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Short Report

Evaluation of methamphetamine assist packs: As-needed antipsychotics for self-management of methamphetamine-associated psychiatric toxicity

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ABSTRACT

Background: Methamphetamine frequently causes substance-induced psychosis and related symptoms. There are currently no interventions to prevent or assist in self-management of these symptoms.
Methods: We evaluated a program providing "Methamphetamine Assist Packs" to patients who were seen in a psychiatric emergency services program for methamphetamine-induced psychosis. Methamphetamine Assist Packs included a small number of tablets of an antipsychotic medication (olanzapine), administration instructions, and referral information. We reviewed medical charts of patients who received Methamphetamine Assist Packs from January 2022 through May 2023 for sociodemographic and emergency visit characteristics. We assessed the changes between the number of psychiatric emergency visits before and after Methamphetamine Assist Pack receipt at two, six, and 12 months using generalized estimating equations.
Results: Ninety-two patients received a Methamphetamine Assist Pack, with a mean age of 40 years; 79 % were male and 49 % Black/African American; 77 % experienced housing instability or homelessness. The most common symptoms were suicidal ideation (54 %), paranoia or delusions (45 %), and hallucinations (40 %); 55 % were on involuntary psychiatric hold, 38 % required medications for agitation, and 18 % required seclusion or physical restraints. The rate of psychiatric emergency visits after Methamphetamine Assist Pack receipt was 0.68 and 0.87 times the rate prior to receipt at two and six months, respectively ($p < 0.001$). There was no difference at 12 months.
Conclusions: Methamphetamine Assist Packs were associated with fewer psychiatric emergency visits for six months after receipt, and represent a promising intervention to address acute psychiatric toxicity from methamphetamine in need of further research.

Introduction

Methamphetamine use and related morbidity and mortality have increased substantially in recent years, with an estimated 24 million people using methamphetamine and other amphetamine-type stimulants globally (Chomchai & Chomchai, 2015). Deaths related to methamphetamine use generally involve cardiovascular or traumatic causes, such as homicide, suicide, or other injuries, many of which may be related to the psychiatric effects of the drug (Stockings et al., 2019). Half of methamphetamine-related emergency department visits in the United States are due to psychiatric symptoms (National Institute on Drug Abuse, 2023; Suen, Davy-Mendez, LeSaint, Riley & Coffin, 2022). Similarly, 47 % of visits to the Zuckerberg San Francisco General Hospital's Psychiatric Emergency Services, a dedicated emergency department that provides specialty care for people with the most serious psychiatric concerns, were related to methamphetamine use in 2017 and 2018 (San Francisco Department of Public Health, 2019). Among patients with eight or more involuntary psychiatric holds, 89 % reported methamphetamine use only, without use of other major drugs (San Francisco Department of Public Health, 2019).

Despite the contribution of methamphetamine to receiving emergency psychiatric care, limited research has focused on methamphetamine toxicity. Methamphetamine toxicity includes symptoms such as anxiety, agitation, hallucinations, paranoid or grandiose delusions,

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impulsivity, chest pain, heart palpitations, and shortness of breath (Davy-Mendez et al., 2021; Moallem, Courtney & Ray, 2018; Riley et al., 2020). Previous research has found that psychiatric toxicity from methamphetamine use, including methamphetamine-induced psychosis, can lead to increased risky and impulsive behaviors, ranging from walking unsafely in streets to physical altercations, which can contribute to injury-related deaths, suicides, or homicides (Stockings et al., 2019).

Antipsychotic medications have been shown to reduce symptoms of methamphetamine-induced psychosis (Fluyau, Mitra & Lorthe, 2019). Building on the model of providing naloxone to treat acute opioid toxicity following use, the San Francisco Department of Public Health piloted Methamphetamine Assist Packs (also called "Chill Packs"). Methamphetamine Assist Packs included oral or dissolving tablets of olanzapine to be self-administered as needed in the event of psychosis, anxiety, agitation, or inability to sleep following methamphetamine use (Thomas & Saadabadi, 2023). Olanzapine is a commonly used second-generation atypical antipsychotic approved in the United States for treatment of schizophrenia and bipolar I disorder (Thomas & Saadabadi, 2023) and is also effective in treating methamphetamine-induced psychosis by reducing the frequency and severity of symptoms more than other commonly used antipsychotics such as risperidone and aripiprazole (Srisurapanont et al., 2021). Among antipsychotic medications, olanzapine has a favorable safety profile, including fewer extrapyramidal side effects (Leelahanaj et al., 2005), minimal drug-drug interactions, and no current street value; metabolic side effects are generally limited to long-term use (Kantrowitz & Citrome, 2008). However, we are unaware of an intervention utilizing self-administered antipsychotic medications on an as-needed basis for methamphetamine-induced psychiatric toxicity, as in the Methamphetamine Assist Pack program.

We sought to describe and evaluate the impact of the pilot Methamphetamine Assist Pack program by describing sociodemographic and clinical characteristics of those served and comparing their use of psychiatric emergency services before and after receipt of the Methamphetamine Assist Pack. We hypothesized that patients would have fewer near-term psychiatric emergency service visits in the two months following receipt of a Methamphetamine Assist Pack.

Methods

Study design

We analyzed retrospective medical record data collected for a programmatic evaluation, including patient and visit-level characteristics, to compare the within-person difference in the number of psychiatric emergency service visits before and after receipt of a Methamphetamine Assist Pack.

Program

Beginning in January 2022, patients at the Zuckerberg San Francisco General Hospital's Psychiatric Emergency Services who presented with methamphetamine-induced psychotic symptoms and no indication for long-term anti-psychotic therapy (i.e., no diagnosis of a primary psychotic disorder such as schizophrenia) were provided with a Methamphetamine Assist Pack consisting of olanzapine and an information and referral sheet. Psychiatric Emergency Services psychiatric providers were oriented to the program and trained to prescribe four tablets of olanzapine 5 mg as needed for psychiatric toxicity, although they had discretion regarding whether or not to provide the Methamphetamine Assist Pack and to adjust any elements of the prescription based on clinical judgment. Patients were provided the Methamphetamine Assist Pack "in-hand" on discharge, instructed to take the medication as needed to self-manage distressing psychiatric symptoms following methamphetamine use, and to refer to the flyer for additional services (see *Supplementary Material*). Providers obtained standard informed consent for medical treatment from patients.

Participants and setting

We reviewed the charts of all patients seen at San Francisco's Psychiatric Emergency Services who received a prescription for olanzapine at discharge from January 2022 through May 2023. In this analysis, we included patients who presented for methamphetamine-related psychiatric complaints and had received the number of olanzapine tablets consistent with receipt of a Methamphetamine Assist Pack. As this was a new program and providers could vary the contents of the Methamphetamine Assist Pack, we also included patients who were provided fewer than 28 doses of 10 mg or less of olanzapine but for whom provider notes stated the intent of providing a Methamphetamine Assist Pack.

We abstracted sociodemographic and index visit (the visit at which they first received a Methamphetamine Assist Pack) characteristics from medical charts. We tallied the number of psychiatric emergency service visits patients had in the 12 months leading up to and following receipt of the Methamphetamine Assist Pack. Data were entered into REDCap (Harris et al., 2019, 2009). Attempts were made to contact patients with telephone numbers that were available in the medical chart to discuss use of the Methamphetamine Assist Packs, however few patients had available numbers and most were disconnected. This analysis of deidentified data from a programmatic evaluation was approved by the University of California San Francisco Institutional Review Board (#23-40490).

Variables

Sociodemographic characteristics included age, sex at birth, gender (cisgender female, cisgender male, transgender female, transgender male), race (American Indian or Alaskan Native, Asian, Black or African American, Native Hawaiian or Pacific Islander, White, other), ethnicity (Hispanic, Latinx, or Spanish origin and not of Hispanic, Latinx, or Spanish origin), spoken language (Cantonese or Mandarin, English, Russian, Spanish, Tagalog, Vietnamese), and unstable housing or homelessness (determined based on a citywide metric indicating utilization of housing and shelter resources indicative of housing instability or homelessness).

Details of the index visit were captured including length of stay, legal status (voluntary visit vs. involuntary hold for danger to oneself, danger to others, or grave disability) (San Francisco Health Network, 2023), psychiatric symptoms present during the psychiatric emergency services intake (abnormal thought process or speech, depression/low mood, mania, paranoia or other delusions, hallucinations [auditory, visual, tactile, etc.], suicidal ideation, homicidal ideation, disorientation, reduced consciousness), application of locked seclusion or physical restraints, medications given for agitation or to reduce underlying symptoms (oral medications given on a schedule, oral medications given as needed, intramuscular medications given as needed), and Methamphetamine Assist Pack characteristics (dose of olanzapine provided on discharge, quantity of tablets provided, and concurrent provision of take-home naloxone).

The primary outcome was the number of psychiatric emergency service visits. Although we collected data for 12 months before and after Methamphetamine Assist Pack receipt, we hypothesized that the intervention would be associated with only a short-term reduction in visits, for two months after receipt.

Analysis

We performed descriptive analysis on all sociodemographic and index visit variables. We reported the mean and standard deviation (SD) for continuous variables that were normally distributed and the median and interquartile range (IQR) for those that were skewed. For

Table 1
Characteristics of methamphetamine assist pack recipients and index visits ($N = 92$).

Sociodemographic Characteristics	*n/mean*	*%/SD*
Age (years)	40	9.8
Sex		
Female	18	20 %
Male	73	79 %
Unknown/Chose not to disclose	1	1 %
Gender		
Cisgender Female	16	17 %
Cisgender Male	67	73 %
Transgender Female	2	2 %
Transgender Male	1	1 %
Unknown/Chose not to disclose	6	7 %
Race*		
American Indian or Alaskan Native	1	1 %
Asian	4	4 %
Black or African American	45	49 %
Native Hawaiian or Pacific Islander	1	1 %
White	28	30 %
Other	16	17 %
Unknown/Chose not to disclose	2	2 %
Ethnicity		
Hispanic, Latine, or Spanish origin	17	18 %
Not of Hispanic, Latinx, or Spanish origin	73	79 %
Unknown/Chose not to disclose	2	2 %
Spoken Language*		
English	88	96 %
Spanish	6	7 %
Portuguese	1	1 %
Unstable housing/homelessness		
Low risk	20	22 %
High risk	71	77 %
Unknown/Chose not to disclose	1	1 %
Characteristics of Index Psychiatric Emergency Visit	***n/median***	***%/IQR***
Length of stay (hours)	31	23–49
Admission volition		
Voluntary	41	45 %
Involuntary psychiatric hold*	51	55 %
Danger to oneself	*23*	*25 %*
Danger to others	*22*	*24 %*
Gravely disabled	*22*	*24 %*
Symptoms present during intake*		
Abnormal thought process or speech	22	24 %
Depression/low mood	15	16 %
Mania	1	1 %
Paranoia or other delusions	41	45 %
Hallucinations (auditory, visual, tactile)	37	40 %
Suicidal ideation	50	54 %
Homicidal ideation	7	8 %
Disoriented	4	4 %
Reduced consciousness	3	3 %
None	5	5 %
Any seclusion or physical restraints	17	18 %
Locked seclusion	*10*	*11 %*
Physical restraints	*12*	*13 %*
Medications given for agitation or symptom management	35	38 %
Oral medications given standing	*7*	*8 %*
Oral medications given as needed	*9*	*10 %*
Intramuscular injection medications given as needed	*19*	*21 %*
None	57	62 %
Methamphetamine Assist Pack Characteristics		
Olanzapine dose provided (mg)		
2.5	1	1 %
5	88	96 %
10	3	3 %
*Number of olanzapine tablets provided***		
2	1	1 %
3	18	20 %
4	42	46 %
5	10	11 %
6	6	7 %
7	2	2 %
8	1	1 %
10	9	10 %
14	1	1 %
20	1	1 %
Also provided with naloxone	78	85 %

* Total exceeds 100 % as patients may have had multiple types of involuntary hold or symptoms.
** One missing response.

categorical data, frequencies and proportions were reported. We conducted generalized estimating equations (GEE) with a log link function for our count outcome to model the expected number of psychiatric emergency service visits before and after Methamphetamine Assist Pack receipt at three time points (two, six, and 12 months). We used an exchangeable correlation structure to account for repeated measures within each patient. A p-value of <0.05 was considered significant and statistical analyses were performed using Stata 17 (StataCorp, College Station, TX).

Results

Descriptive results

Ninety-two patients received a Methamphetamine Assist Pack during the study period. Mean age was 40 years and 79 % were assigned male sex at birth. Almost half (49 %) of patients identified as Black/African American and 18 % were Latine. Three-quarters of patients (77%) were experiencing housing instability or homelessness (Table 1). Over half of the patients (55 %) were on involuntary hold and the most common symptoms were suicidal ideation (54 %), paranoia or other delusions (45 %), and hallucinations (40 %). Over a third of patients (38 %) required medication for agitation and 18 % required seclusion or physical restraints. Median length of stay was 31.4 h. Nearly all patients (96 %) were prescribed olanzapine doses of 5 mg upon discharge and 46 % received four doses; 85 % were also prescribed naloxone for opioid overdose rescue (Table 1).

Psychiatric emergency service visits

Patients had a mean of 2.0, 3.5, and 5.5 psychiatric emergency service visits in the two, six, and 12 months before Methamphetamine Assist Pack receipt, respectively, and a mean of 1.4, 3.1, and 5.3 visits in those periods after receipt. The GEE model demonstrated a rate of psychiatric emergency service visits two months after receipt of the initial Methamphetamine Assist Pack 32 % lower than the rate of visits two months before receipt (incidence rate ratio [IRR] 0.68, 95 % confidence interval [CI] 0.61 to 0.76; $p < 0.001$) (Table 2). Similarly, the rate of visits six months after receipt was 13 % lower than six months before receipt (IRR 0.87, 95 % CI 0.81 to 0.93; $p < 0.001$). There was no difference at 12 months (IRR 0.96, 95 % CI 0.90 to 1.03; $p = 0.30$) (Table 2). Five patients received an additional Methamphetamine Assist Pack in the first two months after the initial provision, with a range of 4 to 53 days between receipt of the first and final Methamphetamine Assist Pack. After 12 months, 24 patients had received at least one additional Methamphetamine Assist Pack (see *Supplementary Material*).

Discussion

To our knowledge, there are no other studies of interventions providing as-needed antipsychotics to this population. Patients who received a Methamphetamine Assist Pack had substantial social and mental health morbidity, including high-risk housing status, frequent use of medications for agitation or need for physical restraint during their index emergency visit, and the majority were on an involuntary psychiatric hold. Patients had significantly fewer psychiatric emergency service visits at both two and six months following initial Methamphetamine Assist Pack provision compared to prior to the intervention. If these observational results were confirmed in a randomized trial, provision of two to four Methamphetamine Assist Packs to a similar population of patients would be expected to avert one psychiatric emergency visit in the following two months.

As expected, we found no difference in psychiatric emergency service visits at 12 months. Each Methamphetamine Assist Pack contained a small number of tablets that would likely be used over a short period of time and most patients did not receive further Methamphetamine Assist Packs. The intervention was not available in other settings and prescribing a Methamphetamine Assist Pack was at the discretion of psychiatric emergency service attendings. While some patients did receive additional Methamphetamine Assist Packs, the sample size was insufficient for a more granular analysis that could address confounders. The hypothesized benefit of a Methamphetamine Assist Pack may be short-term and would therefore require greater availability to be sustained. People who use methamphetamine might also benefit further by pairing the intervention with counseling or other behavioral supports.

While olanzapine and other antipsychotics have demonstrated a benefit in treating methamphetamine-associated psychosis (Fluyau et al., 2019; Leelahanaj et al., 2005), this represents the first evaluation of an intervention providing as needed antipsychotic therapy to this population. This study demonstrates that as needed antipsychotic therapy has the potential to reduce utilization of psychiatric emergency care. More broadly, use of Methamphetamine Assist Packs might result in fewer adverse events related to methamphetamine-induced psychosis, such as physical altercations, involuntary interventions by medical or public safety personnel, or insomnia. These findings support further implementation, evaluation, and rigorous study of this intervention as a means to mitigate the psychiatric morbidity of methamphetamine use both in the United States and internationally.

The Methamphetamine Assist Pack program was designed to support self-management of psychiatric symptoms from methamphetamine use. One concern with Methamphetamine Assist Packs may be the capacity or perceived capacity of patients who experience psychotic symptoms to safely and effectively use a medication to self-manage those symptoms. When naloxone was first provided for overdose prevention, many professionals felt that people who use drugs could neither safely nor effectively utilize naloxone to manage opioid overdose (Bazazi, Zaller, Fu & Rich, 2010), in contrast to what experience and research later demonstrated (Walley et al., 2013). If experience with naloxone provision serves as a lesson for managing psychiatric toxicities from methamphetamine, it is critical that we remain open to self-management of symptoms among this population.

Limitations

The major limitation of this evaluation was reliance upon medical record data. The inability to reach patients for interviews meant we were unable to determine if and how Methamphetamine Assist Packs were used by the patients who received them. Future research is needed to establish what happens to these medications after they are dispensed, including any safety concerns, an effort challenged by the difficulty establishing consistent follow-up in this population. In addition, we followed presentations only at one facility; while San Francisco's Psychiatric Emergency Services program sees a high proportion of severe psychiatric disturbance in the area, patients may also have been seen in other area hospitals. Results may also have limited generalizability to other populations, as our sample had significant psychiatric morbidity;

Table 2
Generalized estimating equation models of psychiatric emergency service visits before and after methamphetamine assist pack receipt. ($N = 92$).

Time before and after receipt of Methamphetamine Assist Pack	Incidence Rate Ratio of Psychiatric Emergency Service visits	95 % Confidence Interval	*p-value*
2 months	0.68	0.61 to 0.76	<0.001
6 months	0.87	0.81 to 0.93	<0.001
12 months	0.96	0.90 to 1.03	0.30

however, the real world setting of this pilot is arguably a contravening strength. Finally, the small sample size and limited data elements did not allow for robust analysis of confounding or for stratifying outcomes by racial or other demographic groupings to better examine potential equity impacts of the Methamphetamine Assist Pack program.

Conclusion

There is no established intervention to prevent or to support self-management of acute psychiatric symptoms due to methamphetamine use. In this pilot of providing Methamphetamine Assist Packs consisting of a small supply of low-dose atypical antipsychotics for self-management of symptoms of methamphetamine-associated psychiatric toxicity, we found significantly fewer psychiatric emergency visits in the two and six months after receipt of the medication. While additional research, such as a randomized controlled trial, is needed to determine if and how this medication is used and to affirm these preliminary findings, results are promising and support further development of Methamphetamine Assist Packs as a public health intervention for populations heavily impacted by methamphetamine use.

Ethics approval

The authors declare that they have obtained ethics approval from an appropriately constituted ethics committee/institutional review board where the research entailed animal or human participation.

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CRediT authorship contribution statement

Phillip O. Coffin: Writing – review & editing, Writing – original draft, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition, Conceptualization. **Yi-Shin Grace Chang:** Writing – review & editing, Writing – original draft, Methodology, Formal analysis. **Megan McDaniel:** Writing – review & editing, Methodology, Data curation. **Mark Leary:** Writing – review & editing, Investigation, Data curation. **David Pating:** Writing – review & editing, Methodology, Conceptualization. **Vanessa M. McMahan:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Formal analysis. **Matthew L. Goldman:** Writing – review & editing, Supervision, Project administration, Methodology, Investigation, Funding acquisition, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.drugpo.2024.104480.

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