Letters to the Editor

Combined Transcranial Magnetic Stimulation and Right Unilateral Electroconvulsive Therapy in Patients With Treatment-Refractory Depression

Dear Editor: Treating patients with refractory depression is a common challenge for psychiatrists. There are several reasons for this. First, a substantial portion of patients starting pharmacologic treatment either fail to respond or cannot tolerate the drug (1,2). Even among responders to antidepressants, residual symptoms are common (3) and have been shown to be associated with a greater likelihood of relapse and a poorer prognosis (4).

Although combination and augmentation treatments are useful in patients with resistant depression (5,6), over one-third do not benefit from multiple combination. The addition of electroconvulsive therapy (ECT), still considered to be the treatment of choice for severe depression, alone or with other pharmacologic agents, leaves 40% of patients with marked depressive symptomatology (7,8).

Transcranial magnetic stimulation (TMS) has been shown to improve depressive symptoms both in uncontrolled (9,10) and in sham-controlled studies (11,12). Pridmore substituted rapid TMS treatments for right unilateral (RUL) ECTs, showing that the TMS-substituted group did as well as the group that continued to receive ECT (13).

We describe below the first successful use of combined RUL ECT and bilateral TMS.

Case Report

The patient is a woman, aged 39 years, referred to the mood disorders service for treatment resistance. Under our care, she received adequate trials with serzone; clomipramine augmented by cytoxen, lithium, and risperidone; phenelzine; parnate up to 100 mg daily augmented by quetiapine; mirtazapine with topiramate and lithium; fluoxetine and tryptophan; nortriptyline; and citalopram augmented by lamotrigine. A full course of bifrontal ECT was associated with severe cognitive disturbances and only partial response.

Our patient, who had shown a partial response when participating in a bilateral TMS study, was offered an open trial of combination and bilateral TMS.

At the start of treatments, her Hamilton Depression Rating Scale (HDRS) and Beck Depression Inventory (BDI) scores were 35 and 55, respectively. On Mondays, Wednesdays, and Fridays, she received 10 ECTs (RUL placement, pulse width 1.0 ms, 60 to 90 Hz, 3 to 4 seconds, and 800 mamp with Mecta [Tualatin, Oregon: Customs Systems Associates]). On Tuesdays and Thursdays, she received high-frequency TMS (that is, 20 trains of 12 Hz stimulation with a train of 8 seconds at 110% of motor threshold) over the left prefrontal cortex and low frequency (that is, 2 trains of 1 Hz stimulation with a train duration of 60 seconds and an intertrain interval of 3 minutes) over the right cortex. At the end of our course, her depression remitted, with HDRS and BDI scores dropping to 4 and 11, respectively. She was discharged home. Her Mini-Mental Status Exam Score was 28 out of 30.

Discussion

Despite the advances in treatment of depression, 10% to 30% of all depression patients remain refractory to treatment. Although ECT is still considered the treatment of choice for severe depression, there is no consensus or guideline suggesting the next steps for patients who do not tolerate or do not respond to a course of ECT. We are therefore describing a treatment-refractory patient with depression who obtained full remission for the first time with a combined treatment of ECT and TMS. The combined treatments were well tolerated.

References


G Abraham, MD, FRCPC
Kingston, Ontario

Re: Treatment Noncompliance With Orally Disintegrating Olanzapine Tablets

Dear Editor: Dr Freudenreich reported on the case of a woman, aged 52 years, with chronic schizophrenia and covert noncompliance with the orally disintegrating formulation of olanzapine (1). The patient was able to “cheek” the medication wafer behind her front teeth near the gum line. Consequently, no clinical improvement was observed. Once this was discovered, the patient was placed on haloperidol decanoate. Dr Freudenreich concluded that fast-dissolving medication is no substitute for parenteral medication.

Although adherence to medication is an important concern, parenteral medication is not always the answer. Treatment compliance to haloperidol decanoate is not guaranteed if the patient fails to attend clinic appointments. Moreover, haloperidol is inferior in terms of effects on negative symptoms, cognition, and mood, compared with atypical antipsychotics (2). It is possible that, by persisting with a treatment course of an atypical antipsychotic, improvements in overall well-being, including cognition and mood, may lead to improved insight and a better functional outcome.

We have also observed the “cheek” of olanzapine wafers in a small minority of
patients. One patient placed the wafer on top of a rear molar, allowing for the surreptitious removal of the agent a few minutes later. Another method is to place a small piece of tissue or paper towel in the mouth, placing the wafer on top of this barrier. All methods can be easily managed by having the patient swish and swallow water after administering the medication. The characteristics of the wafer make it impossible for “cheeking” to occur, compared with regular pills or capsules.

References


Leslie Citrome, MD, MPH
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Reply: Treatment Noncompliance With Orally Disintegrating Olanzapine Tablets

My letter describing a patient with olanzapine wafer noncompliance had one purpose: to alert clinicians to the possibility of “cheeking” wafers. Dr Citrome describes 2 more “cheeking” techniques and offers an easy remedy. I did not suggest that parental drug administration is always (or even usually) the answer to medication non-adherence. I agree with Dr Citrome that persistence with oral atypical antipsychotics (ensuring swishing and swallowing) is preferable to forced parenteral haloperidol, particularly if it leads to a better outcome.

In some cases, however, benefit might never materialize from the patient’s perspective, regardless of the medication administered or the route of administration and regardless of clinical response by objective criteria. How prudent and promising is it to insist on repeating daily the drama of drug administration with its checks and obvious coercive element? I would argue that a fail-safe route of infrequent drug administration (for example, with intramuscular haloperidol decanoate) should remain an option to stabilize patients who have little insight into drug benefit. There is no question that these patients present us with complex issues regarding competency, civil rights, and our duties as physicians.

Oliver Freudenreich, MD
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Quetiapine in the Management of Psychosis Secondary to Huntington’s Disease: A Case Report

Dear Editor: Psychiatric disorders are common in patients with Huntington’s disease (HD) and include mood disorders, anxiety, sexual dysfunction, and psychosis (1–3). Although up to 23% of patients with HD have psychotic symptoms (3), the literature regarding management of psychosis secondary to HD is limited to case reports or series. Agents reported to be effective in the management of HD psychosis include clozapine (4), risperidone (5), and olanzapine (6,7). Recent reports indicate that olanzapine (7) and quetiapine (8) may also improve the motor symptoms of HD. However, to our knowledge, no reports exist describing the efficacy of quetiapine in managing psychotic symptoms associated with HD. We describe the first report of quetiapine in the management of psychosis caused by HD.

Mr A, aged 43 years, has a history of HD and psychosis and was admitted to hospital for management of a psychiatric episode. Prior to admission, the patient’s community treatment team observed that he was not eating, was unable to care for himself, and was experiencing paranoid delusions. He was diagnosed with HD 16 years prior, and his family history was positive for HD. Past treatment of his psychosis included chlorpromazine, haloperidol, lithium, olanzapine, and benzodiazepines. We began treatment with olanzapine, titrating to 20 mg daily.

Olanzapine blood levels were 91 nmol/L at 15 mg daily. Unfortunately, Mr A experienced side effects while taking olanzapine, and his psychosis was poorly controlled. It was decided to discontinue olanzapine, and quetiapine was titrated up to 300 mg daily, while the dosage of olanzapine was tapered over the course of 1 week. We evaluated baseline psychiatric symptomatology, using the Positive and Negative Syndrome Scale (PANSS), on the first day of quetiapine-only therapy and at 8 weeks of quetiapine-only therapy. We evaluated extrapyramidal symptoms (EPS) initially and at 8 weeks, using the Extrapyramidal Symptom Rating Scale (ESRS) (9).

Initially, the total PANSS score was 68, with subsection scores of 19, 12, and 37 on the positive, negative, and general psychopathology subscales, respectively, at a quetiapine dosage of 300 mg daily. At the start of our study period, the ESRS score was 6. At 8 weeks, the total PANSS score was 53, with subsection scores of 12, 12, and 29 on the positive, negative, and general psychopathology scales, at a quetiapine dosage of 500 mg daily. At 8 weeks, the ESRS score was 12. Serum quetiapine levels at the end of our study were 384 nmol/L. Despite the increase in EPS, Mr A felt subjectively better during quetiapine therapy, compared with olanzapine therapy. Quetiapine appears to be effective in treating the positive symptoms of HD psychosis, with little effect on negative symptomatology. The potential worsening of EPS during quetiapine therapy in HD patients warrants caution in its use, and we suggest careful monitoring for EPS to minimize the impact of these side effects while treating psychotic symptoms. Further large-scale studies are required to evaluate the efficacy of quetiapine in the management of psychosis in HD.

References


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Ziprasidone-Induced Lupus Erythematosus

Dear Editor: Ziprasidone is a novel atypical antipsychotic medication that presumably exerts its antipsychotic effects through antagonism of 5-HT2 and D2 receptors (1). Drug-induced lupus erythematosus (DILE) has been documented to occur with the administration of several medications (2). To our knowledge, there have been no reported cases of DILE associated with ziprasidone. Here, we report a case of DILE in an individual receiving ziprasidone.

References


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Lorazepam-Induced Prolongation of the QT Interval in a Patient With Schizoaffective Disorder and Complete AV Block

Dear Editor:

A wide range of noncardiovascular-therapeutic agents have been shown to prolong the QT interval. The large scope of this problem has created an issue for drug developers and health authorities and is of critical importance for attending physicians. The noncardiac agents associated with QT prolongation belong to many different pharmacologic classes, including psychotropic drugs, prokinetic medicines, antimalarial medicines, antibiotics belonging to several different chemical classes, antifungal agents, and nonnarcotic antiasthmatics. In many cases, psychotropic drugs, particularly tricyclic antidepressants and antipsychotic agents, are correlated with iatrogenic prolongation of the QT interval of the ECG. This is associated with dangerous polymorphic ventricular tachyarrhythmias in syndrome de points and sudden death. In addition to the ventricular conduction time, the QT interval of the ECG reflects the duration of the ventricular action potential (AP) at the cellular level. Thus, the prolongation of the QT interval may reflect effects on ion channels involved in ventricular AP generation. However, the QT interval also depends on the heart rate, and therefore, the determination of QT prolongation in patients is usually measured using the heart-rate corrected QT interval. Vulnerability to medication-induced prolongation of the QT interval may also reside in the patient, with respect to the underlying psychiatric diagnosis, any underlying medical illness (especially cardiovascular disease), genetic predisposition to drug-induced QT prolongation, and patient age. The interactions between different psychotropic drugs used in combination or used with other medications that have known effects on the cardiovascular system may also lead to QT prolongation and risk of arrhythmia. QT prolongation duringlorazepam therapy has not been documented in the literature. We present a case of lorazepam-induced severe QT prolongation.

Case report

A woman, aged 40 years, with an acute schizomaniac episode, a third-degree atrioventricular (AV) block, and cardiovascular disease meeting ICD-10 criteria was admitted to our psychiatric hospital. The ECG showed the complete AV block (heart rate 45 bpm, QT interval 394 ms), and the blood tests revealed abnormal findings (elevated creatine kinase and creatine kinase-MB isoenzyme, normal troponin I, and elevated liver enzymes). The electroencephalogram and the brain CT revealed no abnormal findings. Because of the severe symptoms, psychopharmacotherapy with 12.5 mg quetiapine, 100 mg trimipramine, 40 mg pipamperone, and 5 mg diazepam daily was started. The psychopharmacotherapy had no influence on the QT interval. At day 6, 0.5 mg lorazepam was given 3 times, inducing QT prolongation up to 580 ms. Psychopharmacotherapy was discontinued, and the patient was admitted to the medical department for 1 day. The QT prolongation persisted for 7 days, and according to the international treatment criteria, the insertion of a cardiac pacemaker was mandatory. On day 16, a permanent cardiac pacemaker with dual-chamber pacing (that is, DDD mode) was implanted. Afterwards, a sophisticated psychopharmacotherapeutic regimen was established, and the patient responded to the therapy.

In this case, we found a constellation of putative risk factors for the development of QT prolongation. We hypothesize that lorazepam induced the QT prolongation. For a given medication, arrhythmogenic risk must be understood to be partially mechanistically dependent on vulnerability intrinsic to the individual patient with regard to the particular drug. We suggest cautious use of psychotropic drugs in patients with risk factors.

References


Marc Ziegenbein, MD; Stefan Kropp, MD Hanover, Germany

Rheumatology and dermatology consultations were obtained. Both consultants felt that she was likely suffering a reaction to the ziprasidone, rather than a connective tissue disease. Serum autoantibodies, rheumatoid factor, erythrocyte sedimentation rate (sed rate), and punch biopsy were obtained to evaluate the rash. Results of serum tests showed a slightly elevated sed rate at 45 mm/Hr and a positive result for SS-A/Ro autoantibodies at 162.7. Other serum autoantibodies used as markers for drug-induced lupus were negative. Results of punch biopsy with consistent with a drug-induced rash caused by type 3 or 4 hypersensitivity reaction. A literature search on the other medications currently under the scope of this problem has created an issue for drug developers and health authorities but is of critical importance for attending physicians. The noncardiac agents associated with QT prolongation belong to many different pharmacologic classes, including psychotropic drugs, prokinetic medicines, antimalarial medicines, antibiotics belonging to several different chemical classes, antifungal agents, and nonnarcotic antiasthmatics. In many cases, psychotropic drugs, particularly tricyclic antidepressants and antipsychotic agents, are correlated with iatrogenic prolongation of the QT interval of the ECG. This is associated with dangerous polymorphic ventricular tachyarrhythmias in syndrome de points and sudden death. In addition to the ventricular conduction time, the QT interval of the ECG reflects the duration of the ventricular action potential (AP) at the cellular level. Thus, the prolongation of the QT interval may reflect effects on ion channels involved in ventricular AP generation. However, the QT interval also depends on the heart rate, and therefore, the determination of QT prolongation in patients is usually measured using the heart-rate corrected QT interval. Vulnerability to medication-induced prolongation of the QT interval may also reside in the patient, with respect to the underlying psychiatric diagnosis, any underlying medical illness (especially cardiovascular disease), genetic predisposition to drug-induced QT prolongation, and patient age. The interactions between different psychotropic drugs used in combination or used with other medications that have known effects on the cardiovascular system may also lead to QT prolongation and risk of arrhythmia. QT prolongation duringlorazepam therapy has not been documented in the literature. We present a case of lorazepam-induced severe QT prolongation.

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References


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