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Risperidone Augmentation in the Treatment of Severe Adolescent OCD in SSRI-refractory Cases: A Case-series

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Background and Methods. ***The adverse effects and potential clinical value of risperidone as augmentation to selective serotonin reuptake inhibitor (SSRI) treatment in treatment resistant severe adolescent OCD patients were examined in 17 adolescents (15–19 years old, 8 males and 9 females) in an open label trial of risperidone 1–2 mg daily.***
Results. ***After 12 weeks of augmenting treatment, statistically significant improvements were reflected in OCD symptom ratings (mean total Y-BOCS/CY-BOCS scores after treatment with second SSRI 24.2 ± 2.6 versus 19.9 ± 2.9, $p < 0.001$) and global assessment scores (mean CGAS, 69.4 ± 11.4 versus 74.7 ± 9.6, $p < 0.001$). Four patients had moderate improvement of more than 25% reduction in Y-BOCS scores in OCD symptoms. Further 10 patients had a reduction of 10-25% in total score, indicating slight improvement. One patient (6%) dropped from clinical OCD to a subclinical level of OCD (Y-BOCS total score < 15). No patient was found to have worsened during augmentation treatment. Eight cases had weight gain and sedation was reported in four cases.***
Conclusion. ***These preliminary findings suggest that augmentation with risperidone in dosages up to 2 mg daily might be efficient in adolescents with treatment resistant OCD.***

Keywords OCD; Adolescents; Augmentation; Risperidone.

INTRODUCTION

OCD (obsessive-compulsive disorder) is defined as the presence of obsessions and compulsions that cause distress and functional impairment. It affects 2–3% of the adult population and 0.5–1% of the pediatric/adolescent population. For many patients the disorder takes a chronic course (1,2) and the disorder can cause significant functional impairment.

Studies of treatment have clearly demonstrated the efficacy of selective serotonin reuptake inhibitor (SSRI) drugs in both adult and child/adolescent patients (1,3,4). However, in both children and adult patients these treatment strategies seem to reduce rather than remove obsessive-compulsive symptoms, and still there seems to be approximately one fourth of pediatric and adult OCD patients who respond only partially or do not respond at all to different SSRIs (3,4). Current estimates suggest that SSRI response in large scale studies has generally yielded approximately 44–46% responders with mean symptom improvement in the active treatment group of between 20–40% in children as well as in adults (5,6). The recommended treatment for OCD in children and adolescents is cognitive behavioral therapy (CBT) and SSRI medication (7–9). However, when treatment response is insufficient one must first of all analyze the possible reasons for this: low compliance, psychological stress factors (within or outside the family) that seem to maintain the obsessive-compulsive symptoms, whether cognitive behavioral therapy is offered (and carried out appropriately) and that SSRI treatment is performed adequately.

The psychologists Inger Englyst and Karin Christensen, Psychiatric Hospital for Children and Adolescents, University Hospital in Aarhus, have performed some of the CBT, for which they are appreciated.

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Augmentation strategies have been described in adult OCD patients. Augmentation with many different agents has been attempted including lithium, clonazepam, buspirone, pimozide, haloperidol, risperidone, olanzapine, clomipramine, clonidine, all with partial, equivocal or no effect (10). Recently, a controlled study in adult patients showed that OCD patients both with and without comorbid chronic tic disorders or schizotypal personality disorder may respond to the addition of low dose risperidone to ongoing SSRI treatment (11–14). Augmenting strategies are poorly described in children and adolescents. Only a few casuistic reports have indicated the efficacy of antipsychotic augmentation (15), or buspirone (8). Risperidone has recently been used in randomized control trials in treating conduct disorder in children with average or subaverage intelligence providing preliminary evidence that it may be efficacious in this disorder (16,17). Safety aspects of the drug were described: there where demonstrated no changes in laboratory value or electrocardiogram during a 10-week study (dosages 0.5 mg to a maximum of 1.5 mg in the population below 50 kg of weight, a maximum of 3 mg for patients over 50 kg). However, it was concluded that risperidone was associated with weight gain significantly more than in the placebo group (16).

The aim of this study was to describe the efficacy and tolerability of risperidone as an augmenting drug in treatment resistant adolescents with severe OCD. This study analyzes a group of patients treated with both SSRI and cognitive behavioral therapy, that is the optimal treatment strategy for OCD.

METHODS

Subjects

All included patients were consecutively referred as out-patients to Psychiatric Hospital for Children and Adolescents covering the total hospitalized service of child and adolescent psychiatry in the county (inhabitants 550,000).

Inclusion criteria for the study were: aged 18 years or younger; referred for evaluation and/or treatment of OCD; fulfilling DSM-IV criteria for OCD in the evaluation at our hospital.

Exclusion criteria were overt psychosis (i.e. schizophrenia or bipolar disorder); neurological symptoms or disorders including Tourette's syndrome; acute or chronic medical disorders; alcohol or substance abuse; unwilling to accept medication in the treatment of OCD; lack of consent to treatment with medication by parents or child.

All patients were assessed with the CY-BOCS (below 15 years) (18) or Y-BOCS (more than 15 years) (19) and were diagnosed according to the K-SADS interview (20) (Table I). The global function was assessed with the Children's Clinical Global Assessment Scale (CGAS) (21).

Design and Treatment

All patients were treated with adequate dosages of SSRI drugs (sertraline - maximum 200 mg, citalopram - maximum 80 mg (in one case 100 mg), fluoxetine - maximum 80 mg, paroxetine - maximum 80 mg) for at least 12 weeks with the first SSRI drug. The second SSRI drug was tried for a period of minimum 12 weeks. The clinic usually chooses sertraline or citalopram as first choice SSRI drug to children and adolescents with OCD (22–25).

At the time of the study none of the SSRIs were approved for pediatric OCD. However, at the end sertraline was approved for pediatric OCD.

Side effects were evaluated consecutively at the weekly visits and systematically asked for regarding tiredness, sleep problems, agitation, and irritability. The most common side effects from SSRI treatment were the usually reported (Table II). In the description in Table II only side effects evolved after combined treatment was started are described.

All patients received cognitive behavioral therapy (in the initial phase psycho-education to patients and relatives followed by an individual CBT program from 10 to16 sessions and ongoing with booster sessions during the time of combined treatment). The CBT program was performed according to the manual described by March (9) and performed by trained CBT psychotherapists. CBT was continued throughout the study, that is, also during augmentation treatment.

In case of no or minimal improvement following treatment with two different SSRI agents and CBT, augmentation with risperidone was initiated. Treatment resistance has not been categorically defined. In this study, in order to define treatment efficacy, both reduction in total CY-BOCS score and total score at the end of treatment were considered. Treatment resistance was hence defined as a reduction of less than 25% on the CY-BOCS total score (as 25% usually characterizes a positive response), and a CY-BOCS total score after treatment above 20. Risperidone was started in dosages of 0.5 mg. Risperidone was increased by 0.5 mg every two weeks if improvement was not seen until a maximum dose of 2.0 mg was obtained.

Efficacy evaluation of the combined treatment was made by the author after 12 weeks of treatment with an SSRI and risperidone.

Patients

Seventeen adolescent out-patients with severe OCD were treated with two different SSRI drugs. They all had no or insufficient effect from the SSRI treatment and were augmented with risperidone as augmentation to ongoing SSRI treatment (the second SSRI drug). Every patient was evaluated weekly with the CY-BOCS, CGAS-score and weight control in an open label study.

Table I Symptomatology of 17 Adolescents

No./Age/Sex	Age of Onset	Type of OCD-symptom	Comorbid Diagnosis	Family History
1/9/M	14	Checking Fear might harm others	None	Father OCD
2/16/F	12	Repeating rituals Need for assurance	Asperger Syndrome	None
3/15/M	13	Washing rituals Fear of illness	None	Father OCD
4/18/M	14	Fear of illness/contamination Washing rituals	None	None
5/17/F	14	Fear of illness Somatic obsessions Checking	Panic attacks	Brother schizophrenia
6/17/F	15	Checking	Depression (moderate)	Father OCD
7/15/F	13	Repeating rituals Mental rituals Washing rituals	Bipolar disorder	Mother depression
8/18/F	13	Washing rituals	Depression (moderate)	Mother depression
9/17/M	9	Mental rituals	None	None
10/15/F	13	Fear of contamination Washing rituals	None	Mother depression Brother schizophrenia
11/18/M	16	Fear of catastrophy Repeating Different rituals Symmetry rituals	None	Mother depression
12/16/M	14	Sexual obsessions Fear might harm others Aggressive obsessions	None	None
13/17/M	13	Sexual obsessions Religious obsessions Fear of illness	None	None
14/15/F	13	Blinking, Counting Phrases, Symmetry	None	None
15/15/F	12	Sexual obsessions Repeating rituals Different rituals	None	None
16/16/M	14	Fear of cancer Different rituals Washing rituals	None	None
17/17F	13	Washing rituals Repeating Checking	None	None

Efficacy evaluation of combined treatment was made after 12 weeks of treatment with an SSRI and risperidone.

At pre-treatment baseline, all children and adolescents had high scores on the Y-BOCS/CY-BOCS (range 25–36, clinical cut-off = 15), indicating severe OCD (Table II). All patients were significantly socially disabled by their obsessive-compulsive symptoms. The CGAS scores at baseline were in the range of 40–75 (mean 61.8 ± 11.3) indicating poor to moderate impairment of overall social functioning (clinical cut-off = 70) (Table II).

Statistics

A paired T-test for measures was used.

RESULTS

Efficacy

All adolescents fulfilled the DSM-IV criteria for OCD (the mean Y-BOCS at referral was 28.9). There were 8 males and 9 females with the mean age of 16.6, the age range was 15 to 18 years. The mean Y-BOCS and the changes in the total scores can be seen in Table II. The changes in total Y-BOCS and CGAS scores after augmentation with risperidone were statistically significant (see Table III). The patients were treated with augmentation with risperidone in dosages from 1–2 mg per day.

Four patients (24%) had a further reduction in CY-BOCS (after the augmentation with risperidone) of more than 25%

Table II Changes in Y-BOCS and CGAS After Treatment

N	Y-BOCS Scores Before Treatment/ After 2nd SSRI/ After Augmentation	CGAS Score Before/ After 2nd SSRI/ Combined Treatment	1st/2nd SSRI	Risperidone	Side Effects
1	32/25/22	60/75/85	Citalopram/sertraline	1 mg × 2	None
2	28/26/24	40/50/60	Sertraline/paroxetine	0.5 mg × 2	Sedation Weight gain
3	28/22/16	70/75/75	Citalopram/sertraline	1 mg × 2	Weight gain
4	32/30/24	70/80/85	Citalopram/sertraline	1 mg × 2	None
5	34/26/20	70/70/75	Sertraline/citalopram	1 mg × 2	None
6	27/24/18	65/75/85	Citalopram/sertraline	1 mg × 2	None
7	28/23/18	55/65/70	Sertraline/citalopram	1 mg × 2	Sedation Weight gain
8	27/24/20	70/80/80	Citalopram/sertraline	1 mg + 0.5 mg	Weight gain
9	28/26/24	60/60/60	Citalopram/sertraline	1 mg × 2	None
10	25/20/15	70/80/80	Sertraline/paroxetine	1 mg × 2	Weight gain
11	36/28/22	40/60/70	Citalopram/sertraline	1 mg × 2	None
12	28/21/17	70/80/80	Sertraline/citalopram	0.5 mg × 2	Weight gain
13	28/23/18	75/80/80	Sertraline/citalopram	1 mg × 2	Weight gain Sedation
14	26/25/24	75/80/80	Fluoxetine/sertraline	1 mg + 0.5 mg	None
15	28/23/17	50/50/60	Citalopram/sertraline	0.5 mg × 2	Weight gain
16	30/24/20	60/70/85	Sertraline/citalopram	1 mg × 2	None
17	27/21/20	50/50/60	Citalopram/sertraline	1 mg × 2	Sedation

Table III Efficacy of Treatment with SSRI and Risperidone

Variable	Pre-treatment (T_1)	After 2nd SSRI (T_2)	After Augmentation (T_3)	$t(T_1\text{-}T_2)$ p	$t(T_2\text{-}T_3)$	p
Total Y-BOCS or CY-BOCS score	28.9 ± 2.9	24.2 ± 2.6	19.9 ± 2.9	8.83 $p < 0.001$	960	$p < 0.001$
CGAS-score	61.8 ± 11.3	69.4 ± 11.4	74.7 ± 9.6	5.61 $p < 0.001$	424	$p < 0.001$

(i.e. moderate to good improvement), 10 patients had a reduction of 10-25% (i.e. slight to moderate improvement), 3 patients had less than 10% change (characterized as no effect). Nine patients (53%) dropped from severe OCD (Y-BOCS > 23) to moderate OCD (i.e. Y-BOCS 16–23), one patient dropped to a subclinical level of OCD (i.e. Y-BOCS ≤ 15). Males and females did not differ as to reduction in total scores on the Y-BOCS or increase on the CGAS.

Side Effects

None of the patients had a worsening of obsessive-compulsive symptoms following combined treatment. The augmentation with risperidone was tolerated by the patients, however, weight gain (defined as an increase of 10% or more) was reported in 8 cases (41%) and sedation in four cases (23%) (Table II).

The mean change of total weight from baseline to end of observation period was 7.8% (0–33.3%), mean change of weight after addition of risperidone was 2.7% (0–10.3%). Mean change in kilograms was 5.3 kg (0–24 kg). Seven patients had an increase of weight after addition of risperidone of more than 10%. One patient had a total increase in weight of 33.3% (from BMI 14.0 to 20.5) during treatment, and an increase of 10.3% after addition of risperidone. After addition of risperidone three patients had a BMI of 25 or more (maximum 25.7), which indicated overweight. Mean BMI before treatment was 20.9 (14–24.5) and after additional treatment with risperidone (i.e., end of treatment study) 22.5 (18.8–25.7).

DISCUSSION

Very little has been written about the possible role of augmentation to SSRI-treatment in pediatric and adolescent OCD. There is increasing evidence that OCD is a neurobiological disorder with involvement of the serotonergic (and possibly the dopaminergic) system in a manner that is not fully understood. There is some evidence for the

efficacy of the atypical antipsychotics from both case and open-label studies (15). Fitzgerald et al. described four pediatric patients diagnosed with OCD. Risperidone was used as an augmentation to a serotonin reuptake inhibitor. An improved treatment response was observed in all cases. A case-study done by Ramasubbu et al. (26) showed that a linear dose response relationship between increasing doses of olanzapine and improvement in obsessive-compulsive symptoms was observed in an OCD-patient (adult) resistant to 5-HT reuptake inhibitors, and that OC-symptoms induced by low doses of risperidone (1 mg) were reversed by increasing the doses of risperidone (3 mg) suggesting an inverse dose-severity relationship. Some cases in open label-studies suggest the onset or worsening of obsessive-compulsive symptoms with the use of atypical agents, either alone or as augmentation (27), a phenomenon also reported in children (28). However, such a worsening of obsessive-compulsive symptoms induced by risperidone was not reported in the present study. It may be that some intractable OCD patients require dopaminergic modulation in addition to serotonergic agents to obtain symptom relief. It has been suggested that atypical neuroleptic augmentation may affect obsessive-compulsive symptoms through antagonism of serotonergic receptor subtypes that have been down regulated by previous chronic SSRI administration (12). In a study done by Maina et al. on charts of patients with OCD who responded to the addition of an antipsychotic to SSRI it was indicated that antipsychotic augmentation should be maintained for patients who respond to this strategy because the vast majority of subjects who discontinue the antipsychotic relapse within two months (29).

The sample in this study consisted of severely affected, treatment resistant adolescent OCD patients. All of them had tried two different SSRIs for a period of three months. The optimal dosage in the pediatric and adolescent population is not accurately settled. However, all patients were treated with fairly high dosages of SSRI. After augmentation with risperidone a considerable number had a significant reduction in obsessive-compulsive symptoms, 24% of whom had a reduction of more than 25%. Only a few had such significant reduction in total score of the Y-BOCS that they no longer had clinical obsessive-compulsive symptoms, but had OCD on a subclinical level. The clinical implication of this study would be that augmentation should be tried in severe treatment resistant cases in which both SSRI and CBT has been inefficient.

This study is limited in conclusion as it is neither randomized nor blind. However, the study is the first to report of augmenting medication in a fairly high number of treatment resistant adolescent cases with OCD. The number of cases, however, did not allow any analysis of subgroups, that is whether some symptoms (like symmetry) are more likely to respond to the addition of risperidone. It should be noted that none of the patients included in this study had Tourette's Syndrome, which has previously been described as a possible indication for the combination of SSRI and antipsychotic medication (11,12). Another methodological issue of importance is the fact that all patients were offered CBT during the study. CBT could be regarded as a secondary form of augmentation treatment. However, in all cases CBT was given already from the beginning of the pharmacological treatment, that is long before augmentation with risperidone, thereby presumably not affecting or systematically introducing bias on the effect of risperidone.

Although 12 weeks is considered sufficient to evaluate the treatment efficacy of a chosen drug, long term studies indicate that a further reduction of obsessive-compulsive symptoms can be obtained on the same drug (24,25). So, in theory, one would expect a further decrease in OCD severity after prolonged treatment with one of the SSRIs. However, in this population there was no or only very minimal change in OCD severity following treatment with two different SSRIs.

Side Effects

In this treatment resistant, severely affected group with early onset of OCD and at least some years of severe obsessive-compulsive symptoms the addition of an atypical antipsychotic like risperidone might be beneficial. However, there were some side effects associated with this combined treatment.

Weight gain was a considerable problem in almost half of the cases. Apart from this side effect, the augmentation with risperidone was well tolerated in the group of adolescent patients.

CONCLUSION

This study indicates that risperidone may be efficacious as augmenting drug in some treatment resistant adolescents with OCD. Randomized control trials are warranted in the population of treatment resistant children and adolescents with severe OCD. The most common side effect of the combined treatment was weight gain.

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