INPLASY PROTOCOL

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None declared.

The efficacy and tolerability of inhaled N2O in major depressive disorder: a systematic review and meta-analysis

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Review question / Objective: **(1) patient: adult patients diagnosed as MDD; (2) intervention: patients received inhalation of 50% nitrous oxide; (3) comparison: patients received inhalation of 100% oxygen; (4) outcomes: the primary outcome was the change of depression severity scores at different timeline. Secondary outcomes were response and remission. Safety outcomes included the incidence of adverse events. (5) study type: randomized controlled trial (RCT).**
Condition being studied: **Major depressive disorder (MDD) is a common mental illness and has been the leading cause of mortality among mental diseases. As a NMDA receptor, Nitrous oxide (N2O) has been initially used to treat patients with MDD. This meta-analysis aimed to compare the safety and efficacy of N2O inhalation in MDD patients.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 26 February 2023 and was last updated on 26 February 2023 (registration number INPLASY202320113).

INTRODUCTION

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METHODS

Participant or population: Patients diagnosed as MDD based on currently acknowledged guidelines.

Intervention: Patients with inhalation of 50% N2O were classified into intervention group.

Comparator: Patients with inhalation of oxygen were categorized as control group.

Study designs to be included: Randomized controlled trials.

Eligibility criteria: (1) study type: cohort study, case reports, review, letter; (2) language: non-English article; (4) lack of depression measurement results.

Information sources: PubMed, EMBASE, and Cochrane Library.

Main outcome(s): Efficacy outcomes include change of depression severity score which was defined by HAMD or HDRS scales, response and remission which were defined by the included studies. Safety outcome were adverse events occurred after the inhalation.

Data management: We used standard mean difference (SMD) and Relative risk (RR) with their 95% confidence intervals (CI) to assess continuous and dichotomous data. Cochran Q test and I2 test were selected to detect potential heterogeneity. A p 50% was considered substantial heterogeneity.

Quality assessment / Risk of bias analysis: The Cochrane Risk of Bias Tool was used to assess the characteristics of the studies for risk of bias which assessed bias through six domains: sequence generation, allocation concealment, blinding approaches, incomplete outcome data, selective reporting, and other sources of bias.

Strategy of data synthesis: All data in this meta-analysis were performed by STATA 17.0.

Subgroup analysis: Subgroup analysis was conducted on treatment-resistant major depression (TRMD), which was a subgroup of MDD.

Sensitivity analysis: sensitive analysis was performed when heterogeneity was more than 50%.

Language restriction: English.

Country(ies) involved: China.

Keywords: Depression, Major depressive disorder, MDD, N2O, Nitrous oxide, Meta-analysis.

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