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The Use of Stimulant Augmentation of Second Generation Antipsychotics in the Management of Negative Symptoms of Schizophrenia: A Case Report

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Abstract

Background: Negative symptoms of schizophrenia have been demonstrated to be due to decreased dopamine in the mesocortical pathways. Stimulant medications are a class of medications that can increase dopamine activity in the mesocortical pathway. ***Case Presentation:*** We present the case of a patient whose negative symptoms improved from a Positive and Negative Syndrome (PANSS) score of 39 to 11 on the negative symptoms subscale during a three-week trial of dopamine agonist augmentation of antipsychotic therapy. The score on the positive symptoms subscale on PANSS remained low with a two-point reduction at the end of the three-week period. ***Conclusion:*** The potential benefits of using stimulant medications in treating negative symptoms of schizophrenia are discussed.

Keywords: ***Schizophrenia, Negative Symptoms, Atypical Antipsychotics***

Introduction

The use of available antipsychotic medications alone for negative symptoms of schizophrenia have been shown to have modest benefits.[1] Likewise, the expectation that negative symptoms would show differentially improved responsiveness to second generation antipsychotics (SGA) compared to first-generation antipsychotics has not been realized to a degree that is clinically significant. The results from various studies indicate no clear advantage of using SGAs over first-generation antipsychotics in treating negative symptoms.[2] The likely reason is that dopamine hypoactivity in the pre-frontal has been shown to be correlated with negative symptoms of schizophrenia.[3] Most antipsychotic medications are dopamine antagonists and may exacerbate dopamine hypoactivity in the prefrontal cortex.[3] Hence, interventions that increase dopamine activity in the prefrontal cortex, such as stimulants, may improve negative symptoms.[4]

We present the case of a patient hospitalized for schizophrenia with predominantly negative features who has shown minimal response to initial treatment with a second-generation antipsychotic medication. A three-week trial of augmentation with dopamine agonist therapy was initiated to achieve some improvement in the negative symptoms. This improvement in negative symptoms was monitored with the negative symptoms subscale on PANSS. The potential adverse event of worsening positive symptoms of psychosis was also monitored with the positive symptoms subscale on PANSS. The result of the three-week trial of treatment augmentation with dopamine agonist therapy is presented and the possible implication for managing negative symptoms of psychosis discussed.

Case Presentation

The patient is a 48-year-old Caucasian male who was brought to the hospital emergency department from his shelter for medication noncompliance and poor personal hygiene. He presented disheveled, malodorous with extensive body rash and lice noted. It was reported that the patient had not taken a shower for about 4-months prior to arrival in the emergency department. He had profound psychomotor retardation and was motionless on the chair upon initial arrival. He demonstrated affective flattening, anhedonia, paucity of gestures, poor eye contact, affect non-responsivity and lack of vocal inflection. He exhibited alogia with poverty of speech limited to one or two syllables, poverty of content, at times demonstrated thought blocking, and increased

latency response. He showed poor interaction with staff and other patients and exhibited emotional withdrawal. In addition, his speech was of low tone. PANSS score was 39 on negative subscale and 14 on positive subscale. Laboratory findings were within normal limits. Urine toxicology results were unremarkable.

On day 1 of admission, patient was started on Olanzapine 10 mg orally at bedtime with a presumptive diagnosis of schizophrenia with predominantly negative features. He continued to demonstrate poor self-care, with no showering done following admission. He continued to exhibit social withdrawal. He did not engage in group therapy sessions or participate in other treatment activities. On day 5, PANSS score was 39 on negative subscale and 7 on positive subscale. Wellbutrin XL 150 mg orally daily was added for management of possible depressive features and/or negative symptoms of schizophrenia. He continued to remain isolative, and his personal hygiene worsened, as he refrained from showering even after repeated encouragement from the staff. On day 9, Ritalin 5 mg orally daily was added for persisting negative symptoms of schizophrenia. PANSS score was 36 on negative subscale and 6 on positive subscale. This was eventually up titrated to 20 mg orally daily by Day 13.

On Day 15 he began to display improvement of his negative symptoms: he took a shower, began showing reactivity of affect with improvements in eye contact and social interaction. Poverty of speech and thought, apathy, anhedonia, reduced social drive, loss of motivation, and lack of social interest remained unchanged. Memantine 5 mg daily was added. He was noted to show slow but significant and steady improvement of negative symptoms. PANSS score was 21 on negative subscale and 5 on positive subscale. Ritalin 20mg was cross tapered with Amantadine 100mg.

On Day 30, he was discharged with a PANSS score of 11 on negative subscale and 5 on positive subscale. His medications upon discharge were Amantadine 100 mg daily, Olanzapine 10 mg at bedtime and Memantine 5 mg daily. He had concurrent resolution in paranoid beliefs and did not display any new positive symptoms of psychosis. He also reported no side effects on the medications with good tolerability and a desire to continue on the same regimen. Follow up contact post discharge revealed he remained functional and was working with social work services for possible vocational training options.

Discussion

Studies reporting the use of stimulants in treating negative symptoms of schizophrenia are limited. In addition, evidence of the efficacy of such practice is inconclusive at best, and sometimes even contradictory [2, 5]. In a placebo-controlled trial, the use of methylphenidate as an adjuvant for the treatment of Negative symptoms of schizophrenia was reported to have no significant difference in the measured Scale for assessment of Negative Symptoms (SANS) Score.[6] However, some studies have reported a significant improvement in the negative symptoms of schizophrenia with augmentation of antipsychotics with psychostimulants. In a randomized placebo-controlled trial of psychostimulant augmentation of risperidone, by Arbabi et al., significant improvement in negative symptoms was observed which further supports the use of psychostimulants.[7] Furthermore, it was reported by Lieberman et al., in a systematic review that there seems to be an improvement in negative symptoms of schizophrenia in the augmentation of antipsychotics with psychostimulants in select patient's population without a worsening of the positive symptoms.[5] The potential benefit of psychostimulants as an adjunctive treatment has been sparsely explored and documented in recent literature, thereby prompting a call for further review by the Cochrane Collaboration.[4] The potential benefit of psychostimulants is widely recognized, prompting a call for further review by the Cochrane Collaboration.[4] Essali et al suggest that the positive effect of amphetamines on the prefrontal cortex may improve the negative symptoms of schizophrenia.[4]

There is also active but preliminary research on using other stimulants such as Modafinil or Armodafinil as an adjunctive treatment of negative symptoms in schizophrenia.[8-10] During a 4-week, double-blind, placebo-controlled study of the effect of Armodafinil on cognition among schizophrenic patients treated with antipsychotics, those who received 200 mg of Armodafinil daily had significant attenuation of their negative symptoms. Our patient initially presented with signs and symptoms of schizophrenia with predominantly negative symptoms as outlined by his history. Although the first-line treatment is an atypical antipsychotic; a four-week course of Olanzapine showed no significant improvement of symptoms for our patient. The addition of Methylphenidate, however, showed significant improvement of his social functions: his affect, speech, volition to participate in group activities and the general energy level started showing gradual improvement.

Conclusion

The use of stimulants in schizophrenia with predominantly negative symptomatology is seldom and poorly characterized in literature. This case report showed significant clinical improvement after the augmentation of an antipsychotic medication with stimulants. Since no large-scale clinical trials support any particular treatment of negative symptoms of schizophrenia, more clinical research is needed. This report hopes to contribute to the increasing number of literature describing the use of stimulants in schizophrenia which can hopefully lead to a multi-center randomized clinical trial featuring stimulants in refractive schizophrenia with predominant negative symptoms.

List of abbreviations:

PANSS: Positive and Negative Syndrome Score
SGA: Second generation antipsychotics
SANS: Scale for assessment of Negative Symptoms

Consent: The patient's consent was obtained orally.

Conflict of Interest: The authors have no conflicts of interest to declare.

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