Aripiprazole Augmentation in Treatment of Resistant Obsessive Compulsive Disorder

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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
positive clinical response were followed up for periods ranging from 4-12 months. Symptoms. However, one patient developed tremors, but she was on clomipramine as well. Those who showed a
compulsions. A headache was reported in three patients, requiring reduction in dosage but not discontinuation.
Aripiprazole was effective in improving OCD, either obsessions or the combined form of obsessions and
severity in the mild range.

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 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 obsessogetic 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

<table>
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<th>Patient</th>
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<th>Sex</th>
<th>Initial complaints</th>
<th>Pre-YBOCS</th>
<th>Post-YBOCS</th>
<th>Other medications used in combination</th>
<th>Aripiprazole Treatment</th>
<th>Outcome (CSI-score)</th>
<th>Side effects</th>
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<td>1</td>
<td>36</td>
<td>F</td>
<td>Checking gas, taps, lights</td>
<td>19</td>
<td>21</td>
<td>Paroxetine Duloxetine</td>
<td>10mg/d</td>
<td>4 Worsening of rituals, drug discontinued (-1)</td>
<td>Worsening of symptoms (increased checking)</td>
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<td>2</td>
<td>28</td>
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<td>18</td>
<td>7</td>
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<td>10mg/d</td>
<td>10 Improved (+2) Tremors</td>
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<td>32</td>
<td>M</td>
<td>Repetitive religious thoughts</td>
<td>27</td>
<td>25</td>
<td>Escitalopram Fluoxetine</td>
<td>10mg/d</td>
<td>12 No improvement (0) Headaches</td>
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<td>26</td>
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<td>54</td>
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<td>Checking doors and windows</td>
<td>30</td>
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<td>10-15mg/d</td>
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<td>9 Improved (+2) None</td>
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<td>Headaches</td>
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Abbreviation: OCD=obsessive compulsive disorder, CGI-I= Clinical Global Impression-Improvement scale, F=female, M=Male