

Polydipsia as a Precursor of Manic Episode in Bipolar Affective Disorder Patients with Alcohol Use Disorder

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Bipolar affective disorder (BD) diagnosis and initiation of appropriate treatment are often delayed, and this is associated with poorer outcomes, such as rapid cycling or cognitive decline. Therefore, identifying certain warning signs of a probable successive episode during the inter-episode phase is important for early intervention. We present the retrospective data of three cases of BD. Our first case had a history of alcohol use disorder (AUD), where he drank in a dipsomaniac manner, and the other two cases had dipsomaniac alcohol use before their manic attacks, and none of them had any AUD after the mood episode was over. Two brothers also had hypertensive episodes during the manic attacks. None of the cases reported increased fluid intake when they were euthymic. We suggest that polydipsia in BD may be a warning sign of an upcoming manic episode, especially in those patients with AUD. Polydipsia in BD may be caused or facilitated by a combination of hyperdopaminergic activity, hypothalamic dysfunction, and dysregulated renin-angiotensin system. To be able to prevent new episodes, a patient's drinking habits and change in fluid intake should be asked at every visit. Those patients with a history of alcohol abuse should especially be informed about polydipsia and manic episode association.

KEY WORDS: Polydipsia; Manic disorder; Binge drinking; Comorbidity; Alcoholism.

INTRODUCTION

Bipolar affective disorder (BD) causes severe suffering in patients and their relatives and enforces high economic costs on the healthcare system. The total lifetime prevalence estimate for the BD spectrum is 2.4%,¹⁾ and it is the sixth leading cause of disability among mental disorders worldwide.²⁾ Regarding the prevalence and public health costs of BD, it is clear that the research for understanding the pathogenesis, course, and treatment of the disease is paramount.

BD often starts with a depressive episode. During the prodrome phase of a first manic episode, patients have symptoms like mood fluctuation, sleep disturbance, and functional impairment, which are non-specific symptoms that might be seen in other psychiatric syndromes as

well.³⁾ These make it difficult to predict a first hypomanic or manic episode. BD diagnosis and initiation of appropriate treatment are often delayed.⁴⁾ The delay in diagnosis and treatment of BD is associated with poorer outcomes like rapid cycling or cognitive decline.⁵⁾ The staging model of BD suggests that the disease progresses from mild to severe presentations in time. Therefore, the early management of BD is critical to prevent further progression.⁶⁾

In our clinical practice, we have observed some of our patients reporting polydipsia before the onset of a manic episode. Polydipsia is common in schizophrenic patients but is rarely reported in BD.^{7,8)} We suggest that polydipsia may be one of the early signs of a manic episode, especially in those patients with alcohol use disorders (AUD). We will briefly present three BD cases with polydipsia.

CASE

Case 1

A 33-year-old male patient responded to treatment

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with amitriptyline 75 mg/day for major depression (MD). He had a previous history of AUD with episodes of dipsomania. By the end of the third month of antidepressant treatment, his daily intake of water had increased from 4 L/day to 14 L/day. His alcohol consumption didn't change. Soon after these complaints of polydipsia, he became more talkative, had a decreased need for sleep, and was overspending money, so diagnosis of a manic episode was made, and he was started on chlorpromazine 100 mg/day, zuclopenthixol 20 mg/day, and biperiden 2 mg/day. The manic symptoms resolved, and his daily water drinking decreased to 5 L/day after four weeks of treatment. By the third year of remission, his water drinking again increased from 4 L/day to 8 L/day, and a second manic episode ensued.

Case 2

A 35-year-old male patient who had been on paroxetine 20 mg/day and modafinil 100 mg/day treatment for MD for the past six months came to the outpatient clinic complaining of feeling thirstier. He drank more water than usual (5 L/day), had cravings for alcohol, and had a blackout during a dipsomaniac alcohol drinking episode. A week later, his energy levels increased and he became distractible and irritable. Therefore, he was diagnosed with a manic episode. Paroxetine and modafinil were stopped, and he was started on valproic acid 750 mg/day and aripiprazole 10 mg/day. His arterial blood pressure measurements were frequently above 140/90 mmHg; so he was started on amlodipine 5 mg/day. The manic episode resolved in a month, and his thirst decreased. He no longer craved for alcohol. His antihypertensive drug was stopped by the first month because of hypotension. He has been in remission for the past 13 months.

Case 3

Forty-two year-old male patient is the brother of Case 2 who was followed up by the same physician. He also had a diagnosis of BD with MD as the first presenting mood episode. According to his medical records during his two manic episodes, he also had complained about increased thirst, dipsomaniac alcohol drinking, and hypertensive attacks that resolved during euthymic states. He has been in remission for the past eight years with chlorpromazine 25 mg/day and has not been drinking alcohol since because he thinks alcohol triggers the episodes.

DISCUSSION

We have presented three male cases of BD, whose first episodes were MD, and who had polydipsia before the onset of a manic episode. None of the cases had a history of diabetes mellitus or diabetes insipidus that might have induced polydipsia. Even though the information about the third case is retrospective, it is included to support the genetic background of BD and to highlight the co-occurrence of hypertensive episodes with the manic attacks. None of the cases reported increased fluid intake during euthymia.

Polydipsia is defined as drinking more fluids than the physiologic needs of the body, which has been suggested to be more than 3 L/day.⁹⁾ Clinically, the patient drinks large amounts of fluids and has polyuria. Polydipsia may cause hyponatremia and water intoxication, manifested by psychiatric symptoms, nausea, vomiting, delirium, ataxia, seizures, coma, and even death when untreated.¹⁰⁾ Psychogenically induced polydipsia (PPD) is mainly seen in schizophrenia among other psychiatric syndromes⁷⁾ and may be a coping mechanism in stressful conditions.¹¹⁾ PPD is a multifactorial dysfunction of the hypothalamic-pituitary axis (HPA). Chronic consumption of excess fluid might be changing the feedback regulation of HPA.¹²⁾

Polydipsia in BD may share a common etiologic factor with polydipsia in schizophrenia. As previously suggested, elevated levels of dopamine might be stimulating the thirst center.¹³⁾ To explain the development of psychogenic polydipsia in schizophrenia, in an animal model, repeated treatment with D2/D3 agonist quinpirole was shown to induce hyperdipsia¹⁴⁾ in a compulsive manner.¹⁵⁾ Many of the behavioral abnormalities seen in BD may be related to hyperdopaminergic activity,¹⁶⁾ especially in the mesolimbic pathway,¹⁷⁾ which might constitute the basis for hyperdipsia in BD as well. In agreement with this, all of our patients responded to antipsychotic drugs. Hyperdopaminergic activity is temporary in BD during a manic episode, which supports the idea of polydipsia as an early sign of a manic episode. None of our patients had polydipsia after their manic episodes were over.

Our first case had a history of AUD, when he drank in a dipsomaniac manner, and the other two cases had dipsomaniac alcohol use before their manic attacks; however, none of them had any AUD after the mood episode was over. Alcohol abuse may be another factor contributing to

polydipsia. Schizophrenic patients with polydipsia have a more frequent history of alcohol abuse.¹⁸⁾ Harding *et al.*¹⁹⁾ found that chronic alcoholic men had neuronal loss in vasopressin (VP) producing neurons. Generally, VP release is induced in hyperosmolar plasma states, resulting in decreased urine production and increased thirst; however, chronic alcohol use may disrupt VP release, and osmotically inappropriate thirst responses like polydipsia may ensue.²⁰⁾

The two brothers, without any family history of hypertension, had increased arterial hypertension during the manic attacks that resolved when the episode ended. The increase in arterial blood pressure may be related to a common factor that results in abnormal fluid intake. Longitudinal follow-up of these two patients shows that as long as they remain in the euthymic state, they don't report any increase in arterial blood pressure or fluid intake which might strengthen the suggested tie between BD manic episodes and polydipsia and concurrent hypertension. Angiotensin II (AngII) is dipsogenic.²¹⁾ The effects of AngII are mediated by AT1R and AT2R receptors. Hyperactivation of these two receptors is implicated in the pathophysiology of mood disorders by their pro-inflammatory effects.²²⁾ Angiotensins may also have regulatory effects on dopaminergic activity in the brain²³⁾ which might, in part, explain both the manic episode and polydipsia. AngII is also responsible for increased arterial hypertension, so it might be suggested that concurrent hypertension that resolves after a manic episode is over may be caused by the vasoconstrictor effects of AngII. In light of all these, use of AT1R receptor antagonists as previously suggested by de Góis Queiroz *et al.*²²⁾ may be complementary in the management of manic episodes.

As a summary, we have suggested that polydipsia in BD may be a warning sign of an upcoming manic episode especially in those patients with AUD. Polydipsia in BD may be caused or facilitated by a combination of hyperdopaminergic activity, hypothalamic dysfunction, and dysregulated renin-angiotensin system. Interrelations among these three may form the basis or be a consequence of the basic pathophysiology of BD. To be able to prevent new episodes, a patient's drinking habits and change in fluid intake should be asked at every visit. Regarding the hypertensive episodes in our patients, it is clear that arterial blood pressure measurements should be

a regular part of every psychiatric evaluation. Those patients with a history of AUD should be informed about polydipsia and manic episode association.

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