

Anticholinergic medications even in therapeutic range can cause recurrence of psychosis

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ABSTRACT

Anticholinergic drugs are commonly used in psychiatry to attenuate antipsychotic induced extrapyramidal syndrome (EPS). Psychosis as a side effect is generally explained under the rubric of anticholinergic toxicity or induced delirium. Anticholinergic induced worsening of psychosis in patients with normal cognition is extremely rare in literature. Here, we are presenting a case of young female who was prescribed with multiple anticholinergics to reduce EPS, and each time had worsening of psychosis with intact cognition. We then discussed the possible neurobiological explanation with special reference to muscarinic hypothesis of schizophrenia.

INTRODUCTION

Anticholinergic drugs like trihexyphenidyl and procyclidine are often used in schizophrenia to combat antipsychotic-induced extrapyramidal syndrome (EPS). Even though this group of drugs has multiple side effects like constipation, blurring of vision and cognitive deficits, it is inadvertently prescribed in clinical practice.¹ Toxicity due to its overdose has been described in the literature with presentation of mydriasis, drowsiness, urinary frequency, and, in severe cases, psychosis, convulsions, cardiorespiratory collapse and even death. Psychosis as a side effect is generally explained under the rubric of anticholinergic toxicity or induced delirium.^{1 2} Anticholinergic induced worsening of psychosis in patients with normal cognition is extremely rare in literature. Here, we present a case who was prescribed with multiple anticholinergics to reduce EPS, and each time, the person had worsening of psychosis with intact cognition.

CASE HISTORY

A woman aged 21 years, studying in a vocational school with a history of moderate mental retardation (IQ: 40) presented with irritability, decreased social interaction, auditory hallucination, persecutory and

referential delusions, qualified for the diagnosis of schizophrenia (archaically p_{ro}prop schizophrenia).³ The patient also had extrapyramidal syndrome (EPS) (perioral movements which were probably due to the use of olanzapine 10 mg, given elsewhere). However, she was oriented to time, place and person.

In view of no improvement with 10 mg of olanzapine and poor tolerance, she was started on aripiprazole 5 mg, which was gradually increased to 20 mg. On this dose, she had worsening of perioral lip movements and developed pill-rolling type of tremors in the hands. So, aripiprazole was decreased to 10 mg, but extrapyramidal symptoms persisted even after dose reduction. To counter EPS, she was started on trihexyphenidyl 2 mg.

On the same day, she had a significant worsening of psychotic symptoms like visual and auditory hallucinations, anger outbursts, fearfulness and aggressive behaviour; hence, trihexyphenidyl was stopped. One week later, she was started on procyclidine 2.5 mg and she had similar exacerbation of psychotic symptoms, so it was also stopped. Five days later, she was again started on promethazine 25 mg and she showed similar episodes of psychosis, so it was also stopped. As the patient was not tolerating anticholinergic and was not keen on changing aripiprazole, due to its benefits on psychosis, she was started on vitamin E for EPS. This time, she did not have any exacerbation of psychotic symptoms, but there was no improvement in her EPS even with 800 mg of vitamin E for 1 month.

As the EPS was causing disturbances while taking food, she was started on tetrabenazine on which she showed partial improvement of EPS without worsening of psychotic symptoms. Hence, she was kept on 10 mg of aripiprazole with 50 mg of tetrabenazine. Her basic blood parameters and MRI were within normal limits. She never showed any sign of delirium in the whole period of treatment.



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DISCUSSION

Generally psychosis can be induced by anticholinergic drugs only when they are taken in dosages exceeding therapeutic range.⁴ However, in our case, psychosis was induced within therapeutic dosage range itself with no other peripheral or cognitive anticholinergic symptoms. She was prescribed with three different anticholinergics, and each of them had led into psychotic relapses which subsided soon after inciting agent was withdrawn. This proves it as the causative factor as per Naranjo's score of 10.⁵

As vitamin E and tetrabenazine have different mechanisms of action than anticholinergics, it did not show any psychotic relapses. This raises the suspicion of the underlying muscarinic hypothesis of schizophrenia, which states that there are decreased levels of M1 and M4 receptors in the hippocampus and the prefrontal cortex and its subsequent upregulation of neuroinflammatory activity.⁶ This also explains the negative and cognitive symptoms of schizophrenia.⁷ In subjects with schizophrenia, this could be a reason behind the worsening of psychotic symptoms. Moreover, there are evidences of reduced cholinergic activity in intellectual development disorder (IDD).⁸ So in this particular case, as we hypothesised, the patient already had diminished levels of acetylcholine due to IDD and schizophrenia, which, when further challenged with anticholinergic drugs, resulted in florid psychotic relapses even in its therapeutic dose range.

Hence, we should be cautious while prescribing anticholinergics to persons with both psychosis and IDD. Further studies in this area would be worthwhile.

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