Case Report

Paliperidone-induced Polydipsia in Schizophrenia

Yi-Ting Hsieh, M.D., Yi-Yung Hung, M.D., Tiao-Lai Huang, M.D.*

Objective: Polydipsia is an underdiagnosed clinical phenomenon among patients with chronic schizophrenia. Detection and management of polydipsia are clinically important because of its complications such as severe hyponatremia and water intoxication, resulting in epilepsy, coma, and death. The effect of antipsychotic drugs can cause polydipsia remains controversial. Case Report: We report a 37-year-old male patient taking paliperidone (12 mg per day) for chronic schizophrenia. After a three-week treatment with paliperidone, he developed polydipsia (daily water intake being greater than 10 liters) and hyponatremia. He did not have any other medical causes. We switched paliperidone to olanzapine (20 mg per day) due to suspected paliperidone-induced polydipsia. His daily water intake was decreased to 5 liters after two weeks, and all other associated symptoms were subsided. No relapse of polydipsia was noted in the following six months. Conclusion: Polydipsia may be related to paliperidone use. Further investigation of its cause relationship is needed.

Key words: Paliperidone, polydipsia, hyponatremia, antipsychotic

Introduction

Polydipsia which is a common clinical complication of psychiatric patients, has been reported in more than 20% of chronic hospitalized psychiatric patients [1]. Detection and treatment of polydipsia are important clinically because of its serious complications such as hyponatremia and water intoxication, resulting in seizure, coma, and death.

In schizophrenia, the excessive intake of liquid has been associated with positive symptoms, nicotine, inappropriate antidiuretic hormone (ADH) release, and medication side effects [2]. Polydipsia and hyponatremia can occur as a side effect of treatment with different psychotropic medications including tricyclic antidepressants, selective serotonin reuptake inhibitors, monoamine oxidase inhibitors, benzodiazepines, antiepileptic drugs and antipsychotics [3]. Until now, the pathophysiology of polydipsia is still unclear,
and this lack of knowledge limits the possibility of developing an appropriate drug treatment [4]. First-generation antipsychotic drugs have been associated with a worsened polydipsic behavior. The most beneficial effect has been obtained with clozapine [4]. Second-generation antipsychotic drugs such as olanzapine and risperidone, are not clearly useful and their effect remains controversial [4]. A recent report suggests that risperidone can also induce polydipsia and hyponatremia [5].

Paliperidone, a major active metabolite of risperidone, has not been reported to cause polydipsia. Here we report a chronic schizophrenic inpatient who developed severe polydipsia, secondary hyponatremia, body weight gain and bilateral scrotal swelling after paliperidone therapy.

Case Report

A 37-year-old single and unemployed male patient has been diagnosed as chronic schizophrenia, paranoid type according to DSM-IV criteria for five years and was previously admitted to psychiatric ward for four times. He did not have any physical illness or substance abuse except of little alcohol drinking. He had been treated with risperidone at outpatient clinic for two years, and he was found to have mild polydipsic symptoms like excessive water drinking and thirst in the past. But he had poor compliance, resulting in having aggravated psychotic symptoms including auditory hallucinations and delusions of reference. At admission, his positive and negative syndrome scale (PANSS) was 135. The laboratory data showed mild hypokalemia (blood potassium level: 3.4 mEq/dL, normal range: 3.7-5.2 mEq/dL), and no other specific abnormal findings in complete blood count, liver and renal function and blood sodium.

After admission, he took 12 mg/day of paliperidone for recurrent psychosis, and zolpidem 10 mg HS for insomnia. Patient responded well and his PANSS score was decreased to 98 in two weeks. But he developed severe polydipsia and secondary hyponatremia in the third week of the treatment. His daily drinking volume of water was greater than 10 L per day, and he gained 7.6 kg in 20 days. He complained of frequent thirst, and had severe bilateral scrotal swelling. Following excessive water intake he experienced nausea, general malaise, slurred speech and drowsiness, but did not have muscle twitches, cramps, blurred of vision, delirium or coma. The laboratory results showed hyponatremia (blood sodium level: 127 mEq/dL, normal range: 135-145 mEq/dL), elevated antidiuretic hormone (ADH) (blood ADH level: 4.65 pg/ml, normal range: 0.4-2.4 pg/ml) and mild hypokalemia (blood potassium level: 3.4 mEq/dL). His urine sodium, blood osmolality, urine osmolality, thyroid function and blood sugar remained within the normal range. The finding of a brain MRI revealed unremarkable. His paliperidone 12 mg/day was switched to olanzapine 20 mg/day due to the possible role in inducing polydipsia. He also received 3 g of salt per day. His daily water drinking volume was reduced to less than 5 L/day in the following two weeks gradually. His hyponatremia and scrotal swelling were also subsided. However, his psychotic symptoms were relapsed at the same time. We shifted olanzapine to clozapine and titrated gradually to 350 mg per day after two weeks. His psychotic symptoms were stabilized, and he had not had any relapse of polydipsia in the following six months.

Discussion

The patient had used risperidone for two years before admission with poor drug compli-
ance and irregular outpatient clinic follow-up. Previously, he had mild polydipsic symptoms at outpatient clinic. We assumed that his drug compliance was poor when he was on risperidone therapy at the clinic, therefore, his polydipsic symptoms were not severe at that time.

Thirst and excessive water-drinking developed in the three weeks after the patient started to receive paliperidone therapy, and his water-drinking problem was subsided two weeks after discontinuing paliperidone. He did not have any brain lesion, diabetes mellitus or insipidus. He was not on any other medication known to cause polydipsia [3]. He never had the similar symptoms before and after discontinuation of paliperidone, so the psychogenic cause was not likely. The Naranjo adverse drug reaction probability scale for this case is 6, indicating that paliperidone is a probable (score = 5-9) cause of polydipsic symptoms.

How antipsychotic treatment causes neuroendocrine abnormalities is not clear. But syndrome of inappropriate antidiuretic hormone (SIADH) has most frequently been mentioned as the underlying mechanism. SIADH is caused by excessive secretion of antidiuretic hormone (ADH). Long-term D₂ receptor blockade after long-standing antipsychotic use may lead to supersensitivity of dopamine D₂ receptors, resulting in increased ADH levels [6, 7]. Long-term D₂ receptor blockade can also increase peripheral effect to angiotensin II with dipsinogenic activity in humans, and increase angiotensin II-induced thirst in animals [8]. In a report on aripiprazole-induced hyponatremia, the authors suggest that ADH releasing is suspected to be mediated through serotonin, which may be the effect of second-generation antipsychotic drugs [9]. In addition, second-generation antipsychotic drugs induce severe polydipsia by stimulating the thirst center or causing a dry mouth due to anticholinergic effect [10].

Olanzapine and risperidone are not proved effective in treating polydipsic schizophrenic patients, and might worsen the symptoms. On the contrary, clozapine showed efficacy in treating polydipsia among schizophrenic patients. Lower binding affinity for D₂ of clozapine than risperidone and olanzapine might be associated with avoidance of D₂ supersensitivity [4]. Queitapine shows benefit in polydipsic treatment due to its clozapine-like preclinical profile in some case reports, but the data remains limited for a definite conclusion [4, 11].

Paliperidone, 9-hydroxy-risperidone, is a dopamine D₂ and serotonin 5-HT₂ receptor antagonist. In our case, we suspect that paliperidone has the similar effect with risperidone. We suspect that paliperidone induces polydipsia and hyponatremia though the way as excessive ADH releasing, which may be D₂ receptor-related or serotonin-mediated. In addition, the role of increased peripheral effect to angiotensin II and anticholinergic effect cannot be ruled out.

In recent years, paliperidone is increasingly used in schizophrenic patients, and we have reported the first case of paliperidone-induced polydipsia here. This case report is limited for extrapolating this observation to other paliperidone-medicated patients, because we did not re-challenge our patient with paliperidone. The adverse effect of polydipsia and hyponatremia during paliperidone treatment warrant clinical awareness and further investigation.

References


