Case Report

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Aripiprazole can a Viable Choice for Persistant Suppression of Symptoms in Managing Chronic Tic Disorders and Tourette's Disorder Through the Life Span: A Case Series

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ABSTRACT:

Aripiprazole can a viable choice for persistant suppression of symptoms in managing chronic tic disorders and Tourette's disorder through the life span: a case series

Tic disorders may cause impairment both by themselves and associated comorbidities. Medications for tic disorders are indicated when tics are moderate/ severe causing severe impairment and in presence of comorbid disorders responsive to medications. Duration of improvement is still not known as the literature lacks prospective studies with a long follow-up period. This case series aims to report management of tic disorders with aripiprazole in patients with different ages. Here, we describe 8 cases with complex motor tic disorder or Tourette's Disorder in which aripiprazole was used. The ages of patients were varied, from 9 to 57 years. Mean follow-up was 19.6 weeks. Mean dose of aripiprazole for pediatric patients was 15.4 mg/ day while it was 12.5 mg/ day for adult patients. All patients benefited from treatment with aripiprazole in the long term. Our results should be supported with controlled studies.

Keywords: aripiprazole, tic, Tourette's disorder

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INTRODUCTION

Tic disorders are defined in the Diagnostic and Statistical Manual of Mental Disorders (DSM) based on type (motor or vocal), complexity (simple/complex) and duration of tics. Tics themselves are defined as sudden, rapid and non-rhythmic movements. Tic disorders in DSM-IV-TR included transient tic disorder (≥1 months but <12 months), chronic motor/ vocal tic disorder (>12 months), Tourette's disorder (both motor and vocal tics for >12 months) and Tic disorder not otherwise specified (NOS)[1].

DSM-5 published in 2013; changed the definition of tics by removing "stereotyped" from their definition, added specifiers for motor/ vocal tics, removed stimulant use from listed etiologies and changed the nomenclature. Accordingly, tic disorders listed in DSM-5 include other specified tic disorder, unspecified tic disorder, provisional tic disorder, persistent (chronic) motor or vocal tic disorder (specify motor/ vocal), and Tourette's disorder.

Tic disorders may cause impairment both by

themselves and associated comorbidities. Current practice parameters suggest use of psycho-education and behavioral interventions when tics are mild/ moderate in severity and in the presence of comorbid disorders, which are responsive to behavioral interventions[3,4]. Medications for tic disorders are indicated when tics are moderate/ severe causing severe impairment and in presence of comorbid disorders responsive to medications[5-9].

Aripiprazole, an atypical antipsychotic noted for its partial D2 agonist activity along with a low propensity for extrapyramidal effects, has been shown to be efficacious in managing tic disorders in case series and open-trials[10-14]. The efficacy of aripiprazole for tic disorders in children and adolescents has also been demonstrated in a double-blind, placebo controlled study[15]. There is one study which shows efficacy of aripiprazole in adult patients with Tourette's disorder with a relatively long follow-up period of 56 months[16]. Physician surveys also list it along with risperidone as popular choices for initial treatment[17]. There are a number of studies demonstrating the utility of aripiprazole with other dopamine antagonistic agents such as clozapine and pimozide[18,19]. However, the duration of improvement is still not known as the literature lacks prospective studies with a long follow-up period. This case series aims to report management of tic disorders with aripiprazole in patients with different ages. Here, we describe 8 cases with complex motor tic disorder or Tourette's Syndrome, in which aripiprazole was used. All patients were previously treated with pimozide, haloperidol or risperidone before aripiprazole treatment, while one patient also received sulpiride.

CASES

Our case series consists of 8 patients within a wide range of age (9–57) with a mean age of 22.5 years. The sociodemogaphic features of patients, as well as their pre and post-treatment tic severity scale scores and time to tic suppression are listed in Table 1. All of the cases provided informed consent for deidentified use of their psychiatric information to contribute to this article. Mean duration of tics reported by patients were 5.13 years (Range: 1- 20). All patients were given the diagnosis of chronic motor tic disorder or Tourette's disorder according to Diagnostic and Statistical Manual of Mental Disorders–IV criteria. Previous trials with pimozide, risperidone, sulpiride, and haloperidol were all discontinued due to adverse effects, especially sedation and weight gain. Patients were seen at least at monthly intervals for at least one year. Comorbid diagnoses and prior medication trials are listed in Table 2. Patient 3 was also diagnosed with obsessive-compulsive disorder (OCD) and was using fluvoxamine 50 mg/day while patient 6 was had comorbid attention deficit and hyperactivity disorder (ADHD-Combined type), bipolar I disorder (last episode, mixed) and cannabis use disorder and was using valproate 1000 mg/day. Patient 8 had concomitant ADHD and OCD and was using short acting methylphenidate 25 mg/day, guanfacine 2 mg/day

Table 1: Response to aripiprazole in a group of patients of diverse ages with tic disorders

Pt*	Sex†	Age (years)	Dx‡	YGTSS¶ Baseline	YGTSS End	Dose (mg)	Follow-up (weeks)	CGI- TI**	CGI-TI f/u††
1	F	57	CMT§	25	10	10	25	1	1
2	F	45	TD‖	40	25	15	12	2	1
3	M	11	CMT	50	35	15	20	2	1
4	F	9	TD	20	13	5	16	1	1
5	F	14	TD	75	45	15	16	2	2
6	M	16	TD	51	34	20	24	2	1
7	M	17	TD	75	50	30	20	2	1
8	M	9	CMT	59	7	7.5	24	1	1

*Pt: Patient, †Sex: F/M: Female/ Male, ‡Dx: Diagnosis, §CMT: Chronic Motor Tic Disorder, ‖TD: Tourette Disorder, ¶YGTSS: Yale Global Tic Severity Scale, mg: milligrams, **CGI- TI: Clinical Global Impressions- Tics Improvement Scale, ††f/u: after 1 year

Table 2: Psychiatric characteristics of the cases prior to treatment with aripiprazole

Pt*	Sex†	Dx‡	Comorbid Dx‡	Current concomitant medications	Prior Medication Trials	Efficacy of prior medications	Reason for Discont.§
1	F	CMT			Risperidone, Sulpiride Pimozide	Moderate-good	sedation, weight gain
2	F	TD			Haloperidol Pimozide, Risperidone	moderate	EPS††, Weight gain
3	M	CMT	OCD¶	Fluvoxamine	Risperidone	poor	Inadequate response
4	F	TD			Risperidone	good	Weight gain, sedation
5	F	TD			Pimozide	moderate	Galactorrhea, Weight gain
6	M	TD	Bipolar I Disorder, ADHD‖, Cannabis Abuse	Valproate	Risperidone, Pimozide, Sulpiride	poor	Weight gain, sedation
7	M	TD			Risperidone, Pimozide	moderate	EPS, weight gain
8	M	CMT	ADHD, OCD	MPH**, Guanfacine, Sertraline	Risperidone	poor	Weight gain, sedation

*Pt: Patient, †Sex: Female/ Male, ‡Dx: Diagnosis, §Discont.: Discontinuation, || ADHD: Attention Deficit Hyperactivity Disorder, ¶OCD: Obsessive Compulsive Disorder, **MPH: Methyphenidate, ††EPS: Extrapyramidal Side Effects,

and sertraline 100 mg/day, prior to initiation of treatment with aripiprazole, with only minor improvement in tic symptoms (YGTTS: 59 at baseline). While on aripiprazole, one patient reported mild akathisia initially which was successfully managed by a slow upwards titration of dose. Other patients did not report any side effects and were stable at the last evaluation. Overall, the medication was well tolerated. At the 1 year follow-up, all the patients were either free of tics or they had mild simple tics only at times of stress, not lasting for more than 1 month. All patients were still using aripiprazole at above-mentioned doses. At 1-year follow-up, their CGI-tic severity scores were either better or were preserved at the previous value.

DISCUSSION

Here, we report eight patients with Tic Disorders from different age groups who were successfully managed with aripiprazole. All patients had previous trials with other typical or atypical antipsychotics and had to discontinue treatment due to adverse effects. Mean dose of aripiprazole for pediatric patients was 15.4 mg/day while it was 12.5 mg/day for adult patients.

Previous open trials with pediatric patients report favorable response to aripiprazole at doses of 3.3 to 9.8 mg/day and that adverse effects (primarily; hypersomnia, headache and nausea) were observed in one-fifth to one-third of patients[20,21]. The observations of higher mean effective dose and lack of adverse effects may be due to the unique features of our patients (i.e. a wide age range and previous trials with multiple antipsychotics). Similarly, in a large trial of 100 patients, with a mean age of 27 years, mean aripiprazole dose was reported at 17 mg, and 41% of patients did not report any side effects[14]. It may also be argued that tic disorders, by their nature, display a waxing and waning course with spontaneous remissions and as such remissions observed in our patients may be due to other factors. However, histories of tics that span up to 20 years in one patient and 5–10 years in others refractory to pharmacotherapeutic trials with other neuroleptic agents argue otherwise.

Tic disorders, especially chronic ones with comorbid diagnoses have negative impact on patients' lives. Atypical and typical antipsychotics and alpha-2-agonists are effective in managing tics although these are limited by side-effects[4]. Patients often face the dilemma of having tics or side effects of drugs that they are prescribed for controlling tics. This often causes medication non-adherence and hence, the relapse of the tics. This series of patients from various age groups having differing co-morbid diagnoses may suggest aripiprazole as a viable long-term treatment for tic disorders for children and adults. The relatively mild side effect profile of aripiprazole may also increase long-term medication compliance in patients. A recent double blind, placebo controlled trial showed efficacy and tolerability of aripiprazole over placebo in management of Tourette's disorder in children and adolescents[15]. Prospective long-term randomized placebo controlled trials for children and adults are required to establish efficacy and tolerability of aripiprazole in management of tics and Tourette's disorder in all age groups.

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