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Low-threshold extended-release naltrexone for high utilizers of public services with severe alcohol use disorder: A pilot study

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ABSTRACT

Extended-release naltrexone (XRNTX) is an effective treatment for alcohol use disorder (AUD). We sought to evaluate the feasibility, acceptability, and preliminary effectiveness and cost-effectiveness of XRNTX delivered as a stand-alone service to persons with severe AUD who are high utilizers of multiple urgent and emergency medical services (HUMS). Of 15 HUMS persons with severe AUD selected based on chart review, 11 agreed to participate. Participants received a mean of 4.5 injections (range 2–7). Modest benefits from XRNTX were observed in terms of patients' Urge-to-Drink Score and the costs of emergency medical services utilized. Though limited by a small sample size, costs including client utilization and study related expenses during the post-enrollment period were less than client utilization costs in the pre-enrollment period. We also observed non-significant improvements in the number of drinking days, but no change in quality of life as measured by the EQ-5D. Eighty-eight percent of participants perceived XRNTX as helping with their drinking. Findings need to be replicated in a larger study, however if replicated, the cost savings could be substantial.

1. Introduction

Alcohol use disorders (AUD) are associated with significant morbidity and mortality, responsible for 3.8% of all deaths and 4.6% of disability-adjusted life years worldwide (Rehm et al., 2009). Furthermore, AUD represent a major cost to high income countries, estimated at 0.96% of gross domestic product (Mohapatra, Patra, Popova, Duhig, & Rehm, 2010). In San Francisco City and County, AUDs directly result in approximately 110 deaths annually seen by the Office of the Chief Medical Examiner (Hauser, 2016). Efforts to increase access to effective AUD treatment are urgently needed to address this major public health issue.

Pharmacotherapies for AUD have proven critical in managing the disease. The only long-acting formulation of an AUD pharmacotherapy available in the United States is extended-release naltrexone (Vivitrol© in the US, hereinafter referred to as XRNTX). XRNTX overcomes daily adherence barriers to oral treatment and produces moderate effect sizes (Jonas et al., 2014). A recent review of studies suggest that clinicians must treat approximately four individuals with XRNTX to achieve abstinence in one individual, a measure far superior to many pharmacotherapies in medical care (Mannelli, Peindl, Masand, & Patkar, 2014). Additionally, this review evaluating XRNTX as compared to placebo suggests that with a need to treat of 14 individuals, there is a significant reduction in heavy drinking, without the goal of abstinence (Mannelli et al., 2014). Healthcare costs have been shown to decrease with XRNTX given for alcohol or opioid use disorder, including a 34% reduction in total medical costs, 36% reduction in total pharmacy costs, and 52% reduction in alcohol-related hospitalization costs (Mark, 2010). In a study of Aetna claims, receipt of XRNTX was associated with a 13% reduction in ED visits (Un, 2008).

In San Francisco, excessive alcohol consumption is an important driver of health care outcomes and costs among individuals who are "High Users of Multiple Services" (HUMS). In general, HUMS clients have a higher burden of chronic disease due to multiple factors such as alcohol and substance use disorders, significant cognitive impairment, mental illness, and behavioral issues (Martinez, 2014). Many of these individuals also suffer from chronic homelessness and very difficult living

Abbreviations: AUD, alcohol use disorder; CCMS, Coordinated Case Management System database; CM, case manager; ED, emergency department; HUMS, high users of multiple services; ICM, intensive case management; SFDPH, San Francisco Department of Public Health; XRNTX, extended release injectable naltrexone.

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conditions, and a significant proportion (35%) has a severe alcohol use disorder (personal communication, Martinez, 2014). These San Francisco residents are less visible in healthcare systems because they are often not the highest user of a single system, but rather use *multiple services* across the medical, mental health and substance abuse treatment systems, as they struggle with multiple disorders. Notwithstanding an array of substance and mental health treatment, including outreach to the homeless with a housing first model, some people continue to suffer multiple displacements and interrupted episodes of ineffective care (Martinez, 2012). HUMS clients often struggle to engage in health services and tend to rely only on urgent/emergent care. Thus, HUMS clients account for major San Francisco City and County expenditures on urgent and emergent care and preventable hospitalization (Martinez, 2014; Martinez & Parekh, 2011).

XRNTX has been studied in safety-net patient populations with promising results (Collins et al., 2015; Crevecoeur-MacPhail et al., 2012b; Herbeck et al., 2016). These studies examined alcohol-related outcomes, in particular changes in individual's alcohol craving. Although the studies had promising results including both in decreases in alcohol craving and in retention of subjects, the interventions were largely not provided in a low-threshold fashion, but rather in the context of a behavioral AUD treatment program. The viability of utilizing this medication in a low-threshold manner among HUMS clients with multiple chronic health disorders is unknown.

We conducted a pilot study to establish whether XRNTX, as a standalone intervention for non-treatment seeking high utilizer subjects in the context of ongoing case management, would be feasible and acceptable as a low-threshold intervention. In this current study, the clients were included or excluded based on high utilization of system-wide programs. Secondly, we aim to develop preliminary estimates of cost-effectiveness in terms of impact on service utilization and quality of life. Additionally, we explored changes in urge to drink and drinking frequency and monitored medication-related adverse events. Finally, we assessed the logistics of providing XRNTX and explored future implementation strategies through qualitative interviews with key informants in the San Francisco Department of Public Health (SFDPH).

2. Methods

2.1. Research team and setting

This pilot occurred within the SFDPH, with the intervention implemented by clinicians and intensive case managers at a county-funded behavioral health clinic. The behavioral health clinic is a full service partnership providing intensive wraparound services to individuals who are high users of multiple services. Services are clinic-based and off-site, including intensive case management, primary and mental health care, social work, crisis management, individual psychotherapy services, and connections to substance use, psychiatric emergency, and acute medical services. The steering committee included staff from the Substance Use Research Unit of the SF Population Health Division, Community Behavioral Health Services, San Francisco Sobering Center, and the office of the Drug and Alcohol Administrator. Research activities were directed by the Substance Use Research Unit, while pharmacy and steering committee activities were led by Behavioral Health Services. Study activities were approved by the University of California-San Francisco Committee on Human Research (CHR# 12–10,232).

2.2. Eligibility and recruitment

All potential participants were initially identified through the HUMS list created by DPH analysts. Utilizing this annually-generated list of high use individuals, inclusion criteria for potential participants included: assigned to the intensive case management and behavioral health clinic (ICM) program, which facilitated regular contact with the participant throughout the intervention; had severe AUD by the assessment of clinicians at the behavioral health clinic; were not using opioids regularly; and had acceptable clinically-obtained laboratory values (platelets >100, estimated creatinine clearance >50, and transaminases <5 times upper limit of normal).

The Steering Committee met monthly to identify and discuss potential participants. At these meetings, the most recent HUMS list of individuals (sorted by the system wide expenditures they accrued, with the most "expensive" individuals being listed first) was reviewed and clients who were in intensive case management and had known AUD were selected from the top of the list downwards. Safety data were reviewed and a contact plan was devised. The case managers would then offer intervention to the client and, if he or she were interested and provided consent, the case manager arranged for either a lab work visit or the enrollment visit at the Clinic (see Fig. 1). All participants were recruited and enrolled between June 2013 and August 2014. The range of time a potential participant had been enrolled in ICM was not a factor for enrollment. The amount of time a client had participated in the ICM services varied, from one month to over seven years prior to study enrollment, with half the participants enrolled in ICM >3 years prior to the study.

2.3. Procedures

Potential subjects who agreed to participate were escorted to the clinic by their case manager. A clinician confirmed eligibility, performed formal medication consent, and confirmed the absence of chronic opioid use. A urine drug screen was performed prior to medication administration to rule out the presence of opioids and, if the participant had recently consumed opioids based on history, medical chart, or urine screen results, a naloxone challenge test was administered. After eligibility was established, clinic staff contacted the pharmacy to initiate delivery of the XRNTX and paged the evaluation team to consent the participant for research and conduct the research activities. After receipt of XRNTX at the clinic, participants remained on-site for at least 30 min to ensure absence of any serious reaction.

Case managers attempted to follow participants weekly, per their standard clinical protocol, and accompanied participants back to the clinic every 4 weeks to receive their next XRNTX injection. The clinician reviewed any interim labs for changes in hepatic function. Funded through the City and County of San Francisco, the study was designed for a six-month pre-and-post analysis. Although the analysis was concluded after the seventh injection (six months post enrollment), clients were offered XRNTX injections for up to 12 months.

Research staff conducted the evaluation survey in the 30 min it took to prepare medication for administration. In addition, case managers attempted to administer the Urge-to-Drink Scale at weekly visits. Participants were reimbursed with a $5 grocery card for each monthly survey completed, for a total maximum of $35 for participation in this study.

2.4. Measures

The survey included demographics, lifetime and past month alcohol and drug use, the Urge-to-Drink Scale (scored from 0 to 30, with a score of 10 or higher associated with greater risk for relapse (Flannery, Poole, Gallop, & Volpicelli, 2003; Flannery, Volpicelli, & Pettinati, 1999)), drinking days in the past week, quality of life (EQ-5D, including the EQ-VAS visual analog scale, rated from 0 as the worst imaginable health state to 100 as the best imaginable health state (Shaw, Johnson, & Coons, 2005)), Short Index of Problems (SIP-2R, scored from 0 to 45, with a higher score corresponding to more problems with alcohol consumption ("Project MATCH", 1993)), days slept on the street in the past week, perception of treatment (assessed with the question "How much do you think the naltrexone injections helped you with your drinking?"), adverse events, and reasons for continuing or discontinuing treatment. The respectively assigned case managers were tasked with providing the Urge-to-Drink Scale weekly. Our intention was to comprehensively evaluate Urge-to-Drink as a primary metric of evaluation to

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