Stability of Pre-Treatment Suicidal Thoughts in a Clinical Trial of Ketamine's Antisuicidal Effects: A Preliminary Analysis

Ionescu DF[1,2], Baer L[1,2,3], Cusin C[1,2]

[1]Depression Clinical and Research Program, Department of Psychiatry, Massachusetts General Hospital, Boston, MA;
[2]Harvard Medical School, Boston, MA; [3]Department of Psychology, Harvard University, Cambridge, MA

THE METHODOLOGICAL QUESTION

Upon enrolling into a clinical trial, what is the pre-treatment stability of suicidal thoughts in patients with chronic suicidal thinking?

INTRODUCTION

Suicide is the 10th leading cause of death in the Unites States, and unlike other top 10 causes of death (such as heart disease and cancer), suicide rates are on the rise.(1) This highlights the urgent need for studies to assess suicide outcomes and treatments.

However, little is known about the stability of suicidal thoughts upon enrolling into a treatment study, before assignment to a treatment group.
Therefore, we sought to examine the extent to which suicidal thoughts remain stable between the time of enrollment into a clinical trial and the start of treatment. We hypothesized that suicidal thinking would remain stable in depressed patients with suicidal thinking.

METHODS

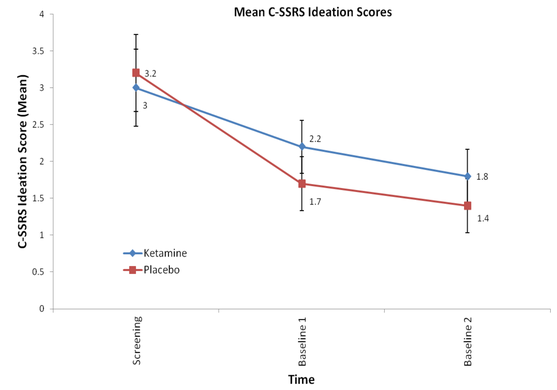
Twenty-six outpatients with severe treatment resistant major depressive disorder and current, chronic (≥ 3 months) suicidal thinking were enrolled and randomized in a double-blind fashion to six infusions over three weeks of ketamine (0.5mg/kg over 45 minutes) or saline placebo ("infusion phase") for the purpose of examining ketamine's antidepressant effects compared to placebo.

Prior to the infusion phase, all patients completed three pre-treatment visits within two weeks; one Screening Visit and two additional Baseline Visits (Baseline 1 and 2). The purpose of multiple pre-treatment visits was to assess continued eligibility prior to randomization.

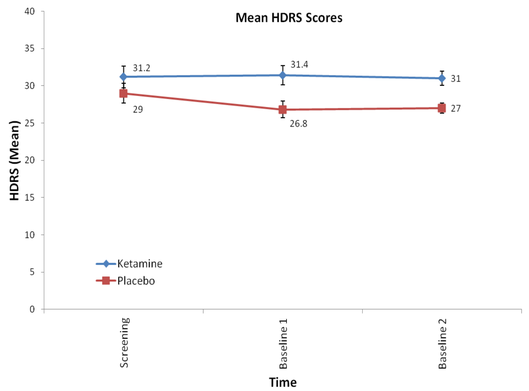
Presence of suicidal thinking was assessed at all visits using the Hamilton Depression Rating Scale (HDRS) Suicide Item (HDRS-SI) Score, C-SSRS Ideation Score (C-SSRS) Ideation and Intensity Scores, and the Concise Health Risk Tracking (CHRT) Scale. Depression severity was assessed with the HDRS Total Score. All scales were clinician-administered, with the exception of the self-administered CHRT. *Post-hoc* analyses with linear mixed models were used to evaluate changes in suicidal thinking and depression across the three pre-infusion visits (from Screening to Baseline 2).

RESULTS

There was a significant effect of time on the C-SSRS Ideation Score, regardless of eventual randomization to ketamine or placebo ($F(23.806)=14.679$, $p<0.001$); specifically, C-SSRS Ideation Scores significantly decreased across the first three pre-infusion visits.



Despite a numerical decrease in other suicide rating scores between the Screening Visit and Baseline 2 (i.e., the visit before the first infusion visit), this decrease did not reach statistical significance for the other suicide rating scales (the HDRS-SI score, the C-SSRS Intensity score, or the CHRT Propensity score (all p's>0.05)). Furthermore, there was no significant increase or decrease of HDRS total scores across the pre-infusion visits ($F(23.084)=0.695$, $p=0.51$).



CONCLUSIONS

Contrary to our hypothesis, suicidal thinking scores decreased prior to randomization, as measured by the C-SSRS Ideation Score. However, there were no significant changes in depression scores as measured by the HDRS Total score during the same period. These data suggest that, unlike depression, suicidal thinking may destabilize upon enrollment into a clinical trial. In turn, this may have implications for the design of clinical trials that seek to examine treatments for suicidal thinking.

Disclosures
One or more authors report the following potential conflicts, which are described in the program: Funding from NIH/NIMH, Brain and Behavior Research Foundation, American Foundation for Suicidal Prevention (AFSP), and Massachusetts General Hospital Executive Committee on Research (ECOR).

References

1. CDC: Injury Prevention & Control: Data & Statistics (WISQARSTM). 2014.