CASE REPORT

Cardiac Considerations in Treatment of Schizophrenia: A Case Report Highlighting the Use of Long-acting Injection Paliperidone Palmitate Depot in Schizophrenia Patient with Comorbid Wolff-Parkinson-White Syndrome

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Abstract

The effect of antipsychotics on electron-conduction abnormalities in already diagnosed Wolff-Parkinson-White (WPW) syndrome is under-evaluated which creates a dilemma among practitioners in choosing an effective antipsychotic with minimal side effects. Paliperidone, a second-generation antipsychotic, is Food and Drug Administration (FDA) approved for treating schizophrenia, but the studies have documented mixed results on its effect on QT prolongation. Hence, we are going to present a case of paranoid schizophrenia with comorbid WPW syndrome showing a remarkable response on long-acting paliperidone palmitate depot with no effect on QT prolongation, even after a 2-month follow-up of electrocardiogram (ECG) report.

Keywords: Case report, Electrocardiogram changes, Paliperidone depot, Schizophrenia, Wolff-Parkinson-White syndrome.

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Introduction

Wolff-Parkinson-White (WPW) syndrome is a cardiac condition characterized by an accessory pathway that bypasses the atrioventricular (AV) node, resulting in abnormally fast ventricular contractions. The specific electrocardiogram (ECG) findings of WPW include a delta wave, a widened QRS complex (>110 ms), and shortened PR interval.[1] The cardiovascular disease is one of the main attributes of premature death in patients with schizophrenia compared to general population due to a sedentary lifestyle, unhealthy dietary habits, substance abuse, illness factors like negative symptoms, and antipsychotic-induced adverse effects.[2] The safety and tolerability of antipsychotics in WPW syndrome are limited to a few case reports and one controlled study, and no long-term follow-up is documented.

The authors are going to present a case of paranoid schizophrenia with comorbid WPW syndrome, highlighting the effectiveness and tolerability of long-acting paliperidone palmitate depot and its effect on QT prolongation after a period of 2 months.

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Case Description

A 32-year-old married female with past history of radiofrequency ablation surgery 2 years back for WPW syndrome with nil contributory family history, and well-adjusted premorbid personality presented with complaints of suspiciousness, the belief that her husband was being replaced by his look alike, unprovoked abusive and aggressive behavior for the past 10 years. Her illness was of insidious in onset, fluctuating in course on irregular intake of medications. On mental state examination (MSE), her affect was irritable. There was documentation of thought withdrawal, delusion of persecution, delusion of infidelity, Capgras syndrome without any perceptual abnormality owing to the diagnosis of paranoid schizophrenia (F20.0). The consent to include in our study was obtained from both the patient and her husband. The baseline ECG during admission showed delta waves suggesting pre-excitation from the accessory bypass tract with a QTc interval of 410 ms. Because of the risk of harm to oneself and others, electroconvulsive therapy (ECT) was considered but declined by guardians. Hence, she was prescribed injection lorazepam 4 mg with the avoidance of injectable antipsychotics. She was referred to a cardiologist, and echocardiogram (ECHO) came out to be normal. She was started on tab. Aripiprazole, considering the mild risk of QT prolongation, and hiked up to 30 mg. No improvement was noticed after a trial of 4 weeks. To address poor compliance in the long term, there was a need for long-acting injection (LAI) depot. Paliperidone palmitate LAI was considered for its rapid onset of action and relatively safe

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cardiac profile, among other LAIs. To establish tolerability with paliperidone LAI, tablet aripiprazole 30 mg was cross tapered with tablet risperidone due to the unavailability of oral paliperidone in our center. Index patients showed improvement in unprovoked aggression, and 25% decline in positive and negative syndrome scale (PANSS) scores from the time of admission on tab risperidone 6 mg. Her repeat ECG documented delta waves with a QTc of 380 ms. Hence, the first dose of paliperidone palmitate LAI 150 mg/mL was administered over the deltoid region while oral tab risperidone 6 mg was gradually tapered off. On the day 10, an injection of paliperidone palmitate depot 100 mg was given in intramuscular route in gluteal region. After 2 weeks, on MSE, the preoccupation and conviction of delusion of persecution and delusion of infidelity were reduced owing to sealing over, and a further decline in PANSS score was documented. Her repeat ECG after two weeks on paliperidone LAI showed a QTc of 376 ms and clinically, no side effects were noticed. Hence, she was planned for discharge with monotherapy of paliperidone palmitate LAI 150 mg every month for the maintenance phase. She came for follow-up after 2 months when she was doing all her household chores with nil unprovoked aggression. On MSE, no active psychopathology was noted. Her 2 months follow-up ECG documented a delta wave with a QTc of 370 ms. During this time, echocardiogram was also found to be normal.

Discussion

In WPW syndrome, also called pre-excitation syndrome, impulses from the sinus node are transmitted down through additional channels that activate the ventricles earlier, causing pre-excitation in part of the ventricular muscles. This pre-excitement of the local myocardium is depicted as a delta wave on the ECG, and one of the most common tachyarrhythmias caused by pre-excitation syndrome is paroxysmal supraventricular tachyarrhythmia.[3] It is predominantly asymptomatic, but rare cases, it can cause sudden cardiac death. Individuals with WPW are at higher risk of QT prolongation from exposure to antipsychotic medications. On the other hand, schizophrenia is a chronic psychiatric illness affecting 1% of the general population, and where the mainstay of treatment relies on antipsychotics. Hence, caution is required when prescribing antipsychotics for already-diagnosed comorbid cardiac disease.

One case report of a 44-year-old patient diagnosed with schizophrenia showed a broad QRS interval and delta wave on the ECG suggestive of WPW syndrome immediately after ECT, and the duration of delta waves increased exponentially during the first 4-months on re-administration of ECT but disappeared later on.[4] Hence, we thought of ECT for acute management of symptoms, but the guardians denied it.

Cardiomyopathy, cardiac arrhythmia, and QT prolongation/torsades-de-pointes were among the most common cardiac side effects induced by antipsychotics. Clozapine and amisulpride were the most notorious among the other 10 antipsychotics included in the study conducted from 2015 to 2020.[5] But the study lacks recommendations the usage of antipsychotics in WPW syndrome. The case report of olanzapine-induced QTc prolongation in WPW syndrome barred us from its use in long term management.[6] In a case series of two separate cases, risperidone at 1 mg twice daily (BID) induced palpitations, QTc prolongation, shortened PR intervals, and the induction of a delta wave on the ECG.[7] There was a case report where an overdose of quetiapine precipitated QTc prolongation with the presentation of palpitation and tachycardiac in a history of diagnosed WPW syndrome, which resolved spontaneously.[8]

In our patient, LAI was preferred over oral antipsychotics in the view of poor compliance. All the LAI of 1st generation antipsychotics were avoided due to the high risk of extrapyramidal side effects. Coming to the available LAI of 2nd generation antipsychotics, the plan of aripiprazole LAI was dropped due to poor response of oral aripiprazole 30 mg. Due to the fear of post-injection syndrome/delirium and the risk of significant weight gain, and later possibility of non-compliance, olanzapine LAI was not considered.[9] Documentation of a good response to tab risperidone 6 mg motivated us towards choosing risperidone LAI or paliperidone LAI, an active metabolite of risperidone. The risperidone LAI took around 3–4 weeks for the first injection to produce therapeutic plasma levels, and hence, for at least 3 weeks, oral antipsychotics were needed to be continued. Whereas, coadministration of oral antipsychotics is not needed after the recommended loading dose of paliperidone LAI. Because, the active level of paliperidone in systemic circulation is available as early as day 1 and reaches maximum plasma concentration by day 13.[10] It blocks the *human ether-a-go-related (hERG)* gene that codes for the cardiac potassium channel, and thus slowing of depolarization and prolongation of the QRS interval can be noticed.[11] In a study, it was highlighted that the dose-dependent QT prolongation of risperidone is because of its active metabolite, 9-hydroxy risperidone which is paliperidone.[12] There were other studies also showing minimal risk of paliperidone extended release (ER) with lower ECG anomalies even in long-term treatment.[13] The effect of QTc prolongation was comparable with paliperidone ER 12 mg (maximum dose), 18 mg (suprathreshold dose), and quetiapine 800 mg without any proarrhythmic potential.[14] Considering the risk-benefit ratio and feasibility, paliperidone palmitate LAI was chosen. Caution was taken in prescribing other psychotropics along with paliperidone as there has been a report of first-degree AV block with tachycardia with an overdose of paliperidone and mirtazapine.[15] Hence, we consider monotherapy with a long-acting injection of paliperidone palmitate depot.

Conclusion

The remarkable response and no QT prolongation to long-acting paliperidone depot over a period of 2 months in our case was an important finding, but further study is needed in this arena. To the best of our knowledge, no case report has been published to evaluate the effectiveness, safety, and tolerability of long-acting paliperidone palmitate depot with a follow-up of 2 months in the background of WPW syndrome.

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References

1. Chhabra L, Goyal A, Benham MD. Wolff-Parkinson-White Syndrome. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2024. Available from: http://www.ncbi.nlm.nih.gov/books/NBK554437/.
2. Galletly CA. Premature death in schizophrenia: Bridging the gap. Lancet Psychiatry 2017;4(4):263–265. DOI: 10.1016/S2215-0366(17)30079-2.
3. Suba S, Dzikowicz DJ, Kozik TM, et al. Narrow vs wide QRS complex tachycardia in a patient with Wolf-Parkinson-White syndrome. Am

J Crit Care Off Publ Am Assoc Crit-Care Nurses 2022;31(3):255–256. DOI: 10.4037/ajcc2022819.
4. Enomoto S, Yoshino A, Takase B, et al. Electroconvulsive therapy-induced Wolff-Parkinson-White syndrome: A case report. Gen Hosp Psychiatry 2013;35(5):575.e7–575.e8. DOI: 10.1016/j.genhosppsych.2013.02.004.
5. He L, Yu Y, Wei Y, et al. Characteristics and spectrum of cardiotoxicity induced by various antipsychotics: A real-world study from 2015 to 2020 based on FAERS. Front Pharmacol 2021;12:815151. DOI: 10.1016/j.genhosppsych.2013.02.004.
6. Su KP, Lane HY, Chuang CL, et al. Olanzapine-induced QTc prolongation in a patient with Wolff-Parkinson-White syndrome. Schizophr Res 2004;66(2–3):191–192. DOI: 10.1016/S0920-9964(03)00182-8.
7. Imran TF, Niazi OT, Amin R, et al. Risperidone unmasking an accessory pathway. Int J Cardiol 2015;187:488–490. DOI: 10.1016/j.ijcard.2015.03.419.
8. Chen M, Gomaa H, Cortez-Resendiz A, et al. Quetiapine and Wolf-Parkinson-White syndrome. Case Rep Psychiatry 2020;2020:e6633385. DOI: 10.1155/2020/6633385.
9. Kochen SA, Hakkers CS, van Gorp F, et al. Olanzapine postinjection delirium/sedation syndrome after long-acting olanzapine depot injection presenting to the emergency department: Practical guidelines for diagnosis and management. Emerg Med J EMJ 2024. DOI: 10.1136/emermed-2024-213972.
10. Citrome L. Paliperidone palmitate - Review of the efficacy, safety and cost of a new second-generation depot antipsychotic medication. Int J Clin Pract 2010;64(2):216–239. DOI: 10.1111/j.1742-1241.2009.02240.x.
11. Lee HJ, Choi JS, Choi BH, et al. Inhibition of cloned hERG potassium channels by risperidone and paliperidone. Naunyn Schmiedebergs Arch Pharmacol 2017;390(6):633–642. DOI: 10.1007/s00210-017-1364-5.
12. Suzuki Y, Fukui N, Watanabe J, et al. QT prolongation of the antipsychotic risperidone is predominantly related to its 9-hydroxy metabolite paliperidone. Hum Psychopharmacol 2012;27(1):39–42. DOI: 10.1002/hup.1258.
13. Spina E, Crupi R. Safety and efficacy of paliperidone extended-release in acute and maintenance treatment of schizophrenia. J Cent Nerv Syst Dis 2011;3:27–41. DOI: 10.4137/JCNSD.S1607.
14. Hough DW, Natarajan J, Vandebosch A, et al. Evaluation of the effect of paliperidone extended release and quetiapine on corrected QT intervals: A randomized, double-blind, placebo-controlled study. Int Clin Psychopharmacol 2011;26(1):25–34. DOI: 10.1097/YIC.0b013e3283400d58.
15. Cheung B, Levy C, Shivkumar A. First-degree atrioventricular block with tachycardia from paliperidone and mirtazapine overdose. Eur J Case Rep Intern Med 2020;7(12):001879. DOI: 10.12890/2020_001879.