Sustained Mood Improvement with Laughing Gas Exposure (SMILE): A Randomized, Placebo-Controlled Pilot Trial of Nitrous Oxide for Treatment-Resistant Depression

Submission ID 3005881

Submission Type Pharmaceutical Pipeline

Topic Depressive Disorders

Status Submitted

Submitter Venkat Bhat

Affiliation University of Toronto

SUBMISSION DETAILS

Request for Proposals Cutting Edge Treatments

Abstract Background: Nitrous oxide may possess antidepressant effects; however, limited data exist on repeated administrations and active placebo-controlled studies in treatment-resistant depression (TRD). We aimed to test the feasibility of a randomized controlled trial (RCT) examining a 4-week course of nitrous oxide or active placebo, midazolam.
Methods: In this randomized, active placebo-controlled pilot trial, 40 participants with TRD were assigned either a 1-hour inhalation of 50% nitrous oxide plus intravenous saline (n=20) or a 1-hour inhalation of 50% oxygen plus intravenous midazolam (0.02 mg/kg, up to 2mg; n=20) once-weekly, for 4 weeks. Feasibility was assessed by examining rates of recruitment, withdrawal, adherence, missing data, and adverse events. The primary clinical efficacy measure was the change in depression severity, assessed by the Montgomery-Åsberg Depression Rating Scale (MADRS) score, from baseline to day 42. Results: The recruitment rate was 22.3% (95% confidence interval [CI]: 16.9-29.0). Withdrawal rates were 10% (95% CI: 2.8-30.1) in both groups and adherence rates were 100.0% (95% CI: 82.4-100) in the nitrous oxide group and 94.4% (95% CI: 74.2-99.0) in the placebo group. There were no missing primary clinical outcome data in either group (0.0%, 95% CI: 0.0-17.6). MADRS score changed by -20.5% (95% CI: -39.6 to -1.3) in the nitrous oxide group and -9.0% (95% CI: -22.6 to 4.6) in the placebo group. Nearly all adverse events were mild to moderate and transient.
Conclusion: The findings support the feasibility and the necessity of conducting a full-scale trial comparing nitrous oxide and midazolam in patients with TRD.

Author Listing

* Presenting Author

First Name	Last Name	Affiliation

Karim	Ladha	Department of Anesthesiology and Pain Medicine, University of Toronto, Toronto, Ontario, Canada.
Jiwon	Lee	Department of Anesthesia, St. Michael's Hospital, Toronto, Ontario, Canada.
Gabriella	Mattina	Department of Anesthesia, St. Michael's Hospital, Toronto, Ontario, Canada.
Janneth	Pazmino-Canizares	Department of Anesthesia, St. Michael's Hospital, Toronto, Ontario, Canada.
Duminda	Wijeysundera	Department of Anesthesiology and Pain Medicine, University of Toronto, Toronto, Ontario, Canada.
Fatemeh	Nezhad	Interventional Psychiatry Program, St. Michael's Hospital, Unity Health Toronto, Toronto, Ontario, Canada.
Vanessa	Tassone	Interventional Psychiatry Program, St. Michael's Hospital, Unity Health Toronto, Toronto, Ontario, Canada.
Fathima	Adamsahib	Interventional Psychiatry Program, St. Michael's Hospital, Unity Health Toronto, Toronto, Ontario, Canada.
Wendy	Lou	Biostatistics Division, Dalla Lana School of Public Health, University of Toronto, Toronto, Ontario, Canada.
Sidney	Kennedy	Department of Psychiatry, Temerty Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada.
Venkat *	Bhat *	University of Toronto