Short Communication

Depression Associated With Discontinuation of Trihexyphenidyl: A Report of Two Cases

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Abstract

The cholinergic-adrenergic hypothesis of mood disorders states that depression is a clinical manifestation of a state of cholinergic dominance, whereas mania reflects adrenergic dominance. In line with cholinergic adrenergic hypothesis of affective disorder, anticholinergic drugs have been suggested to have antidepressant properties, and to cause mania-like state. We report two patients with major mental disorders in whom discontinuation of low dose Trihexyphenidyl (THP), an anticholinergic medication, lead to depressive disorder. This report is of significance as discontinuation of THP is common in clinical practice of psychiatry, and at-least in some subset of patients it may precipitate depressive disorder. Antidepressant properties of THP deserve consideration and future research.

Introduction

The cholinergic-adrenergic hypothesis of mood disorders states that depression is a clinical manifestation of a state of cholinergic dominance, whereas mania reflects adrenergic dominance (1). Interest in this hypothesis has re-emerged due to the therapeutic potential of some of the anticholinergic medications (2). We report two patients with major mental disorders in whom discontinuation of low dose Trihexyphenidyl (THP), an anticholinergic medication, lead to depressive disorder.

Case 1

Mr. P, a 55 year old male with schizophrenia (age of onset 16 years) with family history suggestive of Bi Polar Affective Disorder in a 3rd degree relative, was asymptomatic on 100 mg/d of chlorpromazine and 2 mg/d of THP for the last 8 years. He had been on 2 mg/d of THP since 10 years that had been started for extrapyramidal symptoms (EPS) while he was on higher dose of chlorpromazine (400 mg/d). He had two episodes suggestive of depressive disorder (last episode 2 years back) in the last 6 years, for which he was on fluoxetine 20 mg/d. As he was maintaining well for previous two years and did not have EPS, treating physician decreased THP to 1 mg/day for a month and then stopped. During the follow up, after about 2 weeks of decreasing the dose of THP, patient started having non-pervasive low mood, loss of interest in pleasurable activities, and decreased appetite. After
stopping THP, the depressive symptoms worsened over next few weeks. At the end of 4 weeks of stopping THP, he was noted to have an episode of moderate depressive disorder (as per ICD -10) with pervasive sadness of mood, disturbed biological functions, and suicidal ideas with early morning worsening of symptoms. The score on Hamilton Depressive Rating -17 Scale (HDRS-17) was 21. He did not have any psychotic symptoms or EPS. There was no history of intake of any additional non-prescribed medications, herbal preparations, and recent vaccination. After discussing with the client about the available options, THP was restarted at the dose of 2 mg/d and the rest of the medications were continued at the same dose. By the end of 4 weeks, complete improvement in depressive symptoms was noticed, with a HDRS score of 6. Since 6 months patient is maintaining well on the same medications.

**Case 2**

Mrs. R, a 39 years old female client, with a diagnosis of Bi-Polar Affective Disorder, had a total of 5 episodes of mania and 1 episode of depressive disorder. The last episode of mood disorder was an episode of mania without psychotic symptoms following drug default 2 years back. She was treated with lithium carbonate up to 900 mg/d, risperidone 4 mg/d and THP 2 mg/d. Her serum lithium level was 0.8 mmol/dl. During follow up, tablet risperidone was gradually tapered off, tablet chlorpromazine 100 mg/d was added for sleep initiation difficulties and other medications were continued. Gradually the dose of chlorpromazine was decreased to 50 mg/d and she was well on tablet lithium 900 mg/d, chlorpromazine 50 mg/d and THP 2 mg/d for 6 months. After discussing with the patient, we stopped tablet chlorpromazine and THP and lithium was continued at the same dose. After about 7-10 days of stopping chlorpromazine and THP, patient started having depressive symptoms in the absence of sleep difficulty. Symptoms gradually worsened, and over next 2-3 weeks she developed an episode of moderate depressive disorder with somatic symptoms (ICD 10). She had significant agitation, death wishes and decreased sleep (both initiation and maintenance). She scored 16 on HDRS-17 scale. She was restarted on chlorpromazine up to 100 mg/
practice, and at least in some subset of patients it may precipitate depressive disorder. Antidepressant properties of THP may deserve consideration and future research.

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References


