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Research Paper

Boosting treatment stabilization in patients of amphetamine-type stimulant use disorder

I-Chun Chen[a,b,*], Chur-Jen Chen[c], Yu-Chiao Hsieh[a], Wan-Jan Tsai[a], Tsuo-Hung Lan[a,d]

[a] Department of Psychiatry, Taichung Veterans General Hospital, Taichung City, Taiwan
[b] Ph.D. Program in Translational Medicine, National Chung Hsing University, Taichung City, Taiwan
[c] Department of Applied Mathematics, Tunghai University, Taichung, Taiwan
[d] Faculty of Medicine, National Yang-Ming University, Taipei, Taiwan

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ABSTRACT

Background: To investigate boosting effects on treatment stabilization in the mandatory treatment modality for patients of amphetamine-type stimulant use disorder.
Methods: This is a retrospective follow-up study over a period from January 2013 to December 2018. We analyzed 425 patients of amphetamine-type stimulant use disorder under mandating treatments. Treatment stabilization for a given patient was defined once 4 negative urinalysis had been observed. We developed a dynamic monitoring model of boosting effects informed by the available data, specifically the number of negative urine samples required to reach stabilization, the sum of urinalyses done at the time when the given number of negative urine samples had been observed and who the patient was. To represent the simulated population, a Monte Carlo method was used to generate *p*-values from 1000 experiments conducted on a computer.
Results: In the observed samples, the probability of 4 negative results in urinalysis from 4 outpatient visits was 75.5%. In comparison, the probability for achieving 4th negative results in urinalysis over 4 visits from negative binominal distribution was 57.3%, and from the computer simulation, 49.8%. The observed samples had significantly higher probability of achieving 4 negative results in urinalysis over 4 outpatient visits ($p < 0.001$).
Conclusions: The mandatory treatment modality boosted treatment stabilization for patients of amphetamine-type stimulant use disorder. The major benefit of using the monitoring model is the ability to monitor boosting effects of stabilization. Results supported the effectiveness of this mandatory treatment modality and can be implemented in deferred-prosecution based treatment modality.

Introduction

Globally, 37 million people use amphetamine and prescription stimulants (United National Office on Drugs & Crimes, 2017). The amphetamine-type of stimulants (amphetamine, crystal methamphetamine [or ice], 3,4-Methylenedioxymethamphetamine [Ecstasy]) or abbreviated ATS, are the second most commonly used drug after Cannabis (United Nations Office on Drugs and Crimes [UNODC], 2011). The prevalence of ATS use is exceptionally high in Asia, and is also increasing in America (Lee, Hsu, & Tsay, 2013; Massaro et al., 2017; Shadloo et al., 2017). The use of ATS puts a heavy burden on the medical cost, which is already loaded by the increasing trauma admissions, HIV infections, hepatitis A and B infections (Gemma et al., 2018; Piyaraj et al., 2018; Zhang, Shoptaw, Reback, Yadav, & Nyamathi, 2018).

There is a discrepancy between substantial criminal-related costs and unproportionate number of criminal acts coming from ATS users. The criminal activity of amphetamine-type stimulants users has a zero-inflated distribution (Garrett et al., 2018), which is characterized by a large number of individuals having no recorded criminal acts (Enns et al., 2017). Asian countries (e.g., Taiwan) allow a more liberal drug policy in the past two decades. The approach for ATS use offenders has switched from a detention-base to a deferred prosecution base.

We introduced an mandatory treatment modality for ATS use offenders under deferred prosecution. It focuses on the provision of mandatory urinalysis in conjunction with counselling. Individual is defined as treatment stabilization, if 4 negative results in urinalysis are observed. When the 4th negative result in urinalysis is observed for an

* Corresponding author at: Department of psychiatry, Taichung Veterans General Hospital, No. 450, Section 1, Dongda Road, Xitun District, Taichung City, 407, Taiwan.
E-mail address: i-chun.chen@vghtc.gov.tw (I.-C. Chen).

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individual, the sum of prior urinalysis (including this one) can be calculated. When the 4th negative urine sample occurs at the v th urinalysis, the distribution of v follows a negative binomial distribution (Lloyd-Smith, 2007). The parameter, v, may be used to assess the performance of addiction treatment modality, particularly in the context with contingency management.

The effectiveness of mandatory addiction treatment modality is unclear. Here we aimed to investigate if mandatory treatment modality boosts treatment stabilization for ATS users.

Methods

Observed dataset

This is a retrospective follow-up study. Eligible subjects were 425 patients of ATS users undergoing substance treatment services at the Taichung Veterans General Hospital in Taiwan from January 2013 to December 2018. Inclusion criteria were stimulant use disorder, amphetamine-type, based on diagnostic criteria of Diagnostic and Statistical Manual of Mental Disorders 5th Edition (or DSM-5). Exclusion criteria were those without paying a minimum of 5 or exceeding 20 outpatient visits. According these criteria 37 subjects were excluded. The final study samples were therefore 387 subjects of ATS use offenders under deferred prosecution. This study protocol was approved by the Ethics Review Committee in Taichung Veterans General Hospital.

Treatment protocol

At the beginning of deferred prosecution, the ATS use offenders attended the pre-treatment assessment. Urinalyses for amphetamine and 3,4-Methylenedioxymethamphetamine (MDMA) based on immunoassay was conducted on three kinds of occasions: (a) the day of pre-treatment assessment, (b) the day of beginning mandatory treatment and (c) bi-weekly counselling. For each patient, stabilization was defined as long as a total of 4 negative urine samples had been observed. Upon reaching the state of stabilization, the patient was switched to monthly counselling. Patients attended bi-weekly group psychotherapy starting on the 8th month of mandatory treatments.

Measurements

Results of urinalysis on the day of pre-treatment assessment and at the beginning of mandatory treatments in 387 patients were either one of the followings: (a) negative remaining negative, (b) negative switching to positive, (c) positive remaining positive or (d) positive switching to negative. Among patients with negative urinalyses at the time of pre-treatment, the percentages of patients remaining negative and switching to positive at the treatment beginning were designated p and q respectively. Among patients with positive results of urinalyses at pre-treatment, the percentages of remaining positive and switching to negative at the treatment beginning were designated s and t respectively (Table 1). The outcome measurement was the sum of the total number of urinalyses done when the 4th negative urine sample had been observed. Urinalysis was conducted for each patient during every outpatient visit, and the outcome measurement was the total number of outpatient visits when achieving the 4th negative urine sample.

Table 1
Tables of parameters.

Parameters	Meanings
i	Number of subjects
j	Number of outpatient visits
v	Number of urinalysis upon reaching the 4th negative result in urinalysis
p	Percentage of negative remaining negative in first two urinalysis
q	Percentage of negative switching to positive in first two urinalysis
s	Percentage of positive remaining positive in first two urinalysis
t	Percentage of positive switching to negative in first two urinalysis

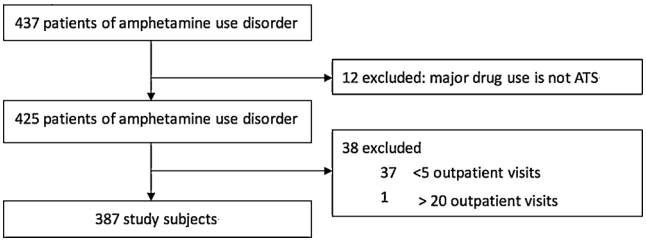

Fig. 1. Flow chart of the study.

Simulation datasets

In comparison, the simulation data used the same parameters including number of subjects which is i (i = 387) and the numbers of outpatient visits, which is j (j = 20), and the same parameters p,q,s,t (see 2.3 Measurements) to represent the transition in next outpatient visit throughout the 20 outpatient visits. Each of the simulated data represented 20 results of urinalysis from each of 387 simulated subjects. We counted for each subject the total number of outpatient visits, which is v (v = 4, 5,6,…, 20), upon reaching the 4th negative result in urinalysis. The first 10 simulated samples are shown in Fig. 1.

Statistical analyses

Computer simulation with the Monte Carlo method 1000 times was used to generate the p-values. The p-value is the proportion of such repetitions with probability of achieving 4 negative urine samples over 4 outpatient visits greater than the observed value. Null hypothesis was that both the observed samples and the simulated population data had the same probability of achieving 4 negative results of urinalysis over 4 outpatient visits. The R software (version 3.4.4) was used for all statistical analyses. Differences were considered significant at $p < 0.001$.

Results

Observed dataset

Among the 387 patients with ATS use disorder, 79.1% of them were male (n = 306), with mean age of 36.0 ± 8.7 years. At the pre-treatment phase, 19.4% of the patients showed positive results in urinalysis. At the beginning of treatment, 13.2% of them showed positive results in urinalysis. We noted that 37.0% of them used the stimulants more than 4 times a week, and 17.3% of them also had alcohol use disorder, and 10.1% had opioid use disorder. Regarding HIV burdens among all the 387 patients, 8.0% of the male had sex with men, and 7.8% were HIV-positive. Also 10.6% of the patients had psychotic disorders, and 1.6% being the bipolar disorder (Table 2).

Regarding the indicator of stabilization, 292 (75.5%) patients took 4 outpatient visits to reach the 4th negative urinalysis result, corresponded to a probability of 75.5%. The probability of reaching the same goal dropped progressively with visits exceeding 4, i.e., 5, 11.9% (n = 46); 6, 3.9% (n = 15); 7, 3.4% (n = 13); 8, 1.3% (n = 5); 9, 1.3% (n = 5) and 10, 1.0% (n = 4). Some patients (1.9%, n = 7) required even more visits (11–18) to reach this goal (Fig. 1). The median time for subjects to reach the 4th negative urinalysis result was 49 days (Table 2).

Among patients with negative results in urinalysis at the pre-treatment stage (n = 312), the percentages of those remaining negative or switching to positive at the start of treatment were 93.9% and 6.1%

Table 2
Descriptive data of 387 patients with amphetamine-type stimulant use disorder.

Baseline	Mean ± SD	Number (%)
Male		306(79.1)
Age	36.0 ± 8.7	
Positive urinalysis result using immunoassay		
Beginning of deferred prosecution		75(19.4)
Beginning of treatment		51(13.2)
Amphetamine use ≧ 4 times/ week		143(37.0)
Alcohol use disorder		67(17.3)
Opioid use disorder		39(10.1)
Men sexed with men		31(8.0)
HIV positive		30(7.8)
Psychotic disorder		41(10.6)
Bipolar disorder		6(1.6)
Indicators of stabilization		Median
Sum of outpatient visits when achieving 4 negative urine samples*		4**
Days of achieving 4 negative urine samples*	49	

*Treatment protocol was a bi-weekly urinalysis schedule.
**Note 292 subjects (75.5%) achieved 4 negative urine samples over 4 outpatient visits.

respectively. Among patients with positive urinalysis at pre-treatment, the percentages of remaining positive or switching to negative at the treatment beginning were 42.7% and 57.3% respectively.

Simulation datasets

In Fig. 2, x-axis represents the number of outpatient visits taken to achieve the 4th negative urinalysis result, and y-axis, the probability of achieving 4th negative result in urinalysis. While the observed probability for achieving 4th negative results in urinalysis over 4 visits was 75.5%, that based on negative binomial distribution was 57.3%. The probability for achieving 4th negative results in urinalysis over 4 visits from 10 computer simulations was averaged 49.8% (Fig. 2).

The 1000 simulated values for the probability of achieving 4 negative urinalysis over 4 outpatient visits ranged from 40.6% to 57.4%. The proportion of such simulated values greater than the observed value (75.5%) occurred at a probability with a p value < 0.001.

Discussion

We found that 75.5% of patients took 4 visits to reach the 4th negative urinalysis result, while the mathematically theoretical counterpart was 57.3%. That from computer simulations had an average of 49.8%. Our mandatory treatment modality had therefore significantly increased the probability of achieving overall negative results in urinalysis over 4 outpatient visits ($p < 0.001$). Results indicated that our mandatory treatment modality had boosted treatment stabilization for patients of ATS disorder.

Drug policy-makers have urged the evaluation on the performance of mandatory addiction treatment (Fazel, Bains, & Doll, 2006; Lunze, 2018). We developed here a dynamic monitoring model of boosting effects, indicated by the available parameters, in particular in urinalysis results the percentages of (a) negative remaining negative, (b) negative switching to positive, (c) positive remaining positive or (d) positive switching to negative and (e) the number of negative urine samples required to reach stabilization, together with (f) the sum of urinalysis done when 4 negative urine sample is being observed.

Our study supported that while prompted by criminal justice system for treatments, subjects have no poorer treatment engagements nor poorer treatment outcomes (Kiluk et al., 2015). Psychodynamics interactions in treatment modality is distinct from the counterpart in the correctional system. Positive results of urinalysis are not allowed in the correctional system under current criminal justice settings. Individuals with intractability of amphetamine use may tamper urine samples during mandatory urinalysis in court settings (Lin, Lee, Lee, & Chen, 2018), whereas results of urinalysis are more likely valid in medical settings. Our treatment modality was of non-judgmental manner, and

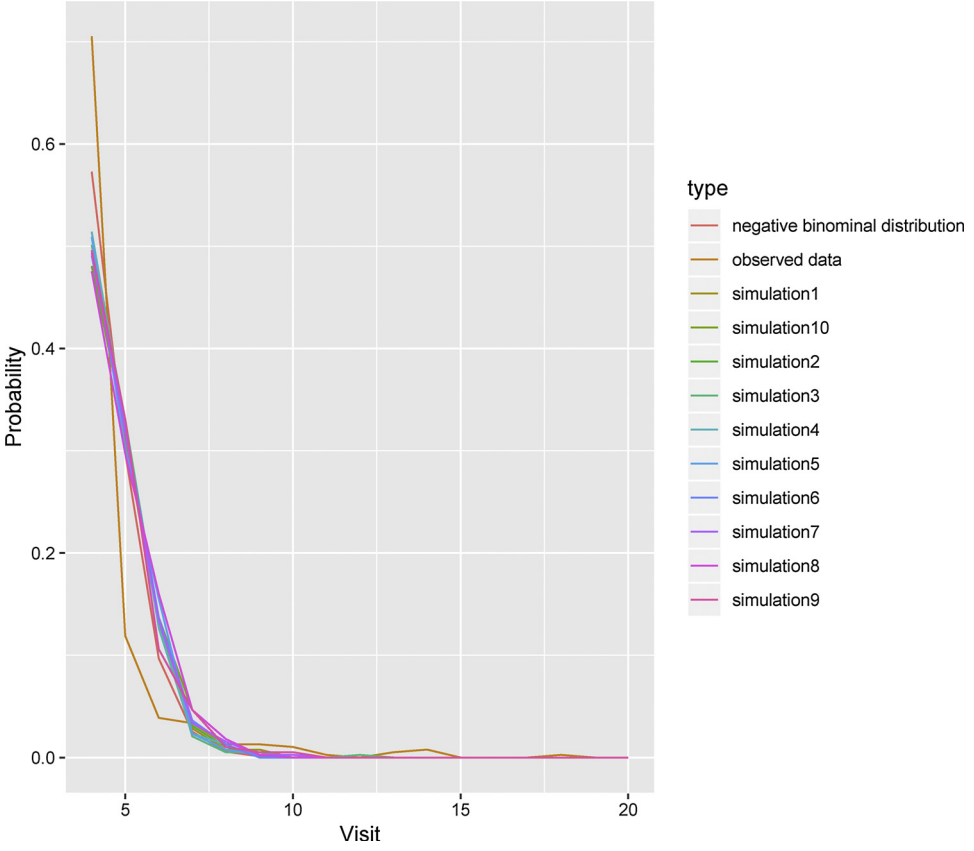

Fig. 2. Number of outpatient visit taken to achieve 4 negative urinalysis results and the corresponding probabilities. X-axis represents the number of outpatient visit taken to achieve 4 negative urinalysis results, and y-axis represents the corresponding probabilities. Note the probability for achieving 4th negative results in urinalysis over 4 visits was 75.5%, that based on negative binomial distribution was 57.3%. The probability for achieving 4th negative results in urinalysis over 4 visits from 10 computer simulations was averaged 49.8%.

was emphasized on mandatory urinalysis. Urinalysis just acted as a treatment necessity, while a positive result of urinalysis initiated a more aggressive treatment approach.

The strengths of the current study are as follows. Firstly, because the result of urinalysis depended largely on the last sample of urinalysis, the study had adjusted for the time-dependent effects using computer simulations. Among patients with negative urinalysis at the stage of pre-treatment, the percentage of remaining negative was 93.9%, and switched to positive (6.1%) at the treatment beginning. Among patients with positive urinalysis at pre-treatment, the percentages of remaining positive and switching to negative at the treatment beginning were 42.7% and 57.3% respectively. The study simulated transitions in the next result of urinalysis using values of the above parameters. Secondly, these parameters represented results of urinalysis at the start of deferred prosecution, simulation samples constrained by these parameters could account for the probability of achieving overall negative results in urinalysis over 4 outpatient visits under judicial-alone influences. Others have reported a reduction of amphetamine-type stimulants use accrue upon treatment entry (Mimiaga et al., 2018).The observed samples of 387 patient were the outcomes under the judicial-plus-therapeutic effects. Thus our study has the strength of differentiating the judicial-alone and judicial-plus-therapeutic effect. Thirdly, our dropout rate throughout the course of treatment was extremely low, i.e., 8.4% (37 out of 437 patients were followed up with < 5 visits, see Fig. 1 study flow chart).

The limitations of the study are as follows. Firstly, the study followed a bi-weekly urinalysis schedule. However, the duration of detectability of amphetamine is two to three days (Wolff et al., 1999). Following more frequent urinalysis schedules (e.g., twice-weekly) should be considered in the future. Secondly, our study excluded patients having < 5 outpatient visits. The number of outpatient visits, particularly having three or more visits, is shown to be negatively associated with days of methamphetamine use (Cucciare et al., 2018). It is possible that our subjects had less compulsive drug-seeking behaviors.

By boosting the treatment stabilization, psychotic symptoms of patients were reduced. This finding is consistent with decreased psychotic symptoms during one-month stimulants abstinence (McKetin, Lubman, Baker, Dawe, & Ali, 2013). For greater impact on preventing HIV transmission, trauma admission and mental health risks, addiction treatment that boosts one-month abstinence is critical. The boosting effects on treatment stabilization can reduce social and medical costs.

Conclusion

Under this mandatory treatment modality, stabilization was boosted among the patients of amphetamine-type stimulant use disorder. We also developed a dynamic monitoring model of the boosting effects. The major benefit of the model is performance evaluation of mandatory addiction treatment. This approach has the potential power of differentiating judicial-alone and judicial-plus-therapeutic effects for amphetamine-type stimulant use patients in mandatory treatment modality.

Conflicts of interest

Authors declared none.

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None.

Author contribution

I-Chun Chen had contributed to conception and design, statistical analysis, interpretation of data and drafting the manuscript. Chur-Jen Chen and Tsuo-Hung Lan had contributed to critical revision of the manuscript for important intellectual content. Yu-Chiao Hsieh and Wan-Jan Tsai, two psychologists, had contributed to acquisition of data and administrative support.

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