Ziprasidone therapy for post-traumatic stress disorder

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We describe the cases of 2 men with chronic combat-induced post-traumatic stress disorder (PTSD) who benefited from therapy with ziprasidone. They did not have active psychotic symptoms. Both the patients had a history of inadequate response to previous trials of different psychotropic agents. Ziprasidone was considered because of its broad-spectrum actions on various neurotransmitters. To our knowledge, this is the first published report of the usefulness of ziprasidone in the pharmacotherapy of PTSD, although atypical antipsychotic agents (e.g., olanzapine, quetiapine and risperidone) have been reported to be beneficial in the treatment of this condition.

Nous décrivons les cas de deux hommes atteints d'un syndrome de stress post-traumatique (SSPT) chronique attribuable au combat et qui ont bénéficié d'une thérapie à la ziprasidone. Ils n'avaient pas de symptômes psychotiques actifs. Les patients avaient déjà répondu inadéquatement à des essais antérieurs de divers agents psychotropes. On a envisagé la ziprasidone en raison du large spectre de ses effets sur divers neurotransmetteurs. Il s'agit, sauf erreur, du premier rapport publié sur l'utilité de la ziprasidone dans la pharmacothérapie du SSPT, même si l'on a déjà signalé que des antipsychotiques atypiques (p. ex., olanzapine, quétiapine et rispéridone) avaient un effet bénéfique dans le traitement de cette affection.

Introduction

The pharmacological treatment for post-traumatic stress disorder (PTSD) begins with selective serotonin reuptake inhibitor antidepressants; however, an inadequate therapeutic response, as well as the presence of psychotic symptoms in some patients, has led to the exploration of additional pharmacological treatment options. Several atypical antipsychotics, including risperidone, olanzapine and quetiapine, have been reported to produce beneficial effects in PTSD.[1-5] To our knowledge, this is the first published report of the usefulness of ziprasidone in the pharmacotherapy of PTSD.

Case 1

The first patient is a 53-year-old man with a history of chronic combat-related PTSD, who was admitted to hospital because of worsening flashbacks, nightmares and insomnia. In addition, he had intrusive thoughts, which consisted of continuous unwanted memories of his past trauma. He had increased irritability, leading to arguments and disagreements with his wife, alternating with passivity and avoidant and withdrawn behaviour. This patient's symptoms were triggered by news reports of military activity in the Middle East. He also experienced significant insomnia, anhedonia, anergy, poor concentration and decreased appetite, but he had no active psychotic symptoms. Because of the distress caused by the increasing severity of his intrusive symptoms, the patient had been drinking 2–3 beers every other day of the week preceding this admission, after extended sobriety. (The patient had a history of alcohol dependence from 1977 to 1980.) Because of his history of depressive disorder and PTSD, he had received previous adequate trials of medications, including venlafaxine, fluoxetine, sertraline, risperidone and imipramine, without an adequate or prolonged response in combination or as monotherapy. In addition, he had been admitted to a psychiatric hospital 4 times during the 4 years before the current admission. His medications at the time of admission were citalopram, 40 mg/d, bupropion, 150 mg/d, and atenolol, 50 mg/d.

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This patient was administered ziprasidone, titrated to 60 mg twice a day, over the course of a week; he responded favourably with good control of the intrusive symptoms and flashbacks, as well as improvement in mood and affect. Zolpidem, 10 mg, was added to help regulate his sleep pattern. Citalopram and bupropion were discontinued. The atenolol was continued for the patient's hypertension. After discharge, ziprasidone was continued on an outpatient basis and was further titrated up to 80 mg twice a day. The patient was advised to attend group therapy twice a month after discharge. Six months later, his clinical status continued to be stable, with no significant symptoms of PTSD or depression. He started to attend group therapy twice a month on a regular basis. This patient also remained sober, with no substance use, at the time of last contact.

Case 2

The second patient is a 55-year-old man with chronic combat-related PTSD who was admitted to hospital because his condition was refractory to treatment and because of the deterioration of his clinical status. At the time of his admission, he was taking trazodone, risperidone, venlafaxine and topiramate. His main symptoms were flashbacks, nightmares, increased vigilance and insomnia; however, he had no active psychotic symptoms. His PTSD resulted from traumatic stress experienced in Vietnam when he was exposed to extensive combat. His flashbacks sometimes included hearing phrases such as "incoming!" or "watch out!" while on other occasions the flashbacks involved seeing rifle muzzle flashes, explosions or smoke. Because of the frequency of his symptoms, he had retired a few years before from a utility company after working for 20 years. He had no history of substance use or abuse, nor any history of abuse as a child. The patient had received adequate therapeutic trials of sertraline, fluoxetine, paroxetine, nefazodone and carbamazepine either as monotherapy or in combination, but no adequate therapeutic response to these medications had been demonstrated. Venlafaxine was discontinued, because the patient was not responding. Risperidone was discontinued, because he was complaining of an extremely dry mouth. He was prescribed ziprasidone, and the dose was titrated to 40 mg, twice a day, over the course of a week. Trazodone, 100 mg, was also continued to help with his sleep. Topiramate was continued at the same dosage. He reported a positive therapeutic response regarding his flashbacks, nightmares and sleep. The dose of ziprasidone was further titrated up to 60 mg, twice a day, resulting in additional improvement. The patient's condition remained stable, and symptoms such as hyperarousal and re-experiencing symptoms were under control at about 4 months' follow-up after discharge from hospital. The patient continued to see his therapist upon discharge at the PTSD clinic and also reported improvement in his mood.

Discussion

Atypical antipsychotic agents (e.g., olanzapine, quetiapine and risperidone) have been reported to be beneficial in the treatment of PTSD.[1–5] Ziprasidone has affinities to serotonin-2A (5-HT_{2A}), dopamine-2 (D_2), 5-HT_{1A}, 5-HT_{1D} and 5-HT_{2C} receptors.[6] Ziprasidone, through 5-HT_{1A} receptor agonist activity, may help in the reduction of anxiety and depressive symptoms. The 5-HT_{2C} affinity of ziprasidone may also confer additional anxiolytic and antidepressant effect.[6] In addition, D_2 receptor antagonism provided by ziprasidone is expected to be beneficial regarding symptoms such as flashbacks, hypervigilance and intrusive thoughts, because these symptoms can be conceptualized as hallucinatory and delusional and, thus, psychotic. Further, the D_2 receptor antagonism is expected to control other symptoms of psychosis such as paranoia and to decrease the aggressive and self-destructive behaviour seen in the more severe cases of PTSD. A selective serotonin reuptake inhibitor–like effect is also demonstrated by ziprasidone because of its reuptake inhibition of serotonin, which is likely to be beneficial regarding symptoms of impulsivity, aggression, depression, panic and withdrawal.

To our knowledge, this is the first published case report of the efficacy of ziprasidone as a treatment for PTSD. However, many questions need to be answered, for example, the optimum dosage and duration of therapy. Additional randomized controlled studies are needed to further elucidate the role of ziprasidone in the treatment of PTSD and related stress spectrum disorders.

Competing interests: None declared for Drs. Siddiqui, Marcil and Ramaswamy. Dr. Bhatia is on the speakers' bureau for Janssen, AstraZeneca, Bristol Myers-Squibb, Shire and Pfizer and has received travel assistance to attend advisory board meetings. Dr. Petty owns stock in Pfizer, has been a paid consultant for Bristol Myers-Squibb and AstraZeneca, has received honoraria from Pfizer, Bristol Myers-Squibb and AstraZeneca, has received speaker fees from Lilly, Bristol Myers-Squibb, Janssen and Abbot, and has received travel asistance from Ortho McNeil.

Contributors: Drs. Siddiqui, Ramaswamy and Petty conceived and designed the study. Dr. Siddiqui collected the data. Drs. Siddiqui, Marcil, Bhatia and Petty analyzed the data. Drs. Siddiqui and Petty wrote the article. Drs. Marcil, Bhatia, Ramaswamy and Petty critically reviewed the article. All authors gave final approval for the article to be published.

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