

Resolution of Tardive Dyskinesia with Clozapine: A Case Report

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Received date: June 09, 2016; Accepted date: July 30, 2016; Published date: August 05, 2016

Citation: Badii Amamou, Nesrine Essid, Amel Mrad, Ahmed Mhalla, Lotfi Gaha (2016) Resolution of Tardive Dyskinesia with Clozapine: A Case Report. Dual Diagn Open Acc 1:19. doi: 10.21767/2472-5048.100019

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Abstract

Tardive dyskinesia is an extrapyramidal side effect that can occur after a prolonged use of antipsychotic medication, it appears to be about 0.4% to 4% worldwide. Prior reports suggest that clozapine may be effective in the management of tardive dyskinesia.

We present the case of a patient with tardive dyskinesia induced by antipsychotics. After treatment failure with other psychotropic medications, clozapine medication was initiated; we used the "evaluation of tardive dyskinesia" scale to assess severity of tardive dyskinesia. We noticed a significant improvement in tardive dyskinesia from the fifth week of treatment with clozapine at the dose of 250 mg per day with a decrease in the scale score for "evaluation of tardive dyskinesia" from 70 to 22.

Clozapine appears to be efficacious in the management of tardive dyskinesia. Larger, randomized, blinded, and controlled prospective studies are needed to confirm these findings and to determine optimal dosage.

Keywords: Tardive dyskinesia; Bipolar disorder; Clozapine

Introduction

Tardive dyskinesia is an extrapyramidal side effect that can occur after a prolonged use of medication that block dopamine receptors; it is characterized by involuntary and persistent muscle contractions frequently causing twisting and repetitive movements or abnormal postures [1]. Tardive dyskinesia commonly involves the head and neck region and can start as a focal dystonia, which can progress to a segmental form, involving two to four body parts [2].

The prevalence of tardive dyskinesia associated with antipsychotics appears to be about 0.4% to 4% worldwide [3]. Almost half of the patients who develop tardive dyskinesia tend to do so in the first 5 years of exposure to antipsychotics, the onset is earlier in men than in women [4]. Several cases of tardive dyskinesia were reported primarily in patients with disorders of schizophrenia spectrum. The tardive dystonia

mechanism is not fully known and Currently, there are no approved drugs for treating tardive dyskinesia, though some have shown efficacy in studies [3,4].

The present study aims to illustrate the effectiveness of clozapine in a patient with tardive dyskinesia induced by antipsychotics. We used the "evaluation of tardive dyskinesia" [5] scale to assess severity of tardive dyskinesia.

Case

A male patient 43 years of age married and father of a daughter. He is followed from the age of 23 for a bipolar disorder. In 2001, the patient was initially treated with Carbamazepine (600 mg daily) and Haloperidol (40 mg daily) treating a manic episode, he developed an induced tardive dyskinesia involving muscles spasm in the neck and nape, which completely resolved after stopping Haloperidol for three weeks. The reintroduction of Haloperidol at doses below 10 mg/day was well tolerated in combination with lithium carbonate treating the second manic relapse.

In 2007, during the third manic relapse, he was treated with Olanzapine (30 mg daily) in combination with lithium carbonate with recurrence of the tardive dyskinesia. The neurological examination and brain scan were in favor of iatrogenic origin. Since 2008 until 2014 and despite a switch by several antipsychotics (to treat the tardive dystonia) in combination with lithium carbonate the patient did not show any improvement and dyskinesia becomes very troublesome with a scale score for "tardive dyskinesia assessment" at 70:

- Ziprasidone (160 mg daily who was arrested during the appearance of long QT)
- medication with antimuscarinic,
- benzodiazepines,
- Pregabalin,
- Injections of botulinum toxin,
- Aripiprazole at the dose of 15 mg daily

In March 2015 we used Clozapine (in combination with Aripiprazole and lithium carbonate) with gradual dose increase to 250 mg daily and regular monitoring of blood counts formula. A significant improvement in tardive dyskinesia was noticed

from the fifth week of treatment with Clozapine at the dose of 250 mg per day with a scale score for "evaluation of tardive dyskinesia" at 22.

The decreasing of Aripiprazole was followed by a depressive relapse then we maintained the combination: Clozapine (250 mg) daily+Aripiprazole (15 mg daily)+lithium carbonate (1500 mg) daily. Since April 2015 the patient showed no relapse neither in mood nor in tardive dyskinesia.

Discussion

This case presents important findings consistent with the available literature regarding the effects of clozapine in tardive dyskinesia showing improvement along the symptom severity. Late dyskinesia has been associated with antipsychotic exposure to both typical and atypical antipsychotic, such as Olanzapine, Risperidone and Ziprasidone [6].

Several pathogenic mechanisms causing tardive dyskinesia has been reported including hypersensitivity of dopamine receptors according to the antagonism of dopamine receptor blockade of serotonin and genetic polymorphisms linked to the D2/D3 receptor alleles [7]. The ability of Clozapine to treat tardive dyskinesia may be related to the antagonism of D1 receptor [8]. Clozapine has a lower risk of developing tardive dyskinesia and have even specifically antidyskinetic properties [9].

It should be noted that without increasing extrapyramidal disorder, Clozapine is used to curb psychotic symptoms induced by antiparkinsonian dopaminergic agonists [10]. In patients with resistant schizophrenia and concomitantly presenting TD, Clozapine is a treatment of choice in the average dose of 400 mg daily to act on both psychotic and motor symptoms [11].

In the indication of treatment of extrapyramidal movement disorders (TD but also akathisia and Parkinsonism) in schizophrenic subjects with residual psychotic symptoms despite first-line treatment, Clozapine can reduce dyskinesia initially, before then improve psychotic symptoms [12]. Uzun et al. reported a clinical case where TD is curbed by the introduction of Clozapine up to 450 mg daily, but, lowering dosages, they reappear [13].

A similar case is reported by Shrivastava et al. With recurrence of TD at the lower doses of Clozapine at 150 mg/day, then again their disappearance following the doses reincreases at 200 mg daily [14]. Yunxin Sim Kwan and Kang [15] reported a clinical case of a patient followed for bipolar disorder suffering from tardive dyskinesia induced by antipsychotics and has improved and resolved completely after 21 months of treatment with Clozapine at the dose of 300 mg per day. He remained symptom-free despite the higher reduction of Clozapine at the current dose of 200 mg per day.

There have also been case reports of tardive dystonia treated with Olanzapine [16] and Quetiapine [17]. Botulinum toxin has been described as effective in the treatment of localized tardive dystonia. However, repeated injections are required because its effects are only temporary (Havaki Kontaxaki et al) [18]. The dopaminergic drugs such as Reserpine and Tetrabenazine can be

effective in the treatment of moderate to severe tardive dystonia [8].

Clonazepam has also been reported to reduce dyskinetic and dystonic movements [19]. In terms of combination therapy, Havaki-Kontaxaki et al. [18] treating a patient with a combination of Clozapine, Clonazepam and Botulinum Toxin showed good results. More recent data have suggested the use of deep brain stimulation areas such as globus pallidus suchas and subthalamic nucleus in the treatment of tardive dystonia [20].

Conclusion

We report a successful resolution of tardive dyskinesia in a bipolar patient using a combination of Clozapine (250 mg) daily +Aripiprazole (15 mg) daily+lithium carbonate (1500 mg) daily. Clozapine may be a reasonable treatment for tardive dystonia in patients with bipolar disorder. However, the risks of clozapine merit caution. Controlled studies are needed to further determine clozapine's role in treating tardive dystonia in patients with bipolar disorder.

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