

REVIEWER'S REPORT

Manuscript No.: IJAR-54017

Date: 24/09/2025

Title: Ketamine Combined With Dextromethorphan-Bupropion for Depression in the Context of Nitrous Oxide Misuse

Recommendation:

Accept as it is ☐☐☒☐..

Accept after minor revision ☐☐☐☐

Accept after major revision ☐☐☐☐☐

Do not accept (*Reasons below*) ☐☐☐

Rating	Excel.	Good	Fair	Poor
Originality	✓			
Techn. Quality		✓		
Clarity		✓		
Significance		✓		

Reviewer Name: Sakshi Jaju

Date: 24/09/2025

Reviewer's Comment for Publication.

The article presents a case of a 27-year-old male with depression linked to nitrous oxide misuse, treated with esketamine and dextromethorphan-bupropion. The combined therapy provided rapid symptom relief and supported abstinence from nitrous oxide use. The case highlights the potential of using clinically supervised NMDA receptor antagonists as alternatives to maladaptive self-medication.

Strengths:

1. Novel therapeutic approach combining two rapid-acting antidepressants.
2. Well-documented case with clear clinical outcomes.
3. Provides biological rationale and references to recent studies.

Weaknesses:

1. Single case report; lacks generalizability.
2. Short follow-up period; long-term outcomes unclear.
3. No comparison with standard treatments or control group.

Overall Assessment:

The article is interesting and clinically relevant, offering insights into innovative treatments for depression with substance misuse. However, larger studies are needed to confirm efficacy and safety before widespread application.

Recommendation:

Manuscript accepted for the publication .