TITLE: **A comparison of a Combination of Aspirin and Oral Ketamine (VTS-K formulation) to Oral Ketamine alone in adult patients presenting to the ED with acute musculoskeletal pain: prospective, randomized, open-label, clinical trial.**

NCT#:

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INTRODUCTION

Acute Pain is one of the most frequent chief complaints and the main reason for visiting the Emergency Department (ED). The acute pain in the ED is largely prevalent across the country with recent literature demonstrating that 61-91% of patients are admitted to the ED due to a variety of acute painful syndromes. There is a lack of good options for pain control in such settings.

STUDY OBJECTIVES

To compare analgesic efficacy and rates of side effects of a proprietary formulation of orally administered aspirin and ketamine (AOK) to a proprietary formulation of Oral Ketamine (OK) (VTS-K formulations) for pain management in adult ED patients presenting to the ED with acute musculoskeletal pain

HYPOTHESIS

We hypothesize that the administration of AOK will provide better analgesia at 60 minutes post-administration in comparison to OK in adult patients presenting to the ED with acute musculoskeletal pain. The primary outcome of this trial is the comparative reduction in participant's pain scores at 60 minutes post-medication administration.

STUDY DESIGN

Subjects: Patients 18 years of age and older presenting to the ED with acute musculoskeletal painful conditions (traumatic and non-traumatic) with an initial pain score of 5 or more on a standard 11- point (0 to 10) numeric rating scale and requiring oral analgesia as determined by the treating attending physician. Patients' screening and enrollment will be performed by study investigators and research assistants. All patients will be enrolled at various times of the day when study investigators will be available for patient enrollment and an ED pharmacist will be available for medication preparation.

Eligibility Criteria: Patients 18 years of age and older presenting to the ED with acute musculoskeletal painful conditions (traumatic and non-traumatic) with an initial pain score of 5 on a standard 11- point (0 to 10) numeric rating scale. Patients will have to be awake, alert, and oriented to person, place, and time, and will be able to demonstrate understanding of the informed consent process and content. Patients also will have to demonstrate ability to verbalize the nature of any adverse effects they might experience as well as to express their pain severity by using the NRS.

Exclusion Criteria: Patients with altered mental status, allergy to aspirin and ketamine, pregnant patients, unstable vital signs (systolic blood pressure <90 or>180 mm Hg, pulse rate <50 or >150 beats/min, and respiration

rate <10 or >30 breaths/min), inability to provide consent, consumption of Aspirin or NSAID's within 6 hours of arrival to the ED, active PUD, history of GI Hemorrhage, history of renal and hepatic insufficiency, past medical history of alcohol or drug abuse, or schizophrenia.

Design: This is a prospective, randomized, open-label trial comparing analgesic efficacy and safety of AOK and OK in patients presenting to the ED of Maimonides Medical Center with acute musculoskeletal pain. Upon meeting the eligibility criteria, patients will be randomized into one of the two study arms: Group I will receive AOK and Group II will receive OK.

Data Collection Procedures: Each patient will be approached by a study investigator for acquisition of written informed consent and Health Insurance Portability and Accountability Act authorization after being evaluated by the treating emergency physician and determined to meet study eligibility criteria. When English will not be the participant's primary language, a language- appropriate consent form will be used and non-investigator, hospital-employed, trained interpreters or licensed telephone interpreter will assist in acquisition of informed consent. Baseline pain score will be determined with an 11-point numeric rating scale (0 to 10), described to the patient as "no pain" being 0 and "the worst pain imaginable" being 10. A study investigator will record the patient's body weight and baseline vital signs. All data will be recorded on data collection sheets, including patients' sex, demographics, medical history, and vital signs, and entered into SPSS (version 24.0; IBM Corp) by the research manager. Confirmation of written consent acquisition for all participants, and statistical analyses will be conducted by the statistician, who will work independently of any data collection.

Data Analysis: Data analyses will include frequency distributions and independent-sample t-test to assess differences in pain scores at the various intervals. Mixed-model linear regression will be used to compare changes in pain numeric rating scale across time points. For categorical outcomes (eg, complete resolution of pain), a X^2 or Fisher's exact test will be used to compare outcomes at 60 minutes. Based on the validation of a verbally administered rating scale of acute pain in the ED and the comparison of verbal and visual pain scales, we will use a primary outcome consisting of a minimal clinically meaningful difference of 2 between two groups at the 60-minute pain assessment.

Sample Size: Assuming 3.0 SD, alpha of 0.05 and 80% power, we will need 29 patients per group to detect a superiority of AOK with minimal statistically significant difference of 2.0 at 60 min.

Expected Outcomes: The primary outcome will include a reduction from baseline of pain scores on numeric rating pain scale (NRS) at 60 minutes. The secondary outcomes will include a need for rescue analgesia and rates of adverse up to 120 minutes.

Adverse Events:
With respect to unique adverse effects of SDK, we will use Side Effect Rating Scale for Dissociative Anesthetics (SERSDA) and Richmond Agitation Sedation Scale (RASS). SERSDA Scale includes fatigue, dizziness, nausea, headache, feeling of unreality, changes in hearing, mood change, general discomfort, and hallucinations with severity of each graded by patients on a five-point scale, with "0" representing the absence of any adverse effects and "4" representing a severely bothersome side effect. RASS evaluates the severity of agitation and/or sedation in accordance to the nine-point scale with scores ranging from "−4" (deeply sedated) to "0" (alert and calm) to "+4" (combative).