Letters to the Editor

Cost Savings With Intramuscular Anticholinergics

Sir: With the advent of atypical antipsychotics, novel anticonvulsant agents, and selective serotonin reuptake inhibitors, the pharmacotherapy of psychiatric disorders has changed tremendously in the last decade. Although these newer medications are generally better tolerated, and, in some cases, lessen associated costs of more frequent hospitalizations, they have greatly impacted hospital pharmacy budgets. With few of these newer medications available generically, there is little opportunity to decrease medication costs except in interventions such as tablet splitting.[1]

In an effort to reduce costs at our institution, we recently identified high-use, high-cost items. As a result, one initiative we undertook was a policy of substituting generic parenteral diphenhydramine, 25 mg, for parenteral benztropine, 1 mg, for the treatment and/or prophylaxis of antipsychotic-induced extrapyramidal symptoms (EPS). Significantly, parenteral benztropine is unavailable generically, but was the medication of choice at our institution for acute EPS or prophylaxis. Further, cost differences between the 2 products were substantial at $7.30 per single-use 2-mL glass ampul of benztropine (1 mg/mL) versus $0.40 per 2-mL multiuse vial of diphenhydramine (50 mg/mL). Although we could locate no controlled clinical efficacy trials of benztropine versus diphenhydramine for EPS, the use of both agents is widely accepted in the treatment of acute dystonic reactions and pseudoparkinsonism.[2–4] Diphenhydramine is generally regarded as the more sedating agent as a result of its antihistamine effects, but this may be beneficial in some patients.[3] Further, some patients may respond more rapidly to diphenhydramine.[4]

The project was implemented via a joint memorandum to all medical staff from the medical director and clinical coordinator for pharmacy services at the institution that outlined the project and potential savings. The medical staff was encouraged to voluntarily comply with the effort.

Compliance with the project was excellent and almost immediate. No adverse events or efficacy problems were reported during the year that intramuscular diphenhydramine was used. Our hospital saved approximately $9000 in drug costs the first year, or $6.90 per dose, with the change to diphenhydramine. This savings is expected to continue on an annual basis.

Our clinical findings are limited since we did not perform a rigorous assessment of individual differences in observed or perceived EPS in patients treated with one agent versus the other. Nonetheless, as a result of our experience and the known effectiveness of both agents, we believe clinicians can consider switching from intramuscular benztropine to diphenhydramine for the treatment or prophylaxis of antipsychotic-induced EPS. However, since diphenhydramine may be more sedating than benztropine, caution is advised to avoid additive pharmacodynamic effects in patients who are already receiving other sedating agents and/or in the elderly, who may be more sensitive to these side effects. This intervention is easily implemented, does not appear to compromise patient care, and results in modest cost savings.

References

1. Bult J, Schiff G, Wisniewski M. Sertraline tablet splitting program. Hosp Pharm 1999;34:996–999
2. Holloman L, Marder S. Management of acute extrapyramidal effects induced by antipsychotic drugs. Am J Health Syst Pharm 1997;54:2461–2477
3. Stanilla J, Simpson G. Treatment of extrapyramidal side effects. In: Schatzberg AF, Nemeroff CB, eds. Textbook of Psychopharmacology. 2nd ed. Washington, DC: American Psychiatric Press; 1998:349–369
4. Tonda ME, Guthrie SK. Treatment of acute neuroleptic-induced movement disorders. Pharmacotherapy 1994;14:543–560

John S. Markowitz, Pharm.D.
Stephen McLeod-Bryant, M.D.
Cherry Wyant Jackson, Pharm.D.
Medical University of South Carolina
Charleston, South Carolina

Problems With Ensuring a Double Blind

Sir: We read with interest the article by Zanardi et al.[1] evaluating the effectiveness of venlafaxine versus fluvoxamine in the treatment of delusional depression. Delusional depression, as the authors point out, is a difficult condition to treat with the limited treatment options available to clinicians. New treatment trials such as that reported in this study are always welcome. We have, however, 2 concerns about the design used by the authors that may have compromised the integrity of the blind in their study.

Firstly, as the authors indicate, venlafaxine and fluvoxamine work on different neurotransmitters. Consequently, the 2 drugs have different side effect profiles, namely, sustained hypertension, dizziness, delayed ejaculation, and somnolence are more common with venlafaxine[2] and gastrointestinal symptoms, malaise, sedation, tremor, and exacerbation of anxiety features are associated with fluvoxamine.[3] The authors report that the side effects were rated by "trained psychiatrists" using the Dosage Records and Treatment Emergent Symptoms Scale (DOTES). Some of the side effects outlined above were experienced by study participants, but the authors do not report the drugs with which they were associated. The blind of the study might have been broken because side effect profiles do provide significant clues about the drug being tried.[4] For instance, one could speculate, even though the authors do not report, that the patient who

dropped out of the study owing to a marked increase in blood pressure was likely to be on venlafaxine treatment. Two interventions have been reported to be helpful in this regard[4]: (1) one blinded psychiatrist monitors the therapeutic response and possible toxicity and another psychiatrist, who is not blinded, receives reports from the first psychiatrist and the laboratory and adjusts the dosage according to the study protocol; (2) the psychiatrists are asked to guess what medication each patient is receiving. If the success rate of having a correct guess is higher than chance, then one could say that the blind is broken.

Secondly, some important details about medication dispensation are missing that are important in ensuring a double blind. These include the number of tablets patients were having to take, the external appearance of the tablets, and who dispensed them to the patients.[4] A conventional way to ensure blinding in studies in which patients have to take different numbers of tablets owing to varying dose strengths is called the "double-placebo method."[4] Each group receives an identical number of tablets made by combining active medication and placebo.

The findings of this pilot study should be interpreted in light of these factors, which could have been best outlined in the discussion of the limitations of the study.

References

1. Zanardi R, Franchini L, Serretti A, et al. Venlafaxine versus fluvoxamine in the treatment of delusional depression: a pilot double-blind controlled study. J Clin Psychiatry 2000;61:26–29
2. Mackay FR, Dunn NR, Martin RM, et al. Newer antidepressants: a comparison of tolerability in general practice. Br J Gen Pract 1999; 49:892–896
3. Edwards JG, Anderson I. Systematic review and guide to selection of selective serotonin re-uptake inhibitors. Drugs 1999;57:507–533
4. Spiker B. Guide to Clinical Trials. New York, NY: Raven Press; 1991

Shailesh Kumar, M.R.C.Psych., M.Phil.
Lakeland Health Limited
Rotorua, New Zealand
Mark Oakley-Browne, Ph.D., F.R.A.N.Z.C.P.
Auckland School of Medicine
Auckland, New Zealand

Zanardi and Colleagues Reply

Sir: Drs. Kumar and Oakley-Browne raised 2 concerns about our study design.[1] The first is related to the possibility of breaking the blind of the study given the different side effect profiles of fluvoxamine and venlafaxine, since the 2 drugs have different mechanisms of action. To address this observation, we point out the following considerations: Firstly, even if the 2 drugs belong to different classes of antidepressants, it should be noted that venlafaxine is a serotonin-norepinephrine reuptake inhibitor, thus sharing with fluvoxamine the action on serotonin reuptake. This probably is why the 2 compounds' side effect profiles frequently show overlapping features. For example, nausea, sexual dysfunction, dizziness, diarrhea, headache, anorexia, asthenia, constipation, and insomnia (just to cite the most frequent ones) are as common with venlafaxine as with fluvoxamine treatment.[2,3] Keeping this in mind, clinicians are quite unlikely to be able to guess which medication a given patient is receiving considering the side effect profile showed. Secondly, the same observation should be made for all comparison studies, particularly those in which the side effect profile of drugs is often different and more easily recognizable (i.e., tricyclic antidepressants versus selective serotonin reuptake inhibitors).

Regarding the second and last concern that Drs. Kumar and Oakley-Browne had about the description of medication dispensation, we cannot help agreeing with them. In fact, being aware of the importance of ensuring that the dispensation of medications did not break the blind, we carefully followed these rules: the external appearance of the capsules was identical for size, consistency, and color; the number of capsules administered was the same in the 2 groups (1 capsule daily for the first 3 days and then 2 capsules daily for each patient); the time of administration for the 2 treatments during the day was the same (1 capsule after dinner on the first 3 days with the addition of the second capsule after breakfast from the fourth day on); and medication dispensation was carried out by a member of the nursing staff. Given these precautions, we feel confident in saying that our trial was not affected at all by such limitations.

In every randomized controlled study we carry out, we stick to the suggestions so clearly outlined in the CONSORT statement.[4] The problem arising from the full description of such guidelines is the need of more space than is usually available in scientific journals.

References

1. Zanardi R, Franchini L, Serretti A, et al. Venlafaxine versus fluvoxamine in the treatment of delusional depression: a pilot double-blind controlled study. J Clin Psychiatry 2000;61:26–29
2. Markham Brown T, Stoudemire A. Psychiatric Side Effects of Prescription and Over-the-Counter Medications. Washington, DC: American Psychiatric Press; 1998
3. Medscape DrugInfo. Available at: http://www.promini.medscape.com/drugdb/search.asp. Accessed January 8, 2000
4. CONSORT Group. Improving the quality of reporting of randomized controlled trials: the CONSORT statement. JAMA 1996;276:637–639

Raffaella Zanardi, M.D.
David Rossini, M.D.
Alessandro Serretti, M.D.
University of Milan
Milan, Italy

Low-Dose Olanzapine for Self-Mutilation Behavior in Patients With Borderline Personality Disorder

Sir: Self-mutilation is a common but difficult symptom to treat. Seen in several different psychiatric disorders, it is an intermittent phenomenon of borderline personality disorder in times of stress. Cutting, burning, and inflicting pain may be self-punishment, parasuicidal behavior, or part of a psychotic-like set of symptoms. There is no specific medication that has an indication for treatment of self-mutilation. Frequently, drugs are prescribed to treat the underlying psychiatric condition. Many medications have been tried with varying degrees of success for borderline personality disorder with self-mutilation. The following 2 case reports describe patients with severe borderline personality disorder whose self-mutilation responded to low-dose olanzapine.

Case 1. Ms. A, a 27-year-old woman who met DSM-IV criteria for borderline personality disorder, presented to the psychiatry clinic in crisis because her husband was leaving for a business trip and the 1-year anniversary of her mother's death was approaching. She reported a number of depressive symptoms and had made superficial lacerations on her left forearm and right thigh. She was started on 20 mg/day of fluoxetine,

followed twice weekly in supportive therapy, and referred to a bereavement group. She continued to have recurrent suicidal thoughts and decompensated 2 weeks later, requiring a 4-day inpatient stay. Her physical examination at admission revealed that she had made new lacerations to her left wrist. The fluoxetine treatment was continued and olanzapine, 5 mg, was started. She continued on olanzapine treatment for 2 months and fluoxetine for 6 months with no further incidents of self-mutilation.

Case 2. Ms. B, a 24-year-old woman with a long history of DSM-IV dysthymic disorder and borderline personality disorder, presented to the psychiatry clinic after a marital conflict. She had symptoms of affective instability, poor self-esteem, unstable interpersonal relationships, and recurrent suicidal threats and gestures. She had been hospitalized for similar symptoms 7 times in the past 4 years. She had made several superficial lacerations and burns to both forearms, stating that she preferred the physical pain to her emotional suffering. She was briefly hospitalized. Olanzapine, 5 mg/day, was started and continued for a month until her marital situation stabilized. There were no further incidents of self-mutilation for at least 7 months, but she was lost to follow-up after the family moved from the area.

There are many articles about the use of psychotropics in the treatment of borderline personality disorder.[1–3] Little, to date, has been written about the use of atypical neuroleptics in the treatment of either borderline personality disorder or self-mutilation.[4–8] Schulz et al.[4] found that low-dose olanzapine substantially reduced overall symptomatology and improved functioning in comorbid borderline personality disorder and dysthymia. The present 2 cases are consistent with those findings.

Olanzapine and other atypical neuroleptics have unique advantages over other psychotropics because of their combination of antipsychotic, antidepressant, and mood stabilization properties and their low risk of neurologic side effects or tardive dyskinesia.[4] The dopamine-blocking effects of the atypical neuroleptics may address psychotic-like symptoms,[5] and the ability of these agents to affect serotonin reuptake may modulate pathologic aggression.[9,10]

In both cases, olanzapine was efficacious and well tolerated and had few side effects. Although it is possible that the benefits of hospitalization and an antidepressant contributed to the recovery of the first patient, the second patient did not respond to either past hospitalizations or trials of various antidepressants.

Future studies of patients with self-mutilation could examine optimal dosing and duration of treatment with atypical neuroleptics. Objective measures could be beneficial but may be difficult to use with a behavior that is intermittent and linked to unpredictable environmental stressors.

Atypical neuroleptics such as olanzapine, when used as part of a comprehensive treatment program, appear to be safe and efficacious agents for the treatment of self-mutilation seen in borderline personality disorder.

The opinions or assertions contained herein are the private views of the author and are not to be construed as official or reflecting the opinions of the Department of the Army, Department of Defense, or the U.S. Government.

References

1. Coccaro EF. Clinical outcome of psychopharmacologic treatment of borderline and schizotypal personality disordered subjects. J Clin Psychiatry 1998;59(suppl 1):30–35
2. Hirschfeld RMA. Pharmacotherapy of borderline personality disorder. J Clin Psychiatry 1997;58(suppl 14):48–52
3. Hollander E. Managing aggressive behavior in patients with obsessive-compulsive disorder and borderline personality disorder. J Clin Psychiatry 1999;60(suppl 15):38–44
4. Schulz SC, Camlin KL, Berry SA, et al. Olanzapine safety and efficacy in patients with borderline personality disorder and comorbid dysthymia. Biol Psychiatry 1999;46:1429–1435
5. Benedetti F, Sforzini L, Colombo C, et al. Low-dose clozapine in acute and continuation treatment of severe borderline personality disorder. J Clin Psychiatry 1998;59:103–107
6. Khouzam HR, Donnelly NJ. Remission of self-mutilation in a patient with borderline personality disorder during risperidone therapy. J Nerv Ment Dis 1997;185:348–349
7. Szigethy EM, Schulz SC. Risperidone in comorbid borderline personality disorder and dysthymia. J Clin Psychopharmacol 1997;17: 326–327
8. Paris J. Is psychopharmacological treatment effective for the symptoms of borderline personality disorder (BPD)? J Psychiatry Neurosci 1999;24:262
9. Fava M. Psychopharmacologic treatment of pathologic aggression. Psychiatr Clin North Am 1997;20:427–451
10. Cornelius JR, Soloff PH, Perel JM, et al. Fluoxetine trial in borderline personality disorder. Psychopharmacol Bull 1990;26:151–154

LTC David W. Hough, M.D.
Madigan Army Medical Center
Tacoma, Washington

Successful Treatment of Nondelusional Body Dysmorphic Disorder With Olanzapine: A Case Report

Sir: Evidence suggests that body dysmorphic disorder (BDD), a preoccupation with an imagined or slight defect in appearance, responds preferentially to serotonin reuptake inhibitors (SRIs).[1,2] Given that BDD symptoms are often psychotic,[3] and given BDD's similarities to OCD,[4] antipsychotic augmentation of BDD is a promising although unstudied treatment strategy. The use of neuroleptics as monotherapy to treat BDD, however, has been limited. Although pimozide has been said to be effective for the delusional form of BDD (monosymptomatic hypochondriacal psychosis),[5] SRI augmentation with pimozide was unsuccessful in a small series of patients.[6] In case reports, typical neuroleptics (loxapine, trifluoperazine, thioridazine) have generally been reported to be ineffective.[7] The following case represents the first reported successful treatment of nondelusional BDD with an atypical neuroleptic, olanzapine.

Case report. Ms. A, a 46-year-old white woman who carries the diagnoses of alcohol dependence and bipolar II disorder, presented to the emergency department intoxicated and suicidal. Upon examination, she fulfilled DSM-IV criteria for alcohol dependence; bipolar II disorder, most recent episode depressed, severe with psychotic features (intermittent auditory hallucinations); and body dysmorphic disorder. She reported an almost constant preoccupation with her hair, looking in a mirror approximately every 5 minutes. Specifically, Ms. A thought her hairline was too far down on her forehead and that this placement of the hairline made her face look too small. She kept trying to brush her hair back off her forehead, hoping to affect the hairline itself over time. Additionally, whenever she left her house, Ms. A wore both a hat to cover her hairline and bright red makeup in order to make her face "look bigger." Her preoccupation with her hair resulted in significant impairment at work and had severely damaged her relationship with her boyfriend. There were no other symptoms consistent with obsessive-compulsive disorder (OCD), and there were no additional Axis I or Axis II diagnoses.

With respect to her appearance-related concerns, there was no evidence of delusionality. Ms. A reported that she felt her defect was probably real and as ugly as she thought it was, but she was not completely convinced of this belief. She also reported that although she was uncertain concerning others' views about her beliefs, she herself was fairly certain that her beliefs were true and that others' views were simply less accurate. Ms. A was willing, however, to consider the possibility that her beliefs may be false.

Ms. A reported that her appearance concerns predated her affective symptoms and her alcohol use. On the basis of a detailed history, Ms. A met DSM-IV criteria for BDD beginning at age 12 years. At that time, Ms. A would spend hours in front of the mirror each morning examining her hairline, frequently resulting in her being late for or absent from school. Subsequently, Ms. A began drinking in her late teen years and recalls a depressed mood with neurovegetative symptoms emerging simultaneously with her alcohol abuse. From a clinical perspective, her drinking did not appear to be related to her BDD.

Ms. A had been taking no medications for approximately 3 years at the time of assessment. Her previous medications included a 1-year trial of fluoxetine, 80 mg/day, which resulted in moderate improvement in depressive symptoms but did not diminish her BDD symptoms. She had received no behavioral, cognitive, or psychodynamic therapy.

On the basis of recent evidence of the possible mood-stabilizing properties of olanzapine,[8] the antidepressant effects olanzapine has demonstrated as an augmenting agent,[9] and the presence of auditory hallucinations, Ms. A was started on 5 mg/day of olanzapine as monotherapy after receiving information on the medication and providing informed consent for neuroleptic treatment. The dose of olanzapine was titrated up to 20 mg/day over the next 2 weeks. She was followed for 3 weeks on this monotherapy. Although she was no longer suicidal, her mood only minimally improved. At the end of 3 weeks, however, she reported no preoccupation with her appearance and no longer met criteria for BDD. This was the first remission of Ms. A's BDD symptoms since their onset at age 12 years. At follow-up approximately 8 weeks later, Ms. A's BDD symptoms were still in remission.

BDD has many phenomenological similarities to OCD, and the evidence that BDD symptoms respond to SRI treatment supports its inclusion as an obsessive-compulsive spectrum disorder.[10] Thus, the neurochemical hypotheses underlying OCD may shed light on BDD and its response to neuroleptics. Although a serotonin deficiency has long been suggested as the etiology of OCD, a serotonin-dopamine hypothesis has also been proposed.[11] Serotonin deficiency may be associated with a reduced inhibitory effect on dopamine neurons and thereby result in a serotonergic-dopaminergic imbalance. Dopamine excess may mediate the repetitive behaviors found in OCD and may explain the role for neuroleptics in treating OCD and BDD. Atypical neuroleptics such as olanzapine are generally antagonists at both serotonin-2A and dopamine-2 receptors, and this dual action may explain their possible efficacy in treating OCD. Clinically, available evidence suggests that augmentation of an SRI with an atypical neuroleptic is generally effective for OCD.[12,13] There is no published evidence, however, that olanzapine or other atypical neuroleptics have been used alone successfully to treat OCD. Except for this case, there is no published evidence that olanzapine is effective for treating the preoccupations found in BDD.

This single case raises some important questions concerning (1) the use of atypical neuroleptics in the treatment of BDD, (2) the neurochemical similarities between OCD and BDD, and (3) the role of serotonin and dopamine in the etiology of BDD. A single case must obviously be viewed with extreme caution from a clinical perspective, particularly given the brief follow-up period. Controlled studies of the use of atypical neuroleptics in the treatment of BDD are necessary to shed light on these questions.

References

1. Phillips KA. Body dysmorphic disorder: diagnostic controversies and treatment challenges. Bull Menninger Clin 2000;64:18–35
2. Hollander E, Allen A, Kwon J, et al. Clomipramine vs desipramine crossover trial in body dysmorphic disorder: selective efficacy of a serotonin reuptake inhibitor in imagined ugliness. Arch Gen Psychiatry 1999;56:1033–1039
3. McElroy SL, Phillips KA, Keck PE Jr, et al. Body dysmorphic disorder: does it have a psychotic subtype? J Clin Psychiatry 1993;54:389–395
4. Phillips KA, Gunderson CG, Mallya G, et al. A comparison study of body dysmorphic disorder and obsessive-compulsive disorder. J Clin Psychiatry 1998;59:568–575
5. Munro A, Chmara J. Monosymptomatic hypochondriacal psychosis: a diagnostic checklist based on 50 cases of the disorder. Can J Psychiatry 1982;27:374–376
6. Phillips KA, McElroy SL, Hudson JI, et al. Body dysmorphic disorder: an obsessive-compulsive spectrum disorder, a form of affective spectrum disorder, or both? J Clin Psychiatry 1995;56(suppl 4):41–52
7. Phillips KA. Body dysmorphic disorder: the distress of imagined ugliness. Am J Psychiatry 1991;148:1138–1149
8. Tohen M, Sanger TM, Tollefson GD, et al. Olanzapine versus placebo in the treatment of acute mania. Am J Psychiatry 1999;156:702–709
9. Shelton R, Tollefson G, Tohen M, et al. The study of olanzapine plus fluoxetine in treatment-resistant major depressive disorder without psychotic features. Presented at the 38th annual meeting of the New Clinical Drug Evaluation Unit; June 10–11, 1998; Boca Raton, Fla
10. McElroy SL, Phillips KA, Keck PE Jr. Obsessive compulsive spectrum disorder. J Clin Psychiatry 1994;55(10, suppl):33–53
11. Austin LS, Lydiard RB, Ballenger JC, et al. Dopamine blocking activity of clomipramine in patients with obsessive-compulsive disorder. Biol Psychiatry 1991;30:225–232
12. Weiss EL, Potenza MN, McDougle CJ, et al. Olanzapine addition in obsessive-compulsive disorder refractory to selective serotonin reuptake inhibitors: an open-label case series. J Clin Psychiatry 1999;60:524–527
13. Potenza MN, Wasylink S, Longhurst JG, et al. Olanzapine augmentation of fluoxetine in the treatment of refractory obsessive-compulsive disorder [letter]. J Clin Psychopharmacol 1998;18:423–424

Jon E. Grant, J.D., M.D.
University of Minnesota Medical School
Minneapolis, Minnesota

Olanzapine in the Treatment of Tardive Dyskinesia: A Report of 2 Cases

Sir: Tardive dyskinesia is an abnormal involuntary movement disorder characterized most commonly by choreoathetoid movements of orofacial muscles and distal limbs. Tardive dyskinesia occurs in predisposed individuals during or after cessation of long-term antipsychotic exposure. The risk of developing tardive dyskinesia increases by an average of approximately 5% per year of antipsychotic exposure to 68% by 25 years.[1] The atypical antipsychotics have been associated with a lower incidence of tardive dyskinesia,[2] and they have also been reported to improve tardive dyskinesia.[3–5] A few case reports exist of improvement in tardive dyskinesia with olanzapine[6–9]; however, no study has been conducted of olanzapine in the

treatment of tardive dyskinesia. The following case studies report improvement in tardive dyskinesia with olanzapine.

Case 1. Mr. A, a 19-year-old man, was diagnosed with mild mental retardation of unknown etiology and undifferentiated schizophrenia (DSM-IV). One year after his initial diagnosis, he was given risperidone, 2 mg/day, which was increased to 6 mg/day after 2 days, along with diazepam, 10 mg/day. After 2 weeks, he started showing improvement in psychotic symptoms but developed extrapyramidal symptoms, leading to the addition of trihexyphenidyl, 4 mg/day, and the cessation of diazepam treatment. His extrapyramidal symptoms improved, as did his psychotic symptoms, but negative symptoms and functional impairment were present after 8 weeks of trihexyphenidyl treatment.

After 3 months of treatment with trihexyphenidyl, Mr. A developed involuntary chewing movements and puckering of the lips. Because these movements were bothersome to him, he became more socially withdrawn. A diagnosis of tardive dyskinesia was made after a review of his medical history and a detailed neurologic examination. Risperidone was decreased to 4 mg/day, but no improvement in tardive dyskinesia was seen in 2 weeks. Thereafter, risperidone was further decreased to 2 mg/day, and trihexyphenidyl treatment was stopped. No improvement in tardive dyskinesia was observed in 2 weeks; thus, risperidone was stopped, and olanzapine, 5 mg/day, was started. Within 2 weeks, Mr. A's involuntary movements began to decrease and stopped completely after 6 weeks. He also showed improvement in negative symptoms and was able to return to his job.

Case 2. Ms. B, a 28-year-old woman, had a diagnosis of paranoid schizophrenia (DSM-IV) for 7 years. She had been treated with typical neuroleptics in the past, but she would stop medication after a few months of treatment, leading to relapse several times. Approximately 7 years after her initial diagnosis, she was administered haloperidol, 10 mg/day. She showed improvement and was maintained on 5 mg/day of haloperidol. After about 9 months of treatment with haloperidol, she developed abnormal chewing movements and movements of the lips and tongue. Ms. B was unable to speak properly because of these movements and was quite troubled by them. A diagnosis of tardive dyskinesia was made after neurologic evaluation. Haloperidol was stopped, and olanzapine, 10 mg/day, was started in divided doses. After 1 month of olanzapine treatment, Ms. B showed improvement in dyskinetic movements, and after an additional 4 weeks, her dyskinetic movements stopped completely. She has remained well on a once-daily dose of olanzapine, 10 mg.

The first patient had exposure to an atypical antipsychotic (risperidone) for only 3 months, whereas the second patient had 5 years of cumulative exposure to typical antipsychotics. Both patients showed rapid remission of tardive dyskinesia during treatment with olanzapine and were thereafter maintained on olanzapine therapy. The rapid response suggests the suppressive effect of olanzapine in tardive dyskinesia. Another possibility is the spontaneous remission of tardive dyskinesia after withdrawal of haloperidol and risperidone. However, improvement in tardive dyskinesia has generally been seen over long periods of time, whereas early exacerbation of dyskinetic movements can occur after withdrawal from the offending agent.[10] A long-term drug-free observation would have been necessary to clarify whether the improvement occurred because of the addition of olanzapine or the withdrawal of haloperidol and risperidone. A remote possibility is that olanzapine has an active therapeutic effect in tardive dyskinesia, as is reported with clozapine.[4] Because olanzapine has a molecular structure and receptor profile closure similar to those of clozapine,[11] it may have a similar effect. However, confirming such an effect would require long-term administration of olanzapine before attempting withdrawal of olanzapine to observe the recurrence of dyskinetic movements.

Because this is a report of only 2 cases, its findings cannot be generalized. Further study is needed to determine the effectiveness of olanzapine in the treatment of tardive dyskinesia.

References

1. Glazer WM, Morgenstern H, Doucette JT. Predicting the long-term risk of tardive dyskinesia in outpatients maintained on neuroleptic medications. J Clin Psychiatry 1993;54:133–139
2. Glazer WM. Expected incidence of tardive dyskinesia associated with atypical antipsychotics. J Clin Psychiatry 2000;61(suppl 4):21–26
3. Lieberman JA, Saltz BL, John CA, et al. The effect of clozapine on tardive dyskinesia. Br J Psychiatry 1991;158:503–510
4. Tamminga CA, Thaker GK, Moran M, et al. Clozapine in tardive dyskinesia: observation from human and animal studies. J Clin Psychiatry 1994;55(9, suppl B):102–106
5. Chouinard G. Effect of risperidone in tardive dyskinesia: an analysis of the Canadian Multicenter Risperidone Study. J Clin Psychopharmacol 1995;15(suppl 1):36–44
6. Almeida OP. Olanzapine for the treatment of tardive dyskinesia [letter]. J Clin Psychiatry 1998;59:380–381
7. Littrell KH, Johnson CG, Littrell S, et al. Marked reduction of tardive dyskinesia with olanzapine [letter]. Arch Gen Psychiatry 1998;5: 279–280
8. O'Brien J, Barber R. Marked improvement in tardive dyskinesia following treatment with olanzapine in an elderly subject [letter]. Br J Psychiatry 1998;172:186
9. Khan M, Farver D. Rapid resolution of antipsychotic induced tardive dyskinesia with olanzapine. S D J Med 2000;53:65–67
10. Dixon L, Thaker G, Conley R, et al. Changes in psychopathology and tardive dyskinesia after neuroleptic withdrawal in a double design. Schizophr Res 1993;10:267–271
11. Reus VI. Olanzapine: a novel atypical neuroleptic agent. Lancet 1997;349:1264–1265. Correction 1997;350:372

Vivek Agarwal, M.D.
Parvesh Kumar, M.D.
Institute of Human Behaviour and Allied Sciences
Delhi, India