Treatment of Visual Hallucinations in Schizophrenia by Acetylcholinesterase Inhibitors: a case report

Nazir Hashemi Abad, MD [1]
Najafi Shala Doulatabad, Msc[2]
Ali Mohammadi, MD [1]
Hamid Reza Ghafarian Srazi PhD [3, 4]

1 Department of Psychiatry, Faculty of Medicine,Yasouj University of Medical Science, Yasouj, Iran .
2 Department of Nursing, College of Nursing & Midwifery, Yasouj University of Medical Science, Yasouj, Iran .
3 Department of Social Medicine, Faculty of Medicine; Yasouj University of Medical Sciences, Yasouj, Iran
4 Department of Epidemiology And Biostatistics, Tehran University of Medical Sciences, School of Public Health, Tehran, Iran.

Corresponding author:
Hamid Reza Ghafarian Shirazi
Department of Social Medicin, School of Medicine, Yasuj University of Medical Sciences, Yasouj, Iran
Tel/Fax:+98 741 2230290
E-mail:ghafarian_h@razi.tums.ac.ir

Schizophrenia and various neurological disorders have some signs and symptoms. Visual hallucinations are one of such disorders. The related studies in some diseases for example Parkinson Disease and Lewy Body Dementia indicate that Acetylcholine (Ach) plays a significant role in neuropsychiatric manifestation and its association with visual hallucination; therefore, visual hallucinations occur due to the depletion of Ach. Drug therapies such as Cholinesterase inhibitors (ChEIs) for increasing Ach level may be beneficial in treating visual hallucination. AchEI's have been used in the treatment of visual hallucinations in Dementia and Parkinson's Disease. We thought that a similar Ach depletion may cause visual hallucinations in patients with schizophrenia and may provide a target for drug treatment. We had a patient with schizophrenia whose psychotic symptoms responded to the treatment plan, but her visual hallucination did not. However, the patient's visual hallucination successfully responded to Rivastigmine (AchEI).
This case illustrates the use of an AchEI in the treatment of refractory visual hallucinations in a patient with schizophrenia.

Keywords: *Acetyl cholinesterase inhibitors, Hallucinations, Schizophrenia, Visual Perception*

Iran J Psychiatry 2011; 6:161-163

The annual incidence of schizophrenia averages 15 per 100000, the point prevalence averages 4.5 per population of 1000(1). Visual hallucinations are one of the symptoms of schizophrenia and of various other neurological disorders (2, 3). Acetylcholine (ACh) plays an important role in a wide variety of cognitive tasks such as perception, selective attention, associative learning, and memory (4). The cholinergic disturbance may contribute to neuropsychiatric manifestation of the disease particularly for such symptoms as hallucination and delusion (5). A more recent study focused on acetylcholine depletion and its association with visual hallucination. The treatment of the visual hallucination often targets the underling illness rather than the symptom (6). Drug therapies to increase the level of Ach, and cholinesterase inhibitors (ChEIs) may be beneficial in treating visual hallucination of various neurological disorders such as Dementia with Lewy Bodies (DLB) and Parkinson's disease. The introduction of Rivastigmine led to improvement in cognitive and functional abilities as well as resolution of behavioral problems and visual hallucinations. As indicated in some researches, Rivastigmine, Donepezil, Galantamine are some ChEIs that may be effective in the treatment of visual hallucination (7, 14).
We had a patient with schizophrenia whose psychotic symptoms responded to treatment plan, but not her visual hallucination. We observed a case presentation by Sachin ,SP: Acetylcholinesterase inhibitors (AchEI,s) for the treatment of visual hallucination in schizophrenia(6) ,and used Rivastigmine (an AchEIs) to treat our patient's resistant and distressing visual hallucination. The patient's visual hallucination successfully responded to Rivastigmine (AchEI).

Case presentation

The case was a 28- year old single female, with primary education degree who had been diagnosed with schizophrenia. She was admitted to the psychiatry ward of the Rajaee Hospital (Yasouj city, south of Iran). When she was admitted, she presented abnormal behavior, agitation, self talking, self laughing, and occasional aggression. She had paranoid delusions, auditory and visual hallucinations of her both parents with their dog, and she had no insight into her illness. Despite managing these symptoms with antipsychotic medications for 6 months, they remained unchanged.

These visual experiences were evident during the day and night, especially when she was alone. The patient had a past history of schizophrenic features since 6 years ago, with 3 exacerbated episodes. She referred to a local physician, received antipsychotic drugs, and as a result her condition improved temporarily. However, she was admitted again following an inability to function in the community due to deterioration in her mental state. She did not respond to treatment strategies, including atypical antipsychotic, and clozapine. In terms of a reduction in paranoid delusions, aggressiveness and auditory hallucinations, she responded well to a combination of clozapine, na-valporate, and clonazepam, but her visual hallucinations were still vivid. The patient was isolated and did not have good relations with family or friends. However, her presentation was not thought to be related to drug and substance (alcohol and opium) misuse or psychosocial stressors. Physical investigations were unremarkable (including lab data, thyroid function tests, copper, caeruloplasmin, autoantibody, MRI and EEG).

At the time of admission, the patient's PANSS (15) score was 81 (p32, n13, g36), and MMSE score was 30/30. The pharmacological treatment plan was na-valporate plus clonazepam and clozapine therapy. After a four - month therapy with clozapine at a dose of 500 mg (100 mg at morning,100 mg at noon, 300 mg at night) daily, na-valporate 200 mg three times daily, clonazepam 1 mg two times daily accompanied by psychological and occupational therapy, the patient's mental state was stabilized and her behavior improved. In addition, her delusions, auditory hallucinations and function were improved, and her PANSS increased to a total score of 49 (p13, n12, g 24). Despite these improvements, the patient continued to experience vivid visual hallucinations of her parents and their dog.

The psychiatric treatment team decided to initiate an AChEI, Rivastigmine, to target visual hallucination symptoms (the same as Sachin SP case). Therefore, 3 mg of Rivastigmine capsule in the mornings, and 3 mg at night was initiated. No changes were made to all other psychotropic medications. After the addition of Rivastigmine capsule to her treatment regimen, PANSS rating scales and MMSE scores were done on two occasions. The patient was supervised by one member of family and an specialist nurse one week prior to administration of Rivastigmine and during admission.

The patient's functioning was improved, she became calm and independent in her self-care, and participated in community outings. The patient's level of occupational and psychological therapy input remained stable throughout the introduction of Rivastigmine and focusing on reducing the distress and interference with daily activities associated with her visual hallucinations. No medication changes were made to her pharmacological therapy, and she did not report any side effects from the Rivastigmine capsule. Two weeks after the addition of Rivastigmine capsule, her PANSS total score was 44 (P 11, N 11, GP 22) and this improvement was maintained as her PANSS total score at the sixth week was 43 (P 10, N 11, GP 22). Over the baseline assessment period, the patient, her family, and the specialist nurse continued to report visual hallucinations throughout the day. Reports of visual hallucinations decreased to one to two times a day on average, and the level of distress also reduced significantly 16 days after addition of Rivastigmine. However, the patient reported one to two appearances of visual hallucinations a day (seeing her parents with a dog). Gradually, even this report became much more ambiguous; the hallucinations were more unclear at night and day. The patient thought that the capsule was helpful, and by taking it, she experienced the hallucinations less frequently than before. She was discharged from the hospital two months after receiving Rivastigmine.After a four- month follow up, she could live independently quite successfully, although supported by her local mental health team. She also remained free from visual hallucinations and continued Rivastigmine capsule plus other pharmacological management.

Conclusion

AchEI's can be used to treat refractory visual hallucinations in schizophrenic patients. In this case, the treatment was to combine current thinking in neurophysiology and therapeutic evidence in related disorders, and we applied them to clinical practice in a targeted way. This was a case report with new therapeutic use. Further research on this issue is suggested.

Conflict of interest

Authors have no conflict of interest to declare that are relevant to the content of this submission.

Authors' contributions

Hashemi N contributed to planning, supervision and writing the report. Najafi S and Mohammadi A reviewed the literature. Najefi S, Mohammadi A and Ghafarian Shirazi HR. each contributed to writing the case presentation.

Consent

Written informed consent was obtained from the patient for publication of this case report.

Acknowledgements:

The authors would like to thank the patient and her parents, the especial nurse, all colleagues in Rajaie Hospital, Research Committee, and Ethic Committee of Yasouj University of Medical Sciences for supporting this study .

References

1. Tandon R, Keshavan M, Nasrallah H. Schizophrenia epidemiology and etiology. Schizophrenia research. 2008; 102: 1-18. doi:10.1016/j.schres.2008.04.011
2. Kersten D, Mamassian P, Yuille A. Object perception as bayesian inference. *Annu Rev Psychology.* 2004; 55:271–304. doi: 10.1146/annurev.psych.55.090902.142005.(Cross Ref)
3. Friston K. A theory of cortical responses. *Phil Trans R Soc B.* 2005; 360: 815–836. doi: 10.1098/rstb.2005.1622.(PMC free article)(PubMed)(Cross Ref)
4. Yu D, Dayan P. Acetylcholine in cortical inference. Neural network. 2002; 15: 719–730. doi: 10.1016/S0893-6080(02)00058-8.(PubMed)(Cross Ref)
5. Jeffery L. Cholinesterase inhibitors: A new class of psychotropic compounds. Am J Psychiatry. 2000;157:4-15
6. Sachin SP, Azizah A, Pamela J, Sukhi S. Acetylcholinesterase inhibitors (AchEI,s) for the treatment of visual hallucination in schizophrenia: a case report. BMC psychiatry. 2010;10: 68. doi:10.1168/147-244x-10-68
7. Edwards K, Royall D, Hershey L, Lichter D, Hake A, Farlow M, Pasquier F, Johnson S. Efficacy and safety of galantamine in patients with dementia with Lewy bodies: a 24 week open-label study. *Dementia and Geriatric Cognitive Disorders.* 2007; 23(6): 401–5. doi: 10.1159/000101512.(PubMed)(Cross Ref)
8. Fabbrini G, Barbanti P, Aurilia C, Pauletti C, Lenzi GL, Meco G. Donepezil in the treatment of hallucinations and delusions in Parkinson's disease. *Neurological Sciences.* 2002; 23(1): 41–43. doi: 10.1007/s100720200022.(Cross Ref)
9. Cummings JL. Cholinesterase Inhibitors: A new Class of Psychotropic Compounds. *Am J Psychiatry.* 2000; 157 :(1) 4-15.
10. Cummings JL, Askin-Edgar S. Evidence for Psychotropic Effects of Acetylcholinesterase Inhibitors. *CNS Drugs.* 2000; 13 :(6) 385–395. doi: 10.2165/00023210-200013060-00001.(Cross Ref)
11. Bullock R, Cameron A. Rivastigmine for the treatment of dementia and visual hallucinations associated with Parkinson's disease: a case series. *Current Medical Research and Opinion.* 2002; 18(5):258–64. doi: 10.1185/030079902125000813.(PubMed)(Cross Ref)
12. David B, Murat E, Ian M, Peter P, Dag A, Chuanchieh H, Roger L. Effect of Rivastigmine in patients with and without visual hallucinations in dementia associated with Parkinson's disease. Movement Disorder.2006;21:1899-1907.doi:10.1002/mds.21077.
13. Edwards KR, Hershey L, Wray L, Bednarczyk EM, Lichter D, Farlow M, Johnson S. Efficacy and Safety of Galantamine in Patients with Dementia with Lewy Bodies: A 12-Week Interim Analysis. Dementia and geriatric cognitive disorder. 2004;17:40-48 (DOI: 10.1159/000074681)
14. Lenzi A, Maltinti E, Poggi E, Fabrizio L, Coli E. Effect of Rivastigmine on cognitive function and quality of life in patients with schizophrenia. Clinical neuropharmacology 2003; 26: 317-32.
15. Kay SR, Fiszbein A, Opler LA. The positive and negative syndrome scale for schizophrenia. Schizophr Bull. 1987; 13: 261–276.