

Trihexyphenidyl Triggered Hypomania in a Bipolar Patient

Eren Yıldızhan¹, Serap Batmaz², Nazan Karagöz Sakallı¹, Erhan Kurt¹

ÖZET:

İki uçlu bozukluklu bir hastada triheksifenidil ile tetiklenen hipomani

Düzenli düşük doz klorpromazin kullanımı sonrasında gelişen bir tardiv diskinezi olgusu bildirmekteyiz. Olgudaki tardiv diskinezinin tedavisinde antikolinergik bir ajan olan triheksifenidil (THX) kullanıldı. Tedavi yanıtı iyi olmakla beraber, THX kullanımı sonrasında kısa süreli hipomanik dönemler görüldü. Hastanın uzun süredir düzenli tedavi altında ve belirtisiz olduğu dikkate alındığında, tedaviye eklenen THX'in hastalık seyrini olumsuz etkilediğinden ya da hipomaniyi tetiklemiş olabileceğinden şüphelendik. Söz konusu hipomanik dönemler kısa süreli idi ve olanzapin kullanımı ile kontrol altına alındı. THX dozunu artırdığımızda ise hastanın mizacında yükselme olduğunu saptadık. Ailesinde iki uçlu bozukluk öyküsü olması ve iki uçlu bozukluğun erken başlangıçlı tipine sahip olması olgumuzda tardiv hareket bozukluğunun görülmesi olasılığını artırmış olan diğer etkenlerdi. THX tardiv diskinezi tedavisinde etkili bir seçenek olarak kabul edilmekle birlikte, bu ajanın iki uçlu olan hastalarda hastalık seyrinde değişikliğe yol açma olasılığı incelemeye değerdir.

Anahtar sözcükler: triheksifenidil, hipomani, tardiv diskinezi

Journal of Mood Disorders 2012;2(2):77-9

ABSTRACT:

Trihexyphenidyl triggered hypomania in a bipolar patient

We observed a case of tardive dyskinesia after regular use of low dose chlorpromazine. An anticholinergic agent; trihexyphenidyl (THX) was prescribed to treat the tardive dyskinesia. The treatment response was satisfactory, but brief hypomanic episodes occurred. Because the patient was symptom free for long periods of time, we suspected that THX might have had a negative effect on the course of the disease or it might have induced hypomania. The hypomanic episodes were controlled with short term use of olanzapine. When the dose of THX was further increased, elevation of mood occurred. The history of bipolar disorder in his family and having the early onset type of bipolar disorder were features of our case that made the tardive movement disorder more likely. Although THX may be an effective option in tardive dyskinesia, possible impact on the course of the disorder in bipolar patients should be considered.

Key words: trihexyphenidyl, hypomania, tardive dyskinesia

Journal of Mood Disorders 2012;2(2):77-9

¹MD, Bakırköy Research and Training Hospital For Psychiatry, Neurology and Neurosurgery, Department of Psychiatry, Istanbul-Turkey
²MD, Istanbul University, Medical Faculty of Istanbul, Department of Psychiatry, Istanbul-Turkey;

Yazışma Adresi / Address reprint requests to: Eren Yıldızhan, Prof. Dr. Mazhar Osman Bakırköy Ruh Sağlığı ve Sinir Hastalıkları Eğitim ve Araştırma Hastanesi, İstanbul-Türkiye

Telefon / Phone: +90-212-543-6565

Elektronik posta adresi / E-mail address: erenyildizhan@hotmail.com

Kabul tarihi / Date of acceptance: 06 Nisan 2012 / April 06, 2012

Bağını beyanı:

E.Y., S.B., N.K.S., E.K.: Yazarlar bu makale ile ilgili olarak herhangi bir çıkar çatışması bildirmemişlerdir.

Declaration of interest:

E.Y., S.B., N.K.S., E.K.: The authors reported no conflict of interest related to this article.

INTRODUCTION

Anticholinergic agents are frequently used in the treatment of drug induced acute extrapyramidal side effects but effectiveness of these agents in tardive movement disorders is enigmatic. On the contrary, it has been suggested that antipsychotic agents may be even worsening tardive dyskinesia

We report a case of bipolar man with tardive dyskinesia. Brief episodes of hypomania were induced by trihexyphenidyl (THX) which had been used to treat the tardive dyskinesia.

CASE REPORT

MRA.T. was a 41 years old Caucasian man with 26 years history of bipolar disorder. He had history of bipolar disorder in three of his brothers.

His first hospitalization was when he was 15 years old. He was treated with haloperidole which was substituted with chlorpromazine after a few days because of acute dystonia due to haloperidole. He was given lithium or chlorpromazine and lithium combination as maintenance treatment. For seven years (from 1994 to 2001) he was symptom free with monotherapy of lithium 1200mg/day.

After this period, he admitted to the clinic with a hypomanic episode. He was given chlorpromazine 400mg/day and biperiden 4 mg/day as an adjunct to lithium monotherapy and chlorpromazine was decreased to 50 mg/day because of parkinsonism which subsided after dose reduction. His new maintenance treatment was chlorpromazine 50 mg/day and lithium 1200mg/day and this was followed by another seven years of symptom free period.

After seven years of continuous chlorpromazine (50mg/day) and lithium therapy, the patient admitted to the clinic with dystonic movements of face, head, neck and arms. He was diagnosed tardive dyskinesia according to the DSM IV and Abnormal Involuntary Movements Scale (AIMS) score was 18. Chlorpromazine was discontinued and quetiapine with varying doses (400mg/day, 600mg/day and 200 mg/day) was prescribed but no improvement was observed. He was given clozapine 12,5 mg/day but he could not tolerate because of intense restlessness and dysphoria. Valproic acid 1000 mg/day and propranolol 60 mg/day was prescribed and that was not also effective.

Modest improvement in tardive dyskinesia was observed after addition of the anticholinergic agent which is trihexyphenidyl 2 mg/day. After that, his AIMS score was 12.

His treatment regimen at that time was lithium 1200mg/day, valproic acid 1000mg/day, THX 2 mg/day. After partial improvement of dyskinetic movements, an episode of hypomania occurred; he was euphoric with excessive energy so that he was sometimes singing in public buses, he was sleeping less than normal and his amount of talking was increased that could easily be seen during the interview.

This episode of hypomania subsided with addition of olanzapine 5mg/day for 10 days. In this index visit, the blood levels of mood stabilizers were in the therapeutic range (serum levels; lithium: 0.78 mmol/L, valproate: 86.12 µg/ml).

Afterwards, reserpine 0,50mg/day and chlortalidone 100 mg/day was prescribed but modest improvement was observed. 6 months later another hypomanic episode that is similar in severity to the previous one occurred. Young mania rating score was 12 (serum levels; lithium: 0.51 mmol/L, valproate: 74.37 µg/ml). This episode was controlled with olanzapine 5 mg/day for 5 days and that is followed by a subsyndromal depressive episode. When

THX was titrated up to 4 mg/day, a further improvement in dystonic movements was observed with spontaneous relief from the depressive symptoms, his AIMS score was 8.

His current medication is now lithium 900 mg/day, valproic acid 1000 mg/day, THX 4 mg/day, reserpine/chlortalidone 0.50/ 100 mg/day, clonazepam 2 mg/day. If he forgets taking his medication, the dystonic movements worsen and when he takes his medication they improve again.

DISCUSSION

The patient has history of acute dystonia with haloperidole and this is relieved by substituting that agent with chlorpromazine. Tardive movements that occurred later may be speculated to be a side effect of haloperidole, but it should be noted that he hadn't been prescribed haloperidole since 1994 and tardive dyskinesia first occurred in 2008, following 7 years of symptom free treatment with chlorpromazine and lithium.

In 2001, a brief period of parkinsonism was observed after titration of chlorpromazine to 400mg/day because of hypomania, and this parkinsonian symptoms were relieved by dose reduction to 50mg/day. That might have been a sign of increasing dopamine hypersensitivity in the patient. At that moment, when the parkinsonism had been observed, discontinuing chlorpromazine might have been more appropriate instead of dose reduction, but the evidences favoring this decision is still inadequate.

The role of lithium in this case is difficult to interpret because of the confounding results in the literature, there are evidences that lithium has potential to decrease the risk of tardive dyskinesia, but long term lithium treatment is also associated with increased tardive dyskinesia risk (3,4). In our case, there is continuous lithium treatment without cessation.

Hayashi et al. (5) reported a case of tardive dystonia which is effectively treated with THX. Euphoric effects of anticholinergic agents has been known from the literature (6) but although we found reports of psychosis induced by anticholinergic agents (7), we didn't find any cases of hypomania induced by THX. Despite he was on continuous lithium and valproate protection, THX induced hypomania. In 1983, Tollefson and Senogles (8) suggested a cholinergic role in the mechanism of lithium in mania. The addition of THX might have a role of diminishing the

effectiveness of lithium prophylaxis. Disappearance of the subsyndromal depression after titrating.

THX up to 4 mg also suggest that THX may have an effect of elevating the mood. Koszewska and Rybanowski (9) reported in their retrospective study that mood conversions from depression to mania occurs more frequently in tricyclic antidepressants than non tricyclic antidepressants and added that it might be the anticholinergic activity that causes the higher frequency of

mood conversion during tricyclic antidepressant therapy. THX could have induced the hypomania with such a mechanism in our case. For Mr.A.T., strongly positive family history of bipolar disorder and early onset of the disorder are other risk factors for manic switch (10).

THX is a treatment option in tardive dyskinesia although induction of hypomania in bipolar patients is a possibility. Rather than discontinuing THX, addition of antipsychotic treatment can be effective.

References:

1. Kane JM, Jeste DV, Barnes TRE et al. Tardive dyskinesia: a task force report of the American Psychiatric Association. Washington: American Psychiatric Press 1992.
2. Waddington JL, Youssef HA. Tardive dyskinesia in bipolar affective disorder: aging, cognitive dysfunction, course of illness, and exposure to neuroleptics and lithium. *Am J Psychiatry* 1988;145:613-616.
3. Kane JM, Jeste DV, Barnes TRE. Tardive dyskinesia in affective disorders. *Journal of Clinical Psychiatry* 1999;60:43-47.
4. Pert A, Rosenblatt JE, Sivit C, Pert CB, Bunney WeJr. Long-term treatment with lithium prevents the development of dopamine receptor supersensitivity. *Science* 1979;135:509-514.
5. Hayashi Y, Ohyagi Y, Inoue I et al. A case of amoxapine induced tardive dystonia successfully treated with a low dose anticholinergic agent. *Rinsho Shinkeigaku* 2000;40:367-371.
6. Fleischhacker WW, Barnas C, Günther V, Meise U, Stuppach C, Unterweger B. Mood-altering effects of biperiden in healthy volunteers. *J Affect Disord* 1987;12:153-157.
7. Clarke LA, Cassidy CW, Catalano MC. Psychosis induced by smoking cessation clinic administered anticholinergic overload. *Annals of Clinical Psychiatry*, 2004;16:171-175.
8. Tollefson GD, Senogles S. A cholinergic role in the mechanism of lithium in mania. *Biol Psychiatry* 1983;18:467-479.
9. Koszewska I, Rybakowski JK. Antidepressant-induced mood conversions in bipolar disorder: a retrospective study of tricyclic antidepressant drugs. *Neuropsychobiology* 2009;59:12-6.
10. Othmer E, Desouza CM, Penick EC et al. Indicators of mania in depressed outpatients: a retrospective analysis of data from the Kansas 1500 study. *J Clin Psychiatry* 2007;68:47-51.