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Presentation 1

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Title: Bridging Patients from Oral to Intramuscular Naltrexone After Near-Fatal Overdose

Background: Experts suspect that near-fatal opiod overdoses outnumber fatal overdoses by 20 to 1 (or more) [1]. In some settings, half the individuals who died of an overdose presented to care for a non-fatal overdose in the preceding 5 years [2]. Patients who have recently started therapy for opiod addiction may also be at increased risk for death from overdose [3]. The majority of patients who receive naloxone from police or EMS personnel are transported to an emergency department (ED), making the ED the preferred location in which to study patients after near-fatal overdose. These encounters represent a critical opportunity for initiation of addiction treatment and initiation of medication assisted treatment for opioid dependence in a high risk and vulnerable population [4].

In our population, up to 67% of patients who required naloxone reversal for an opioid overdose describe a single relapse with heroin after an extended period of abstinence [5]. These patients are often unwilling to consider opioid agonist (or partial agonist) therapy because they are no longer opioid dependent. The role of ED-initiated opioid antagonist therapy with naltrexone has not been rigorously explored, despite evidence demonstrating the efficacy of depot naltrexone (Vivitrol) in preventing fatal overdose [6]. One obstacle to starting naltrexone from the ED is the recommended 7 to 10 days of abstinence preceding the depot injection.

Prior research has demonstrated that small doses of oral naltrexone in an appropriately selected population does not precipitate severe withdrawal symptoms and can improve engagement with long-term medication-assisted therapy [7]. In addition, metabolites of oral naltrexone may effectively block opioid receptors while precipitating less withdrawal than the parent compound [8]. Accordingly, we anticipate that use of low-dose oral naltrexone as a bridge to long-term injectable therapy may lead to more patients being successfully treated with long-term opioid antagonist therapy.

Aims:

1) To assess barriers to naltrexone treatment among patients recruited from the Emergency Department after near-fatal overdose. In this aim, we will conduct semi-structured interviews with 20 ED patients presenting after non-fatal overdose to assess their knowledge, attitudes, beliefs, and practical barriers (e.g., insurance, cost, transportation) regarding successful engagement in naltrexone therapy.

2) To evaluate the impact of an escalating oral naltrexone regimen on successful enrollment in depot naltrexone treatment. In this aim, we will evaluate the proportion of study participants successfully starting depot naltrexone injection therapy after an Emergency Department presentation for near-fatal overdose who are receiving either standard therapy, or escalating doses of oral naltrexone (n=20 in each arm). Additionally, we will compare comfort medication use, and self-reported opioid withdrawal scores between the two groups.

Methods: We will screen any patient who presents after naloxone reversal for a reported heroin relapse (by EMS, then confirmed by patient). Patients will be eligible for participation if: 1) they report a single relapse event after more than 14 days of abstinence. 2) are otherwise medically cleared and being discharged from the emergency department.

The initial phase of the study will consist of interviews to evaluate our patient's willingness to begin naltrexone, and identify potential obstacles to engagement in depot naltrexone treatment. The aim of this is to perform qualitative assessments of ED patients presenting after near-fatal overdose regarding barriers to naltrexone treatment. We hope to be able to address some of the barriers identified when our study move into its treatment phase.

In the treatment phase of the study, upon discharge from the emergency department, all patients will receive prescriptions for comfort medications and a referral for outpatient treatment and to receive an injection of depot naltrexone. 40 patients will be enrolled. Of this group, 20 will receive a prescription for escalating oral doses of naltrexone. All patients will be called daily by RA's to evaluate their Subjective Opiod Withdrawal Scale (SOWS) score and use of comfort medications. Coordination with an outpatient treatment center to arrange for treatment with depot naltrexone will be arranged for the patient to receive the medication in 7-10 days after discharge from the emergency department.

Self reported opiod withdrawal symptoms will be evaluated between the naltrexone treatment group and usual care. We will also analyze the number of doses of comfort medication utilized between the two groups. Rates of successful treatment between patients in usual care and escalating doses of oral naltrexone will be measured and compared. We also hope to follow up on patients at one and two months post treatment to assess long-term efficacy of this approach.

Major Limitations/Questions: Our initial study will focus on injection drug users who are not on long-term opiod therapy or abuse oral prescription opiods. This will exclude a large number of patients who may benefit from this or similar therapy, but we feel that these patients' risk for precipitated withdrawal may be greater and we wish to prove safety in a simpler situation of uncomplicated IV opiod abuse after a period abstinence.

This trial will be performed as an intention-to-treat analysis, there will not be any mechanisms to ensure compliance with the proscribed naltrexone regimen. However, we do feel as though this does mimic the real-world scenario of non-compliance with treatment regimens.
The risk of precipitated withdrawal symptoms in patients who have been previously opiod naive has not been well studied. Although in the initial phase of this study, we will use doses of naltrexone that have previously been shown to be well tolerated by patients who are opiod dependent [9], we hope to use higher doses in the future as a proxy for earlier treatment with depot naltrexone once safety of treating these previously naïve patients has been established with the hopes of limiting the amount of time a patient is required to be opioid abstinent to receive depot naltrexone injection

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