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Case Report

### Successful Treatment of Methamphetamine Use Disorder Using Oral Naltrexone and Bupropion: A Case Report

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### ABSTRACT

**Background:** Methamphetamine use disorder (MUD) remains a significant challenge due to the absence of approved pharmacological treatments. Recent studies have shown promise in combining naltrexone and bupropion to reduce craving and use.

**Case presentation:** We report the case of a 41-year-old single male with severe methamphetamine dependence who presented with daily intravenous use, self-neglect, paranoia and auditory hallucinations. He had no prior psychiatric or medical history. Treatment with oral naltrexone 50 mg daily and bupropion extended-release 150 mg daily was initiated, alongside regular follow-up every two weeks. Over the following months, his methamphetamine use progressively decreased, cravings diminished and psychotic features resolved. After six months, he achieved complete abstinence for three consecutive months, with no relapse or significant side effects.

**Conclusion:** This case supports the emerging evidence for the combination of naltrexone and bupropion in the management of methamphetamine use disorder. Oral formulations may be a practical and accessible alternative where injectable naltrexone is unavailable. Further clinical studies are warranted.

**Keywords:** Methamphetamine; Disorder; Oral formulation; Naltrexone

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### Introduction

Methamphetamine use disorder (MUD) is a growing global public health problem associated with severe psychiatric, medical and social consequences. Despite its high prevalence and substantial morbidity, there are currently no approved pharmacotherapies for MUD. Psychosocial interventions remain the mainstay of treatment; however, relapse rates remain high.

Recent clinical trials, including the Accelerated Development of Additive Pharmacotherapy Treatment for Methamphetamine Use Disorder (ADAPT-2) study, have suggested that the combination of extended-release injectable naltrexone and oral bupropion may reduce methamphetamine use and craving<sup>1</sup>. However, data on the effectiveness of oral naltrexone combined with bupropion remain limited. This report presents a successful case using this oral combination in a patient with severe

methamphetamine dependence.

## Case Presentation

A 41-year-old single, unemployed male presented to the psychiatric outpatient clinic seeking help for crystal methamphetamine use. He reported daily intravenous methamphetamine use for approximately two years prior to presentation, resulting in significant self-neglect and social isolation. His family had expelled him from their home due to behavioural disturbance and he was living alone. He denied the use of other substances or alcohol.

During periods of heavy methamphetamine use, he experienced paranoid ideas and auditory hallucinations. He had previously been prescribed antipsychotic medication by another psychiatrist but reported minimal benefit. There was no prior psychiatric or medical history.

Mental state examination at presentation revealed a dishevelled, restless and suspicious man. His mood was anxious with intermittent low mood. Speech was coherent, with no formal thought disorder. He expressed paranoid ideation but denied current auditory hallucinations or suicidal thoughts. Cognition and insight were preserved.

## Intervention and follow-up

Given his motivation to stop using methamphetamine and

his awareness of the consequences, pharmacological treatment was initiated with bupropion extended-release 150 mg once daily and oral naltrexone 50 mg once daily. After two weeks, bupropion was increased to 300 mg once daily, with biweekly outpatient follow-up.

Craving severity and substance use patterns were assessed clinically at each visit based on patient self-report corroborated by clinician evaluation. Craving severity was described descriptively as severe, moderate, mild or minimal, reflecting intensity and functional impact.

At the two-week review, the patient reported good medication tolerability with a modest reduction in methamphetamine use and craving severity. Over the subsequent month, craving severity decreased further, methamphetamine use reduced to approximately three times per week and paranoid symptoms improved significantly. Clinical changes over time are summarized in (Table 1).

By six weeks, methamphetamine use had decreased to twice weekly with minimal craving. After two months, the patient demonstrated continued clinical and social improvement. At three months, he reported complete abstinence with no craving or relapse. No adverse effects were observed during the treatment period. Urine toxicology screening was initially positive for amphetamines but became negative after two months and remained negative thereafter.

**Table 1:** Changes in Craving Severity, Methamphetamine Use, Medications and Clinical Features Over Follow-Up.

Time point	Medication and dosage	Craving severity (clinician-rated)	Methamphetamine use	Mental status	Urine toxicology
Baseline	None	Severe	Approximately 3 grams per week, near-daily intravenous use	Paranoid delusions and auditory hallucinations	Positive for amphetamines
After 2 weeks	Bupropion XR 150 mg/day; Naltrexone 50 mg/day	Moderate	Approximately 2 grams per week, around four days per week	Persistent paranoid delusions and auditory hallucinations	Positive for amphetamines
After 6 weeks	Bupropion XR 300 mg/day; Naltrexone 50 mg/day	Mild	Approximately 1 gram per week	Paranoid delusions present; auditory hallucinations resolved	Positive for amphetamines
After 2 months	Bupropion XR 300 mg/day; Naltrexone 50 mg/day	Minimal	Single reported use	No psychotic symptoms	Negative
After 3 months	Bupropion XR 300 mg/day; Naltrexone 50 mg/day	None	Complete abstinence	No psychotic symptoms	Negative

## Discussion

This case demonstrates a successful outcome using oral naltrexone combined with bupropion for the treatment of methamphetamine use disorder. The proposed mechanism underlying this combination involves modulation of both dopaminergic and opioid reward pathways.

Bupropion is a dual norepinephrine and dopamine reuptake inhibitor at clinically relevant doses and may reduce stimulant craving and withdrawal symptoms<sup>2</sup>. Naltrexone, a  $\mu$ -opioid receptor antagonist, is thought to reduce the reinforcing effects of methamphetamine and attenuate reward-driven use.

The ADAPT-2 trial provided evidence for the efficacy of extended-release injectable naltrexone combined with oral bupropion in reducing methamphetamine use<sup>1</sup>. However, access to injectable formulations remains limited in many regions. This case adds to emerging clinical evidence suggesting that oral naltrexone in combination with bupropion may also be an effective and pragmatic treatment option. Previous studies have shown that bupropion alone may reduce methamphetamine use in selected patients<sup>3</sup>.

The patient's gradual improvement is consistent with neurobiological adaptation and behavioural stabilization over time. Motivation for change and structured follow-up likely contributed significantly to the positive outcome. Overall, the treatment was well tolerated and associated with marked reductions in craving severity, psychotic symptoms and methamphetamine use.

## Limitations

This report is limited by its single-case design, which restricts generalizability and precludes causal inference. Psychosocial factors, including patient motivation and engagement with follow-up, may have influenced outcomes. Additionally, although urine toxicology was used to corroborate abstinence, objective measures were not obtained at every follow-up visit. Larger controlled studies are needed to establish efficacy, optimal dosing and duration of oral naltrexone and bupropion combination therapy for methamphetamine use disorder.

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