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A case report of guardian-consent forced paliperidone palmitate for behavioral disturbance due to traumatic brain injury

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Abstract

Psychosis after traumatic brain injury (TBI) occurs in up to 10% of cases. Although guideline consensus is lacking regarding drugs of choice for this condition, current literature points to the use of atypical antipsychotics. This case describes a 58-year-old male with major neurocognitive disorder due to TBI with behavioral disturbance that was successfully treated with paliperidone palmitate. In addition to the off-label use of paliperidone, this case also explores the use of forced medication as the initial injection was given per guardian consent. After completion of a literature review, this appears to be the first case report describing the use of a long-acting antipsychotic for the treatment of TBI-related psychosis. This case suggests that paliperidone palmitate may be efficacious for psychosis following TBI; however, further study is warranted.

Keywords: forced, off-label, antipsychotics, psychosis, traumatic brain injury, long-acting injectables, paliperidone palmitate

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Background

Various neuropsychiatric syndromes may occur following a traumatic brain injury (TBI). As defined by the *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition,[1] the diagnosis of behavioral disturbance due to TBI includes mood disturbance, agitation, apathy, psychotic symptoms, or other behavioral symptoms. There are an estimated 1.4 million cases of TBI annually in the United States, and approximately 10% of these patients will develop TBI-associated psychosis.[2-4] Psychotic symptoms following TBI often present as hallucinations, delusions, and disorganized thought content.[3] There are currently no medications that are Food and Drug Administration (FDA)–approved for post-TBI psychosis, and there is a paucity of evidence on the pharmacologic treatment approach in this population. The 2006 guidelines[5] for the pharmacologic treatment of neurobehavioral sequelae of TBI discuss olanzapine at the level of "option" for treatment based on 2 case reports; however, they also concluded that there was insufficient evidence to support the development of standards for TBI-related psychosis. A 2016 systematic review[6] on drugs for behavior disorders after TBI reports on a few case-control antipsychotic studies (low evidence) and concludes that atypical antipsychotics are preferred but does not give preference to a specific agent. The 2016 Veterans Affairs and Department of Defense treatment guidelines[7] for mild TBI encourage the use of the respective clinical practice guidelines for the condition or symptoms present. Although it is typically considered best practice to avoid antipsychotics in the TBI population due to negative impacts on neuronal plasticity, these agents have been suggested to be beneficial for those with psychosis, especially delusional-type symptoms.[3,6]

Even though it is common practice in many countries, an area with ongoing debate is the issue of forced or coercive treatment with psychotropics.[8,9] "Forced medication"[8(p3)] has been defined as using manual restraint or strong psychological pressure to administer medication against the patient's will. This is another topic with a gap in the literature, especially regarding long-acting injectable (LAI) antipsychotics. Immediate-release formulations, such as haloperidol lactate, are most commonly used, and only one article was identified reporting on the use of a forced LAI, risperidone microspheres.[10] By current standards, providers may recommend forced medication if a patient is considered to be a harm to the patient's self or others, significantly disabled, or has been diagnosed with a mental health condition and has impaired judgment or lack of capacity.[9]

The legal process for approval of forced medications most often is initiated after the patient has been determined to be incapacitated due to mental illness. The patient will have an involuntary commitment court hearing, and the judge may determine that the patient would benefit from additional treatment, including medication intervention. If family members are present during this court proceeding, the judge may appoint a family member to have power of attorney (POA) if no other identified person has been granted decision-making capabilities. When a patient is unable to provide consent for medications due to cognition, one must determine if the patient has a guardian of person, a durable POA, or a POA for health care. If there is no guardian of person or durable POA/POA for health care, the last resort would be to present the case to the therapeutic review committee. The therapeutic review committee is composed of psychiatric team members who are not currently providing care to the patient and must include a psychiatrist. The therapeutic review committee provides recommendations to the treating members of the team as well as consent or denial for medicating the patient regardless of his or her consent. The legal process described is from the institution's informed consent policies, which are based on federal (Veterans Affairs) guidance. The current report describes a forced administration of paliperidone palmitate in a patient with behavioral disturbance due to TBI. Internal institution review was completed and approved for publication.

Case

The patient was a 56-year-old African American male who was admitted involuntarily from a group home due to paranoia, increased outbursts, and aggression. He was hospitalized at a Veterans Affairs medical center for 66 days in 2017 and had a past medical history of hypertension, hyperlipidemia, and vitamin D deficiency treated with hydrochlorothiazide, lisinopril, simvastatin, and cholecalciferol. As documented by the attending physician, past neurological and psychiatric history included TBI associated with a motor vehicle accident in 1987, seizure disorder status post-TBI, major neurocognitive disorder due to TBI with behavioral disturbance, and rule out psychotic disorder due to another medical condition with delusions. The patient's home regimen of divalproex (delayed release) 750 mg twice daily and topiramate 200 mg twice daily for seizure disorder were continued on admission. The patient was first admitted to this facility in 2012 with a diagnosis of dementia not otherwise specified secondary to TBI and mood disorder not otherwise specified secondary to TBI and admitted again in 2015 with a diagnosis of major neurocognitive disorder due to TBI with behavioral disturbance. Previous psychotropics included aripiprazole and risperidone; however, it is unclear when psychosis emerged. In 2015, he was adherent with some doses of risperidone up to 6 mg/d, but it was tapered prior to discharge due to medication refusal.

The patient remained paranoid, argumentative, and perseverated on persecutory delusions during the first 2 weeks of the hospital stay. Chart review indicated that the patient had experienced at least 1 seizure monthly for 1 year prior to admission. Upon admission, the patient's valproic acid level was 99.7 mcg/mL, confirming compliance in the outpatient setting. The patient experienced a seizure on hospital day (HD) 2 accompanied by urinary incontinence. He refused imaging and part of the postseizure workup, insisting that he did not experience a seizure. It was determined the seizure may have occurred due to intermittent refusal of antiepileptics; however, the first time those medications were refused during the stay was the evening of HD 2 postseizure. In an attempt to further stabilize the patient, divalproex was increased to 1000 mg twice daily and further laboratory workup was attempted per neurology consult recommendation. However, the patient refused medication adjustments and therefore, remained on divalproex 750 mg twice daily.

The patient's paranoia included his belief that providers were making medication adjustments to keep him hospitalized. He was given an opportunity to convert from involuntary admission status to voluntary status, but he refused to sign any paperwork and remained preoccupied with the conspiracy theory that medical staff were plotting against him. The patient was determined to have impaired insight and judgment and, therefore, lacked capacity to make medical decisions. Accordingly, medical decisions were deferred to the patient's mother, who had been granted his POA.

The attending psychiatrist attributed persistent paranoia and persecutory delusions to TBI-associated psychosis; therefore, the team determined that the patient would

benefit from an antipsychotic. Risperidone 1 mg daily was initiated on admission; however, it was consistently refused. After multiple failed attempts to educate the patient on potential benefits of antipsychotics and due to his history of medication nonadherence, it was determined that he would benefit from an LAI. After refusal of voluntary administration, a forced injection of paliperidone palmitate 234 mg was given on HD 15 with POA consent.

Based on daily interviews by the attending psychiatrist and nursing reports, there was a dramatic improvement in symptoms within a week of the first injection, and he willingly accepted the next injections of 156 mg on HDs 22 and 50. Within a few weeks, his paranoia lessened, and he ceased to comment on collusion of staff against him. The patient experienced a second seizure on HD 24 with urinary incontinence witnessed by nursing staff and a possible third seizure on HD 62 that was unwitnessed, evidenced by lethargy and nighttime incontinence. During the seizure on HD 24, the patient fell and had a head impact. Unlike the first episode, the patient was compliant with head imaging and labs, which were nonremarkable. Of note, serum creatinine and sodium were normal during admission and ranged from 0.95 to 1.07 mg/dL and 141 to 146 mEq/L, respectively. The patient remained adherent with medications and continued to show signs of improvement in psychosis and paranoia. Other than the aforementioned seizures, there were no other acute neurological or psychiatric events documented.

Discussion

A literature search was performed using PubMed to identify articles published in English with a combination of the following keywords: forced, off-label, antipsychotics, psychosis, TBI, long-acting injectables, and paliperidone palmitate. The search was not limited to year of publication, and any pertinent articles identified were utilized.

There are few studies that explore the connection between TBI and psychosis; however, post-TBI psychosis has an incidence 2-3 times greater than the general population.[4,11] The onset of TBI-associated psychosis may be acute or delayed, and when there are comorbid seizures, may occur in the peri-ictal period or interictally.[2,11] In this case, the patient appeared to have interictal psychosis as the symptoms were chronic in nature versus episodic. Hallucinations and delusions with retained insight are common in TBI-related psychosis, and patients will frequently report paranoia characterized by hypervigilance, suspiciousness, and systematized persecutory delusions.[2,11]

General treatment guidance for post-TBI psychosis includes using very low doses and preferential use of second-generation antipsychotics (SGAs), except clozapine, over first-generation antipsychotics.[2,11] Efficacy of antipsychotics can be seen as early as within 2 weeks of administration of the first dose.[12,13] Paliperidone is an SGA that is a major active metabolite of risperidone. The proposed therapeutic activity for psychosis is mediated by dopamine D_2 and serotonin $5HT_{2A}$ antagonism in the central nervous system. It is FDA-approved for the treatment of schizophrenia and schizoaffective disorder.[14] Although paliperidone does not have an FDA indication for post-TBI psychosis, there is documented success with risperidone, olanzapine, and ziprasidone.[5,6,15,16] A review[17] published in 2011 reports on various off-label uses for 8 SGAs, including paliperidone, which covered behavioral symptoms of dementia, obsessive-convulsive disorder, eating disorders, personality disorders, depression, anxiety, and substance use. Adverse effects noted in the 2011 analysis are in line with known effects when using for approved psychotic disorders, such as weight gain, sedation, and extrapyramidal symptoms.[17] A known risk of all antipsychotics is the potential for lowering of the seizure threshold, which was of concern for this patient with TBI and uncontrolled seizures. Clozapine should generally be avoided, at least initially, due to the known risk and black box warning of seizures. Although conflicting evidence exists, incidence rates are generally low for most SGAs with the exception of clozapine (incidence rate of up to 5%).[18-20] Lertxundi et al[18] found that paliperidone had fewer reported seizure cases compared to other SGAs. In addition, it was prudent to monitor for neuroleptic malignant syndrome in this case as post-TBI patients have a greater risk of developing this syndrome.[6]

Besides the controversial off-label use of an antipsychotic, this case also included coercive use of medication, which continues to be debated. This practice is avoided unless absolutely necessary, and several reports discuss the use of forced medication.[9,10,21-24] In this case, the patient's guardian was contacted to discuss risks versus benefits of paliperidone LAI, including improvement of psychosis, increased medication adherence in the future, the black box warning of increased mortality in dementia-related psychosis, arrhythmias, extrapyramidal symptoms, metabolic syndrome, tardive dyskinesia, sedation, and alternatives to this treatment compared to no treatment. After this discussion, the guardian consented to the patient receiving paliperidone LAI. Despite this patient's wish to decline paliperidone, it was administered due to the guardian's full decision-making capabilities in accordance with the facility's policies.

This case demonstrates the successful use of a forced injection of paliperidone palmitate for psychosis after TBI. Only the first injection was coerced as the patient willingly accepted the next 2 injections during the hospital stay. Paliperidone palmitate was effective for treating psychosis, and the patient was stabilized for placement upon discharge. Although a witnessed seizure occurred after

paliperidone palmitate was initiated, it is unknown if this event was medication-related due to the patient's history of uncontrolled epilepsy. There were no other confirmed seizures or adverse medication events noted for the remainder of the admission. Despite the limitations of this case report format and the lack of formal monitoring of symptomatology, such as using a rating scale throughout the stay, this case demonstrates efficacy with paliperidone palmitate for behavioral disturbance due to TBI.

Conclusions

This case describes a patient who required guardian-consent forced use of an SGA for the treatment of TBI-associated psychosis. To our knowledge, we report the first case of successful off-label use of paliperidone LAI for the treatment of TBI-associated behavioral disturbance. After initial use of coercive administration, the patient became willing to accept subsequent treatment. Further study is warranted to better understand the relationship of behavioral disturbance following TBI and the use of antipsychotics in this population.

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