

# Cocaine-Induced Psychosis and Asenapine as Treatment: A Case Study

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*ABSTRACT ~ Cocaine-induced psychotic disorder (CIPD) is one of the most serious consequences of cocaine use. Despite the high frequency of CIPD, specific treatment for CIPD has been scarcely researched. Although supportive measures are the first approach, antipsychotic use is often necessary due to clinical severity and CIPD consequences. We report a 38-years-old man with substance use disorders in methadone maintenance treatment who relapsed on cocaine use and presented CIPD that was satisfactorily treated with asenapine. It is important further research on CIPD management, especially on asenapine and other second-generation antipsychotics due to its possible role in its treatment. Psychopharmacology Bulletin. 2019;49(1):92-97.*

## INTRODUCTION

Cocaine use is a social and health problem with more than 17 million past-year users around the world in 2017, being North America, Oceania and Western/Central Europe the main markets.<sup>1</sup> Cocaine use is related to several neuropsychiatric issues and disorders.<sup>2</sup> The most serious neuropsychiatric consequence is psychosis, ranging its prevalence between 29% and 86.5% depending on the study variables.<sup>3</sup> The most common symptoms are delusions (referential and persecution) and hallucinations (auditory, visual, kinesthetic).<sup>2-5</sup> Furthermore, agitation and violent behavior are frequently observed during intoxication.<sup>2,3</sup> Cocaine-induced psychotic symptoms could be transient (presented only during cocaine intoxication) or be experienced for a longer time than a simple cocaine intoxication, in the latter case it is known as cocaine-induced psychotic disorder (CIPD).<sup>2-5</sup>

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There is limited literature regarding CIPD management and treatment.<sup>2,6</sup> Overall, supportive measures are the first approach, such as monitoring hydration and vital signs accompanied by security measures such as offering a nonstimulating environment.<sup>2,5</sup> Pharmacotherapy for CIPD is not well established, being the clinical targets particularly agitation, psychotic symptoms and the anxiety.<sup>4</sup> During intoxication the use of benzodiazepines is reasonable if anxiety or agitation is present.<sup>5,7</sup> However, the use of antipsychotic is frequently needed not only in the acute approach,<sup>2</sup> but also it could continue in short periods if psychotic symptoms are not self-limited (i.e., CIPD is present).<sup>2</sup> There are scarce investigations on antipsychotics and CIPD and some authors indicate that sedative<sup>4</sup> and second-generation antipsychotics should be considered, among them olanzapine, quetiapine, risperidone, and even ziprasidone.<sup>2</sup> There is not information on other new antipsychotics such as aripiprazole or asenapine, despite they have strong evidence in primary psychosis.<sup>8-10</sup> Based on the foregoing, it is needed more research in this area, and in this line, we report a patient with CIPD that was successfully treated with asenapine.

## CASE

A 38 years old man who has only as medical record a hepatitis C virus infection that was treated when he was 36 years old. In his psychiatric history, he began intravenous heroin and intranasal cocaine use at the age of 19. He initiated treatment for substance use disorder (SUD) when he was 23 years old. The patient was included in methadone maintenance program since the first moment, with a stable dose of methadone (60 mg/day) for the last two years. The patient reached heroin abstinence with methadone and cocaine decreased (he has not achieved cocaine abstinence for prolonged periods). Pregabalin has been prescribed in some periods for anxiety disorder no specified. During follow-up, the patient presented several episodes of psychotic symptoms related to cocaine use, those episodes remained some days (sometimes until 10 days), and usually with high behavioral repercussion and great severity of symptoms (irritability, anxiety, restlessness, persecutory delusions, auditory and kinesthetic hallucinations). Due to this severe clinical presentation has been prescribed antipsychotics in some occasions during short periods (no more than 10 days), among antipsychotics used in the past are: olanzapine, quetiapine, risperidone and paliperidone. The patient presented bad tolerance to those antipsychotics, and they were not always effective to control anxiety and/or psychotic symptoms. Risperidone (until 3 mg/day) and paliperidone

(until 6 mg/day) were bad tolerated due to extrapyramidal symptoms and no anxiety control, however the patient report good psychosis control with them. Olanzapine (15 mg/day) and quetiapine (250 mg/day) produced drowsiness, the patient described that both decreased anxiety but only olanzapine controlled psychotic symptoms.

The current episode began after a cocaine relapse (3 days of intranasal cocaine consumption) with psychotic symptoms associated. The patient sought help for anxiety and psychotic symptoms. He referred auditory and kinesthetic hallucinations and persecutory delusions, plus presented irritability, anxiety and psychomotor restlessness. Urine toxicological analysis was positive only for cocaine and methadone. It was prescribed asenapine 10 mg/day due to bad tolerance to previous antipsychotics, and a daily control with psychiatrist was performed at the outpatient center. Two days later, the patient presented no psychomotor restlessness and less irritability and anxiety, but psychotic symptoms did not improve until fourth day. He reported improvement of auditory hallucinations on the fourth day and no delusions on the fifth day. The full remission of psychotic symptoms was reported on seventh days, and asenapine was stopped on tenth day. He did not report any specific side effect with the medication except by a mild nasty taste in the mouth while was in treatment. The patient was receiving methadone (60 mg/day) and pregabalin (150 mg/day) before and during the current episode.

## DISCUSSION

To the best of our knowledge, this is the first report of asenapine use in CIPD, showing a good profile in this issue. CIPD treatment is not well established and usually supportive measures are performed.<sup>2</sup> Antipsychotic use sometimes is needed during the intoxication and when the psychotic symptoms persist,<sup>2</sup> this case represents well how antipsychotics could be used in CIPD.

Asenapine has been extensively researched in schizophrenia and bipolar disorder,<sup>9,10</sup> and in some reports describe potential uses in other issues such as borderline personality disorder<sup>11</sup> and psychotic anxiety.<sup>12</sup> The antipsychotic effect of asenapine is related to antagonist activity at dopamine D2 and serotonin 5-HT<sub>2A</sub> receptor.<sup>13</sup> Therefore, it is probable that the antipsychotic effect of asenapine on CIPD could be related to the dopaminergic activity, as cocaine has a direct effect on dopaminergic system.<sup>14</sup> Besides biochemical profile, asenapine seems to cover important clinical targets when CIPD is approached such as anxiety,<sup>12</sup> aggressive behavior<sup>15</sup> and obviously psychotic symptoms.<sup>9</sup>

No specific clinical trial has been performed on antipsychotics and CIPD, however one case report have described that first generation antipsychotic (chlorpromazine and haloperidol) could be useful for psychotic symptoms.<sup>16</sup> Additionally, some authors describe that second generation antipsychotic may be useful.<sup>2</sup> There are specific clinical trials on other psychostimulant-induced psychosis. Thus, on methamphetamine or amphetamine-induced psychosis (MIP) have been successfully assessed aripiprazole,<sup>17</sup> haloperidol,<sup>18–20</sup> olanzapine,<sup>18,20</sup> risperidone,<sup>17,19,21</sup> and quetiapine.<sup>22</sup> Despite good evidence about antipsychotics in MIP, it is important to mention that cocaine and methamphetamine users have differences in psychopathology and outcomes.<sup>23</sup> Finally, it is important to mention that aside from antipsychotics, there is one case series on lithium as an effective CIPD treatment.<sup>24</sup>

A limitation to extrapolate this case is that we did not use any specific tool to measure psychotic symptoms and its improvement. Additionally, asenapine was used as off-label medication, although off-label use is common among SUD patients and comorbid psychosis.<sup>25</sup> Finally, it is possible that current psychotic symptoms could have been transient, however, the patient presented psychotic symptoms longer than a transient psychosis and this episode was similar to the past psychotic episodes. In any event, it is important to research more on CIPD treatment, especially on antipsychotic treatment. Asenapine and other second-generation antipsychotics may be useful for CIPD treatment. ❖

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## CONFLICT OF INTEREST

Dr. Palma-Álvarez has received fees to give talks for MSD, Mundipharma and Exeltis.

Dr. Ros-Cucurull has received fees to give talks for Janssen-Cilag, Lundbeck, Otsuka, Pfizer, Lilly, Servier, Rovi, Juste. She has received financial compensation for projects with Lundbeck, Esteve, Pfizer, Rovi, Exeltis, Servier. She has received financial compensation for her participation as a board member of Janssen-Cilag. She has no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict.

Dr. Ramos-Quiroga has received fees as speaker from Janssen-Cilag, Shire, Lilly, Ferrer, Medice and Rubió. He has received research funding from Janssen-Cilag, Lilly, Ferrer, Lundbeck and Rubió.

Dr. Roncero has received fees to give lectures for Janssen-Cilag, Ferrer-Brainfarma, Pfizer, Indivior, Lundbeck, Otsuka, Servier, GSK, Rovi, Astra, Gilead, MSD, Sanofi and Exeltis. He has received financial compensation for his participation as a board member of Janssen-Cilag, Lundbeck, Gilead, MSD, Indivior and Mundipharma. He has carried out the PROTEUS project, which was funded by a grant from Reckitt-Benckiser/Indivior. He received a medical education grant for Gilead.

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