

Could allopurinol be used in the treatment of schizophrenia?

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Dear Editor,

Typical and atypical antipsychotic medications used in the treatment of schizophrenia may not be sufficient to improve all symptoms. Approximately one-third of patients with schizophrenia respond partially to treatment with available antipsychotics. The severity of positive symptoms in schizophrenia is associated with poor prognosis. For this reason, there is a search for new treatments, especially in cases that are resistant to treatment or do not respond (Capuzzi et al., 2023). In particular, new options are being investigated to increase the effectiveness of antipsychotic treatment. Allopurinol, a xanthine oxidase inhibitor used in the treatment of hyperuricemia and gout, is one of them (Suhas et al., 2022). There are studies reporting that it reduces the number and rate of aggressive events in patients resistant to other treatments (Carr et al., 2017; Miyauchi, 2021).

The 34-year-old, married patient applied to our psychiatry outpatient clinic due to demoralization, not wanting to go to work, thinking that his wife was cheating on him, and having frequent problems with his friends at work. The patient, who stated that he came to the interview at his father's request and that he did not have any psychiatric problems or illness, first became suspicious of strangers and friends, became introverted, and distanced himself from people 10 years ago, when he was studying at university. The patient, who stated that people stared at him while walking on the road and that cars passing by on the street were trying to hint at him by honking their horns, was unable to continue his schooling that year. The patient was taken to the psychiatric clinic by his relatives and received inpatient treatment for 2 months. After discharge, he used his medications for a while and stopped taking them on the grounds that he was getting better. During the same period, the patient complained of swelling and pain in his right big toe and was diagnosed with gout and treated with allopurinol 600mg/day. The patient, who used the current treatment regularly until two months ago, completed his schooling without any problems, has been working for 6 years, and got married three years ago, has never had a psychiatric application other than the treatment he received during his student period. His current psychiatric symptoms emerged after he stopped allopurinol treatment without a physician's advice. His father stated that the patient had been quiet, introverted, had few friends, and had a touchy and suspicious nature since childhood. He stated that his son, whom he had been talking to on the phone in recent weeks,

said that he was stagnant and joyless, that they were having marital problems, and that everyone at work was dealing with him. In addition, his daughter-in-law, who gave birth a month ago, called him and said, 'Your son has changed a lot, he does not go to work, he constantly says that I am cheating on him, he talks to himself, he does not sleep, he says he will have a test for the baby, this is not from me, he does not even drink water from my hand, he does not eat the food I cook and throws it in the trash. He also stated that 'we have been staying in separate rooms for the last week...'. Thereupon, the father came to his son and found the patient lying on a bed in a room of the house. When his father saw that the patient had not gone to work for a while, was living at home with the curtains closed, and was talking and laughing to himself, he convinced him to consult a doctor.

It was learned that two of the patient's cousins were treated for schizophrenia and one of his uncles died by suicide. On physical examination, redness and deformity were observed in both big toe joints.

The male patient, who looked his age and whose clothing was compatible with his socioeconomic level, made eye contact and had moderate self-care. His speech was clear, fluent, understandable, purposeful, with short sentences and normal volume. His affect was irritable and superficial, consistent with his mood state. Consciousness was clear, orientation and memory were in place. Auditory hallucinations were detected in perception. His assessment and judgment of reality was impaired and his thought process slowed down. His thought content included jealousy, persecution, and delusions of reference towards his wife. After psychiatric evaluation, the patient was recommended to receive inpatient treatment with a diagnosis of schizophrenia according to DSM-5. However, the patient's father and the patient did not accept this suggestion. Thereupon, aripiprazole 5mg/day treatment was started and the drug dose was gradually increased. He was invited to weekly meetings. At the third weekly meeting, when the patient mentioned gout disease and its treatment, which he had not mentioned before, tests were performed in this regard. Internal medicine and physical therapy and rehabilitation departments were consulted. Allopurinol 600mg/day treatment of the patient, who was learned to have voluntarily discontinued the medication and whose serum uric acid level was high, was rearranged. At the end of one month, a significant

improvement was observed in the psychotic symptoms of the patient, who lived with his father and attended regular weekly check-ups. The patient talked to his wife on the phone at the end of the sixth week and started living with his wife 2 months later. It was learned that the patient's complaints disappeared, his relationship with his wife improved, and he continued to work. Informed consent was obtained from the patient before writing this article.

The issue that adenosine agonists such as allopurinol may have a place in the treatment of schizophrenia is on the agenda of clinicians. With the adenosine dysfunction hypothesis, it has been suggested that adenosine may play a role in the pathophysiology of schizophrenia via dopamine and glutamate (Hirota & Kishi, 2013). Increased adenosinergic transmission reduces the affinity of dopamine agonists to dopamine receptors. Adenosine agonists antagonize dopamine activity in the ventral striatum of the brain, and thus adenosine agonists such as allopurinol show dopamine antagonist or antipsychotic-like results. In other words, because adenosine agonists have similar effects to dopamine antagonists, increased adenosine levels may mediate the improvement of schizophrenia symptoms (Linden et al., 2014). Adding allopurinol to antipsychotic treatment may be a treatment option, especially in treatment-resistant cases. Because in our case, there were no psychiatric signs or symptoms during the period when he was using allopurinol for the treatment of gout, and the exacerbation of psychotic symptoms following the sudden discontinuation of allopurinol is what makes the case interesting. It suggests that

other biological systems, such as immunity or metabolism, may be the subject of future research to identify pharmacological targets for the positive symptoms of schizophrenia. However, the lack of replication of studies prevents definitive conclusions from being drawn, and future studies are needed to confirm the results presented in this overview.

References

- Capuzzi, E., Caldiroli, A., Quitadamo, C., Butturini, F., Surace, T., Clerici, M., & Buoli, M. (2023). Novel pharmacotherapy targeting the positive symptoms of schizophrenia. *Expert Opinion on Pharmacotherapy*, 24(14), 1623-1648.
- Carr, C. N., Straley, C. M., & Baugh, T. B. (2017). Allopurinol for the treatment of refractory aggression: A case series. *Pharmacotherapy*, 37(6), 748-754.
- Hirota, T., & Kishi, T. (2013). Adenosine hypothesis in schizophrenia and bipolar disorder: a systematic review and meta-analysis of randomized controlled trial of adjuvant purinergic modulators. *Schizophrenia Research*, 149(1-3), 88-95.
- Linden, N., Onwuanibe, A., & Sandson, N. (2014). Rapid resolution of psychotic symptoms in a patient with schizophrenia using allopurinol as an adjuvant: a case report. *Clinical Schizophrenia & Related Psychoses*, 7(4), 231-234.
- Miyauchi, T. (2021). Long-term improvement of aggression in a patient with schizophrenia using allopurinol as an adjuvant: A case report. *Journal of Clinical Psychopharmacology*, 41(2), 212-214.
- Suhas, S., Sreeraj, V. S., Amrutha, C., Desai, G., & Venkatasubramanian, G. (2022). Is allopurinol a marvel in the end-game of ultra-resistant schizophrenia? *Schizophrenia Research*, 241, 12-13.

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