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POLIDIPSIA PSICÓGENA EN LA DISCAPACIDAD INTELECTUAL - UN DESAFÍO CLÍNICO

PSYCHOGENIC POLYDIPSIA IN INTELLECTUAL DISABILITY – A CLINICAL CHALLENGE

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ABSTRACT

Introduction: Primary polydipsia (PP), or psychogenic polydipsia, is the excessive liquid intake (> 3 litres per day) that is not explained by any other medical condition. It can occur in up to 14% of psychiatric patients and the origin of the water-seeking behaviour among these patients remains unknown. When uncontrolled, patients drink beyond their renal capacity of excretion, developing hyponatremia, which can progress to water intoxication with nausea, vomiting, confusion, ataxia and can even be fatal.

Methods: Case presentation based on the observation of the patient in the inpatient unit, analytical studies and the patient's clinical records. We present a non-systematic review of the literature on the possible mechanisms that may be at the origin of the primary polydipsia and treatment approaches that have been suggested.

Case presentation: We present a case of an individual with an intellectual disability medicated with risperidone for several years suffering from primary polydipsia and consequent severe water intoxication. After stopping risperidone and switching to low dose clozapine, the polydiptic behaviour stopped. One month after discharge it hadn't resurged and the patient remained analytically normal.

Discussion: Antipsychotics have been suggested to be associated with primary polydipsia due to their high affinity to dopamine D2 receptors with consequent receptor hypersensitivity in the hypothalamic-pituitary-adrenal axis and centre of thirst. Fluid restriction is important to correct hyponatremia. A pharmacological approach is often imperative to help patients to become more permeable to behavioural strategies. Unlike other antipsychotics, clozapine does not induce D2 hypersensitivity in the centre of thirst, therefore, it can be a reasonable treatment option.

Conclusion: It is important to elucidate clinicians about this condition since it is common in psychiatric patients and often goes unnoticed or inadequately approached. Further investigations on the link between primary polydipsia and mental diseases are needed, as they are greatly under-researched, in order to find new treatments and management approaches to this condition.

Keywords: Primary polydipsia; Psychogenic polydipsia; Intellectual disability; Water intoxication; Antipsychotics; Clozapine.

RESUMEN

Introducción: La polidipsia primaria (PP), o polidipsia psicógena, es la ingestión excesiva de líquidos (> 3 litros por día) que no se explica por ninguna otra condición médica. Puede ocurrir hasta en el 14% de los pacientes psiquiátricos y se desconoce el origen del comportamiento de búsqueda de agua de estos pacientes. Cuando no se controla, los pacientes beben más allá de su capacidad renal de excreción, desarrollando una hiponatremia que puede progresar a una intoxicación hídrica con náuseas, vómitos, confusión, ataxia e incluso puede ser fatal.

Métodos: Presentación de casos basada en la observación del paciente en la unidad de hospitalización, los estudios analíticos y las historias clínicas del paciente. Se presenta una revisión no sistemática sobre los posibles mecanismos que pueden estar en el origen de la polidipsia primaria y los enfoques de tratamiento que se han sugerido.

Presentación de caso: Presentamos el caso de una persona con discapacidad intelectual medicada con risperidona durante varios años que padece polidipsia primaria y la consiguiente intoxicación grave por el agua. Tras dejar de tomar la risperidona y cambiar a una dosis baja de clozapina, el comportamiento polidíptico se detuvo. Un mes después de la alta hospitalaria, la polidipsia no habia resurgido y el paciente se mantenia analiticamente normal.

Discusión: Se ha sugerido que los antipsicóticos se asocian con la polidipsia primaria debido a su alta afinidad con los receptores de dopamina D2, con la consiguiente hipersensibilidad de los receptores en el eje hipotalámico-pituitaria-suprarrenal y el centro de la sed. La restricción de líquidos es importante para corregir la hiponatremia. A menudo es imprescindible un enfoque farmacológico para ayudar a los pacientes a ser más permeables a las estrategias de comportamiento. A diferencia de otros antipsicóticos, la clozapina no induce hipersensibilidad al D2 en el centro de la sed, por lo que puede ser una opción de tratamiento razonable.

Conclusión: Es importante aclarar a los médicos acerca de esta afección ya que es común en los pacientes psiquiátricos y a menudo pasa desapercibida o se aborda de manera inadecuada. Se necesitan más investigaciones sobre el vínculo entre la polidipsia primaria y las enfermedades mentales, ya que están muy poco investigadas, a fin de encontrar nuevos tratamientos y enfoques de gestión de esta afección.

Palabras clave: Polidipsia primaria; Polidipsia psicogénica; Discapacidad intelectual; Intoxicación por agua; Antipsicóticos; Clozapina.

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INTRODUCTION

Primary polydipsia (PP) is characterised by an increased fluid intake with a consistent excretion of great quantities of dilute urine over an extended period, without any underlying medical cause. Polydipsia can occur in up to 14% of psychiatric patients, therefore, it is also called psychogenic polydipsia. Although most commonly seen in patients with schizophrenia, it has been described in patients with affective and anxiety disorders, intellectual disability and personality disorders (Mercier-Guidez & Loas, 2000).

Generally, PP develops in three phases, beginning with polydipsia and polyuria, followed by hyponatremia (when the kidney's capacity to excrete water is exceeded) and, finally, water intoxication that manifests as nausea, vomiting, delirium, ataxia, seizures, coma and can even be fatal (Bhatia, Goyal, Saha, & Doval, 2017). Unfortunately, it can still go unnoticed or be incorrectly diagnosed, especially in milder cases, which can be mistaken with worsening of the primary psychiatric illness. It is crucial to determine the exact diagnosis since treatment options vary substantially.

Interestingly, antipsychotic therapy can promote the development of this condition. The most commonly associated are the typical antipsychotics. In regard to atypical antipsychotics (risperidone, in particular), the results are still scarce and controversial (Bersani, Pesaresi, Orlandi, Gherardelli, & Pancheri, 2007; Kar, Sharma, Tolar, Pai, & Balasubramanian, 2002; Kawai, Baba, & Suzuki, 2002). This article describes a case of polydipsia with a possible association with the long-term use of risperidone.

METHODS

Case presentation based on the observation of the patient in the inpatient unit, analytical studies and the patient's clinical records. We made a non-systematic review of the literature on the possible mechanisms that may be at the origin of the primary polydipsia in this patient and the best treatment approaches that have been suggested.

CASE PRESENTATION

A 38-year-old male with a diagnosis of intellectual disability, a previous history of childhood meningitis and a malignant testicular tumour treated with surgery and chemotherapy (two years before), was admitted to our inpatient psychiatric unit due to exacerbated polydipsia, with four years of evolution. He had been treated several times for hyponatremia (as low as 105mmol/L), associated with nausea, vomiting, dizziness and ataxia. His parents reported worsening of the excessive water intake behaviour, including drinking water from the toilet and sink, since he stopped attending the day care centre. Blood and urine testing, at one time he went to the emergency department, revealed low plasma sodium (119 mmol/L), low plasma osmolality (248 mOsmol/Kg), lower limit of normal urinary osmolality (96 mOsmol/Kg), and low urinary sodium (16mEq/L). He was previously medicated with valproic acid 500mg bid, risperidone 2mg bid and clonazepam 2mg bid for control of disruptive behaviour.

The differential diagnosis included primary polydipsia, syndrome of inappropriate antidiuretic hormone secretion (SIADH), diabetes insipidus (DI), hyperthyroidism and primary adrenal insufficiency. During hospitalization, 24-hour urinary output confirmed polyuria. Thyroid function, calcium, urea, creatinine, glucose, fasting aldosterone and cortisol were within normal range. Brain MRI excluded hypothalamic/pituitary lesions or tumours and a thoracoabdominal CT scan showed no causes for the condition. Initially, room containment for fluid restriction was necessary, with polyuria resolution and normalization of plasma sodium and urinary and plasma osmolalities. However, uncontrollable thirst and constant water-seeking behaviour persisted, predisposing to psychomotor agitation and emotional lability. Due to the absence of behavioural improvement under the prescribed therapy (risperidone 2 mg bid, clonazepam 1mg id, and lorazepam 2.5mg id), risperidone was stopped and clozapine 12.5mg was introduced. Progressive remission of the water-seeking behaviour was obtained with no complaints of thirst, urinary and plasma osmolality remained normal, as well as plasma sodium. One month after discharge, there was no recurrence of compulsive fluid intake, and blood/urine testing remained normal.

DISCUSSION

Despite the frequency of this condition, polydipsia remains difficult to manage and treat. Since the first reports of the association between polydipsia and mental disease, diverse contributing factors have been suggested, however, the ethiopathogenesis of this disorder still remains uncertain.

Most studies have been carried out with schizophrenic patients. These studies propose that ventricular enlargement may lead to hypothalamic structural defects and, consequently, to abnormalities in the regulation of the thirst centre (Goldman et al., 2007).

Dopamine in the most implicated neurotransmitter in thirst and excessive water intake behaviour in animal models. This has been tested with exogenous dopamine which increased thirst (Amato, Müller, & Badiani, 2012). A recent systematic review showed that the most common antipsychotics used before the onset of polydipsia were those with high affinity to dopamine D2 receptors, which include typical antipsychotics and the atypical antipsychotic risperidone (Kirino et al., 2020). Chronic blockade of D2 receptors can cause dopamine receptor hypersensitivity in the hypothalamic-pituitary-adrenal axis and centre of thirst (Bersani et al., 2007; Verghese, De Leon, & Simpson, 1993). This hypersensitivity explains why polydipsia can occur several years after the continued exposure to antipsychotics (Verghese et al., 1993). At higher doses, risperidone increasingly blocks the dopamine D2 receptors, thereby acting more like a typical antipsychotic (Nyberg, Eriksson, Oxenstierna, Halldin, & Farde, 1999) Despite the controversial results in relation to the effect of risperidone in the treatment of polydipsia, there are case reports that describe improvement of the condition with low dose risperidone (Kawai et al., 2002; Kruse et al., 2001). Nonetheless, it is important to notice that, in our patient, polydipsia stopped after risperidone was withdrawn.

States of anxiety and stress can manifest with primary polydipsia as they can induce an increase in dopamine levels and, consequently, induce thirst. The compulsive drinking behaviour can also be seen as a coping strategy, since it produces a feeling of pleasure and reward with activation of the prefrontal cortex (Saker et al., 2014). This is particularly important in mentally retarded patients, as the compulsive drinking behaviour can be cyclical and coincident with anxiety periods, suggesting that this may be an attempt to mediate stress (Klemperer, 1991). Over the years, excessive water intake can lead to hypothalamic secondary structural defects with repercussions in the feedback of thirst osmoregulation on the hypothalamic-pituitary axis. This maintains the deviant behaviour even in the presence of low plasma osmolality (Siegel, Baldessarini, Klepser, & McDonald, 1998). In PP cases severe enough to cause hyponatremia, as in this patient, have a very high volume intake with consequent very low ADH levels and low urine osmolality (Verghese et al., 1993).

Another important factor is that thirst can be stimulated by the anticholinergic collateral effects of antipsychotics that can cause dry mouth, intensifying water intake to counteract this side effect (Bhatia et al., 2017).

The first step in the diagnosis is to collect the patient's medical and psychiatric history, assess the presence of uncontrollable thirst, current medication and run a complete analytical study to exclude secondary causes of polydipsia. The next step is to check for the presence of polyuria by collecting 24-hour urine, measure plasma and urinary osmolalities and plasma electrolytes. The diagnosis of SIADH is unlikely in this patient considering the presence of polydipsia, polyuria and a decreased urine osmolality. PP is part of the polyuria-polydipsia syndrome, so differential diagnosis with DI is necessary. PP is primarily characterised by an increased fluid intake and polyuria is secondary to the renal excretion of excess water due to a physiologic suppression of ADH (as a result of low plasma osmolality) (Nigro, Grossmann, Chiang, & Inder, 2018). DI is determined by polyuria due to impaired ADH secretion (central DI) or renal ADH resistance (nephrogenic DI – normal/high ADH secretion) and consequent polydipsia, adaptative in an attempt to compensate for the excessive loss of water by the kidney (Bersani et al., 2007; Sailer, Winzeler, & Christ-Crain, 2017). A normal or low plasma sodium and a low plasma and urinary osmolalities are indicative of PP (Sailer et al., 2017). However, the gold standard for making the differential diagnosis is a water deprivation test. In PP, after the water deprivation test, urinary and plasma osmolalities will normalize, as well as plasma sodium (Nigro et al., 2018). Instead, in DI, urinary osmolality will remain below the normal range, polyuria will persist and patients will eventually develop hypernatremia. Due to the lack of support of specialized medical skills necessary for the water deprivation test procedure, it was not possible to perform it in our psychiatric ward. The diagnosis was based on previous osmolalities and plasma sodium levels and their normalization after fluid restriction.

Controlled fluid restriction is the key treatment for PP. However, it often fails due to patient´s non-compliance, who suffers from a compulsive drinking behaviour. Behavioural interventions show some beneficial effects in higher-functioning patients, but they demand close monitoring from medical staff, so they usually need hospitalization. Our patient has an intellectual disability, so any attempt of a behavioural strategy was difficult to implement and for him to adhere, in extreme, needing seclusion from all water resources.

All pharmacological options are considered of low evidence, as they consist of case reports or small prospective studies. Atypical antipsychotics have shown some success in alleviating symptoms of PP. However, as mentioned before,

the impact of risperidone is still controversial. There are reports indicating that risperidone decreases water consumption, possibly secondary to the improvement of psychotic symptoms and helping patients to become more compliant to behavioural therapy (Millson, Emes, & Glackman, 1996; Saker et al., 2014). In contrast with other antipsychotics, clozapine has a relatively low affinity for dopamine D2 receptors and high affinity for serotonin 5HT2A receptors. It may be a reasonable treatment option for polydipsia as it does not induce hypersensitivity in D2 receptors, which has been proposed to generate or worsen polydipsia (Kapur & Seeman, 2001). Furthermore, clozapine can improve polydipsia regardless of the improvement of psychosis, since it has a role in the correction and stabilization of sodium and water metabolism and thirst regulation in some cases (Verghese, de Leon, & Josiassen, 1996). Although its doubtful efficacy due to non-existence of large trials, our patient was medicated with low dose clozapine, showing a clear improvement in the compulsive fluid intake behaviour.

Many other medications have been studied, namely those that affect body water balance. Clonidine (an α-adrenergic blocker) and enalapril (an ACE inhibitor) showed improvement in fluid consumption, and irbesartan (an angiotensin receptor blocker) had positive effects in another case report (Kruse et al., 2001). Naltrexone can possibly play a role in improving compulsive drinking behaviour by the blockade of opioid neurotransmission in the paraventricular and supraoptic hypothalamic nuclei, which has an effect on the thirst mechanism and reduction of diurnal weight change (Becker, Goldman, Alam, & Luchins, 1995).

CONCLUSION

The pathophysiology of PP is complex and far from fully understood. PP is associated with a wide spectrum of psychiatric comorbidities beyond schizophrenia. It is important to elucidate clinicians about this condition since it is common in psychiatric patients and often goes unnoticed and inadequately approached in clinical practice. Evaluation of patients warrants a comprehensive evaluation for other medical causes of polydipsia. A well established communication channel between psychiatry and other specialties is crucial to make the definitive diagnosis.

Fluid restriction is a successful measure to correct hyponatremia complications. However, long-term treatment options for this typically chronic condition are scarce. The current literature is not consistent about which treatment is most effective, mostly because there is a lack of large trials. Additionally, polydipsia is frequently episodic, making interpretation of findings from case reports even more difficult.

Since antipsychotics can serve both as cause and treatment of polydipsia, it is of extreme clinical relevance to clarify the relationship between polydipsia and antipsychotics. In this case report, risperidone was stopped and clozapine was started right away, therefore, it is not possible to identify the real impact of the drug interventions. Further investigations are needed, especially in other mental diseases other than schizophrenia, as they are greatly under-researched, in order to find new treatment and management approaches to this condition.

DECLARATION OF AUTHORSHIP, GOOD PRACTICES AND ASSIGNMENT OF RIGHTS

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