



Successful Management of Polysubstance Dependence Syndrome with Endoxifen – A Case Report

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Abstract

This is a case report of a 32-year-old male, a known case of polysubstance dependence syndrome, including cannabis, alcohol, nicotine, and cocaine, with a history of multiple relapses. He was admitted to a psychiatric facility multiple times for detoxification and psychotherapy. After being treated with endoxifen, the patient was able to maintain abstinence from substances for 18 months. This case highlights the successful Management of polysubstance dependence syndrome with endoxifen.

ARTICLE INFO

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Dates:

Received: 10-01-2025
Accepted: 04-03-2025
Published: 30-06-2025

Keywords:

Polysubstance
dependence syndrome,
Endoxifen, Quetiapine,
Disorder, Relapse
prevention.

How to Cite:

Saluja J. Successful
Management of
Polysubstance
Dependence Syndrome
with Endoxifen – A Case
Report. *Indian Journal
of Clinical Psychiatry.*
2025;5(1): 45-47.
doi: 10.54169/ijocp.v5i01.09

INTRODUCTION

Substance use disorders pose a significant public health concern, characterized by repeated and compulsive use of substances despite negative consequences. Commonly abused substances include alcohol, tobacco, cannabis, opioids, and stimulants.¹ These abuse disorders often lead to devastating consequences on individuals, families, and even communities, leading to health problems, social dysfunction, and economic burdens. Current treatment approaches for substance use disorders include behavioral therapies, pharmacotherapies, and a combination of both. Though there have been substantial advancements in their treatment, relapse rates still remain high, highlighting the need for novel therapeutic strategies.² Protein kinase C (PKC), particularly the PKC δ isoform, mediates the neuropsychological effects of drugs of abuse like methamphetamine, including oxidative stress, neuroinflammation, and dopaminergic degeneration. Inhibition of PKC, such as the PKC β isoform, can attenuate the dopamine-releasing effects of amphetamine-type stimulants.³ Some published case reports suggest endoxifen, a direct protein kinase C inhibitor, to have a beneficial role in substance use disorders.^{4,5,6}

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CASE PRESENTATION

The case: A 32-year-old businessman presented to our psychiatry clinic three years back with complaints of aggression, disturbed daily routine, disturbed sleep, mood fluctuations, interpersonal conflicts, along with abusive and violent behavior. The patient also reported a history of a recent financial loss. The patient was a known case of alcohol, tobacco, cannabis, opioids, and stimulant abuse.

Past history: He started substance use at the age of 15 years by smoking nicotine cigarettes with his peers. At 16, he was introduced to cannabis in the form of hash rolled with tobacco, and he started drinking beer at social gatherings. He continued his education until he was 18 years old, when he was enrolled in college and was exposed to additional substances, including LSD, cocaine, mushrooms, and ecstasy. His substance use escalated over time, leading to frequent use of cocaine, tobacco, and cannabis, often accompanied by alcohol. This pattern caused a decline in his interest in college and business. At 27 years of age, he was admitted to a psychiatry facility for detoxification and psychotherapy; subsequently, he was discharged on a daily regimen of quetiapine 200 mg, naltrexone 50 mg, and baclofen 30 mg. However, he relapsed on alcohol and cannabis within 14 days of discharge. Afterwards, he stopped showing up in the clinic and tried to manage his condition independently for several months. Despite his efforts, he continued to experience frequent relapses, consuming up to two bottles of whiskey in 24 hours.

Examination findings: At the time of presentation, he had normal psychomotor activity and no evidence of formal thought disorder. His higher mental functions, including judgment and insight, were intact, suggesting that he was able to make rational decisions and understand his condition. The patient underwent multiple laboratory investigations, including CBsC, LFT, RFT, RBS, HbA1c, Thyroid profile, ECG, and lipid Profile. No significant abnormalities were found in the investigation reports. He was diagnosed with polysubstance dependence syndrome.

He was prescribed endoxifen 8 mg to be taken in the morning and quetiapine 50 mg at night for

sleep. After two months, he reported a reduction in substance use in the form of drinking alcohol only once or twice a week and consuming cannabis twice a month.

For the last 3 years, the patient has been continuing on the same dose of endoxifen and quetiapine without any relapse or adverse events. The patient has been regularly coming for follow-up every month and undergoing a cannabis urine screening test, which has been negative for the past 20 months. He has completely stopped taking alcohol and other substances for the last 20 months and has maintained an absolute abstinence from all the substances. He is also managing his business well, with no arguments or quarrels at home, maintaining a good daily routine with regular sleep. During last visit, the patient was subjected to routine laboratory investigations in which no significant abnormality was found.

DISCUSSION

This case report highlights the successful Management of polysubstance dependence syndrome with endoxifen and quetiapine. The use of endoxifen, a direct inhibitor of protein kinase C (PKC), has been shown to be effective in reducing manic symptoms associated with bipolar disorder. Case reports demonstrating the efficacy of endoxifen in managing comorbid substance use disorders among patients with bipolar mania are available.⁴⁻⁶ A case report by Dubey (2022) showed that long-term treatment with 8 mg twice daily for 3 months proved efficacious in controlling severe manic symptoms, with no adverse effects and reduced alcohol consumption.⁴ Another case report by Thanvi V. (2022) reported nil craving for stimulant use when the patient was put on endoxifen therapy.⁵ Along similar lines, the present case was able to maintain complete abstinence from all substances, including alcohol, tobacco, cannabis, opioids, and other stimulants, for a long period of 20 months. The outcomes suggest that endoxifen was effective in addressing the underlying neurobiological mechanisms that contributed to his substance use disorder. Throughout the treatment period, the patient underwent comprehensive investigations to

monitor his overall health and to ensure the safety of the prescribed medications. Endoxifen treatment did not cause any significant adverse effects. The addition of quetiapine, an atypical antipsychotic, helped to manage the patient's sleep disturbances.

CONCLUSION

According to our knowledge, this is the first case report demonstrating the effectiveness of endoxifen in patients with polysubstance dependence syndrome for an extensive period of 3 years. Endoxifen can be a potential option for the Management of substance use disorder, though randomized controlled trials are warranted to confirm the same.

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