prevalence of METH increased from 2015 (0.78%) to 2016 (1.06%), then decreased to 2017 (0.55%) and 2018 (0.17%), showed similar trends with the consumption.
Conclusions: The obvious reduction trends of METH consumption via WBE over the period in Dalian provides objective evidence for declined METH consumption in local population. The reduction is probably due to the severe crack-down of illicit drugs by the government.

1. Introduction

The abuse of illicit drugs has attracted worldwide attention. According to the Annual Report on Drug Control in China (2014–2016) (Office of China National Narcotic Cotrol Commission, 2014, 2015, 2016a), the percentage of synthetic drug abusers increased significantly, from 49.4% in 2014 to 60.5% in 2016. More than 80% of synthetic drug abusers mainly use methamphetamine (METH). The abuse of METH can not only seriously affect the abuser's health (Degenhardt et al., 2011), but can also indirectly cause numerous social problems (Tscharke et al., 2016). Therefore, it is particularly important to monitor the level of METH abuse in population. Meanwhile, anti-drug policies can be formulated more reasonably and measures can be implemented more effectively.

The direct questionnaires survey method is a major component of traditional methods for monitoring illicit drug abuse (Ort et al., 2014). However, the surveys are labor-intensive and time-consuming (Wang et al., 2016a), and the obtained results may be subject to errors arising from reporting biases and low response rates (Lai et al., 2013b). In addition, illicit drug consumption obtained from integrating with other indirect consumers' data, such as crime statistics, medical records, drug production and seizure rates, can also introduce an additional error due to the time lags (Maida et al., 2017). To address the inherent limitations of traditional methods, a new method for monitoring drug abuse has been proposed, namely Wastewater-based epidemiology (WBE). It is based on the determination of the concentrations of the drugs themselves and/or their metabolites excreted by drug users in raw wastewater. Combined with the information of daily flow rate, the population served by wastewater treatment plants (WWTPs) and the human metabolic parameters of related drugs, the concentrations were used to

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https://doi.org/10.1016/j.drugalcdep.2018.10.023
Received 9 August 2018; Received in revised form 21 October 2018; Accepted 23 October 2018
Available online 14 November 2018
0376-8716/

Table 1
Flow rate, concentrations of METH and NH_4-N in wastewater, NH_4-N population, the coefficient of population variation, mass load, consumption and prevalence of METH for each WWTP.

WWTPs	Flow rate ($\times 10^4\,m^3$/d)	CMETH (ng/L)	CNH4-N (mg/L)	Population ($\times 10^4$)	Population CV (%)	Mass load (mg/day/1000 people)	Consumption (mg/day/1000 people)	Prevalence (%)
CYI	8	186 ± 132	25.7 ± 6.29	34.3 ± 8.17	23.8	49.6 ± 49.1	184 ± 182	0.50
CER	12	257 ± 271	32.8 ± 7.67	64.8 ± 16.1	24.8	55.0 ± 68.1	204 ± 252	0.54
MYI	10	234 ± 221	24.3 ± 9.77	40.1 ± 16.7	41.7	58.1 ± 54.8	215 ± 203	0.67
MER	8.15	249 ± 183	28.3 ± 9.16	38.5 ± 12.8	33.3	50.8 ± 36.8	188 ± 136	0.61
LSH	5.5	164 ± 211	24.9 ± 10.7	22.3 ± 9.21	41.4	34.7 ± 43.2	128 ± 160	0.45
QSH	3.4	304 ± 288	37.1 ± 14.0	20.7 ± 7.88	38.0	43.0 ± 38.5	159 ± 142	0.57
SEG	8	293 ± 292	24.3 ± 10.9	31.1 ± 13.6	43.7	78.7 ± 88.1	291 ± 326	0.83
XJH	3	311 ± 447	35.5 ± 11.7	17.7 ± 5.61	31.7	51.5 ± 72.8	190 ± 269	0.60
FJZ	0.7	235 ± 392	16.1 ± 3.65	1.87 ± 0.395	21.1	92.2 ± 148	341 ± 548	1.01
LHT	8	250 ± 443	17.2 ± 8.22	22.1 ± 10.3	46.8	81.4 ± 112	301 ± 414	1.00
HTX	2.5	126 ± 123	13.9 ± 5.70	5.60 ± 2.32	41.5	60.6 ± 68.5	224 ± 253	0.63

back-calculate drug consumption in almost real time (Archer et al., 2018; Castiglioni et al., 2014; Daughton, 2001).

WBE has been used to assess patterns of METH consumption over different time periods and across different regions in China. It has been applied to estimate the daily, diurnal, or seasonal variations (Lai et al., 2013a; Zhang et al., 2017). As reported, the method was successfully applied to investigate variations between the urban center and suburban areas in Beijing (Li et al., 2014), four megacities (Khan et al., 2014) and 18 major cities across China (Du et al., 2015). In addition, Pei et al. (2016) assessed uncertainty and variability of METH use by Monte Carlo simulation and reported the number of abusers and prevalence of METH use among the general population in China for the first time.

Long-term monitoring on METH can provide some meaningful information about patterns of drug abuse over time. Although most studies in China provided useful insights on METH consumption, long-term monitoring studies have not yet been conducted in China. Studies about long-term monitoring of METH consumption through WBE were mainly reported in Australia, including two studies in the capital of the state of South Australia (Tscharke et al., 2015, 2016) and three in South East Queensland (Bruno et al., 2018; Gao et al., 2018; Lai et al., 2016). Additionally, a few long-term monitoring studies have measured METH consumption in European countries, such as Italy (Zuccato et al., 2011), Belgium (Been et al., 2016), Spain (Mastroianni et al., 2017) and multiple other European cities (European Monitoring Centre for Drugs and Drug Addiction, 2018; Ort et al., 2014). These studies covered different periods of time, but showed the same upward trends and most of the results through WBE showed good agreement with traditional reports.

However, it remains challenging to carry out long-time monitoring of population drug consumption through WBE, due to population fluctuation in the sampling areas, different characteristics of users, and a smaller sample size, which might not accurately reflect the overall trend (Boogaerts et al., 2016). Thus, it is important to use dynamic populations to reflect population mobility and collect large numbers of samples for analysis in long-term monitoring techniques (van Nuijs et al., 2011a).

Census data of population were mainly used in previous long-term monitoring studies. However, updating census data is a time-consuming process, and it does not reflect the variations of population in real time. Moreover, water quality parameters, such as biological oxygen demand (BOD_5), nitrogen (N), phosphorus (P) and chemical oxygen demand (COD), were also applied in some studies to obtain population size (van Nuijs et al., 2011b; Zuccato et al., 2016), but these parameters are easily influenced by industrial pollution sources, which can reduce the accuracy of experimental results. In order to better reflect the fluctuation of population during the long-term drug abuse monitoring, ammonium nitrogen (NH_4-N) is proposed for back-calculation in this study, which serves as an indirect marker of urine and is supposed to be less affected by industrial pollution sources (Been et al., 2014; Zheng et al., 2017). In this way, the fluctuation of population can be reflected effectively.

This study was designed to assess the trend of METH consumption in Dalian. To achieve this, more than 170 raw wastewater samples collected from the wastewater treatment plants from 2015 to 2018 were analyzed using GC–MS. The population was calculated from mass load of NH_4-N to obtain an accurate reflection of population variation. The final variation trend of METH consumption was obtained by combining the concentrations of METH in wastewater, flow rate, population size and the correction factor.

2. Material and methods

2.1. Reagents and materials

METH was purchased from Cerilliant (Round Rock, TX, USA) with concentrations of 1 mg/mL in methanol (MeOH). Trifluoroacetic anhydride (TFA) was obtained from Sigma–Aldrich Inc. (Saint Louis, MO, USA). MeOH and ethyl acetate (EAC) were of pesticide grade purity (J.T. Baker, USA). Oasis MCX (60 mg, 3 mL) solid-phase extraction (SPE) cartridges and vacuum pump manifold with twenty connections were acquired from Waters Corporation (Waters, USA).

2.2. Wastewater sampling

The sampling sites were set up in Dalian, which is a popular tourist city in China. Composite 24-h samples without any chemical and physical treatment were collected from the inlet of 11 municipal WWTPs (CYI, CER, MYI, MER, LSH, QSH, SEG, XJH, FJZ, LHT, and HTX) by sampling wastewater every 30 min for 24 h with an automatic sampler JC-8000D (Qingdao Juchuang Environmental Co., Ltd, Qingdao). They are located in the four central districts of Dalian. More details of the WWTPs were given in the Table S1 and Figure S1. More details on daily flow rate of WWTPs are shown in Table 1. The sampling campaign consisted of the following months: June and November 2015, August and September 2016, January, March-October, and December 2017, February and May 2018. A total of 178 samples were collected over the period of four years. The samples were acidified to pH 2 using HCl and then stored at −20 °C until analysis.

2.3. Extraction and analysis

The wastewater samples were passed through 0.45 μm glass filters to remove solid particles. Fifty (50) mL of filtered water were extracted with an Oasis MCX SPE cartridge, which was preconditioned with 6 mL of MeOH, 4 mL of Milli-Q water, and 4 mL of Milli-Q water at pH 2, consecutively. After loading with wastewater, the cartridges were dried for five minutes under vacuum to remove excess water. The analytes were finally eluted with 4 mL of MeOH and 4 mL of 4% NH_3 in MeOH. The eluate was dried under a soft stream of nitrogen and redissolved to 200 µL of EAC. For derivatization, 25 µL TFA was then added into the solution and reacted for 60 min at 45 °C. After reaction, a certain amount of 10% $NaHCO_3$ solution was added to remove the remaining derivative reagent and adjust the solution to be neutral. The mixture was centrifuged at 2000 rpm for 3 min. The obtained organic phase was transferred to the chromatographic bottle and spiked with the internal standard of nap-d8 (50 ng/L) before analysis.

The samples were analyzed by an Agilent 7890B gas chromatograph connected to an Agilent 5977 A mass spectrometer (GC–MS) equipped with an HP-1 column (30 m × 0.25 mm × 0.25 µm, JandW Scientific). Oven temperature was as follows: the initial temperature was set at 90 °C, then increased to 180 °C at a rate of 10 °C /min. The injection volume was 1.0 µL. The injector temperature was set to 230 °C. The mass spectrometry was operated in an electron impact ionization source maintained at 230 °C and 70 eV and quadrupole was maintained at 150 °C. The retention time and mass ions of compounds are listed in Table S2.

Linearity was evaluated from the calibration curves obtained by analysis of seven standard solutions at the following concentrations for METH-TFA: 0, 10, 20, 50, 100, 200, and 500 ng/L. The regression coefficient (r^2) calculated by linear regression was 0.998. The recoveries of spiked experiments performed by comparing 50 mL super pure water spiked at the standard 200 ng/L were 109 ± 23% for METH-TFA. The limit of quantification (LOQ) for METH, calculated as 10 times signal to noise ratio, showed 2.86 ng/L. The procedure blank using ultrapure water was run for every 10 wastewater samples and following the same pretreatment steps as wastewater sample. All the target compounds were below detection limit. Detailed method validation information was presented in Table S1[2].

The determination of NH4-N was performed according to the standard methods 350.1 from the United States Environmental Protection Agency with the Nessler Method (EPA, 1993).

2.4. Back calculation of methamphetamine abuse

The daily mass load of METH per capita (m_{METH}) at a specific WWTP was estimated using the following equation:

$$m_{METH,i} = \frac{C_{METH,i} \times F_i}{P_i} \tag{1}$$

where $C_{METH,i}$ is the concentration of METH in a WWTP of i; F_i is the flow rate of raw wastewater in a WWTP of i; and P_i is the population served by a WWTP of i.

NH_4-N is used as an indirect marker of the population. The population estimated by NH_4-N is calculated as follows:

$$P_i = \frac{C_{NH_4-N,i} \times F_i}{m_{NH_4-N}} \tag{2}$$

where $C_{NH_4-N,i}$ is the concentration of NH_4-N measured in wastewater from WWTPs of i; m_{NH_4-N} is the average amount of daily NH_4-N production of each person. The value of m_{NH_4-N} was determined to be 6 g/day/capita (Zheng et al., 2017). Therefore, Eq. (1), used to calculate the mass load of METH, can be simplified as follows:

$$m_{METH,i} = \frac{C_{METH,i} \times m_{NH_4-N,i}}{C_{NH_4-N,i}} \tag{3}$$

The consumption of METH (J_{METH}) can be derived from the mass load by multiplying correction factors, and J_{METH} from each WWTPs are calculated as follows:

$$J_{METH,i} = \mathrm{m}_{METH,i} \times f \tag{4}$$

where f is the correction factor for METH, and the value of f used in this study was estimated to be 3.7 based on the excretion rate 27% of smoking (Wang, 2018).

Prevalence of METH (PR_{METH}) is important to evaluate the change trends of abusing and can be compared conveniently between different areas or different times.

$$PR(\%) = \frac{J_{METH,i}}{D \times n_D \times R_{15-64}} \times 100\% \tag{5}$$

where D is the single dose of METH abuse, and n_D is the frequency of METH abuse, R_{15-64} is the proportion of adult population aged 15–64 years among general population. D was estimated at 135 ± 80 mg in China (Pei et al., 2016). The value of n_D was determined to be 0.31 ± 0.31 dose/day/capita in China (Pei et al., 2016). The value R_{15-64} was determined to be 76.9%.

2.5. Statistical analysis

METH consumption between 2015 and 2018 was analyzed to compare the difference. Before comparing the data, the Kolmogorov-Smirnov algorithm was used to determine whether the data had a normal distribution. If it was applicable, we used the one-way ANOVA followed by the Tukey-Kramer test for multiple comparisons, or else we used the non-parametric Kruskal-Wallis test. Linear fitting was performed to test for trends in detections of METH across each year of study. All calculations and statistical tests were performed using SPSS and Origin 8.0 software, and p-value of < 0.05 was regarded as statistically significant.

3. Results

3.1. Temporal trends of METH concentrations

METH was detected in all the wastewater samples ($n = 178$) with concentrations ranging from 2.96 to 1870 ng/L (median: 159 ng/L) (Table 1 and Table S3). The METH concentrations in 11 WWTPs during four years period were shown in Fig. 1. Different trends were shown among these WWTPs. Three WWTPs (CYI, CER and MYI) showed a continuous decline trend of METH concentrations. Concentrations of METH in LSH decreased slightly from 2015 to 2016, then remained stable in 2017 and decreased in 2018. While, the results of other seven WWTPs (MYI, QSH, SEG, XJH, FJZ, LHT and HTX) presented increasing trends from 2015 to 2016 and then decreasing in the following two years.

During the sampling period (2015–2018), a tendency of obvious reduction of METH concentrations in Dalian was found (Fig. S2). The average concentrations of METH in Dalian increased slowly from 315 ± 243 ng/L in 2015 to 523 ± 549 ng/L in 2016 ($p > 0.05$, Kruskal-Wallis test), followed by a significant decrease with the concentrations at 188 ± 187 ng/L in 2017 and 54.6 ± 42.9 ng/L in 2018 ($p < 0.05$, Kruskal-Wallis test).

3.2. Population estimation

To evaluate the size of population more accurately, concentrations of NH_4-N were monitored and applied for population calculation. NH_4-N concentrations varied from 2.88 to 57.1 mg/L with the median at 24.1 mg/L (Table 1 and Table S3[3]). The concentrations of NH_4-N in 11 WWTPs during the sampling period were showed in Fig. S3. NH_4-N showed a significant difference from 2015 to 2018 ($p < 0.05$, Kruskal-Wallis test). The average concentrations of NH_4-N in 11 WWTPs remained stable between 2015 (30.2 mg/L) and 2016 (31.4 mg/L) ($p > 0.05$, Kruskal-Wallis test). Significant decrease occurred in the following two years, with the concentrations at 23.3 mg/L in 2017 and 22.8 mg/L in 2018 (2015 or 2016 vs. 2017 or 2018, $p < 0.05$, Kruskal-Wallis test).

Based on the Eq. (2), the population was calculated for each WWTP. The coefficient of variation (CV) was used to describe the variation of population over the sampling period. An average of 35.3 ± 8.9% in 11

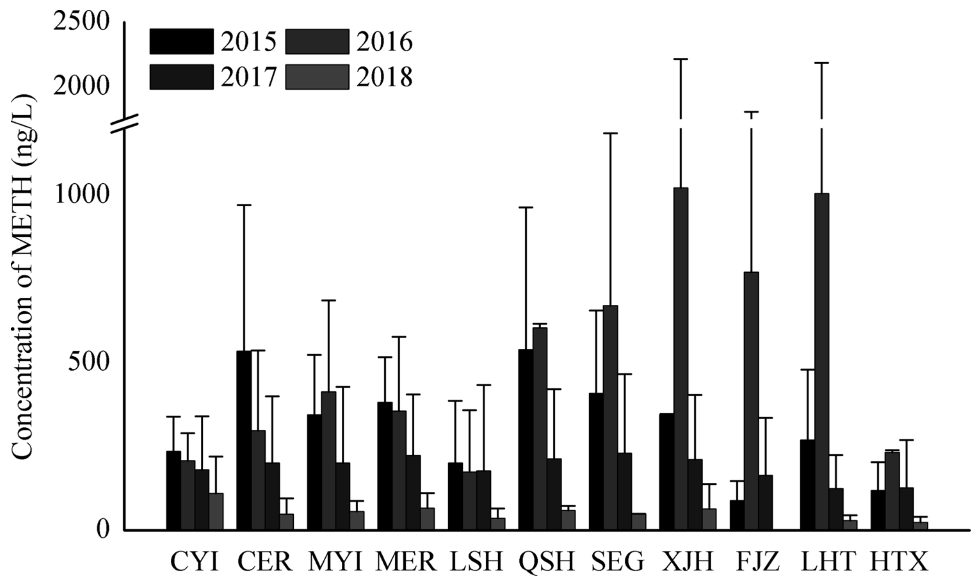

Fig. 1. Concentrations of METH in 11 WWTPs in.2015–2018.

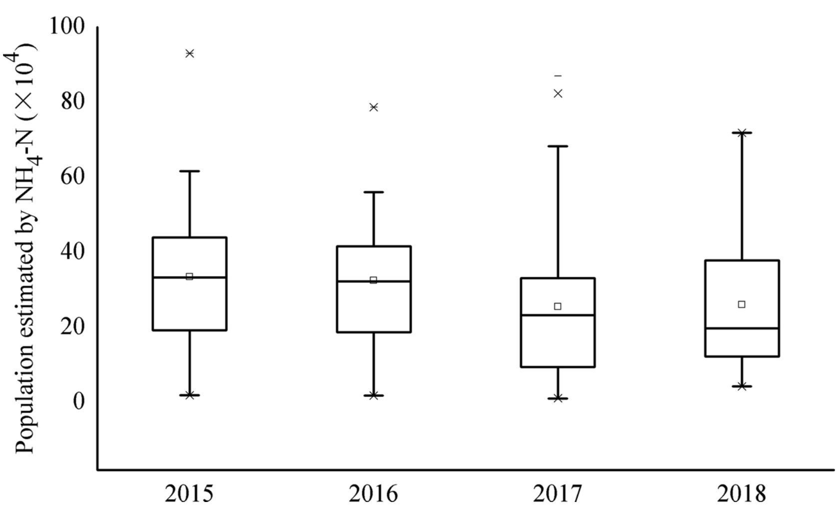

Fig. 2. Population estimated by NH4-N in.2015–2018.

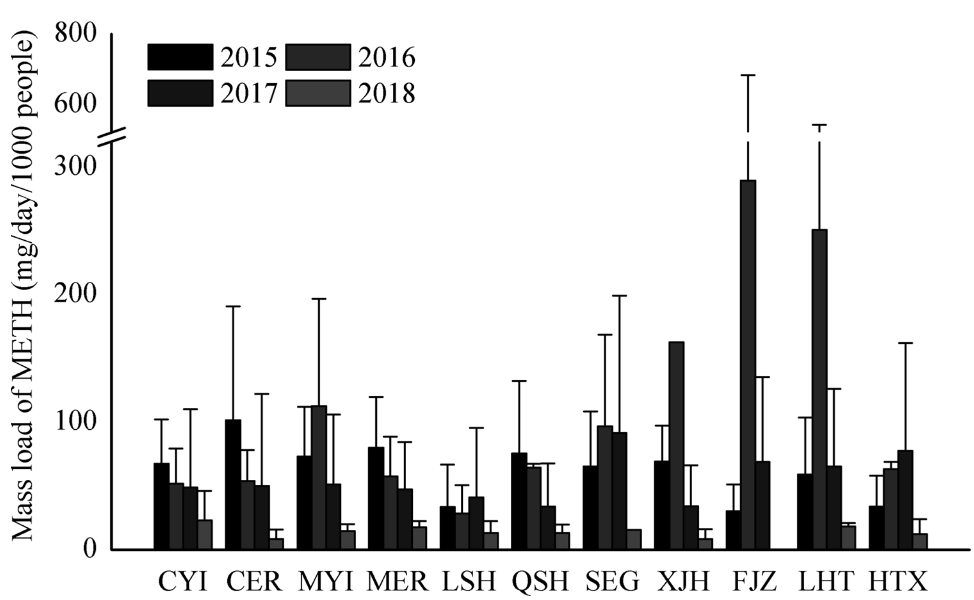

Fig. 3. Mass loads of METH in 11 WWTPs in.2015–2018.

WWTPs was obtained, which indicated the fluctuation of population over the periods. The CVs of each WWTP were showed in Table 1. The population served by the 11 WWTPs during the completed sampling period was shown in Fig. S4. The largest variation was observed in LHT (CV = 46.8%), followed by the SEG (CV = 43.7%). The population served by these two WWTPs from 2015 to 2018 reduced by more than a half. As for other WWTPs, it fluctuated slightly during the sampling period. There was no significant difference in the population in 11 WWTPs over four years ($p > 0.05$, Kruskal-Wallis test) (Fig. 2).

3.3. Mass loads of METH

The mass loads of METH in all WWTPs showed a significant difference during the sampling period ($p < 0.05$, Kruskal-Wallis test), ranging from 0.86 to 568 mg/day/1000 people with a median of 35.8 mg/day/1000 people (Table 1). A different trend of METH mass load was also observed in each WWTP. The mass loads of METH in CY, CER, MER and QSH showed a continuous decline trend from 2015 to 2018. In WWTPs of MYI, SEG, XJH, FJZ and LHT, the mass loads reached the highest in 2016 and then decreased suddenly in 2017 and 2018. In the other two WWTPs (LSH and HTX) the mass loads were higher in 2016 or 2017, but both decreased in 2018. METH mass loads in all 11 WWTPs fluctuated with an overall downward trend in 2015 to 2018 (Fig. 3).

Annual changes in the pattern of mass loads of METH was accessed in Dalian (Fig. S5). It was 62.5 mg/day/1000 people in 2015 and increased gradually to 112 mg/day/1000 people in 2016 ($p > 0.05$, Kruskal-Wallis test), then decreased dramatically for the following two years, reaching to 14.6 mg/day/1000 people in 2018, an approximately eight-fold decrease between 2016 and 2018 ($p < 0.05$, Kruskal-Wallis test).

3.4. Temporal trends of METH consumptions

Consumptions of METH were derived from the back-calculation by Eq. (4). As shown in Fig. 4, there was a gradual increase from 231 to 414 mg/day/1000 people between 2015 and 2016 ($p > 0.05$, Kruskal-Wallis test) and a significant linear decrease occurred since 2016, reaching to 206 mg/day/1000 people in 2017 and 53.9 mg/day/1000 people in 2018 (2015 or 2016 vs. 2017 or 2018, $p < 0.05$, Kruskal-Wallis test). The results demonstrated an overall downward trend of METH use during 2015–2018 ($p < 0.05$; $R^2 = 0.75$). The consumptions of METH in 11 WWTPs during the sampling period were shown in Fig. S6.

3.5. Prevalence of METH among adults (15–64 years old)

Based on Eq. (5), the prevalence of METH use among the adult population aged 15–64 years over the four years was estimated in Dalian. The result showed a similar tendency to the METH consumption, which increased between 2015 (0.78%) and 2016 (1.06%), and decreased noticeably to 2017 (0.55%) and 2018 (0.17%) (Fig. 5).

4. Discussion

Several studies have demonstrated the feasibility of using WBE method to distinguish the precursors and manufacturing processes used to manufacture METH (Castrignanò et al., 2017; Gao et al., 2018; Kasprzyk-Hordern and Baker, 2012). METH manufactured by pseudoephedrine or ephedrine is mainly composed of S(+)-METH, while METH manufactured by phenyl-2-epene is mainly composed of R(-)-METH (Xu et al., 2017). While some studies reported that S(+)-METH is the predominant enantiomer in major Chinese cities, these results suggested that the abuse of METH in China is mainly centered around the derivative manufactured by pseudoephedrine or ephedrine (Wang et al., 2015; Xu et al., 2017). Thus, the enantiomer problem is not considered in this study.

METH concentrations of all samples were above LOQ in 11 WWTPs, demonstrating pervasive abuse in Dalian. Compared with other studies in China, METH concentrations in this study in 2015 and 2016 were higher than the national level (227 ng/L) (Du et al., 2015) and the average concentration (401 ng/L) of four Chinese megacities (Khan et al., 2014). However, METH concentrations in 2017 and 2018 were much lower than these two studies. The significant reduction of METH concentrations in 11 WWTPs may be attributable to the drug crackdown by the anti-drug department or the decreasing use of METH since 2016 in Dalian.

The fluctuations in the size of the investigated population directly affect the accuracy of the results in wastewater studies. The population estimated by NH_4-N in 11 WWTPs was observed with large variations during the sampling period, especially in LHT and SEG. This may be due to the fact that LHT and SEG are close to a tourist attraction and SEG is located next to LHT. The average of coefficient of variation (CV) in 11 WWTPs is higher than the variation of 18% over 235 days in Brussels (van Nuijs et al., 2011b) and 15.6% over 311 monitoring days in South East Queensland (Lai et al., 2014). The situation in Dalian - that millions of people flow in and out in such a tourist city may lead to the result. However, the population estimation based NH_4-N concentration can effectively reflect the fluctuation of population in real time and is suitable for long-term monitoring of METH use in cities with large

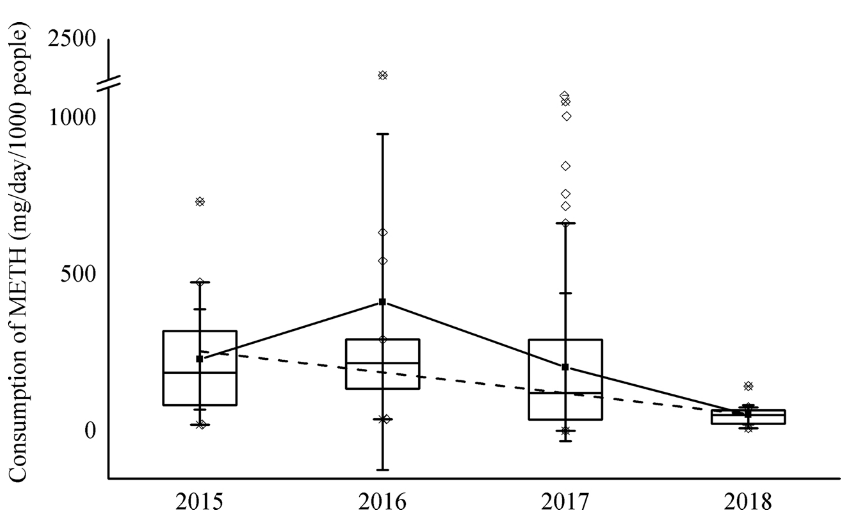

Fig. 4. Estimated consumptions of METH in the 11 WWTPs in 2015–2018. Data is presented in the box plot, with the linear trend (dashed line).

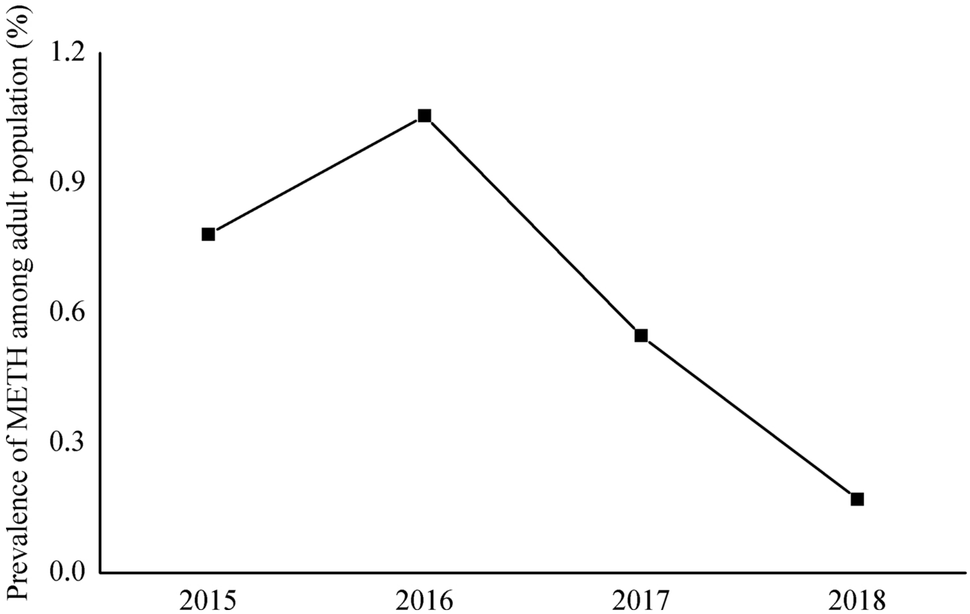

Fig. 5. Prevalence of METH among adult population aged 15–64 years old in.2015–2018.

floating population.

The average mass load of METH in Dalian (58.2 mg/day/1000 people) was at the same level as the results in major Chinese cities (69.5 mg/day/1000 people) (Du et al., 2015) and Oslo (55.7 mg/day/1000 people) (Löve et al., 2018). However, it was much higher than the loads reported in South Korea (10.4 mg/day/1000 people) (Kim et al., 2015) and most European countries (Löve et al., 2018), such as Reykjavik (32.7 mg/day/1000 people), Stockholm (25.3 mg/day/1000 people), Torshavn (4.61 mg/day/1000 people), and Germany (2.05 mg/day/1000 people) (Meyer et al., 2015). In addition, it is much lower than the mass load of METH in Australia (397 mg/day/1000 people) (Tscharke et al., 2015) and slightly lower than that in Helsinki (83.4 mg/day/1000 people) (Fig. S7). This finding is in line with the fact that the METH market in Oceania and Asia is larger than that in Europe (United Nations Office on Drugs and Crime, 2016). Considering the differences in the correction factors selected in different studies, we calculated and compared the consumption in different regions respectively. The comparison results were similar to that of mass load;, that is, the METH consumption in Oceania and Asia was still higher than that in Europe (Fig. S8).

The prevalence in our study of 2016 is much higher than the value (0.58%) in Beijing (Pei et al., 2016) and also actually higher than the 12-month prevalence (best estimate = 0.57%, range of 0.22–1.29%) of the use of amphetamine-type stimulants in East and South-East Asia (United Nations Office on Drugs and Crime, 2016). The high prevalence of METH in Dalian is probably linked to the high levels of METH availability and cheap price. North Korea's METH production also largely contributes to the high prevalence of METH given close proximity of the two locations (Fish, 2011) (Fig. S9). Wang et al. also reported the high mass loads of METH in the Yalu River, due to the location on the border of China and North Korea (Wang et al., 2016b). There is no prevalence in 2017 and 2018 in traditional reports, the results in this study show the advantage of WBE, which can estimate the prevalence in real-time.

WBE can provide supplementary information through long-term monitoring studies compared to traditional methods. However, there are also some sources of variability, such as the metabolic rate in different individuals, sampling period, population fluctuation in the sampling areas and other factors (Castiglioni et al., 2014). For the metabolic rate, it is believable that the effect on the results can be effectively reduced with large numbers of samples (Zuccato et al., 2011). In the long-term monitoring study, the setting of sampling time is very important. However, due to the limitation of time, funds and so on, it is difficult to collect wastewater samples every day during such a long sampling period. To this end, we have made every effort to reduce the variability by collecting samples during at least two months of each sample year. In view of the fluctuation of population in the area served by WWTPs, we used NH_4-N population for back-calculation. This is different from those reported articles, most of which use census or BOD_5 population data. The rationality and accuracy of NH_4-N population data has been proved and accepted, because NH_4-N is an indirect marker of urine and is considered less affected by industrial pollution sources (Been et al., 2014; Zheng et al., 2017). Therefore, more reliable results were obtained in this study through adopting reasonable solutions to reduce the variability from various sources.

In this study, the trend of METH consumption detected by WBE showed a dramatic decline over four years. On the contrary, most of the previous long-term monitoring studies on METH consumption reported an upward trend in other cities. The studies in Australia covered different periods of time, but the results all showed upward trends, such as two times increase in Adelaide from 2010 to 2013 (Tscharke et al., 2015), a five-fold increase (2009–2015) (Lai et al., 2016) and 2.4 times increase (2011–2017) (Gao et al., 2018) in the urban area of South East Queensland. Moreover, the studies in European countries also experienced an increase in METH consumption. For example, the research in Barcelona (NE Spain; 2011 to 2015) (Mastroianni et al., 2017), in Milan from 2005 to 2009 (Zuccato et al., 2011) and in two big cities (Antwerp and Brussels) of Belgium (2011 to 2015) (Been et al., 2016). As mentioned previously, in the current study, the trend of METH consumption presented a completely different picture than the previous studies.

The consumption trend of METH in this study analyzed by WBE was consistent with the Annual Report on Drug Situation in China in 2015 and 2016 showing an increase in the number of synthetic drug abusers (Office of China National Narcotic Cotrol Commission, 2015, 2016a), while the consumption of METH has shown a decline for two consecutive years (2017–2018). However, according to the Annual Report on Drug Control in China in 2017 (Office of China National Narcotic Cotrol Commission, 2017a), the total number of registered drug users has continued to increase and the number of synthetic drug abusers also showed an overall upward trend, although the growth rate has slowed down. Therefore, we proposed some possible explanations for the reduction in METH consumption. For example, the decrease of drug purity, or the increase of anti-drug efforts by government, which may lead to the increase in the retail price of drugs, the change in consumers' behavior, such as decreasing dosage or/and frequency of METH abuse, or even a turn towards other substances, etc.

Regarding drug purity, there were limited surveys in China. In one study, the range of METH purity in china was 55–81% between 2008 and 2014, with an upward trend over the period (Wang et al., 2015). It was much higher than other countries and regions such as Finland (< 30% in 2016) (Kankaanpaa et al., 2016), Iran (33–95% in 2012) (Khajeamiri et al., 2012) and Queensland (71–82% in 2014–2015) (Bruno et al., 2018). Besides, the Annual report on drug abuse illustrates that the percentage of MaGu (a mixture of METH and caffeine) abuse decreased continuously (China Food and Drug Administration, 2016). It excludes the possibility that the purity of METH decreased indirectly due to the increase of MaGu abuse. Therefore, it is not reasonable to link the decrease of METH consumption in Dalian (2015–2018) and the increasing drug purity.

With regard to the anti-drug efforts by government, there were some detailed discussions. In 2015, the Chinese government proposed a series of anti-drug measures, which have been implemented successively since mid-2016 until now. On the one hand, the government tried to combat the source and circulation of drugs. The "4.14″-drug manufacture crack-down task force mechanism, which aims to crack down on drug production and the "5.14″-drug source interception mechanism with the view of curbing the entry and circulation of drugs in our country, was enacted. Remarkable results have been achieved, which are shown by the increasing number of seized drugs and precursor chemicals, 18.8% and 50.5% higher in 2017 than in 2016, respectively (Office of China National Narcotic Cotrol Commission, 2016b, 2017b). On the other hand, the government tried to resist drugs through preventive education and rehabilitation. Among these efforts are the "6.27″-juvenile drug prevention and education project, which aims to establish and improve the youth drug prevention education system, strengthen youth drug prevention education and the "8.31″ community-based drug rehabilitation and treatment project, which aims to help drug abusers overcome addiction and return to society healthily. The former project has also achieved remarkable results, which is shown by the decreasing number of drug abusers under 35 years old, 19% lower in 2017 than in 2016 (Office of China National Narcotic Cotrol Commission, 2016b, 2017b).

In early 2018, based on the previous measures, our country deployed two more major actions. One of the actions is the special campaign to crack down on criminal forces; the action clearly points out that it is necessary to vigorously crack down on these criminal forces that are manipulating and operating illegal activities such as prostitution, gambling and drugs. The other one aims to crack down on the drug production and drug trafficking, as well as control the drug-making items and the number of drug abusers. The implementation of these two actions directly led to another decline in METH consumption in 2018.

Based on the above discussion, it is found that the implementation of anti-drug measures may produce a variety of results, including reduction of drug entry, decrease of production and increase of drug prices, etc. However, according to the information from the local police, the price of METH has increased from 200 RMB/g to 800 RMB/g in recent years. The increase in drug prices can prove the effective implementation of anti-drug measures in our country. Therefore, we conclude that the crack-down actions by the government have contributed significantly to the decline in METH consumption. The correlation between the findings and government behaviors suggests that we can provide data support for policy development in government departments and assess the impact of government drug control policies in the future.

5. Conclusions

This study applied WBE to detect temporal changes of METH consumption in Dalian between 2015 and 2018. Although the study cannot provide details about the abusers and their habits, it allows us to draw rough image of the changing trend of METH abuse in Dalian. This is the first study to report METH abuse in a long-term monitoring format in China. It is worth noting that it is the first time a downward trend in METH consumption has been observed. The final result suggested significant changes in METH consumption over the four years, with a large contraction overall. The significant reduction of METH use from 2015 to 2018 is probably attributable to the drug crack-down by the anti-drug department.

Role of the funding source

Funding: This work was supported by the Fundamental Research Funds for the Central Universities [grant numbers 3132016327, 3132016328].

Contributors

All authors contributed to and have approved the final manuscript.

Conflict of interest

No conflict declared.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.drugalcdep.2018.10.023.

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