



Letter to the Editor

Can low-dose aripiprazole reverse some of the adverse effects from a long-acting injectable?



Keywords:

Aripiprazole
Reverse
Adverse
Effects
Long-acting
Injectable

To the Editor

Long-acting injectables (LAIs) are one of the most effective tools to address medication non-adherence in patients with schizophrenia. However, if a patient develops adverse effects, such as extrapyramidal symptoms (EPS) and hyperprolactinemia with an LAI, s/he can suffer from those adverse effects for an extended period of time. Although anticholinergic medications are the first line of treatment for EPS, they are usually not effective for akathisia. Aripiprazole is a potent partial agonist which has the ability to displace concomitantly-administered antipsychotic drugs that antagonize D2Rs, which may help reduce EPS and hyperprolactinemia. Presented here is the case of a patient in whom LAI-induced EPS and hyperprolactinemia were successfully reduced with low-dose aripiprazole without any increase in psychosis.

History

A 32-year-old petite Caucasian female, born with developmental delay, with a long history of behavioral problems, a low BMI, and a diagnosis of schizoaffective disorder, bipolar type, was readmitted to a state facility for the fifth time due to worsening behavior, and reportedly manic symptoms with psychosis. Approximately 8 months prior to this hospital admission the patient had attempted suicide, which resulted in an anoxic brain injury. After this event she did not return to her baseline level of function and could not survive in the community. She was subsequently court committed for hospitalization at a state psychiatric facility. During her admission she failed to respond to high doses of haloperidol and developed significant adverse effects (AE) including EPS, especially akathisia and hyperprolactinemia. When the patient began to refuse her oral medication, she was started on a long-acting injectable (LAI) paliperidone palmitate to improve adherence. However, within days of administering a loading dose of the LAI, her akathisia became significantly worse and she was found to have an extremely high level of prolactin (i.e., 138 ng/mL) and a noticeable increase in agitation and aggression. Since bextropine was ineffective in treating her akathisia, a trial with 5 mg of aripiprazole was initiated to address the patient's AEs. The following day, the patient's AEs as well as her behavior improved significantly and she became more cooperative and less agitated. Her prolactin normalized over the next month.

However, as plasma levels of LAI paliperidone started to decline post-discontinuation, she decompensated. Aripiprazole at a higher dose of 20 mg a day was not effective as a monotherapy. Eventually aripiprazole was switched to low-dose haloperidol, which successfully decreased the patient's psychosis, behavior problems, akathisia and prolactin levels.

Discussion

If a patient develops AEs from an LAI, especially at its steady state, it may take several weeks for these AEs to cease after the LAI is discontinued. Some of these AEs, such as akathisia and tardive dyskinesia are not adequately managed with anticholinergic medications (Pringsheim et al., 2018; Soares-Weiser et al., 1997). In addition, anticholinergic medications have their own set of nuisance AEs, which may significantly compromise patients' bodily and brain functions, especially in elderly patients (Tune, 2001). Partial agonists at D2Rs may offer a novel and theoretically plausible alternative to anticholinergic medications in patients suffering from long-term AEs with an LAI. Aripiprazole has one of the most potent binding affinities for D2Rs, but functions as a partial agonist and not an antagonist (De Bartolomeis et al., 2015). With such high affinity for D2Rs, aripiprazole has the potential to displace antipsychotic drugs that are D2R antagonists, such as paliperidone, thus replacing antagonism with partial agonism, resulting in reduced EPS and hyperprolactinemia. However, clinical use of this strategy is complex and may require multiple fine adjustments of aripiprazole dosage to find an amount that reduces EPS and hyperprolactinemia but does not worsen psychosis. We believe that in most patients this goal may be achieved with lower dosages of aripiprazole, as higher dosages of aripiprazole may increase the risk for rebound psychosis and even discontinuation EPS (Chouinard et al., 2017). In our patient, a low-dose of 5 mg/day of aripiprazole was successful in reducing persistent EPS and hyperprolactinemia due to a loading intramuscular injection of paliperidone at 234 mg.

It is worth mentioning that most patients tolerate the loading and the maintenance doses of paliperidone palmitate, but our patient had a low BMI and a significant history of anoxic brain injury, which may explain her low threshold to develop EPS and hyperprolactinemia with a generally well-tolerated dose of paliperidone.

Conclusion

Even though aripiprazole may not be an effective antipsychotic treatment for a significant number of schizophrenia patients, it may be a safe and tolerable alternative to reduce LAI-induced AEs, especially akathisia not addressed by the anticholinergic medications.

Authors' contributions

Corresponding author, Mujeeb U. Shad conceived the idea of presenting this interesting case report and all authors equally contributed

to the drafting the manuscript. MS reviewed the final version of the manuscript. All authors read and approved the final manuscript.

Conflict of interest

None of the authors have any conflict of interest in relation to this case report.

Funding source

None.

Acknowledgements

Nursing and other unit staff that takes care of the patients.

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1 August 2018