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LETTER TO THE EDITOR

Open-label olanzapine in obsessive-compulsive disorder refractory to antidepressant treatment

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Olanzapine / Obsessive–compulsive disorder / Augmentation therapy / Treatment–unresponsive OCD

Augmentation strategies have been suggested in patients with obsessive–compulsive disorder (OCD) who have persisting symptoms despite antidepressant drug treatment. Olanzapine augmentation has been reported in recent case reports [1,2] and open trials [3-5].

We treated eight DSM-IV OCD patients (*table I*) (mean age ± S.D.: 38 ± 19.8 years; range: 16–61) who had shown unsatisfactory response to antidepressant treatment of adequate duration. In seven cases, olanzapine was added to the current antidepressant drug; in patient 8, it was started 1 week after venlafaxine discontinuation. Olanzapine was initiated at a dose of 5 mg/d. If needed, dosage was adjusted at 2-week intervals with 5 mg increments. Response was defined as a CGI-I score of "much improved" or "very much improved."

Seven of the eight patients improved within 2 weeks (*table I*). They described a reduction of the pressure or drive associated with obsessions and compulsions. Patient 7 had presented with OCD symptoms for over 10 years, and had a first-degree relative with OCD; her OCD symptoms improved slightly with olanzapine, but returned to the previous level of severity after she discontinued the drug because of her fear of gaining weight. Patient 8 had suffered OCD symptoms for over 1 year, and had presented with rare auditory hallucination symptoms in the last 3 months; olanzapine produced a definite improvement of her OCD symptoms, independent of the positive effect on psychotic symptoms. Improvement was obtained with low doses of olanzapine. Responders received a mean final olanzapine dose of 6.67 mg/d (S.D.: ±2.58; range: 5–10). The two non-responders received comparatively higher doses (15 mg/d for subject 5; and 5 mg/d for subject 7, with comorbid anorexia nervosa and a body weight of 42.5 kg (BMI: 16.6)). Response was not related to gender, comorbid diagnoses, types of OCD symptoms, or concomitant antidepressant drug. Weight gain was observed in five patients. Sedation was reported at the start of treatment but did not seem to problematic, maybe because low doses were used.

The CGI-I is largely used in antipsychotic drug trials, but a specific scale, e.g. the Yale-Brown Obsessive Compulsive Scale, would have been preferable. To our knowledge, there is no controlled study investigating the efficacy of olanzapine in antidepressant-refractory OCD patients. A placebo-controlled investigation of risperidone augmentation of SSRI treatment documented a 50% response rate [6]. A placebo-controlled trial with haloperidol [7] suggested that OCD patients with a comorbid chronic tic disorder constitute a subtype requiring conjoint SSRI/neuroleptic therapy. However, in our series, improvement was not limited to patients presenting with motor tic disorder or psychotic symptoms. The effect of olanzapine is unlikely to

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Table I. Characteristics of patients and response to treatment.

Patient	1	2	3	4	5	6	7	8
Sex	M	F	M	F	M	M	F	F
Age	42	61	61	57	30	17	20	16
Comorbid diagnosis	GAD[b]	Dysthymic disorder	Dysthymic disorder	GAD	Chronic motor tic disorder	Chronic motor tic disorder	Dysthymic disorder Anorexia nervosa	Brief psychotic disorder Depressive disorder NOS[c]
Primary obsessive-compulsive symptoms	Counting Checking	Doubt	Checking	Hoarding	Checking Counting	Ordering	Fear of contamination Obsessions	Fear of contamination Ordering
Past antidepressant dose (mg/d)	None	Fluoxetine (60)		Mirtazapine (45)	Sertraline (150)	None	Paroxetine (40)	Venlafaxine (37.5)
Current antidepressant dose (mg/d)	Fluoxetine (60)	Venlafaxine (300)	Paroxetine (20)	Venlafaxine (150)	Fluoxetine (40)	Venlafaxine (225)	Venlafaxine (75)	None
Dose of olanzapine (mg/d)	5	10	5	5	15	10	5	5
Duration of olanzapine treatment (weeks)	14	41	74	38	15	23	16	4
Adverse effects	Weight gain	None	Weight gain	Weight gain	None	Weight gain	Weight gain	None
CGI-I[a] score at 4 weeks of olanzapine treatment	2	1	1	2	4	1	3	2

[a]CGI-I = Clinical Global Impression Global Improvement item (1 = very much improved, 2 = much improved, 3 = minimally improved, 4 = no change, 5 = minimally worse, 6 = much worse, and 7 = very much worse).
[b]GAD = Generalized Anxiety Disorder.
[c]NOS = not otherwise specified.

be mediated by interactions affecting the pharmacokinetics of antidepressant drugs. Olanzapine, with its broad receptor binding profile [8], might act on obsessive–compulsive symptoms through serotonergic pathways or other mechanisms. Olanzapine's moderate affinity for $5HT_{1B}$ and $5HT_{1D}$ receptor subtypes is worth mentioning, since they have been postulated as targets for the treatment of OCD [9].

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