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Case Report

Improvement of schizoaffective disorder with endoxifen treatment: a case report

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ABSTRACT

Schizoaffective disorder shares symptomatology and pathophysiology with schizophrenia and bipolar disorder. Studies related to treatment option and their efficacy in schizoaffective disorder are limited; thus, no current consensus treatment guidelines exist. Patients with schizoaffective disorders are treated mainly with combination of antipsychotics and mood stabilizers or antidepressants. Here, the author presents a case of schizoaffective disorders that was successfully treated with endoxifen, which had efficacy issues with amisulpride, quetiapine, and risoperidone and safety issues with clozapine.

Keywords: Improvement, Schizoaffective disorder, Symptomatology

INTRODUCTION

Schizoaffective disorder is a severe mental illness with a prevalence of around 0.3%.[1] Patients with schizoaffective disorder may have features of either manic or depressive type, or in some cases, both. As per the DSM-5 diagnostic criteria, to be diagnosed with schizoaffective disorder, at least two psychotic symptoms must be present along with mood symptoms.[2]

It has been evident from molecular studies that protein kinase C (PKC) plays a major role in the pathogenesis of bipolar disorder as well as schizophrenia.[3,4] Pathophysiology of schizoaffective disorder reflects the changes seen in schizophrenia as well as bipolar disorder, pointing towards the potential use of PKC inhibitors like endoxifen in it.[5] The author hereby presents the case of a patient with schizoaffective disorder who was treated with endoxifen.

CASE REPORT

A 55-year-old, unemployed, married man, living with family (wife and son) who had applied for a correspondence course at IIT, Kanpur, reported to the psychiatry clinic with an established diagnosis of schizoaffective disorder for the last 30 years. Patient presented with manic episode with symptoms of schizophrenia. Medical history revealed that he was a known case of diabetes.

He was treated initially with amisulpiride (200 mg BID), quetiapine (50 mg OD) and risperidone (3 mg BID). Patient's symptoms were not improved even after three different antipsychotics tried for 6 weeks. Hence, the decision of change to clozapine was made. Clozapine and lithium were initiated at a dose of 50 mg per day and 450 mg twice daily respectively along with cross-tapering of other antipsychotic therapy. Later on, patient was stabilized on clozapine (150 mg in divided doses) and lithium (450 mg BID). Though adherence to the prescribed treatment was high, the patient developed severe drowsiness and sialorrhea which were assumed to be due to clozapine therapy. To tackle the sialorrhea, 2 mg of glycopyrrolate was initiated. Additionally, the dose of clozapine was tapered down which improved drowsiness but also led to development of symptoms like auditory hallucinations, circumstantiality of speech suggestive of relapse with brief psychiatric rating scale score of 85.

Meanwhile, he was also suffering from the depressive episode. At this point of time, decision to add endoxifen to the treatment regimen was made after due discussion with his family members.

Endoxifen was prescribed at a dose of 8 mg per day initially, which was increased to 16 mg per day after 2 weeks. Doses of clozapine and lithium were reduced to 50 mg per day and 300 mg BID, respectively. The Young Mania rating scale (YMRS) and Montgomery-Åsberg depression rating scale (MADRS) scores at initiation of endoxifen therapy were 12 and 36, respectively.

Improvement in mood started becoming visible within 2 weeks of endoxifen therapy. On further follow-up at 1 month, the symptoms of schizoaffective disorder were further improved, with noticeable improvement in circumstantiality of speech, concentration, and daytime drowsiness. The dose of lithium was further reduced to 450 mg once daily. The BPRS score, following 1 month of endoxifen therapy, came down to 39. The YMRS and MADRS scores also improved to 10 and 24, respectively. Endoxifen was further continued for 4 months during which, the effectiveness of endoxifen continued without any adverse events or changes in blood glucose level.

The patient was stable on 16 mg of daily dose of endoxifen during the latest visit (4 months) and also reported that he had passed his first semester of marketing management and was independently traveling to IIT Kanpur from Vizag for examination.

Table 1: Treatment course (diagnosis: schizoaffective disorder with diabetes).

Mood episode	Treatment 1	Treatment 2	Treatment 3
	Manic episode	**Manic episode**	**Depressive episode**
Prescribed drugs	Amisulpiride (200 mg BID), quetiapine (50 mg OD), risperidone (3 mg BID)	Clozapine was initiated at 200 mg per day, which later stabilized at 150 mg per day, lithium (450 mg BID)	Clozapine (50 mg), lithium (300 mg BD), further reduced to 450 mg OD, endoxifen (8 mg) for 2 weeks, then increased to 16 mg per day
Treatment duration	3 years	4 years	4 months
Reasons for change in treatment	Not responding to 2 different antipsychotics with a sufficient duration of 6 weeks	Patient developed adverse events, drowsiness and sialorrhoea, the dose of clozapine was reduced due to the development of adverse events, which led to relapse	
YMRS score	12	10	6
MADRS score	36	24	6
BPRS score	94	85	18

DISCUSSION

Over-activity of PKC has been observed among patients with schizophrenia and also with bipolar disorders.[3,4] schizoaffective disorder shares symptomatology with schizophrenia and bipolar disorder.[2] schizoaffective disorder pathophysiology also reflects the changes seen in schizophrenia as well as bipolar disorder directing towards potential use of PKC inhibitors. Hence, endoxifen was prescribed in these patients as it works by inhibition of PKC.[6]

Psychostimulants like amphetamine and methamphetamine work through PKC activation, which is responsible for the pathogenesis of bipolar disorder as well as schizophrenia.[7] As endoxifen works through PKC inhibition, it may be the reason endoxifen is effective in the treatment of schizoaffective disorder.[6]

Rigorous studies of treatment efficacy in schizoaffective disorder are limited; thus, no current consensus treatment guidelines exist.[8] Only paliperidone is approved by the EMA and FDA for the management of patients with schizoaffective disorder.[9] Antipsychotic treatment remains the mainstay of pharmacotherapy. For patients with schizoaffective disorder, depressive type, treatment with combination antipsychotic and antidepressant therapy is reasonable, while for patients with schizoaffective disorder, bipolar type, mood stabilizers may be a better choice, particularly when irritability or aggression is present.[8] These medicines have their drawbacks, like extrapyramidal symptoms, metabolic syndromes, drowsiness, and sialorrhoea. Hence, there has been an unmet need for a long time for an effective drug with a better safety and tolerability profile. An experimental study showed the crucial role of PKCβ in the clozapine-induced weight gain. The authors also proposed PKCβ blockade as a new therapeutic strategy to prevent the metabolic side effects of clozapine without interfering with its psychomotor properties.[10] Hence, I hypothesized that endoxifen, which acts by directly inhibiting PKC, hits a major pathophysiological process and is also helpful to reduce adverse events related to long-term antipsychotic therapy. This hypothesis was further strengthened by a case report published by Singh et al, which unveiled the

potential role of endoxifen in patients with schizoaffective disorder.[11]

Herewith, the author reported a patient with schizoaffective disorder who was completely improved by amisulpride, quetiapine, and risperidone; while clozapine was effective, but led to adverse events. Hence, endoxifen was tried and was subsequently found to be effective and safe.

CONCLUSION

Endoxifen, a direct inhibitor of the PKC signalling pathway, was found to be effective and safe in the patient with schizoaffective disorder. Further studies are warranted to study and validate the efficacy and safety of endoxifen as a treatment option for schizoaffective disorder.

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