# It is illegal to post this copyrighted PDF on any website. Long-Acting Aripiprazole in the Management of Violence in Treatment Nonadherent Schizophrenia

Tommaso Toffanin, MD, PhD<sup>a,\*</sup>; Alessandro Miola, MD<sup>a</sup>; Benedetta Salvati, MD<sup>a</sup>; Francesco Folena Comini, MD<sup>a</sup>; Chiara Pavan, MD, PhD<sup>a</sup>; Giorgio Pigato, MD<sup>a</sup>; and Fabio Sambataro, MD, PhD<sup>a</sup>

he risk of violent behavior is higher in patients with schizophrenia relative to the general population. Violence can be prevented using antipsychotic drugs, with clozapine being the gold standard. Regrettably, the nonadherence rate for oral treatments is very high in schizophrenia, ranging from 40% to 80%, and it is one of the principal factors contributing to violent behavior.<sup>1</sup> The introduction of atypical long-acting injectable (LAI) antipsychotics, with faster titration schemes and better tolerability, can improve treatment adherence. Preventing violent activity can reduce criminal behavior in patients with schizophrenia and allow for participation in rehabilitation programs.<sup>2</sup> We report on the long-term effectiveness of aripiprazole LAI monotherapy in reducing criminal violent behavior in a treatment nonadherent patient with severe psychosis admitted to an acute ward per court-ordered commitment.

## **Case Report**

Mr A, a 36-year-old man, was arrested for assaulting a neighbor in a first-degree murder attempt with a cutting instrument and then promptly transferred to the acute inpatient psychiatric unit. There was no prior history of psychiatric illness or illicit drug or alcohol use. The physical and neurologic examinations and routine blood tests were negative. He was diagnosed with schizophreniform disorder (*DSM-5* criteria). The Historical-Clinical-Risk Management-20, Version 3 (HCR-20V3) score was 23, indicating a high risk of violent behavior.<sup>3</sup> At the psychiatric assessment, he presented as tense, apathetic, and suspicious; his speech was disorganized; and persecutory and ruin delusions were evident. In particular, he explained that the assault was a strategy to get arrested and defeat a death plot against him.

Mr A was started on intramuscular aripiprazole 30 mg/d and lorazepam 10 mg/d. After 3 days, the intramuscular

\*Corresponding author: Tommaso Toffanin, MD, PhD, Department of Neuroscience, Psychiatry Unit, University-Hospital of Padova, Via Giustiniani 2, 35128 Padova, Italy (tommaso.toffanin@aopd.veneto.it). Prim Care Companion CNS Disord 2021;23(1):20102623

*To cite:* Toffanin T, Miola A, Salvati B, et al. Long-acting aripiprazole in the management of violence in treatment nonadherent schizophrenia. *Prim Care Companion CNS Disord*. 2021;23(1):20102623.

To share: https://doi.org/10.4088/PCC.20l02623

© Copyright 2021 Physicians Postgraduate Press, Inc.

treatment was stopped, and he was started on tablet aripiprazole 30 mg/d and lorazepam 6 mg/d. Two weeks later, Mr A was started on aripiprazole LAI 400 mg/ month with oral administration of 10 mg/d for the first 15 days. Furthermore, lorazepam was reduced to 2.5 mg/d and stopped after 2 months. Aripiprazole LAI was well tolerated, and he voluntarily took the monthly injection with substantial reduction of psychosis. After 6 months, the patient's violence risk was considerably reduced (his HCR-20V3 score was 8, which indicates low risk).<sup>3</sup> Thus, Mr A was not mandated by the court to a long-term commitment in a forensic long-term mental health facility, and he could enter a psychosocial residential rehabilitation program.

### Discussion

Aside from clozapine, LAIs have proven superior to oral antipsychotics for prevention of criminal violence, addressing adherence and recidivism.<sup>4,5</sup> LAI treatment can allow clinical stability, improve everyday functioning,<sup>6,7</sup> and facilitate interventions aimed at rehabilitating patients with schizophrenia.<sup>8</sup> For the high-risk recidivist patients, the development of life skills may also reduce the crime risk, thanks to a regained ability to live independently in supported environments and interact more appropriately with others. In particular, among atypical antipsychotics aripiprazole has shown a synergistic effect with rehabilitation including working memory and processing speed that are crucial in everyday functioning.<sup>9</sup>

Aripiprazole modulates dopamine and serotonin pathways in several cortical areas<sup>10</sup> and can stabilize dopamine output in frontal areas involved in the regulation of behavior and cognition. Moreover, aripiprazole may act as a partial agonist on 5-HT<sub>1A</sub> serotonin postsynaptic receptors, which are involved in modulating and suppressing aggressive behaviors associated with altered connectivity of the amygdala with the orbital frontal cortex and anterior cingulate cortex and the limbic regions.<sup>11–13</sup>

In conclusion, aripiprazole is a viable treatment for patients with psychosis and violent conduct due to its behavioral and cognitive effects. The adherence following LAI administration allows for a stable treatment that prevents violence and allows a reintegration of patients into the general community.

Published online: January 14, 2021. Potential conflicts of interest: None. Funding/support: None.

<sup>&</sup>lt;sup>a</sup>Department of Neurosciences, Psychiatry Unit, University-Hospital of Padova, Padova, Italy

# ou are prohibited from making this PDF publicly available

# Toffanin et al **Patient consent:** Consent was received from the patient to publish the report **S** Ascher-Svanum H, Novick D, Haro JM, et al. Long-term functional

and information has been de-identified to protect anonymity.

## REFERENCES

- 1. Witt K, van Dorn R, Fazel S. Risk factors for violence in psychosis: systematic review and meta-regression analysis of 110 studies. *PLoS One*. 2013;8(2):e55942.
- Muñoz-Negro JE, Cervilla JA. A systematic review on the pharmacological treatment of delusional disorder. J Clin Psychopharmacol. 2016;36(6):684–690.
- 3. Douglas KS. Version 3 of the Historical-Clinical-Risk Management-20 (HCR-20V3): relevance to violence risk assessment and management in forensic conditional release contexts. *Behav Sci Law*. 2014;32(5):557–576.
- Strassnig MT, Nascimento V, Deckler E, et al. Pharmacological treatment of violence in schizophrenia. CNS Spectr. 2020;25(2):207–215.
- Sajatovic M, Ramirez LF, Fuentes-Casiano E, et al. A 6-month prospective trial of a personalized behavioral intervention + long-acting injectable antipsychotic in individuals with schizophrenia at risk of treatment nonadherence and homelessness. J Clin Psychopharmacol. 2017;37(6):702–707.

- improvements in the 2-year treatment of schizophrenia outpatients with olanzapine long-acting injection. *Neuropsychiatr Dis Treat*. 2014;10:1125–1131.
- Correll CU, Citrome L, Haddad PM, et al. The use of long-acting injectable antipsychotics in Schizophrenia: evaluating the evidence. *J Clin Psychiatry*. 2016;77(suppl 3):1-24.
- 8. Montemagni C, Frieri T, Rocca P. Second-generation long-acting injectable antipsychotics in schizophrenia: patient functioning and quality of life. *Neuropsychiatr Dis Treat*. 2016;12:917–929.
- 9. Matsuda Y, Sato S, Iwata K, et al. Effects of risperidone and aripiprazole on neurocognitive rehabilitation for schizophrenia. *Psychiatry Clin Neurosci.* 2014;68(6):425–431.
- Newman-Tancredi A, Kleven MS. Comparative pharmacology of antipsychotics possessing combined dopamine D2 and serotonin 5-HT1A receptor properties. *Psychopharmacology (Berl)*. 2011;216(4):451–473.
- 11. Rosell DR, Siever LJ. The neurobiology of aggression and violence. CNS Spectr. 2015;20(3):254–279.
- 12. Siever LJ. Neurobiology of aggression and violence. *Am J Psychiatry*. 2008;165(4):429–442.
- Carhart-Harris RL, Nutt DJ. Serotonin and brain function: a tale of two receptors. J Psychopharmacol. 2017;31(9):1091–1120.