Case report

Archives of Psychiatry Research 2024;60:061-066

DOI:10.20471/feb.2024.60.01.08
Received March 27, 2023
Accepted after revision May 25, 2023

"It's a Psychiatric Patient": Misdiagnosing of Somatic Symptoms in Patients with Mental Disorders Due to Stigma and Inadequate Diagnostic Treatment

Sara Bračko[1], Andreja Čelofiga[2]

[1]Medical Faculty, University of Maribor, Maribor, Slovenia, [2]Department of Psychiatry, University Medical Centre Maribor, Maribor, Slovenia

Keywords

Mental disorders; stereotyping; antipsychotic agents; amiodarone; thyrotoxicosis

Abstract

Aim: People with mental illness have more somatic comorbidities and are frequently mistreated. Misdiagnosis occurs for a variety of reasons, including stigma, poor communication, lack of knowledge of psychiatric pathology, and a tendency to attribute physical symptoms to a mental disorder. **Case report:** The factors listed above, as well as the unique circumstances of the covid-19 pandemic led to the misdiagnosis in the case discussed in this paper. The patient was a middle-aged man diagnosed with an ICD-10 diagnosis of a chronic mental disorder in the F2 category and multiple somatic comorbidities in whom amiodarone-induced thyrotoxicosis was undiagnosed and somatic symptoms were attributed to antipsychotic-induced parkinsonism. The mechanism of amiodarone-induced thyrotoxicosis and antipsychotic-induced extrapyramidal symptoms will be described, together with the factors that caused our patient to be misdiagnosed. **Conclusion:** Psychiatric patients are often specific in their communication and behaviour, therefore interaction must be adapted, with a focus on destigmatizing and educating health workers.

Introduction

Individuals with severe mental illness face an increased risk of somatic comorbidities and premature mortality, with a life expectancy that is approximately 30 % shorter than the general population [1-3]. There are several contributing factors to this disparity, including the potential for severe somatic diseases to go undiagnosed or untreated in these patients [2,4]. Certain symptoms associated with mental illness, such as negative symptoms, lack of insight, cognitive impairment, and social isolation, can make it challenging to recognize and treat comorbidities. Patients with severe mental illness are also more likely to experience substance misuse and the long-term effects of psychotropic medications [2]. Additionally, studies have found that as many as 50 % of patients taking chronic psychiatric medication do not follow their treatment plans, and 25 - 90 % of psychiatric patients do not adhere to their prescribed treatment

Correspondence to:
Sara Bračko
Medical Faculty, University of Maribor
Taborska Ulica 8, 2000 Maribor, Slovenia
Phone: + 386 70 663 181
E-mail: sara.bracko@student.um.si

plans [5]. Unfortunately, the quality of medical care provided to patients with severe mental illness is often poor and inadequate [3]. Stigma, poor communication, inadequate knowledge of psychiatric pathology, and a tendency to attribute physical symptoms to a mental disorder are among the most common reasons for this [3,6]. The stigma surrounding mental health disorders contributes to the stigma surrounding somatic problems in these patients [6]. Access to and adequacy of medical care for patients with severe mental illness can also be problematic, with some patients lacking a general practitioner and reporting difficulty accessing health care and medical specialists [7,8]. During the COVID-19 pandemic, all of these challenges have been exacerbated. Pandemic-related restrictions and fear of exposure to the virus have significantly reduced access to health services and treatments [9,10]. Unfortunately, this opened a great possibility of undetected and untreated diseases [11]. We present the case of a patient with a chronic mental disorder and multiple somatic comorbidities in whom amiodarone-induced thyrotoxicosis was undiagnosed and the symptoms were attributed to antipsychotic-induced parkinsonism. No information that might reveal the identity of the patient has been included. Personal information of the patient that is not relevant for the presentation for this case report has been removed.

Case report

A middle-aged man was hospitalised after experiencing hypersalivation, slurred speech, slowed movement (particularly walking), and impaired thinking for a few weeks. He had experienced fatigue, bilateral pretibial oedema, and diarrhoea. He was a multimorbid patient with an ICD-10 diagnosis of chronic mental disorder in the F2 category, cardiovascular and pulmonary diseases. Before the hospitalization, he visited the emergency room twice due to dysarthria and generalized weakness. On his first visit CT, ECG and laboratory tests were normal, so he was discharged. On the second visit (two days later) he was diagnosed with secondary parkinsonism due to antipsychotic therapy and got a referral for an MRI and psychiatric consultation.

During both visits, clinical exams revealed tachycardia (about 110 bpm) and dyspnoea, it was noticed that his arms were not synchronized with his legs while walking. Other diagnostic tests were inconclusive. One day later he was admitted to the psychiatric unit. When admitted, he displayed mental, verbal, and motor slowness, he was hypomimic, hypobulic, while his speech was dysarthric and difficult to understand (possibly due to hypersalivation). He was without delusions or perceptual disturbances. Cognitive slowness with impaired attention has been described and formal thought disorders have been indicated. The symptoms were attributed to a combination of drug-induced parkinsonism and cognitive decline secondary to a chronic mental disorder.

He was diagnosed with a chronic mental disorder more than 20 years ago and had been hospitalized 4 times, otherwise, he was stable. His regular psychiatric therapy consisted of Valproic acid 1500 mg (since 2011), Haloperidol depot (since 1994), Risperidone oral 2 mg (since 2018) and Clonazepam 6 mg. He also had a regular prescription for Amiodarone, Furosemide, Bisoprolol, Rivaroxaban and Ramipril.

Additional laboratory tests were performed during hospitalization in the psychiatric ward. An abnormality was revealed in his thyroid hormones, where an extremely low thyroid-stimulating hormone (TSH) level was found (TSH < 0.005 mU/L, reference interval: 0.27 - 4.2), while the thyroxine (FT4) level was greatly elevated (FT4 > 100.0, reference interval: 12.0 - 22.0 pmol/L). An increase in triiodothyronine (FT3) level was also observed (FT3 = 27.22 pmol/L, reference interval: 3.1 - 6.8 pmol/L). Due to suspicion of a thyroid storm, the patient was transferred to the internal medicine department.

Amiodarone and thyroid dysfunction

Amiodarone is a drug used to treat cardiac arrhythmias. Approximately 37 % of its compound consists of iodine, 10% of which is de-iodinated to form free iodine. It is stored in adipose tissue, the liver, lungs, and myocardium and therefore has an extremely long half-life of 100 days. As a result, excess iodine elimination may persist for months, and toxic effects of amiodarone may occur even after discontinuation of the drug [12-14].

Amiodarone affects both thyroid hormone synthesis and metabolism. When large amounts of iodide are released during amiodarone metabolism, an adaptive blockage of further thyroidal iodide uptake and hormone biosynthesis happens (the Wolf-Chaikoff effect) [14].

Intrinsically, amiodarone blocks thyroid hormone entry into cells, inhibits 5'-deiodinase types 1 and 2, reduces FT3 binding to its receptor (resulting in thyroid hormone antagonism and possible tissue hypothyroidism), and causes thyroid cytotoxicity, also called destructive thyroiditis, which is often seen in amiodarone-induced thyrotoxicosis type 2 (AIT2). Inhibition of 5'deiodinase types 1 and 2 increases total and FT4, reverse triiodothyronine (rT3), TSH and decreases FT3. Due to the inhibition of 5'-monodeiodinase type 1, fractional conversion of FT4 to FT3 is inhibited, mainly in the thyroid gland and the liver (the main extrathyroidal FT3 production site). The inhibition persists for months after amiodarone treatment, further explaining the decreased plasma and tissue FT3 concentrations. On the other hand, inhibition of 5'-deiodinase type 2 results in decreased intrapituitary concentrations of FT3 and causes increased serum TSH levels. Additionally, amiodarone indirectly alters thyroid hormone metabolism by inhibiting cellular thyroid hormone uptake. Consequently, there is decreased transfer of FT4 from the plasma pool to tissue pools, such as the liver. This results in reduced availability of intracellular FT4 and therefore reduced FT3 production [12,14]. Amiodarone can cause either hypothyroidism or hyperthyroidism [12].

Table 1. The Akamizu diagnostic criteria for a thyroid storm [34]

Number	Diagnostic elements for thyroid storm	
1	Pre-requisite for diagnosis of thyroid storm:	
	Elevated serum-free T3 or free T4	
2a	CNS manifestations:	
	Restlessness Delirium Mental aberration Psychosis Somnolence Lethargy Convulsion Coma ≥ 1 point on the Japan Coma Scale ≤ 14 points on the Glasgow Coma Scale	
2b	Non-CNS manifestations:	
	Fever (≥ 38°C)	
	Tachycardia (≥ 130 b. p. m.)	
	Congestive heart failure	
	Gastrointestinal and hepatic	
	Diagnosis	
	Definite diagnosis	Elevated thyroid hormones AND at least one CNS symptom in 2a AND at least one non-CNS manifestation in 2b OR elevated thyroid hormones AND at least three non-CNS manifestations in 2b
	Suspect diagnosis	Fulfilling definite criteria with the exception of not being able to determine raised thyroid hormones AND a history of thyroid disease AND exophthalmos AND goitre

Table adapted and referenced from Akamizu, et al. (2012) [34].

Amiodarone induced thyrotoxicosis

AIT occurs in 2 - 12 % of patients on chronic amiodarone treatment. The incidence varies with dietary iodine intake and is more prevalent in iodine-deficient areas [14]. In the patient's country of residence, iodine consumption is sufficient [15]. Type 1 of AIT is seen in individuals with pre-existing thyroid abnormalities. It is caused by iodine-induced excessive thyroid hormone synthesis. This occurs due to an iodine overload on abnormal thyroid glands. Due to altered intrinsic autoregulatory mechanisms and excess iodine, hyperthyroidism occurs in susceptible individuals. Therefore, in patients with AIT1, amiodarone may reveal underlying thyroid abnormalities or iodine deficiency [14]. Type 2 of AIT occurs in patients with a normal thyroid gland. Thyrotoxicosis results from glandular damage and the consequent release of preformed thyroid hormones into the circulation, in other words, leakage from follicular cells due to destructive thyroiditis [16]. Thyrotoxicosis in patients with AIT2 is usually self-limiting, due to the dose-dependent cytotoxic effect of amiodarone. However, when a certain threshold of intrathyroidal amiodarone concentration is exceeded, cell damage causes thyrotoxicosis as thyroid contents leak into the bloodstream [14]. A study by Anfinsen and Lima has also found that the risk of developing AIT2 increases with the cumulative dose of amiodarone. They describe a median time to onset of AIT2 of 30 months, with the possibility of occurrence even after amiodarone discontinuation. This is caused by the extremely long half-life of amiodarone, which leads to the presence of its contents in the body even after a year (the duration of five half-lives) [16]. This was also found by Basaria and Cooper, who confirm that in the case of AIT2, the duration of amiodarone treatment is usually longer than 2 years [12].

During the first months of treatment, there is a 20 - 40 % increase of FT4, a 30 % decrease in FT3, and an increase in TSH. After three to six months, a new equilibrium is established, and hormone levels return to normal values [16]. Thyroid dysfunction, specifically hyperthyroidism, is characterized by elevated free T4 and decreased TSH [12,17]. Studies have found that TSH levels in exogenous hyperthyroidism are low or normal. Total serum T4 and T3, however, are increased [18]. Similar results have been found by Anfinsen and Lima who describe suppressed TSH, high FT4 and high or normal FT3 [16]. The onset of thyrotoxicosis is usually sudden and explosive, and the symptoms are nonspecific, making the correct diagnosis difficult [12,19]. Symptoms such as weight loss, sweating, tremor, sinus tachycardia and worsening of the underlying heart disease can occur. A small, tender goitre may also be found upon examination [14]. Other symptoms mentioned in literature include generalized weakness, fatigue, heat intolerance, diaphoresis, fever, palpitations, diarrhoea, hair loss, diplopia, eye irritation, pale skin, dyspnoea, tachycardia, pretibial myxoedema, atrial fibrillation, congestive heart failure, nausea, vomiting, hepatic failure, and hyperpyrexia. Psychiatric symptoms are also mentioned, most commonly confusion, agitation, anxiety, emotional liability, delirium, psychosis, stupor and coma [17,19,20]. An uncommon symptom of hyperthyroidism (specifically Graves'

disease) is also sialorrhea, which can affect speech and cause drooling [21].

A meta-analysis of studies in Africa showed that the most common symptoms of thyrotoxicosis are palpitations, weight loss, heat intolerance, fatigue, increased appetite, excessive sweating, insomnia, nervousness, dyspnoea, hyperdefaecation and so on [19]. The Akamizu diagnostic criteria can be used to identify whether a patient is experiencing a thyroid storm. It includes the following diagnostic elements: elevated serum-free T3 or free T4, CNS and non-CNS manifestations [18] (Table 1).

Extrapyramidal symptoms induced by antipsychotics

Most antipsychotic medications function by inhibiting dopaminergic transmission. This inhibition in the mesocortical system leads to the reduction of psychotic symptoms; however, it also causes extrapyramidal symptoms (EPS) by blocking the nigrostriatal system. The affinity of antipsychotics to block dopamine D2 receptors is associated with an increased risk of EPS. Typical antipsychotics have a higher affinity for dopamine D2 receptors, which explains their increased risk of EPS. On the other hand, second and third-generation antipsychotics have a lower affinity and bind more transiently to D2 receptors than dopamine, which allows for normal dopamine transmission. Although dopamine receptor blockade is immediate, the onset of EPS symptoms is delayed, ranging from days to weeks, for reasons that are not yet clear [22].

Several studies have shown that the risk of developing EPS increases when D2 receptor occupancy reaches 70 – 80 % [23–25]. Risperidone has a high occupancy rate for D2 receptors and is therefore associated with a higher risk of EPS, although it also has a high affinity for 5 - HT2 receptors [24]. Antipsychotics can be classified into three groups based on their binding affinity to the D2 receptor. Risperidone, for example, is classified into group number three, which indicates a high affinity and increased risk for EPS [24].

According to a study conducted by Thanvi and Treadwell in 2009, almost 80 % of individuals taking antipsychotics exhibit extrapyramidal symptoms, while 25 % experience drug-induced parkinsonism. Several risk factors are associated with drug-induced parkinsonism, including older age, female gender, the type of agent used, cognitive impairment, AIDS, tardive dyskinesia, and pre-existing EPS. The occurrence of drug-induced parkinsonism is both dose- and duration-dependent, with typical antipsychotics such as haloperidol, calcium channel agents, antiemetics, atypical antipsychotics such as risperidone (particularly at higher doses), antihypertensive agents, and tetrabenazine being the most common causative agents. Less frequently, drugs such as amiodarone, antidepressants, anticonvulsants like sodium valproate, lithium, and other drugs can also cause EPS [22]. Amiodarone as a possible cause of drug-induced parkinsonism is also mentioned in a study by Lopez-Sendon, Mena and de Yebenes [23].

Clinical onset is usually subacute, with bilateral and symmetrical symptoms [22]. Approximately 50 - 75 % of cases occur within the first month and 90 % of cases within the first three months [26]. Drug-induced parkinsonism presents with rigidity, resting tremor, masked faces, generalized slowing of movement, and cogwheel rigidity [24]. The first symptom may be a reduced arm swing when walking [23]. Masked facial expressions present an additional difficulty in making the correct diagnosis, making it easy to misdiagnose a patient with negative symptoms of schizophrenia or depression. Mental abnormalities such as emotional blunting, apathy, anhedonia, and social withdrawal can also be observed [23,24,26,27]. Non-motoric symptoms may include cognitive impairment, depression, apathy, orthostatic hypotension, gastrointestinal disorders, urinary symptoms, sleep disorders, and sensory abnormalities or pain [28].

A study by Savica and associates created diagnostic criteria for drug-induced parkinsonism. The first part consists of the definition of parkinsonism in the context of the syndrome. It is defined as the presence of at least two of the four main signs which include rest tremor, bradykinesia, rigidity, and impaired postural reflexes. The second part defines drug-induced parkinsonism when three of the following are present: symptom onset within 6 months of treatment with dopamine-blocking or dopamine-depleting drugs, no parkinsonism symptoms before treatment and resolution of symptoms within 6 months of withdrawal of treatment. If the treatment has never been discontinued, the first two criteria of the second part are sufficient [29].

Discussion

The patient in our case showed symptoms that could be indicative of both AIT and EPS. AIT typically has a sudden onset with mostly nonspecific symptoms and occurs within a median time of 30 months, even after discontinuation of amiodarone [12,16]. Based on the patient's symptoms, signs, and laboratory findings, AIT is the most likely diagnosis. The patient's TSH levels were low, and serum total T3 and T4 were elevated, which is consistent with findings in the literature [16,18]. Symptoms and signs that may be associated with AIT and were present in our case report include confusion, dyspnoea, tachycardia, pretibial myxoedema, palpitations, subfebrile body temperature, fatigue, sialorrhea and speech difficulties [17-21]. These findings satisfy the Akamizu criteria, which our patient fulfils (elevated thyroid hormones, CNS symptoms, and at least one non-CNS manifestation), leading to a diagnosis of thyroid storm [18].

There are, however, several findings that support a diagnosis of EPS, including reduced arm swing during walking, difficulty walking, speech difficulties, masked facial expression (hypomimia), generalized slowness of movement, and cognitive impairment. In our case, the combination of haloperidol and risperidone makes

EPS a likely diagnosis. However, given the long duration of treatment (> 20 years with haloperidol and 3 years with risperidone), it would be unusual for EPS to occur this late, as its onset is typically subacute and mostly occurs within the first 3 months. Additionally, our patient did not exhibit the typical motor symptoms of EPS [22-24,26,28]. When applying the diagnostic criteria for drug-induced parkinsonism, our patient does not meet all the requirements. He had only one symptom from the first part of the criteria (bradykinesia with hypomimia and speech changes), and in the second part, he only fulfils the second criterion, which is insufficient to confirm the diagnosis [29].

Diagnosing a patient with multiple medical conditions can be challenging. Some of the nonspecific symptoms experienced by the patient may be due to somatic comorbidities. For example, oedema, tachycardia, dyspnoea, and generalized weakness could be explained by heart failure, which could be exacerbated by long-term psychiatric pharmacotherapy. However, symptoms such as dysarthria, hypersalivation, and diarrhoea cannot be definitively attributed to either condition. Therefore, it was crucial to perform further diagnostic tests on the patient to determine the underlying cause of his symptoms.

When patients are taking multiple medications alongside psychiatric therapy, extra caution is necessary to monitor for potential drug interactions, especially if there is a risk of worsening the primary disease. Our patient was taking amiodarone, which is a CYP3A4 inhibitor, while its metabolite, desethylamiodarone, is a CYP2D6 inhibitor. Both enzymes are involved in the metabolism of risperidone and haloperidol [29-31]. In theory, inhibition of the enzymes may lead to increased risperidone and haloperidol concentrations and therefore increase the possibility of EPS development. It is worth noting that a study conducted by Lopez-Sendon, Mena, and de Yebenes discovered that both antipsychotic and non-antipsychotic medications can cause EPS [23]. Of the medications mentioned, our patient had been prescribed haloperidol, risperidone, amiodarone, and valproic acid. This emphasizes the importance of appropriate treatment and follow-up visits, which our patient did not receive. Lack of follow-up and insufficient attention to possible drug interactions are associated with the risk of mistreatment. It is essential to have regular follow-up visits with healthcare providers to ensure that medication regimens are appropriately monitored, and any potential drug interactions can be addressed promptly to prevent potentially harmful consequences.

Thyroid function tests should be conducted in all patients receiving amiodarone, prior to starting treatment, during treatment, and after discontinuation. Guidelines for amiodarone therapy recommend monitoring thyroid function every six months, especially in the elderly [32]. Unfortunately, our patient did not receive any thyroid function tests before or during the three years he was taking amiodarone. While the lack of monitoring after starting treatment could be attributed to the COVID-19 pandemic, it is essential to note that the pandemic has disproportionately affected vulnerable psychiatric patients, who often have inadequate access to medical care or are poorly treated for somatic diseases [33]. However, this does not justify the substandard or unprofessional treatment of any patient.

The misdiagnosis of our patient was a result of several contributing factors, including the stigma associated with mental illness, multimorbidity, the impact of polypharmacy, the unprecedented COVID-19 pandemic, and a non-specific presentation of symptoms. In the future, it is crucial to address the stigma associated with chronic psychiatric patients and ensure that they receive high-quality and equitable care. This effort requires a coordinated long-term approach by a diverse group of healthcare and non-healthcare professionals and a shift in societal attitudes towards people with mental disorders.

Acknowledgments

None.

Conflict of Interest

None to declare.

Funding Sources

None.

References

1. Cradock-O'Leary J, Young AS, Yano EM, Wang M, Lee ML. Use of general medical services by VA patients with psychiatric disorders. Psychiatr Serv. 2002;53:874-8.
2. Phelan M, Stradins L, Morrison S. Physical health of people with severe mental illness. BMJ. 2001;322:443-4.
3. Colton CW, Manderscheid RW. Congruencies in increased mortality rates, years of potential life lost, and causes of death among public mental health clients in eight states. Prev Chronic Dis. 2006;3:A42.
4. McIntyre RS, Soczynska JK, Beyer JL, Woldeyohannes HO, Law CW, Miranda A, et al. Medical comorbidity in bipolar disorder: reprioritizing unmet needs. Curr Opin Psychiatry. 2007;20:406-16.
5. Chakrabarti S. What's in a name? Compliance, adherence and concordance in chronic psychiatric disorders. World J Psychiatry. 2014;4:30-6.
6. Küey L. The impact of stigma on somatic treatment and care for people with comorbid mental and somatic disorders. Curr Opin Psychiatry. 2008;21:403-11.
7. Zeber JE, Copeland LA, McCarthy JF, Bauer MS, Kilbourne AM. Perceived access to general medical and psychiatric care among veterans with bipolar disorder. Am J Public Health. 2009:99:720-7.
8. Kilbourne AM, McCarthy JF, Post EP, Welsh D, Pincus HA, Bauer MS, et al. Access to and satisfaction with care comparing patients with and without serious mental illness. Int J Psychiatry Med. 2006;36:383-99.
9. Núñez A, Sreeganga SD, Ramaprasad A. Access to Healthcare during COVID-19. Int J Environ Res Public Health. 2021;18:2980.
10. Murphy L, Markey K, O' Donnell C, Moloney M, Doody O. The impact of the COVID-19 pandemic and its related restrictions on people with pre-existent mental health conditions: a scoping review. Arch Psychiatr Nurs. 2021;35:375-94.
11. Arolas HPI, Vidal-Alaball J, Gil J, López F, Nicodemo C, Saez M. Missing diagnoses during the covid-19 pandemic: a year in review. Int J Environ Res Public Health. 2021;18:5335.
12. Basaria S, Cooper DS. Amiodarone and the thyroid. Am J Med. 2005;118:706-14.
13. Martino E, Bartalena L, Bogazzi F, Braverman LE. The Effects of amiodarone on the thyroid. Endocr Rev. 2001;22:240-54.
14. Loh K. Amiodarone-induced thyroid disorders: a clinical review. Postgrad Med J. 2000;76:133-40.
15. Nacionalni inštitut za javno zdravlje (NIJZ). Jod v prehrani in tveganja čezmernega vnosa [Internet]. Ljubljana (SI): NIJZ. 2010 [updated 2010; cited 2023 Mar 22]. Available from: https://nijz.si/moje-okolje/varnost-zivil/jod-v-prehrani-in-tveganja-cezmernega-vnosa/
16. Anfinsen OG, Lima K. Amiodarone-induced thyrotoxicosis. Tidsskrift Nor Legeforen. 2021;141.
17. Swee DS, Chng CL, Lim A. Clinical characteristics and outcome of thyroid storm: A case series and review of neuropsychiatric derangements in thyrotoxicosis. Endocr Pract. 2015;21:182–9.
18. Idrose AM. Acute and emergency care for thyrotoxicosis and thyroid storm. Acute Med Surg. 2015;2:147-57.
19. Azeez TA, Adetunji TA, Adio M. Thyrotoxicosis in Africa: a systematic review and meta-analysis of the clinical presentation. Egypt J Intern Med. 2022;34.
20. Stan MN, Sathananthan M, Warnes C, Brennan M, Thapa P, Bahn R. Amiodarone-induced thyrotoxicosis in adults with congenital heart disease - clinical presentation and response to therapy. Endocr Pract. 2014;20:33-40.
21. Mills R, Abbara A, Hui E, Meeran K, Wynne K. Sialorrhoea: an uncommon symptom of Graves' disease. Endocrine Abstracts. 2011;25:350.
22. Thanvi B, Treadwell S. Drug induced parkinsonism: a common cause of parkinsonism in older people. Postgrad Med J. 2009;85:322–6.
23. López-Sendón J, Mena MA, De Yébenes JG. Drug-induced parkinsonism. Expert Opin Drug Saf. 2013;12:487-96.
24. Shirzadi AA, Ghaemi SN. Side effects of atypical antipsychotics: extrapyramidal symptoms and the metabolic syndrome. Harv Rev Psychiatry. 2006;14:152-64.
25. Pierre JM. extrapyramidal symptoms with atypical antipsychotics incidence, prevention and management. Drug Saf. 2005;28:191-208.
26. Ward KM, Citrome L. Antipsychotic-related movement disorders: drug-induced parkinsonism vs. tardive dyskinesia-key differences in pathophysiology and clinical management. Neurol Ther. 2018;7:233-48.
27. Dayalu P, Chou KL. Antipsychotic-induced extrapyramidal symptoms and their management. Expert Opin Pharmacother. 2008;9:1451-62.
28. Levin OS, Chimagomedova AS, Skripkina NA, Lyashenko EA, Babkina OV. Nonmotor symptoms in vascular and other secondary parkinsonism. Int Rev Neurobiol. 2017;134:1303-34.
29. Savica R, Grossardt BR, Bower JH, Ahlskog JE, Mielke MM, Rocca WA. Incidence and time trends of drug-induced parkinsonism: a 30-year population-based study. Mov Disord. 2017;32:227-34.
30. Dean L. Risperidone Therapy and CYP2D6 Genotype. In: Pratt VM, Scott SA, Pirmohamed M, Esquivel B, Kattman BL, Malheiro AJ, eds. Medical Genetics Summaries. Bethesda (US): National Center for Biotechnology Information; 2012.
31. Kudo S, Ishizaki T. Pharmacokinetics of haloperidol. Clin Pharmacokinet. 1999;37:435-56.
32. Ennogen Pharma Ltd. Amiodarone Hydrochloride 200 mg Tablets [Internet]. Dartford (GB): Ennogen Pharma Ltd; 2023 [updated 2023; cited 2023 Mar 22]. Available from: https://www.medicines.org.uk/emc/product/13964/smpc#gref
33. Diaz A, Baweja R, Bonatakis JK, Baweja R. Global health disparities in vulnerable populations of psychiatric patients during the COVID-19 pandemic. World J Psychiatry. 2021;11:94-108.
34. Akamizu T, Satoh T, Isozaki O, Suzuki A, Wakino S, Iburi T, et al. Diagnostic criteria, clinical features, and incidence of thyroid storm based on nationwide surveys. Thyroid. 2012;22:661–79.