Clinical note

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Ziprasidone as coadjuvant treatment in resistant obsessive-compulsive disorder treatment

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Data suggest that atypical antipsychotics may be useful in the treatment of obsessive-compulsive disorder (OCD). We report the case of a patient diagnosed of serious OCD resistant to various antidepressant and antipsychotic treatments (including clozapine). The patient had clinically significant improvement (measured by decrease in the score of the Yale-Brown Obsessive Compulsive (Y-BOCS) and the Clinical Global Impression (CGI) scales) in the four weeks alter switching from clozapine to ziprasidone, improvement that was subsequently maintained. The pharmacodynamic characteristics of ziprasidone could make this drug more effective than other antipsychotics as coadjuvant treatment in OCD.

Key words:
Ziprasidone. Venlafaxine. Obsessive-compulsive disorder.

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La ziprasidona como tratamiento coadyuvante en el tratamiento del trastorno obsesivo-compulsivo resistente

Existen datos que sugieren que los antipsicóticos atípicos pueden ser útiles en el tratamiento del trastorno obsesivo-compulsivo (TOC). El presente trabajo presenta el caso de una paciente diagnosticada de TOC grave y resistente a distintos tratamientos antidepresivos y antipsicóticos (incluyendo clozapina). La paciente presentó mejoría clínicamente significativa (medida por una disminución en la puntuación en las escalas Y-BOCS e ICG) en las 4 semanas posteriores a la sustitución de clozapina por ziprasidona, mejoría que se mantuvo posteriormente. Las peculiaridades famacodinámicas de la ziprasidona podrían hacer a este fármaco más eficaz que otros antipsicóticos como tratamiento coadyuvante en el TOC.

Key words:
Ziprasidone. Venlafaxine. Trastorno obsesivo-compulsivo.

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INTRODUCTION

There is evidence that a percentage of patients with obsessive-compulsive disorder (OCD) do not improve in spite of treatment. From 20 %-30 % respond to psychotropic drug with a 30 % to 60 % reduction in symptoms[1]. Their situation does not improve when behavioral therapy is associated[2].

Among the psychopharmacological treatments, efficacy of the selective serotonin re-uptake inhibitors (SSRI) supports the role of serotoninergic system in treatment of the disorder[3]. However, adequate treatment regimes with these drugs only provide significant improvement in 50 % of the patients[4]. Venlafaxine (selective serotonin and noradrenaline inhibitor) has also been shown to be useful in OCD treatment, although its results are not better than those of the SSRI[5]. Several potentiation strategies with other drugs such as lithium, buspirone or pindolol have been described for drug treatment of monotherapy resistant OCD cases. Association of SSRI plus antispychotics have also been used with positive results: at first, classical antipsychotics and more recently atypical antipsychotics such as clozapine[6], risperidone[4,7], olanzapine[8] or quetiapine[9]. In some cases, the anti-obsessive effect is obtained with low doses, while high doses may cause exacerbations of the obsessive-compulsive symptoms[10]. The case described in the following concerns a patient with obsessive-compulsive disorder resistant to different therapeutic regimes in which antidepressants and atypical antipsychotics (including clozapine) were included and who responded positively to the ziprasidone and venlafaxine combination.

CLINICAL CASE

Mrs. A is a 56 year old patient diagnosed of an obsessive-compulsive disorder with progressive deterioration in the last four years in spite of the psychopharmacological and psychological (relaxation, behavioral psychotherapy) treatment. The patient was referred to our day hospital due to serious obsessive symptoms, accompanied by very intense symptoms of anxiety, both physical (tremors, muscular ten-

sion, sweating, restlessness) and psychic (great mental tension that only mildly decreased in intensity on waking up). Her appearance was downheartened and neglected, intense mood decrease, physical exhaustion, and great despair and fear of the future. Obsession with cleanliness, compulsions (she had even gotten undressed completely before entering her home to not introduce dirt from the street) and progressive slow-down in the performance of tasks almost totally paralyzed her activity, preventing her from performing most the daily tasks. The Yale-Brown scale score on admission was 32. Psychotherapeutic strategies and previous psychopharmacological treatments did not show efficacy in the control of the obsessive symptoms or mood state. The following were included among these psychopharmacological treatments; clorimipramine (up to 225 mg/d), fluoxetine (up to 60 mg/d) maintained for months and associated to clonazepam, trazodone, gapapentin or quetiapine at variable doses. Due to persistence and episodic exacerbation of the symptoms, the out-patient consultations with the psychiatrist and psychologist were not sufficient and the patient had to come to the hospital emergency service on several occasions.

Treatment on admission consisted in: clorimipramine, 75 mg/d; fluoxetine, 60 mg/d, and clonazepam, 4 mg/d, and was replaced with venlafaxine (300 mg/d), clozapine (100 mg/d) and lorazepam (10 mg/d), observing a gradual decrease of anxiety and restlessness. One month after initiating treatment, psychic and somatic anxiety had improved, obsessive thoughts were maintained with similar intensity and the patient had asthenia, discouragement and lack of motivation. The anxiety was more tolerable, but the lack of vital tone and, above all, sensation of psychomotor delay, indifference and «wanting but not being able to» caused the incapacity to be maintained in similar levels to those of the beginning. Decrease of clozapine dose to 25 mg/d caused a slight improvement in the psychomotor slow-down, in the obsessive symptoms and mood.

In the third month of treatment, the obsessive symptoms, anxiety and mood had improved, becoming supportable for the patient. However, she still had great incapacity to perform tasks that produced suffering to her and the sensation of not being able to think clearly. Yale Brown scale score was 14. At this time, clozapine was replaced by ziprasidone (40 mg/d). The patient's situation was normalizing during the following month, obsessions progressively decreasing and personal independence improving. This permitted the patient to perform the domestic tasks «with reasonable effort» and renew social relationships. In this period, and for approximately one month, the patient had nighttime headaches and sweating, above all in the evening, that spontaneously abated. Subsequently, it was possible to decrease the benzodiazepine dose, stabilizing the treatment with: ziprasidone (40 mg/d), venlafaxine (300 mg/d) and lorazepam (2.5 mg/d). This treatment regime allowed for the almost complete normalization of the clinical and life situation of the patient who had a total score of 5 on the Yale-Brown scale. During the treatment period clinical global impression scale went from 6 at the time of admission to 4 when the patient was being treated with venlafaxine and clozapine and to 2 with the venlafaxine and ziprasidone treatment.

DISCUSSION

Ziprasidone is the antipsychotic that has the best affinity ratio for the $5HT_{2A}/_{D2}$ and $5HT_{2C}/_{D2}$ receptors[11]. In the extent in which blockage of the $5HT_{2C}$ receptors may disinhibit the dopaminergic and noradrenergic neurons in the cortex, low doses of ziprasidone would produce a desirable potentiation of dopamine and noradrenaline release in this cerebral zone[12,13]. This could produce activating effects (relief of fatigue) and contribute to improvement of cognitive function[14]. The greater affinity ratio for $5HT_{1A}$ and $5HT_{1D}$[11] may also cause a beneficial effect on anxiety and affective symptoms[15,16]. On the other hand, blockage of the serotonin, noradrenaline and dopamine reuptake sites could also contribute to regulating mood state[11,17,18]. In the case presented, the treatment regime proposed is clearly more effective than the previous ones and the use of low doses of ziprasidone entails improvement in symptoms that had not improved with other atypical antipsychotics, that correspond with the characteristics of its pharmacodynamic profile.

REFERENCES

1. White K, Cole J. Pharmacotherapy. En: Bellack AS, Hersen M, editores. Handbook of comparative treatments. New York: John Wiley and Sons, 1990.
2. Rachman SJ, Hodgson RJ. Obsession and compulsions. Englewood Cliffs: Prentice Hall, 1980.
3. Goodman WK, Price LH, Rasmussen SA, Delgado PL, Heninger GR, Charney DS. Efficacy of fluvoxamine in obsessive-compulsive disorder. A double blind comparision with placebo. Arch Gen Psychiatry 1989;46:36-44.
4. McDougle CJ, Epperson CN, Pelton GH, Wasylink S, Price LH. A double-blind, placebo-controlled study of risperidone addition in serotonin reuptake inhibitor-refractory obsessive-compulsive disorder. Arch Gen Psychiatry 2000;59:472-3.
5. Denys D, van Megen HJ, van der Wee N, Westenberg HG. A double-blind switch study of paroxetine and venlafaxine in obsessive-compulsive disorder. J Clin Psychiatry 2004;65:37-43.
6. Young CR, Bostic JQ, McDonald CL. Clozapine and refractory obsessive-compulsive disorder: a case report. J Clin Psychopharmacology 1994;14:209-11.
7. Saxena S, Wang D, Bystritsky A, Baxter LR Jr. Risperidone augmentation of SRI treatment for refractory obsessive-compulsive disorder. J Clin Psychiatry 1996;57:303-6.
8. Poyurovsky M, Dorfman-Etrog P, Haggai-Hermes H, Munitz H, Tollefson GD, Weizman A. Beneficial effect of olanzapine in schizophrenic patients with obsessive-sompulsive symptoms. Internat Clin Psychopharmacol 2000;15:169-73.

9. Denys D, Van Megen H, Westenberg H. Quetiapine addition to serotonin reuptake inhibitor treatment in patients with treatment-refractory obsessive-compulsive disorder: an open-label study. J Clin Psychiatry 2002;63:700-3.
10. McDougle CJ. Udate on pharmacologic management of OCD: Agents and augmentation. J Clin Psychiatry 1997;58:11-7.
11. Schmidt AW, Lebel LA, Howard HR. Ziprasidone: a novel antipsychotic agent with a unique human receptor binding profile. Eur J Pharmacol 2001;425:197-201.
12. Pozzy L, Acconcia S, Ceglia I, Invernizzi RW, Samanin R. Stimulation of 5-hydroxytryptamine (5-HT2C) receptors in the ventrotegmental area inhibits stress-induced but not basal dopamine release in the rat prefrontal cortex. J Neurochem 2002;82:93-100.
13. Bonaccorso S, Meltzer HY, Li Z, Day J, Alboszta AR, Ichikawa J. SR46349-B, a 5-HT (2A/2C) receptor antagonist, potentiates haloperidol-induced dopamine release in rat medial prefrontal cortex and nucleus accumbens. Neuropsychopharmacology 2002;27:430-41.
14. Bymaster FP, Katner JS, Nelson DL, Hemrik-Luecke SK, Threlkeld PG, et al. Atomoxetine increases extracellular levels of norepinephrine and dopamine in prefrontal cortex of rat: a potential mechanism for efficacy in attention deficit/hyperactivity disorder. Neuropsychopharmacology 2002;27:699-711.
16. Millan MJ. Improving the treatment of schizophrenia: focus on serotonin (5-HT1A) receptors. J Pharmacol Exp Ther 2000;295: 853-61.
17. Briley M, Moret C. Neurobiological mechanism involved in antidepressant therapies. Clin Neuropharmcol 1993;16:387-400.
18. Seeger TF, Seymour PA, Schmidt AW, Schmidt AW, Zorn SH, Schulz DW, et al. Ziprasidone (CP-88,059): a new antipsychotic with combined dopamine and serotonin receptor activity. J Pharmacol Exp Ther 1995;275:101-13.
19. Tatsumi M, Jansen K, Blakely RD, Richelson E. Pharmacological profile of neuroleptics at human monoamine transporters. Eur J Pharmacology 1999;368:277-83.