Ketamine: its effects on suicidal ideations and inpatient hospital length of stay.

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RESEARCH PROTOCOL

Title	Ketamine: its effects on suicidal ideations and inpatient hospital length of stay
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Abstract	Patients admitted to the University of Mississippi Medical Center's (UMMC) inpatient psychiatry unit for suicidal ideations will be given the opportunity to participate in the study. Within 24 hours of arriving to the inpatient psychiatric floor, patients who choose to participate will be randomized to receive either a placebo saline infusion or a ketamine infusion of 0.5 mg/kg over the course of 45 minutes. Infusions will take place in the UMMC Post Anesthesia Care Unit and/or Short Stay Procedure Area. Patients will be monitored for 30 minutes after the completion of their infusion. We will assess all patients' suicidal ideations daily while they are inpatient at UMMC and our primary outcome will be their inpatient hospital course length.
Background	Recent studies demonstrate ketamine can positively impact a patient experiencing suicidal ideations. Ketamine is a NMDA receptor antagonist and has also been shown to have anti-inflammatory effects. There is an association between depression and tumor necrosis factor-alpha as well as interleukin-6 and ketamine has been demonstrated to inhibit both tumor necrosis factor-alpha and interleukin-6. Ketamine works quickly, and the anti-depressant effects have repeatedly been shown to be statistically significant in 24 hours or less. Though ketamine has repeatedly been proven to decrease depressive symptoms, no studies have been conducted evaluating whether or not ketamine shortens the hospital course of a patient admitted with suicidal ideations. Decreasing the inpatient hospital course of a patient admitted for suicidal ideations by as little as one day would save thousands in healthcare dollars.
Purpose	The hypothesis is that ketamine infusions administered to patients with suicidal ideation will help resolve the suicidal ideation more quickly and result in a shorter length of stay than in patients receiving the placebo infusions. The patients will also be assessed for improvement of their suicidal ideations by utilizing the Scale of Suicidal Ideation.
Specific Aim(s)	Our aim is to decrease the length of patients' inpatient hospital course.
Study Period (inclusive years)	Approximately one year to conduct study and an additional six months to follow-up on subjects and assess readmission rates.

Study Design	Patients with suicidal ideations who agree to participate in this study will be enrolled within 24 hours of being admitted to the UMMC inpatient psychiatric service. In order to assess the patient's decisional capacity, a structured protocol will be followed. Only IRB-approved research team members trained in the consent process will consent subjects. During the consent process the investigator will perform a structured assessment of the subjects' capacity to make decisions regarding participating in our protocol. The assessment will occur after the investigator has reviewed the protocol with the patient and the patient has had an opportunity to read the consent form. Introducing the study and obtaining consent will occur in a private area. The investigator's review of the protocol will highlight the following: • participation is voluntary • the purpose of the protocol is to determine if the experimental medication reduces the length of hospitalization • the name of the experimental medication (in this case ketamine) • the potential side effects of the medication • that participating will require placement of a needle in their vein to administer the study medication • the fact that they have a 50% chance of receiving placebo instead of the experimental medication and that they will not be told which they are getting. • the fact that the patient will not be penalized if they decide to not participate in the study Prior to signing the consent form the potential subject will be asked to answer the following list of multiple choice questions designed to test the subject's decisional capacity related to consenting for the protocol. • Which of the following is true? 1. I must sign the consent form and I have to participate in this study. 2. I do not have to sign the consent form or participate in this study if I do not want to participate. 3. I do not have to participate in this study but if I choose not to participate I must leave the hospital. 4. I do not have to participate in this study but if I do I will earn money. • The purpose of the study is to determine if the experimental medication: 1. causes hallucinations 2. improves sleep 3. reduces the length of hospitalization 4. reduces anxiety • The name of the medication tested in this study? 1. Ketamine 2. Zofran 3. Ativan 4. Prozac • Which of the following are potential side effects from the medication used in this study?

Study Design (continued)	1. insomnia, anxiety, headaches 2. hair loss, diarrhea, tingling in the feet 3. ringing or the ears, loss of smell, tooth pain 4. racing heartbeat, high blood pressure, hallucinations • Is getting stuck with a needle part of the study? 1. Yes, an IV which is a needle in the vein 2. No, getting stuck with a needle is not part of the study 3. Yes, an injection in the shoulder. 4. Yes, a prick of the finger to get a blood sample • Will you definitely receive the experimental medication? 1. Yes, I will definitely receive the real medication 2. No, I might not receive the real medication but I will be told if I do not. 3. No, I will not know if I get the fake or real medicine 4. No, I will definitely receive the fake medicine The investigators will consider greater than two incorrect responses 1) evidence of a deficiency in decisional capacity related to the consent process and 2) a criterion for excluding the potential subject from the study. If the potential subject gives no more than two incorrect responses the investigator will ask the subject to explain the incorrect responses. If in discussion of the incorrect responses the investigator feels that the potential subject actually has a correct understanding of the issues covered in the incorrectly answered questions, the investigator will 1) record on the questionnaire why he believes the potential subject understands the incorrectly answered issues and 2) proceed with the consent process. The investigator will consider the potential subject's failure to understand even one of the issues 1) evidence of a deficiency in decisional capacity and 2) criteria for excluding the potential subject from the study. Correct answers for all the questions will serve as evidence of decisional capacity and the potential subject's ability to consent to participate. If the potential subject agrees to participate, he/she will be assured that participation in the study is confidential. After appropriate decisional capacity has been assured, the patient will be assigned at random to one of the following groups: • Group A: receives ketamine intravenous (IV) infusion over 45 minutes • Group B: receives saline (salt solution) over 45 minutes The infusion will be administered in either the Post-Anesthesia Care Unit (PACU) or Short Stay Procedure Area (SSPA). After receiving the infusion, the patient will be monitored for an additional 30 minutes by medical personnel in either the PACU or SSPA. This study will be a randomized, double blind cohort study, so neither the patient nor the study doctor will know which infusion is being administered. While receiving the infusion, the patient's vital signs (including heart rate, heart rhythm, blood pressure, respiratory rate, and temperature) will be monitored on an anesthesia paper chart. After the patient is discharged from the hospital, the treatment team will analyze the patient's medical record and compare the length of hospital stay between the control and treatment groups. The only information about the patient's hospital stay that will be analyzed will be the length of hospital stay.

Study Design (continued)	If a patient is a woman of childbearing age, a urine pregnancy test will be performed after you agree to enroll in the study. The cost of this test will be covered by the University of Mississippi Departments of Anesthesiology and Psychiatry. If you are found to be pregnant, you will not be able to participate in the study. Patients admitted after suicidal attempt may be enrolled in the study. Those who attempted suicide by medication overdose may participate in the study, but must be cleared by a medical toxicology specialist prior to enrollment. Due to cardiovascular adverse effects of ketamine, all participants will receive a 12-lead EKG to screen for cardiac arrhythmias. The cost of this test will be covered by the university of Mississippi Departments of Anesthesiology and Psychiatry. Any rhythm other than sinus rhythm will result in exclusion from the study. The patient's length of hospital stay will be recorded. Patients will be called at three and six months post-discharge to assess for any adverse events or medication reactions. Readmission rates will be assessed at six months post-discharge.
Inclusion Criteria	1. *Men and women between the ages of 18 and 64* 2. *Patients admitted to the UMMC inpatient psychiatry service with suicidal ideations*
Exclusion Criteria	1. Lifetime history of schizophrenia or other primary psychotic disorder 2. Current psychotic or manic symptoms 3. Substance use disorder within one month of admission 4. Positive urine toxicology at admission 5. Any lifetime abuse of ketamine or phencyclidine 6. Systolic BP >180 mmHg or diastolic BP >110 mmHg 7. Any patient who has eaten food within 8 hours prior to receiving the ketamine infusion or who has drank clear liquids within 2 hours prior to receiving the infusion 8. Known CNS mass 9. CNS abnormalities 10. Hydrocephalus 11. Glaucoma 12. Acute globe injury 13. Porphyria 14. Untreated thyroid disease 15. Known coronary artery disease with poor functional capacity 16. Pregnancy 17. Currently breast-feeding 18. Abnormal EKG
Number of Subjects (anticipated)	100 (50 in the control group, 50 in the treatment group)
Outcome Measures	The primary outcome will be the number of hours a patient is admitted to the inpatient psychiatry service after receiving the infusion. A secondary outcome will be improvement in their Scale of Suicidal Ideation score.

Study Endpoints	The study will end upon a patient's discharge orders from the inpatient psychiatry ward being signed in Epic. Patients will be encouraged to notify their nurse when they feel they are ready for discharge, and subsequently will be evaluated by a psychiatrist to determine if they improved significantly enough to leave the inpatient facility.
Private Health Information	The PHI that will be accessed includes the entire patient's medical record within Epic. The only PHI that will be collected is the patient's length of hospital stay. All private health information will be stored on a password-protected USB drive that will be stored in a locked filing cabinet in Dr. Kenneth Oswalt's office at UMMC. Prior to submitting data for statistical analysis, all medical record numbers will be substituted for numerical values ranging from 1 to 100.
Statistical Methodology	Michelle Tucci, PhD, was consulted to determine the power of our study and evaluate for confounding variables. She determined that if a difference in length of stay between the treatment and control groups of two days was expected, then a treatment group of 50 people would be sufficient to potentially find a statistical difference.

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