LETTER TO THE EDITOR

Xanomeline and Trospium: Potential substitute for conventional antipsychotics

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Dear Madam, Schizophrenia is a chronic mental illness with a global prevalence of 24 million people.[1] With paucity of researches mounting the exact prevalence of schizophrenia in Pakistan, the treatment of this illness becomes even harder to combat. This condition is typically managed with antipsychotics, which work by blocking the D2 dopamine receptors but recent advances in research also suggest that the muscarinic cholinergic system is also involved in its pathophysiology.[2] The drug Xanomeline is an oral muscarinic cholinergic receptor agonist that activates M1 and M4 receptors. Xanomeline however causes side effects like vomiting, nausea, diarrhoea, sweating and hypersalivation. To bypass these effects, Trospium was added, which acts by blocking peripheral muscarinic cholinergic receptors.[3,4] To observe the reduction of psychosis in schizophrenics, a double-blinded clinical trial was done with promising results: reduction of both, positive and negative symptoms of Schizophrenia, good tolerance and no evidence of weight gain.[4] Side effects included constipation, nausea, dry mouth, dyspepsia, and vomiting although the incidence of these effects reduced over the course of the trial. However, there is a dearth of research when it comes to comparison of this combination drug (called KARXT) with the usual antipsychotics. Therefore, further research regarding the safety of KARXT, and its efficacy needs to be explored for potential amelioration of symptoms. Moreover, studies comparing the efficacy of this drug with the commonly used antipsychotics need to be explored in order to effectively assess the advantage and potential replacement benefits of this drug.

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References

1. World Health Organization (WHO). Schizophrenia: Fact Sheets. News release. The WHO Media Center. [Online] 2021 [Cited 2022 January 22]. Available from URL: http://www.who.int/news-room/fact-sheets/detail/schizophrenia.
2. Erskine D, Taylor JP, Bakker G, Brown AJH, Tasker T, Nathan PJ. Cholinergic muscarinic M1 and M4 receptors as therapeutic targets for cognitive, behavioural, and psychological symptoms in psychiatric and neurological disorders. Drug Discov Today 2019;24:2307-14. doi: 10.1016/j.drudis.2019.08.009.
3. Thorn CA, Moon J, Bourbonais CA, Harms J, Edgerton JR, Stark E, et al. Striatal, Hippocampal, and Cortical Networks Are Differentially Responsive to the M4- and M1-Muscarinic Acetylcholine Receptor Mediated Effects of Xanomeline. ACS Chem Neurosci 2019;10:1753-64. doi: 10.1021/acschemneuro.8b00625.
4. Brannan SK, Sawchak S, Miller AC, Lieberman JA, Paul SM, Breier A. Muscarinic Cholinergic Receptor Agonist and Peripheral Antagonist for Schizophrenia. N Engl J Med 2021;384:717-26. doi: 10.1056/NEJMoa2017015.