

Aripiprazole Augmentation in Treatment of Resistant Obsessive Compulsive Disorder

Karim Abdel Aziz¹, Nisrin M El-Saadouni², Mohammed Hashim E. Elamin³, Dina Aly El-Gabry⁴, and Hamdy F Moseley¹

1. College of Medicine, UAE University, UAE, AL Ain P O Box 17 666

2. Faculty of Medicine, Mansoura University, Egypt

3. Behavior Sciences Institute, Al Ain Hospital, UAE, AL Ain P O Box 17 666

4. Institute of Psychiatry, Ain Shams University, Egypt

* Email: hamdy.fouad@uaeu.ac.ae

Abstract

Background: Aripiprazole is a novel antipsychotic medication that has been tried in the treatment of several psychiatric disorders. In an open clinical study, we evaluated the safety and efficacy of aripiprazole in patients with obsessive compulsive disorder resistant to normal regimen of treatment.

Method: A total of nine hundred and sixty one patients were admitted over three year period of time (January 2012- December 2014) to the psychiatric department of Al Ain hospital, United Arab Emirates. All patients whose been fulfilled DSM-IV diagnosis of obsessive compulsive disorder (OCD) (36 patients) screened for further assessment. Patients with a diagnosis of schizophrenia (22 patients) and one patient with eating disorder were excluded. Thirteen patients were contacted to be involved in the study. Participants were unstable although they were adherent to their medications (SSRIs) when seen in the outpatient clinic two weeks after their discharge. One patient refused to participate in the study. A final number of 12 agreed to participate in the study. twelve patients aged 22 to 65 years who had DSM-IV diagnosis of OCD were treated with aripiprazole besides their normal treatment for a period of three months with daily doses ranging from ten to 20 mg daily.

Results: a positive clinical response was noted in eight of the 12 patients within three months of study recruitment according to the Clinical Global Impression-Improvement scale. Aripiprazole was well tolerated by most of the patients. The most commonly reported side effect was headache.

Conclusion: our findings suggest that aripiprazole may be an effective adjuvant and safe treatment for resistant OCD.

Key words: OCD, aripiprazole, augmentation therapy

Introduction

Obsessive compulsive disorder (OCD) is an illness that considerably influences social, occupational, and families of patients. Current treatments for OCD rely on serotonergic mechanisms. Many authors have recommended serotonergic antidepressants (SSRIs) for obsessive compulsive disorder [1]. However, their use raises some problems. Drug effects do not last beyond a few months, relapses are common after drug withdrawal [2] and side effects can be a problem [3]. In addition, 30% of patients do not respond to serotonin reuptake inhibitors and remain chronically ill [4]. In a recently published study [4], 8-week, single-blind, randomized trial comparing risperidone versus olanzapine augmentation of serotonin reuptake inhibitors in treatment-resistant OCD, found that patient in both groups responded significantly, without differences between the two treatment groups. Fineberg et al [5] reviewed the evidence for co-administration of antipsychotics in SRI-resistant cases of OCD, based upon, whenever possible, randomized controlled trials. They concluded that the results favour the use of second generation antipsychotics such as risperidone and quetiapine as a first-line strategy for augmentation in resistant OCD. Several reports have suggested successful augmentation with aripiprazole in SRI refractory patients with OCD [6, 7, 8, 9, 10]. This article reports on the open clinical experience of treating 12 patients who had an obsessive compulsive disorder with aripiprazole, as adjuvant medication.

Participants and Procedure:

A total of nine hundred and sixty one patients were admitted over three year period of time (January 2012- December 2014) to the psychiatric department of Al Ain hospital, United Arab Emirates. All patients whose been fulfilled DSM-IV diagnosis of obsessive compulsive disorder (OCD) (36 patients) screened for further assessment. Patients with a diagnosis of schizophrenia (22 patients) and one patient with eating disorder were excluded. Thirteen patients were contacted to be involved in the study. Participants were unstable although they were adherent to their medications (SSRIs) when seen in the outpatient clinic two weeks after their discharge. One patient refused to participate in the study. A final number of 12 agreed to participate in the study. The nature and scope of the study were

discussed with each subject and written informed consent was obtained from all subjects prior to distribution of the questionnaire.

Participants were interviewed in the outpatient at Al Ain teaching Hospital, in Al Ain city, United Arab Emirates in accordance with the Al Ain Medical District Human Research Ethics Committee. Diagnosis was based on the Diagnostic and Statistical Manual of Mental disorders 4th Edition Text Revision (DSM-IV-TR) clinical criteria (APA 2000) by way of a semi-structured interview, comprehensive medical and psychiatric history taking, mental state examination and collateral information from family members.

The subjects' age ranged from 22years to 65years (mean=37.7 years), eight males and four females. There was a wide variation in ethnicity: two patients were Syrian, two were Pakistani, and two were German, one Jordanian, two Indonesian and three Egyptians. Mean duration of obsessive compulsive disorder was 12.7 years. The duration of any SRI medication prior to add aripiprazole was at least 3 months without response. All the patients were in contact with service for an average of two years. Informed consent was constantly obtained from the patients, and Declaration of Helsinki guidelines were followed.

Diagnosis was made according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM IV) [11]. Comorbid diagnoses were ruled out during the interview for common psychiatric diagnoses. Principal measure for OCD severity of symptoms was Yale-Brown Obsessive Compulsive Scale (Y-BOCS) [12]. During the initial evaluation, the mean Y-BOCS scores for the responder group were 25.5; this corresponds to a global severity in the severe range. OCD was present in all the patients (4 had the 'obsessions' subtype and eight had the combination of obsession and compulsions subtype of OCD) (Table 1).

Aripiprazole treatment was started in doses of ten mg once daily and increased gradually (in increments of five per two weeks) to a maximum of 20 mg per day. Clinical efficacy was assessed on a fortnightly basis using Clinical Global Impression-Improvement scale (CGI-I) [13], and patients were prompted to report commonly observed side effects such as insomnia, headaches, fatigue, dizziness, nausea, vomiting, sedation, and dyspepsia and extrapyramidal side effects.

Results

Clinical improvement was noted in eight patients within six weeks of recruitment into the study (table 1): scores on CGI-I showed mild improvement (score of +1) in three patients (cases 5, 7, 10), moderate improvement (score of +2) in five (cases 2, 8, 9, 11, 12), significant improvement (score of +3) in one (case 6) and no change (score 0) in two (cases 3, 4). Symptoms were reported to be worse (score of -1) in one patient (case 1). The mean Y- BOCS score of the responder group at the end of the three months was 9; this corresponds to a global severity in the mild range.

Aripiprazole was effective in improving OCD, either obsessions or the combined form of obsessions and compulsions. A headache was reported in three patients, requiring reduction in dosage but not discontinuation. The other side effects reported included tiredness and insomnia. No patients experienced extrapyramidal symptoms. However, one patient developed tremors, but she was on clomipramine as well. Those who showed a positive clinical response were followed up for periods ranging from 4-12 months.

Discussion

Although SSRI remain the mainstay of pharmacologic treatment for OCD, they may not be tolerated by some patients, may be ineffective in some, and in yet others may exacerbate a comorbid medical condition such as nausea and delayed orgasm [3]. Furthermore, side effect profile of the conventional antidepressant (clomipramine) used in this situation includes symptoms typical of both potent 5-HT reuptake inhibitors and tricyclics. In our cohort, aripiprazole was used for periods of up to 12 months with no undesirable effects. However, it is important to evaluate the longer-term effectiveness and safety of aripiprazole in this population.

Aripiprazole has been noted to be useful for controlling acute agitation in patients with schizophrenia or schizoaffective disorder [14, 15] and bipolar disorder [16] and in primary and comorbid anxiety symptoms [17]. Our findings showed that aripiprazole was effective in improving both obsessions and compulsions in OCD. These suggest that aripiprazole has promise for treatment of patients with OCD disorder. Furthermore, there was improvement in coexisting anxiety and agitation problems. The drug was well tolerated by the patients in dosage used (10-20 mg). The most common side effect reported by patients was headaches in three patients, followed by tiredness and insomnia in one patient each.

There have been few controlled evaluations of pharmacological approaches to OCD patients who have not responded to an adequate trial of a 5-HT reuptake inhibitor alone. In an open case series, some OCD patients seemed to benefit from the addition of low doses of antipsychotic medication to SSRI treatment [18]. Meanwhile, other reports suggest that some atypical antipsychotics may have obsesogenetic as well as antiobsessional effects. Given their higher affinity for serotonin 5HT2 receptors than dopamine D2 receptors, it has been speculated that atypical antipsychotics may induce obsessive-compulsive symptoms, even at low

doses, on account of high 5HT2 antagonism, whereas improvement in obsessive-compulsive symptoms is assumed to occur only at high doses in consequence of high D2 antagonism [19]. However, aripiprazole is a novel antipsychotic agent, is assumed to be a “dopamine-serotonin system stabilizer”. According to preclinical studies, aripiprazole exerts partial agonist on D2 and 5-HT1A receptors. Thus, it may block a receptor if it is over stimulated and stimulate a receptor when activity is needed. It also has the antagonist properties at 5-HT2A receptors [20]. In our cohort there was no effect on 2 cases but symptoms were slightly exacerbated in one case which supports the uniqueness of action of aripiprazole compared with other antipsychotic medications. Substantial methodological limitations, particularly the lack of double-blind placebo for a randomly assigned control, preclude any current generalizations from these findings. Further double blind placebo controlled studies will be needed to support this work.

References

- [1] Besiroglu L, Uguz F, Yilmaz E, Yucel Agargun M, Askin R, Aydin A. psychopharmacological treatment and quality of life in obsessive compulsive disorder. *Turk Psikiyatri Drg* 2008; 19 (1): 38-45
- [2] Thoren R, Asberg M, Cronholm B, Jonerstedt L, and Traskman L. clomipramine treatment of obsessive compulsive disorder: a controlled study. *Arch Gen Psychiatry* 1980; 37: 1281-1285
- [3] Monteiro W, Lelliott P, Marks I and Noshirvani H. anorgasmia from clomipramine in obsessive compulsive disorder. *Br J Psychiatry* 1986; 151: 197-112
- [4] Maina G, Pessina E, Albert U, Bogetto F. 8-week, single-blind, randomized trial comparing risperidone versus olanzapine augmentation of serotonin reuptake inhibitors in treatment-resistant obsessive compulsive disorder. *Eur Neuropsychopharmacol* 2008; 18 (5): 364-372
- [5] Fineberg NA, Gale TM, Sivakumaran T. a review of antipsychotics in the treatment of OCD. *J Psychopharmacology* 2006; 20 (1): 97-103
- [6] Storch EA, Lehmkuhl H, Geffken GR, Touchton A, Muephy TK. Aripiprazole augmentation of incomplete treatment response in an adolescent male with obsessive-compulsive disorder. *Depress Anxiety* 2008; 25 (2): 172-174
- [7] Conor KM, Payne VM, Gadde KM, Zhang W, Davidson JR. the use of aripiprazole in obsessive-compulsive disorder: preliminary observations in eight patients. *J Clin Psychiatry* 2005, 66(1): 49-51
- [8] Filardi da Roch F, Correa H. successful augmentation with aripiprazole in clomipramine-refractory OCD. *Progress in Neuro-Psychopharmacology and Biological Psychiatry* 2007; 7: 1550-1551
- [9] Marino J, Mascarenas CA, Saklad SR, Simpson JA. Case report: aripiprazole for treatment of resistant OCD. *JCNP* 2007: 1-5
- [10] Sarkar R, Klein J, Kruger S. Aripiprazole augmentation in treatment refractory OCD. *Psychopharmacology* 2008; 197 (4): 687-688
- [11] American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. Fourth Edition, Washington, DC: American Psychiatric Association; 1994
- [12] Guy W. ECDEU Assessment Manual for Psychopharmacology. US Dept Health, Education, and Welfare publication (ADM) 76-338. Rockville, Md: National Institute of Mental Health; 1976: 218-222
- [13] Goodman WK, Price LH, Rasmussen SA, Mazure C, Fleischmann R, Hill C, Heninger GR, Charney DS. The Yale-Brown Obsessive Compulsive Scale (Y-BOCS): Part I. development, use and reliability. *Arch Gen Psychiatry* 1989; 46: 1006-1011
- [14] Andrezina R, Josaiassen RC, Marcus RN, Oren DA, Manos G, Stock E, Carson WH, Iwamoto T. intramuscular aripiprazole for the treatment of acute agitation in patients with schizophrenia or schizoaffective disorder: a double-blind, placebo-controlled comparison with intramuscular haloperidol. *Psychopharmacology* 2006; 188(3): 281-292
- [15] Tran-Johnson TK, Sack DA, Marcus RN, Auby P, McQuade RD, Oren DA. Efficacy and safety of intramuscular aripiprazole in patients with acute agitation: a randomized, double-blind, placebo-controlled trial. *J Clin Psychiatry* 2007; 68(1): 111-119
- [16] Currier GW, Citrome LL, Zimbroff DL, Oren D, Manos G, McQuade R, Pikalov AA 3rd, Crandall DT. Intramuscular aripiprazole in the control of agitation. *J Psychiatry Pract* 2007; 13(3): 159-169
- [17] Gao K, Muzina D, Gajwani P, Calabrese JR. Efficacy of typical and atypical antipsychotics for primary and comorbid anxiety symptoms or disorders: a review. *J Clin Psychiatry* 2006; 67(9): 1327-1340
- [18] McDougle CJ, Goodman WK, Price LH, Delgado PL, Krystal JH, Charney DS, Heninger GR. Neuroleptic addition in fluvoxamine-refractory OCD. *Amer Psychiatr Assoc New Res Abstract#NR350*
- [19] Ramasubbu R, Ravindran A, Lapierre Y. serotonin and dopamine antagonism in obsessive-compulsive disorder: effect of atypical antipsychotic drugs. *Pharmacopsychiatry* 2000; 33(^): 236-238
- [20] Bandelow B and Meier A. aripiprazole, a 'dopamine-serotonin system stabilizer' in treatment of psychosis. *German J Psychiatry* 2003; 6: 9-16

Table 1: Characteristics of patients with OCD treated with aripiprazole

Patient	Age (years)	Sex	Initial complaints	Pre-YBOCS	Post-YBOCS	Other medications used in combination	Aripiprazole Treatment		Outcome (CSI-score)	Side effects
							Dose	Duration of follow up in months		
1	36	F	Checking gas, taps, lights	19	21	Paroxetine Duloxetine	10mg/d	4	Worsening of rituals, drug discontinued (-1)	Worsening of symptoms (increased checking)
2	28	F	excessive cleaning for hands	18	7	Flouextine Clomipramine	10mg/d	10	Improved (+2)	Tremors
3	32	M	Repetitive religious thoughts	27	25	Escitalopram Fluoxetine	10mg/d	12	No improvement (0)	Headaches
4	22	F	Repeating prayers a number of times	30	26	Paroxetine Clomipramine	10mg/d	12	No improvement (0) drug discontinued	None
5	54	M	Counting rituals	31	15	Paroxetine Sertraline	10-15mg/d	12	Improved (+1)	Headaches
6	32	M	Checking doors and windows	30	8	Fluoxetine Clomipramine	10-15mg/d	8	Improved (+3)	Tiredness
7	65	F	Repetitive frightening thoughts about children	28	10	Paroxetine clomipramine	10-15mg/d	8	Improved (+1)	None
8	41	M	Repeating prayers a number of times	20	6	Fluoxetine Clomipramine	15-20mg/d	9	Improved (+2)	None
9	27	M	Repeating things a number of times	30	8	Sertraline Escitalopram	15-20mg/d	12	Improved (+2)	None
10	30	M	Repeating thoughts of harming others	23	22	Fluoxetine Paroxetine	15/20mg/d	9	Improved (+1)	Insomnia

11	38	M	excessive cleaning for hands	27	9	Clomipramine Paroxetine	10- 15mg/d	7	Improved (+2)	None
12	46	M	Feeling of incompleteness related to religious practice	20	10	Fluoxetine Clomipramine	10mg/d	6	Improved (+2)	Headaches

Abbreviation: OCD=obsessive compulsive disorder, CGI-I= Clinical Global Impression-Improvement scale, F=female, M=male