Dear Editor: The selective serotonin reuptake inhibitors (SSRIs) are used to treat a wide array of psychiatric conditions (1). Patients experience fewer side effects, compared with the older antidepressants (2). However, sexual dysfunction may occur in up to 75% of patients taking antidepressants (3). I report a case in which a patient taking sertraline experienced decreased to almost nonexistent erections, with a return to his baseline functioning following treatment with vardenafil. To my knowledge, this is the first reported case of vardenafil used to treat antidepressant-induced sexual dysfunction.

Mr A, aged 32 years, was diagnosed with dysthymic disorder according to DSM-IV criteria. He was in good health and did not use alcohol, tobacco, or illicit substances. He had been married for 6 years and described his marriage as excellent. He was active in psychotherapy and referred for medication. He agreed to a trial of sertraline started at 50 mg daily and titrated to 150 mg at 3 weeks’ time. I obtained a baseline sexual history prior to his starting the sertraline and informed him that the medication could affect his sexual functioning. Mr A stated that he understood and agreed to a trial. Within 2 weeks of initiating sertraline, he began to notice diminished erections but no change in libido. Although he was discouraged about this side effect, he had noted an improvement in his dysthymic symptoms and desired to remain on sertraline. He was interested in adding bupropion sustained release (SR) in an attempt to improve sexual functioning. He began bupropion SR 100 mg daily with no improvement at 1 week, and the dosage was increased to 150 mg daily, with no success after 1 week. The bupropion SR was increased to 200 mg daily; again, there was no success at the end of 1 week, and it was discontinued. A trial of vardenafil 10 mg taken 30 minutes prior to sexual activity was initiated, with noted improvement within 3 days of initiation. Mr A has on occasion taken it 15 minutes prior to sexual activity, with positive results. The patient tolerated the medication without any noted side effects. Mr A has returned to his baseline sexual functioning and is fully satisfied with the quality of his erections.

As noted, a baseline sexual functioning history was taken prior to initiating treatment with sertraline, and the patient was informed about the possibility of sexual dysfunction. These factors facilitated discussion of this commonly occurring problem in patients treated with antidepressants. Taking this history also allows clinicians to distinguish between an antidepressant side effect or a pre-existing condition that can occur in up to 31% of men (4). Clinicians frequently are called upon to manage sexual dysfunction as a result of antidepressants. According to a recent survey by Dording and others, 43% of psychiatrists add bupropion to existing medication (5). Bupropion SR has been shown to be beneficial at dosages between 100 and 200 mg taken once daily, with most improvement noted within the first 2 weeks of treatment (6). My patient did not benefit from this strategy and required an alternate agent. I chose vardenafil, a new a phosphodiesterase 5 (PDE5) inhibitor, on the basis of work by Fava and others (7) and Nurnberg and others (8). These authors successfully treated patients suffering from antidepressant-induced sexual dysfunction with sildenafil, a PDE5 inhibitor. Vardenafil is a highly selective PDE5 inhibitor used to treat erectile dysfunction (9). It is generally well tolerated and significantly enhances sexual functioning (10). Improvement in other aspects of sexual functioning, including confidence, orgasmic functions, and satisfaction, were noted in a recent review of vardenafil (11). Although my patient experienced the successful return of his pretreatment sexual functioning, caution is advised when interpreting case report results. Vardenafil may be valuable in expanding treatment options for clinicians managing the common side effect of antidepressant-induced sexual dysfunction, but further controlled studies will be needed.

References

spondyilitis, Crohn’s disease, and hepatitis C. He has a history of child abuse and treated chronic depression. He had an episode of postoperative delirium but no other prior psychiatric symptoms. His 9 daily medications included prednisone, ranitidine, sertraline, and high dosages of morphine.

Because of its delirious effects, Mr W’s morphee was decreased from 360 mg daily to 300 mg daily. He was begun on olanzapine 2.5 mg daily, which was increased to 10 mg daily within 3 days. He remained on the higher dosage of olanzapine for 1 week with no change in his symptoms or agitation. At this point, he met the “1-month” criteria for delusional disorder, somatic type. He was switched to pimozide 2 mg daily. Within 10 days, complete resolution of his symptoms occurred. He was discharged home on pimozide, which was tapered to 1 mg after 1 month. At 6 weeks, he had no recurrent symptoms. The pimozide will be discontinued at 2 months.

Discussion

Pimozide therapy was first reported to be beneficial for somatic delusions in 5 patients in 1975 (7). Several small, noncontrolled studies have reported its benefits, which include recovery from delusions of parasitosis in up to 90% of patients (1).

Newer studies suggest that atypical antipsychotics are equally effective (2). The serotonergic activity of atypicals is suggested to have the additional benefit of reducing the obsessive–compulsive and self-mutilatory features of somatic delusions (2).

Case reports have found response to risperidone in various somatic delusional disorders (4–6). In a 1997 study, treatment with risperidone eliminated symptoms in 3 patients with long histories of delusions of parasitosis who did not respond to haloperidol or pimozide (3). Recently, treatment with low-dosage olanzapine led to complete resolution of symptoms in a case of delusions of infestation (8). Most patients in these studies presented with long-standing histories, having experienced delusions for months to years.

In our case, the older, typical neuroleptic pimozide was effective in treating the new-onset delusion of infestation. More rigorous study into the benefits of treatment with pimozide vs the newer neuroleptics would be useful, not only for treating somatic delusions but also for patients presenting with early symptoms.

Consequently, numerous medications known to influence different receptors are reported to delay ejaculation. These include serotonergic drugs such as selective serotonin reuptake inhibitors (SSRIs) and clomipramine, alpha-adrenergic antagonists such as prazosin, and benzodiazepines such as clonazepam (3). I report the successful use of gabapentin, an anticonvulsant, in the treatment of PE.

Case Report

Mr X, aged 40 years, has a DSM-IV diagnosis of PE, lifelong situational type attributable to combined factors. Stop-pause, stop-squeeze coital alignment techniques and the use of a condom with topical anesthetic (5% lidocaine) were associated with limited response. Conventional pharmacotherapies were also minimally effective and had dose-limiting side effects. Treatment with paroxetine, sertraline, and to a lesser extent, venlafaxine was associated with restless legs, gastrointestinal disturbance, headache, decreased libido, and erectile dysfunction. Trazodone and lorazepam caused sedation and cognitive slowing, while buproprion accelerated ejaculation. Mr X had previously found that alcohol produced satisfactory ejaculatory delay with no loss of erectile capacity, but clearly this was not a feasible regular option. A trial of gabapentin 300 mg taken 1 to 2 hours prior to intercourse resulted in a similar effect with no side effects. Higher doses of 600 mg resulted in further retardation of ejaculation but also in somnolence.

The mechanism of action of gabapentin is not clear, but it is believed to increase GABA through increased GABA release and synthesis and to decrease the release of monoamine neurotransmitters (4). Since benzodiazepines and alcohol can also delay ejaculation and are also GABAergic through a direct action on GABA-A receptors, it is postulated that gabapentin’s effect on ejaculation may be mediated via its action on GABA. Further, anorgasmia has been described in a male patient with bipolar disorder receiving gabapentin (5).

Currently, there are no specific treatments for PE, although dapoxetine, an SSRI-type drug with a short half-life, is undergoing clinical trials. Thus, gabapentin merits further consideration, particularly in those men for whom other therapies are ineffective or poorly tolerated.

References

Suspected Propranolol-Induced Delirium

Dear Editor: Propranolol has been used for many years in internal medicine, neurology, and psychiatry. Surprisingly, only a few case reports of propranolol-induced delirium have been published to date, according to Medline and Toxline databases. In 1979, Kuhr reported a case of prolonged delirium with propranolol use (1). Two cases of delirium, the first associated with combined propranolol and maprotiline and the second associated with combined propranolol, benzotropine, and fluphenazine decanoate, have also been described (2,3). In 1994, Chen reported 3 cases of elderly patients with recent cerebral infarction and preexisting brain dysfunction who were receiving 30 to 60 mg of propranolol daily (4). Watanabe found adjunctive propranolol, scopolamine, and (or) flurazepam before or after surgery to be the strongest predictor of delirium in postoperative orthopedic patients (5). It remains uncertain whether propranolol-induced delirium is very rare or just not reported.

Case Report
A man aged 74 years, a retired joiner, was first admitted to the psychogeriatric unit owing to increasing aggressiveness that was first noticed 3 years earlier. Family members reported paranoid delusions. On admission, he was oriented in time and place. His Mini-Mental State Examination (MMSE) score was 21. Blood counts, bilirubin, aspartate transaminase, alanine aminotransferase, alkaline phosphatase, albumin, potassium, sodium, calcium, glucose, creatinine, urea, and thyroid hormones were within normal limits. ECG revealed sinus arrhythmia. Because he suffered from prostatic carcinoma, the patient had been treated with ciproterone 200 mg daily for 4 years. Olanzapine 5 mg daily was started for treatment of his paranoid delusions. Propranolol had been suggested earlier by a neurologist to alleviate essential tremor, but the patient never started this treatment. On the fifth day after admission, propranolol was started at 40 mg daily and gradually increased to 120 mg daily, when delirium was noticed at night. The patient became sleepless, restless, and disoriented and showed impaired consciousness. During the day, he was tired but without impaired consciousness. On the third day, propranolol was discontinued. Symptoms of delirium disappeared the next day. A decrease in diastolic blood pressure of only 10 mm Hg was measured during the treatment with propranolol.

It is well known that delirium is more often a consequence of multiple etiologic factors than a consequence of a single one. Delirium may be attributed to central beta blockade; in our case, however, preexisting cognitive decline, old age, and other physical illnesses may have predisposed the patient to propranolol toxicity. That said, the time of beginning and resolving the delirium strongly suggest propranolol as the main etiologic factor. The patient’s tremor was later successfully alleviated with gabapentin.

References

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A Curious Case of Neuroleptic Malignant Syndrome

Dear Editor: The patient, a white male, aged 51 years and suffering from schizophrenia, had recently been switched from thioridazine to risperidone. His illness began in the early 1970s and was initially characterized by deteriorating psychosocial level of functioning. He demonstrated poor concentration, poor impulse control, and persecutory delusions. A movement disorder was present, characterized by choreiform movements of his limbs and facial grimaces, which eventually subsided. At the time, these were felt to be abnormal movements, though they were not considered tardive dyskinesia. At that time, he was also switched from haloperidol to thioridazine. The patient had been maintained on thioridazine and was doing extremely well until about 11 days before coming to medical attention, when he was switched from thioridazine to risperidone. The patient

References

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Recognizing Social Anxiety Disorder

Dear Editor: Social anxiety disorder (SAD), formerly known as social phobia, is among the most common of all psychiatric disorders. Indeed, the National Comorbidity Study found SAD to be the third most common psychiatric disorder, after major depression and alcohol dependence, with a lifetime prevalence of 13.3% (1). Despite its high prevalence and the negative impact it has on quality of life, SAD remains underrecognized (2).

Below is a mnemonic (memory aid) that describes the symptoms of social anxiety disorder as listed in the most recent diagnostic and statistical manual of mental disorders (3).

The mnemonic is FAINT, with the letters representing the symptoms, as follows:

F: Fear of one or more social or performance situations in which the person may feel scrutinized, humiliated, or embarrassed.
A: Anxiety when exposed to the feared situations and Avoidance of the situation.
I: Insight into the unreasonableness of the fear and Interference with daily routine, occupational functioning, or social life.
N: Not due to medication, drug abuse, or a general medical condition.
T: Timing. In individuals under age 18 years, symptom duration is at least 6 months.

It is hoped that this mnemonic will improve recognition of social anxiety disorder and will result in more timely treatment for those suffering from this common condition.

References

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Admission, his evaluation comprised a detailed psychiatric, medical, substance abuse, and psychosocial history as well as the relevant laboratory studies. He had a white blood cell count of 6.6; hemoglobin count, 14.7; hematocrit count, 44.8; and platelet count, 285,000. Electrocardiogram on admission revealed QTc interval of 428 milliseconds. Admission vital signs were the following: temperature 97.7, pulse 75, respirations 20, blood pressure 115/74.

We noted that Mr X, who had been sober and involved in substance abuse treatment prior to the week before admission, had failed at least 2 trials of typical and atypical neuroleptics. In light of the history and severity of symptoms, we decided a trial of clozapine would be the most appropriate course of treatment. Haloperidol was discontinued. Mr X was started on 25 mg daily of clozapine, with the dosage gradually increased to 150 mg in 2 weeks. Electrocardiogram (EKG) and laboratory values were monitored regularly. Within 14 days of clozapine treatment, QTc interval had increased to 472 milliseconds, and the patient was tachycardic, with heart rate over 100 beats per minute. At this point, an internal medicine consult was obtained. The recommendation was to immediately discontinue clozapine because of the risk for potentially fatal arrhythmia, such as torsade de pointes. Thus clozapine, which had so far been effective in controlling psychotic symptoms, was discontinued. Quetiapine was initiated the next day, and monitoring of vital signs, laboratory values, and EKG was continued. Over the next 3 days, the QTc interval returned to baseline of 428 milliseconds and remained at baseline throughout the patient’s hospitalization. Vital signs also remained stable with heart rate returning to baseline level. To treat Mr X’s psychosis effectively, quetiapine dosage was titrated to the maximum recommended daily dosage of 800 mg. Mr X tolerated quetiapine well and was safely discharged from the hospital in 2 weeks time. He continues in outpatient treatment and remains stable.

Drug-induced QTc prolongation, though not very common, is potentially fatal. Usually, multiple risk factors need to be present to precipitate arrhythmia, including drug use, such as cocaine (1). In contrast, substance abuse is common among schizophrenia patients, with up to 50% meeting criteria for comorbid substance abuse or dependence. Cocaine abuse is especially problematic because it complicates psychosis and has been shown to prolong QT and QTc intervals and to lead to lethal arrhythmias (2). As our case shows, comorbid cocaine abuse can increase the risk of antipsychotic-induced cardiotoxicity. Though clozapine pharmacotherapy remains an important option for patients with treatment resistant schizophrenia, with other treatment resistant psychotic disorders, and (or) with severe tardive dyskinesia, other treatment options such as quetiapine can be highly effective (3), as shown in our case. Patient safety depends on careful screening for risk factors associated with QT/QTc interval prolongation, especially comorbid substance abuse; close monitoring once antipsychotic treatment is initiated; and appropriate follow-up treatment, both for the primary psychotic disorder and for comorbid substance abuse.

References

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Using Depression Inventories: Not a Replacement for Clinical Judgment

The Children’s Depression Inventory (1) is one of the most common psychometric tools used in assessing childhood depression (2). It is a self-report questionnaire that is considered to have a high internal consistency and a satisfactory reliability. Despite the fact that Kovacs never intended for the CDI to be used to diagnose depression and that its ability to discriminate between children with and without depression is questionable (3), there are many instances when the CDI has been employed to do just this (1).

Case Report
Allan, aged 11 years, was referred for psychiatric assessment of depressive symptoms. His presenting symptoms of fatigue, initial insomnia, hyperphagia, and decreased concentration had been ongoing for 1 year. His teachers had begun to report a decline in his academic and social functioning at school; however, his parents said that his presenting...
symptoms did not seem to interfere with their son’s functioning when the task at hand was of interest to Allan. At the time of assessment, Allan denied experiencing any suicidal ideation or a history of suicide attempts, but he reported vague thoughts that life was no longer worth living. Neither he nor his parents were able to identify any recent stressors, but there was a long-standing history of bullying by peers regarding his obesity. The provisional diagnosis after initial psychiatric interview was adjustment disorder with depressed mood. Psychometric testing revealed Allan to have average to superior abilities but a large discrepancy between verbal and performance IQ. On the Children’s Depression Inventory (CDI), Allan endorsed several depressive symptoms, including suicidal ideation, with a total raw score of 27. This prompted an immediate risk assessment by the urgent care psychiatrist who failed to identify the patient as being at risk. That psychiatrist’s clinical impression was adjustment disorder with depressed mood, with the significant stressor being bullying at school.

In this case, a child with depressive symptoms but no suicidal ideation on clinical exam received a nondepression diagnosis from 2 independent psychiatrists. Conversely, assessment using the CDI rated this boy as very much above average for depressive symptoms and as experiencing suicidal ideation. This case suggests that the CDI may be an indicator of distress but not necessarily of depressive illness. It further supports the use of psychometric tools (in this case, the CDI) as adjuncts to clinical diagnosis. While such tools are valuable in assessment, they should not be considered a reliable substitute for the clinical interviewing process in determining diagnosis or suicidal risk.

References


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Treatment With Risperidone and Occurrence of Blurred Vision: A Question of Higher Dosage

The more frequently encountered ophthalmologic adverse events of neuropsychiatric agents include thioridazine-induced retinopathy, tricyclic antidepressant-induced accommodation interference and glaucoma, and lithium carbonate-induced exophthalmos and papilloedema. Clozapine may produce blurred vision, but this side effect is usually time-limited (1). According to available evidence, episodes of transient visual disturbances appear during treatment with risperidone but disappear when medication with risperidone is reduced to a lower daily dosage (2,3).

Methods

We assessed clinical somatic state, using laboratory values, ophthalmoscopy, biochemistry, EEG, and brain magnetic resonance imaging (MRI). We assessed psychic profiles, using the Positive and Negative Syndrome Scale for Schizophrenia (PANSS) and the Clinical Global Impressions (CGI). We assessed side effects, using the Simpson–Angus Rating Scale for Extrapyramidal Syndrome, the Barnes Akathisia Scale (BAS), and the Extrapyramidal Symptom Rating Scale (ESRS).

Case Report

In June 2002, because of psychotic symptoms, the patient (aged 36 years, single, with no children, and an economist) was hospitalized in our clinic with a discharge diagnosis of psychosis schizoaffective according to DSM-IV (4). After admission to our clinic, we continued therapy with promazine 400 mg daily, along with alprazolam 0.75 mg daily, zolpidem 10 mg daily, and fluoxetine 20 mg daily, and we started therapy with risperidone 2 mg daily. At baseline visit (that is, the first day of therapy with risperidone), we performed the PANSS, CGI, Simpson–Angus Rating Scale for Extrapyramidal Syndrome, BAS, and ESRS. The patient’s total PANSS score was 86, and the CGI score was markedly ill. The values of hematology, biochemistry, and urinalysis were in referent range. EEG was normal. Because of persisting positive symptoms, we increased the dosage of risperidone to 12 mg daily. Promazine was discontinued from therapy. The patient became fully remitted after 4 weeks and was discharged. After 6 weeks of risperidone therapy (4 weeks as an inpatient and 2 weeks as an outpatient), the patient reported blurred vision. To clarify the origin of blurred vision, we assessed clinical somatic state. The values of hematology, biochemistry, and urinalysis were in referent range. The results of the neuropsychological assessment excluded lesions caused by cranial trauma, diffuse brain damage, or lesions caused with slow progressive process. The patient’s brain MRI was normal, and the biomicroscopy results revealed no abnormalities. Ophthalmoscopy showed no pigment mottling or disturbances in the macular regions. Subsequently, the dosage of risperidone was reduced to 4 mg daily, and 2 weeks later, the patient reported full recovery of vision without worsening her mental condition. The diagnostic procedure showed no organic cause of the blurred vision. Also, blurred vision was not related to concomitant therapy.

Conclusion

Blurred vision is a side effect associated with treatment with risperidone in higher dosages, which may disappear, without worsening of symptoms, after decreasing the daily dosage of risperidone. Further observation is necessary for more precise understanding of these conditions, which is essential for diagnosis and appropriate treatment.

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Late Onset Neutropenia With Clozapine

The risk of neutropenia with clozapine has been well established and is greatest in the first 18 weeks of treatment. There have been
scant reports of neutropenia occurring later in treatment.

We describe a case of nonleukopenic neutropenia 3 years after initiation of clozapine.

Mr D is aged 34 years and suffers from paranoid schizophrenia, first diagnosed in April 1992. Since 1994, he had been managed on a combination of haloperidol decanoate, carbamazepine, and fluoxetine. Several full blood pictures (FBPs) performed were within normal ranges.

Because of ongoing delusional thinking and the appearance of mild dyskinetic movements, clozapine was initiated in June 1998. The patient’s medical history comprised a grand mal epileptic seizure after a head injury in 1986. He had been seizure free since 1995.

Prior to starting clozapine, carbamazepine was replaced by sodium valproate. Baseline FBP showed a hemoglobin level of 160 g/L, a platelet count of 146 × 10⁹/L, a white cell count (WCC) of 6.7 × 10⁹/L with a neutrophil differential of 3.48 × 10⁹/L, lymphocytes 2.55 × 10⁹/L, monocytes of 0.4 × 10⁹/L, eosinophils of 0.2 × 10⁹/L, and basophils of 0.07 × 10⁹/L. Following initiation of clozapine, medications included clozapine 300 mg daily, sodium valproate 1 g in the morning, and 1.5 g at night, sertraline 50 mg daily. There was a significant clinical response. In December 1999, monthly FBP revealed mild neutropenia (1.86 × 10⁹/L), with both a normal WCC (4.53 × 10⁹/L) and other white cell indices. The neutrophil count increased to 2.22 × 10⁹/L 2 days later and remained above 2 × 10⁹/L. There were 3 further episodes when Mr D’s neutrophil count dropped below 2 × 10⁹/L with normal WCCs and other FBP parameters, all of which resolved spontaneously.

In July 2001, his clozapine dosage was reduced to 250 mg daily following a further transient drop in his neutrophil count. Morning and afternoon testing yielded similarly low levels of neutrophils, excluding morning neutropenia. In August 2001, the neutrophil count dropped to 1.42 × 10⁹/L (with normal indices hemoglobin 156 g/L, platelets 153 × 10⁹/L, WCC 5.84 × 10⁹/L, lymphocytes 3.59 × 10⁹/L, eosinophils 0.10 × 10⁹/L). Two days later, when the neutrophil count remained below 1.5 × 10⁹/L, clozapine was ceased.

Urea and electrolytes, liver function test, erythrocyte sedimentation rate (ESR), and C-reactive protein level were found to be normal. Physical examination for each episode of neutropenia was normal. Clozapine blood levels before stopping clozapine were 916 mcg/l; norclozapine levels were 214 mcg/l. Following discontinuation of clozapine, the neutrophil count remained between 1.5 × 10⁹/L and 2 × 10⁹/L for 3 weeks before increasing by the fifth week to 2.73 × 10⁹/L. At this time, Mr D began to show signs of relapse of his paranoid schizophrenia and was commenced on risperidone. Eight weeks following discontinuation, the neutrophil count was 2.93 × 10⁹/L.

This case is uncharacteristic of the usual picture of clozapine-associated neutropenia, which occurs much earlier after clozapine initiation, has a more rapid recovery time, and has been associated with eosinophilia or elevations in the WCC that might predate the neutropenia.

The primary etiological role of clozapine appears likely given the gradual resolution of the neutropenia upon cessation of clozapine. Further, there was no discernible evidence for a physical cause of the neutropenia.

The role of concomitant medication, especially valproic acid, remains unclear. This case confirms the necessity for ongoing hematological vigilance in patients taking clozapine.

References

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