CASE REPORT

Efficacy of Aripiprazole in Comorbid Addiction in Bipolar Disorder Pierre Alexis Geoffroy,^{1,2} Guillaume Goddefroy,^{1,2} Benjamin Rolland^{1,2,3} & Olivier Cottencin^{1,2,4}¹ University of Lille Nord de France, Lille, France² Department of Addiction Medicine, CHU Lille, Lille, France³ EA 1046, Lille, France⁴ UDSL, LNFP, EA4559, Lille, France**Keywords**

Addiction; Antipsychotic medication; Bipolar Disorder; Dopamine agonist; Substance use disorder.

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Introduction

Comorbid substance use is a very common problem in bipolar disorder (BD) [1]. Few controlled pharmacological studies have examined its treatment, while comorbidity often complicates BD's diagnosis and treatment and worsens the course of illness and prognosis [2].

Aripiprazole is the first partial agonist dopaminergic antipsychotic with an action on D2/D3 dopamine receptors and a low side-effect profile. Aripiprazole has been proven to be useful during all phases of bipolar illness [3]. In substance-dependence treatment, early results with aripiprazole are promising and warrant further exploration [4,5]. We report, to the best of our knowledge, the first case of a patient presenting with type II BD and polysubstance use (PSU) successfully treated by aripiprazole for both disorders at the 6-month follow-up.

Case Report

A 41-year-old man presenting with a 27-year history of mood disorders and PSU was admitted to our addiction treatment unit for medical PSU detoxification. He presented with alcohol and cannabis-dependence according to DSM-IV TR criteria [6] and with weekly to daily consumption of cocaine and less frequent use of ecstasy. His addiction history reports that his alcohol and

Table 1 Summary of patient drug use history

Age (years old)	Drug use
14	Cannabis and alcohol
15	Cannabis, alcohol, cocaine, heroin, ecstasy, and amphetamine
15–41	Several drug detoxifications and treatments without efficacy (maximal abstinence period of one month)
26	Opioid substitution therapy (OST) with buprenorphine Cannabis, alcohol, cocaine, ecstasy, and amphetamine
40	Buprenorphine (6 mg a day), cannabis, alcohol, and cocaine
41	Today drug detoxification for cannabis, alcohol, and cocaine Maintaining OST (buprenorphine)

cannabis consumption began at 14 years old and was quickly followed by PSU, including cocaine, heroin, ecstasy, and amphetamine. The patient has been using buprenorphine since the age of 26 years old (6 mg/day now for 1 year). Drug use history is summarized in Table 1.

In his past medical history, he presented with a first suicide attempt at 18 years old after using of hypnotics and alcohol, followed by several hospitalizations in the Department of Psychiatry for Major Depressive Disorder (MDD) according to DSM-IV TR criteria [6]. His family history showed alcohol dependence (father

and sister), and his sister committed suicide. Moreover, his three brothers are suffering from PSU without information in favor of current mental illness.

He attempted several drug detoxifications in our department (his first one in 1985) and unfortunately presented with a maximal abstinence period of 1 month. The patient attributed relapses to mood symptoms. His past therapeutic history is marked by many therapeutic attempts, including antidepressants (escitalopram, fluoxetine, and venlafaxine) and mood stabilizers (olanzapine and valpromide), without efficacy on both addictive and thymic symptoms, leading to subsequent relapse and resurgent mood symptoms.

During each hospitalization, his main complaint was depressive symptoms. Due to a careful history and evaluation for the presence of manic or hypomanic symptoms, we noticed many hypomanic episodes. Moreover, the patient indicated psychostimulant intakes with the objective to regain his hypomanic states. At the current admission in our unit, we performed a hypomania rating scale of Angst et al. [7] and determined a score of 19/20, suggesting the diagnosis of bipolar II disorder according to the DSM-IV TR criteria [6]. Thus, we stopped venlafaxine (150 mg/day for the past 6 months) and introduced a mood stabilizer: aripiprazole (10 mg/day). At the same time, we moved the patient on to PSU detoxification (alcohol, cannabis, and cocaine) with diazepam (80 mg/day the first day then reduced each 72 h by 10 mg/day), hydroxyzine (200 mg/day), paracetamol (3 g/day in case of pain), B1, B6, and PP vitamins and hydration. Opiate substitution treatment with buprenorphine (6 mg/day) was continued.

Because the BD type II history and PSU were closely related, the aim of our treatment was to obtain a significant improvement in both affective and addiction symptoms. Affective symptoms (sadness) improved after the first week of hospitalization, and after 2 weeks, the patient no longer craved alcohol, cannabis, or cocaine for the first time in 27 years.

A 6-month follow-up showed that he had wholly stopped PSU, which was confirmed by weekly random alcohol and drug tests. Aripiprazole was continued at 10 mg/day and no adverse effect was reported during the 6-month follow-up. The absence of craving prompted us to consider reducing the opiate substitution treatment but the patient refused. Diazepam was wholly stopped during the first 1-month follow-up. The patient did not consume alcohol or other drugs anymore (except buprenorphine treatment 6 mg/day) and did not develop affective symptoms. He currently exhibits improved functional status and found employment 4 months ago as a landscaper.

Discussion

In this case, olanzapine and valpromide were administered for years. Both are recommended in BD but did not present any efficacy on PSU here. We think that aripiprazole helped to treat the patient's addictive and psychiatric symptoms. Furthermore, experimental studies suggest that aripiprazole could help in improving the relative hypoactivity of dopaminergic pathways during psychostimulant withdrawal [8]. Pilla et al. suggested that the action of aripiprazole on addictive disorders results from the partial agonist action on dopamine D2 and D3 receptors in the nucleus accumbens, whose receptors are involved in addictive behavior when stimulated by dopamine [9]. Only one open study (with a small sample size) aimed to replace the previous antipsychotic treatment with aripiprazole in patients treated for BD or schizoaffective disorder who displayed signs of substance abuse. This approach resulted in a significant reduction in the craving for alcohol and cocaine over a 3-month follow-up [10]. New research needs to be conducted in comorbid substance use treatment, and we may expect promising results with aripiprazole, especially in BD patients with PSU.

References

1. Stinson FS, Grant BF, Dawson DA, Ruan WJ, Huang B, Saha T. Comorbidity between DSM-IV alcohol and specific drug use disorders in the United States: Results from the National Epidemiologic Survey on alcohol and related conditions. *Drug Alcohol Depend* 2005;**80**: 105–116.
2. Singh JB, Zarate CA, Jr. Pharmacological treatment of psychiatric comorbidity in bipolar disorder: A review of controlled trials. *Bipolar Disord* 2006;**8**(6): 696–709.
3. Fountoulakis KN, Vieta E, Schmidt F. Aripiprazole monotherapy in the treatment of bipolar disorder: A meta-analysis. *J Affect Disord* 2011;**133**: 361–370.
4. Feltenstein MW, Do PH, See RE. Repeated aripiprazole administration attenuates cocaine seeking in a rat model of relapse. *Psychopharmacology (Berl)* 2009;**207**:401–411.
5. Vergne DE, Anton RF. Aripiprazole: A drug with a novel mechanism of action and possible efficacy for alcohol dependence. *CNS Neurol Disord Drug Targets* 2010;**9**: 50–54.
6. Association AP. *Diagnostic and statistical manual of mental disorders DSM-IV-TR*, 4th ed. Arlington, USA: American Psychiatric Publishing, Inc., 2000.
7. Angst J, Adolfsson R, Benazzi F, et al. The HCL-32: Towards a self-assessment tool for hypomanic symptoms in outpatients. *J Affect Disord* 2005;**88**: 217–233.
8. Schwabe K, Koch M. Effects of aripiprazole on operant responding for a natural reward after psychostimulant withdrawal in rats. *Psychopharmacology (Berl)* 2007;**191**:759–765.
9. Pilla M, Perachon S, Sautel F, et al. Selective inhibition of cocaine-seeking behaviour by a partial dopamine D3 receptor agonist. *Nature* 1999;**400**:371–375.
10. Brown ES, Jeffress J, Liggin JDM, Garza M, Beard L. Switching outpatients with bipolar or schizoaffective disorders and substance abuse from their current antipsychotic to aripiprazole. *J Clin Psychiatry* 2005;**66**:756–760.