

## DAILY DOSE OF 105 MG ARIPIPIRAZOLE BECAUSE OF DELUSIONAL ORIGIN: A CASE REPORT

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### INTRODUCTION

In clinical practice psychiatrists mainly deal with psychotic experiences considered as reality by the patients. The opposite situation occurs when patients perceive reality as a symptom of their illness. This second state is relatively rare. To our knowledge this is the first case report describing a patient with schizophrenia who took reality as a psychotic symptom and as a result significantly increased the dose of her antipsychotic drug for two weeks. We briefly discuss the relevant psychopathological and pharmacodynamic aspects of the case.

### CASE REPORT

The first psychiatric symptoms of this 30-year old Caucasian woman appeared at the age of twenty. At that time she was convinced that her mother's friend was her biological mother. Her behavior was disorganized, she had conflicts with her roommates at the student hostel and she neglected her basic needs such as personal hygiene, clothing and feeding.

Her first hospitalization took place in 2004 and was caused by visual hallucinations and other more typical symptoms of schizophrenia including delusional misidentification and delusions of reference. Psychological investigations (Rorschach, Benton and Bender tests) and a brain MRI did not confirm any organic brain damage. She was diagnosed with paranoid schizophrenia (F20.00) according to the ICD-10 criteria and was treated with sulpiride 300 mg/day, which she had stopped after discharge. During the next 4 years she was hospitalized three times due to paranoid syndromes. In the course of her illness she experienced visual hallucinations of faces on the wall and also delusions of misidentification concerning her parents. She received consecutively perphenazine, olanzapine and zuclopenthixol.

In 2008, as no expected improvement occurred, she was prescribed aripiprazole 15mg/day. At that time she started reading psychiatry textbooks, searched the Internet for information about schizophrenia, and watched the film 'A Beautiful Mind' about a genius mathematician, who suffered from schizophrenia with visual hallucinations (Howard 2001). Her parents divor-

ced and in this period of time she lived with her father who drank heavily. Seeing her father under the influence of alcohol, based on the film and her previous psychotic symptoms, she assumed that this was not reality, but a visual hallucination. This belief led her to increase the dose of aripiprazole and she took 105 mg/day in two equally divided doses. She explained that she had read the drug leaflet about aripiprazole saying that it reduces hallucinations and that she hoped that her drunken father would disappear after she had increased the dose.

The patient took the increased dose for 14 days until she ran out of the medication. While taking 105 mg daily dose of aripiprazole she felt slightly restless, but her delusions were still present, and she reported that 'her drunk father did not disappear'.

During her psychiatric examination she was mildly restless, had problems concentrating, her thinking was disrupted, she had no hallucinations but had delusions of reference and persecution, and her affect was blunted. The extrapyramidal symptoms (EPS) were evaluated by the Simpson Angus Scale (SAS) (Simpson & Angus 1970), on which she scored 5 points. Akathisia was assessed with the Barnes Akathisia Rating Scale (BARS) (Barnes 1989). Her total score was 3 points with the Objective and the two Subjective items of the BARS. On the 6-point Global Clinical Assessment of Akathisia scale of the BARS she scored 2 points, which also refers to mild akathisia.

As persecutory delusions and delusions of reference still persisted while taking the high doses of aripiprazole, her treatment was modified. She then gradually improved on combined zuclopenthixol and perazine medication.

### DISCUSSION

There are two main aspects of this case report. One is psychopathological, concerning poor insight, low level of compliance and false interpretation of reality as a psychotic symptom. The patient assumed that seeing her drunk father was a hallucination and this false belief led her to increase the dose of aripiprazole. Interestingly the delusion caused an extraordinary type of noncompliance in the form of overdose.

The second aspect is pharmacodynamic, concerning processes after increasing the dose of aripiprazole. The patient's reaction to the extremely high doses of aripiprazole can be described by three major elements: no improvement in psychotic symptoms, appearance of some restlessness/akathisia and relatively good tolerance.

Aripiprazole acts as a partial agonist of D2 receptors, meaning it has a full receptor affinity but limited intrinsic activity. At higher than the recommended maximum daily dose (30mg) the occupancy of D2 receptors exceeds 80% (Mamo et al. 2007), but the partial agonist effect is strong enough to prevent or limit EPSs (Deleon et al. 2004). Furthermore, due to its unique dopaminergic mechanism of action, aripiprazole has also been reported as an effective agent in catatonia (Voros et al. 2009).

In addition, aripiprazole also displays affinity for 5-HT<sub>1A</sub> and 5-HT<sub>2</sub> receptors producing respectively partial agonism and antagonism (Deleon et al. 2004; Šagud et al. 2011). The affinity of therapeutic doses of aripiprazole to 5-HT<sub>2</sub> receptors is much lower than to D2 (52% and 87%, respectively) (Mamo et al. 2007). We can assume that the daily dose of 105mg has a stronger effect on serotonergic system, because its dopaminergic action cannot further increase. Partial agonism on 5-HT<sub>1A</sub> receptors can cause akathisia (Thone 2007). On the other hand, 5-HT<sub>2</sub> antagonism decreases akathisia (Poyurovsky & Weizman 2001, Poyurovsky 2010) and that is probably why this symptom did not increase markedly during the 14 days of taking 105 mg of aripiprazole. Furthermore, subsequent increase in 5-HT<sub>2</sub> occupancy stimulates dopaminergic transmission, which protects the patient from an increase of EPSs.

## CONCLUSION

This case report highlights the patient's non-compliance caused by an unusual reason. It is also an example of unique pharmacodynamics of aripiprazole causing only mild EPS and akathisia in spite of a sustained significant overdose. Although this case report is limited by the lack of blood level measurement of the antipsychotic agent, the use of aripiprazole 3.5 times

higher than maximum recommended daily dose was relatively well tolerated. Despite this, no further relevant clinical improvement was detected.

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