Letters to the Editor

Biological Factors and Adolescent Alcohol Use

Dear Editor:

Several papers on the effect of psychosocial factors on adolescent alcohol use have been published over the past several years. Undoubtedly, psychosocial influences play an important part in alcohol use. However, biological factors and their interaction with environmental factors also play an important role in the development of alcohol use disorders in adolescents.

Alcohol misuse tends to run in families, and it is estimated that 40% to 60% of the variance in risk is explained by genetic influences (1,2). Numerous well-designed twin and adoption studies have demonstrated that genetic factors are important in determining vulnerability to alcoholism (3–5). Children of patients with alcohol dependence are 5 times more likely to develop alcohol-related problems than are children of nonalcohol-dependent individuals (6,7). There is a tendency for people who misuse alcohol to marry individuals who also abuse alcohol (assortative mating) (8). Thus, many adolescent alcohol misusers are from families with a high proportion of alcohol abuse or dependence. Some of these adolescents were exposed to alcohol in utero. Familial loading for alcohol dependence is a risk factor for developing psychiatric and neurological disorders in children and adolescents (9,10). A recent study suggests that offspring from families with a high proportion of alcoholism differ in both neuroanatomical and neurophysiological characteristics. These differences could not be explained by a personal history of alcohol consumption or by specific childhood or adolescent psychopathology (10). Ethanol use during adolescence may disrupt maturational processes in certain brain regions (11). Dopamine projection regions, for example, are undergoing developmental change during adolescence (11). The importance of dopaminergic mechanisms in the biology of alcohol-induced award is well known (12–14). Withdrawal from alcohol is associated with decreased firing of dopaminergic neurons in the ventral tegmental area and decreased dopamine release in the nucleus accumbens (15).

In summary, genetic, developmental, and acquired biological factors affect adolescent alcohol use. Many adolescent drinkers have subtle or overt developmental deficits or psychiatric disorders that require appropriate treatments. Further studies of the role of biological factors in initiation and continuation of adolescent alcohol use are necessary.

References


Leo Sher, MD
New York, New York

Minor Strokes Related to Paroxetine Discontinuation in an Elderly Subject: Emergent Adverse Events

Dear Editor:

Abrupt interruption of extended treatment with selective serotonin reuptake inhibitors (SSRIs) may lead to the emergence of discontinuation syndrome. SSRI discontinuation syndrome may manifest with diverse psychological and physical symptoms, including dizziness, shock-like sensory symptoms, anxiety, irritability, agitation, insomnia, and depression (1). Stroke-like neurological symptoms have been reported in 2 patients who developed severe SSRl-induced discontinuation syndrome (2). However, this is the first report that illustrates an elderly man with cerebrovascular disease developing minor strokes following abrupt discontinuation of long-term paroxetine treatment.

Case Report

Mr A, aged 67 years, had chronic depression. He was investigated for dementia secondary to cerebrovascular disease because he developed memory deficits in the background of type 2 diabetes mellitus, hypertension, and coronary artery disease. He was diagnosed with recurrent major depression over 10 years ago and remained normothymic on long-term maintenance treatment with paroxetine 40 mg daily. Review of his history suggested that he had developed minor strokes involving vertebralbasilar artery territory on 2 occasions following abrupt discontinuation of paroxetine. On the first occasion, 24 to 48 hours after...
accidentally stopping paroxetine treatment, he became anxious, agitated, irritable, confused, showing severe gait ataxia and bilateral motor weakness. He was admitted to a tertiary care hospital and investigated for vertebrobasilar insufficiency. Magnetic resonance imaging (MRI) showed extensive hyperintense T2 signal foci within cerebrum white matter, as well as in the left pons, suggesting nonspecific small-vessel ischemic disease. Magnetic resonance angiography revealed mild occlusion or hypoplasia of the right A1 segment of the anterior cerebral artery.

His blood pressure was elevated to 150/100 mm Hg. The symptoms of agitation, anxiety, insomnia, gait ataxia, and bilateral motor weakness were cleared 24 to 48 hours after paroxetine treatment was reinstalled at the previous dosage. Four months later, his cardiologist abruptly discontinued paroxetine treatment, owing to potential anticholinergic and cardiac side effects. The patient was readmitted to the same tertiary hospital with anxiety, agitation, confusion, gait ataxia, and bilateral motor weakness. A repeat MRI showed no progression in cortical white matter and pontine ischemic changes. The discontinuation symptoms, ataxia, and motor weakness resolved within 48 hours after the reintroduction of paroxetine treatment at the previous dosage. Because vertebrobasilar insufficiency lasted for more than 24 hours and brain parenchyma might be irreversibly altered owing to prolonged ischemic attack, the diagnosis of ministroke involving vertebrobasilar territory was considered.

Discussion
The emergence of anxiety, agitation, and insomnia within 24 to 48 hours of abrupt discontinuation of paroxetine maintenance treatment and the resolution of these symptoms after reinstarting the previous paroxetine treatment concurs with the diagnosis of SSRI discontinuation syndrome (1). This patient suffered minor strokes involving vertebrobasilar territory, as determined by neurological investigations and stroke neurologists. Hence, in this patient manifested ataxia and motor weakness during a discontinuation phase may indicate minor stroke involving vertebrobasilar territory, rather than the physical symptoms of discontinuation syndrome. Moreover, in the presence of cerebrovascular disease, ataxia and motor weakness could not be considered as discontinuation symptoms. Further, since there was a temporal relation between the onset of minor strokes and the discontinuation of paroxetine treatment on both occasions, it is unlikely that these minor strokes were just coincidental manifestations of the underlying cerebrovascular disease. The possibilities of SSRI treatment–associated cerebrovascular bleeding and vasoconstrictive stroke may be irrelevant: this patient developed minor strokes after the discontinuation of paroxetine maintenance treatment (3,4).

Paroxetine has been frequently implicated in SSRI discontinuation syndrome, owing to its short half-life (5). Cholinergic overdrive activating monoaminergic systems, coupled with hyperserotonergic state after the discontinuation of paroxetine treatment, may be responsible for discontinuation symptoms (6,7). Elevated blood pressure and a possible decrease in cerebrovascular reserve because of activation of catecholamines and resulting anxiety during discontinuation syndrome might have contributed to minor strokes in this patient (8,9). Given the possibility of cerebrovascular events as consequences to anxiety and agitation during discontinuation syndrome, it is imperative to minimize discontinuation symptoms by slowly tapering SSRI treatment in elderly subjects with cerebrovascular disease.

References

Rajamannar Ramasubbu MD, FRCPC
Calgary, Alberta

Quetiapine Reduces Flashbacks in Chronic Posttraumatic Stress Disorder

Dear Editor:

Chronic posttraumatic stress disorder (PTSD) is a severe and resistant disorder involving complex symptom clusters and comorbid psychiatric diagnoses that often respond poorly to antidepressants (1–3). Combination therapy is almost always necessary, with antidepressants associated with mood stabilizers and, more recently, with atypical antipsychotics, for which there are preliminary efficacy data (3–13).

We treated 5 patients with chronic PTSD: 3 men with PTSD after Bosnia missions some 10 years ago and 2 women, 1 of whom was physically attacked by her husband during their divorce 2 years earlier and 1 of whom was raped by a stranger.

All 5 patients had already been treated with combination therapy using selective serotonin reuptake inhibitors (SSRIs) or venlafaxine plus gabapentin, and 1 patient had been prescribed lamotrigine. This last patient was the only one who presented with psychotic symptoms. All patients had seen an improvement in anxiety, aggressivity, and sleep but were still haunted by flashbacks.

Quetiapine was gradually added to their regimen, up to 150 mg or 200 mg daily, and all 4 patients noted a dramatic reduction in their diurnal flashbacks, without excessive sedation. The flashbacks, which occurred many times daily, became much less frequent, happening only a few times (or fewer) weekly. In all 5 patients, we were able to gradually

Dear Editor:

Quetiapine Reduces Flashbacks in Chronic Posttraumatic Stress Disorder

Chronic posttraumatic stress disorder (PTSD) is a severe and resistant disorder involving complex symptom clusters and comorbid psychiatric diagnoses that often respond poorly to antidepressants (1–3). Combination therapy is almost always necessary, with antidepressants associated with mood stabilizers and, more recently, with atypical antipsychotics, for which there are preliminary efficacy data (3–13).

We treated 5 patients with chronic PTSD: 3 men with PTSD after Bosnia missions some 10 years ago and 2 women, 1 of whom was physically attacked by her husband during their divorce 2 years earlier and 1 of whom was raped by a stranger.

All 5 patients had already been treated with combination therapy using selective serotonin reuptake inhibitors (SSRIs) or venlafaxine plus gabapentin, and 1 patient had been prescribed lamotrigine. This last patient was the only one who presented with psychotic symptoms. All patients had seen an improvement in anxiety, aggressivity, and sleep but were still haunted by flashbacks.

Quetiapine was gradually added to their regimen, up to 150 mg or 200 mg daily, and all 4 patients noted a dramatic reduction in their diurnal flashbacks, without excessive sedation. The flashbacks, which occurred many times daily, became much less frequent, happening only a few times (or fewer) weekly. In all 5 patients, we were able to gradually
reduce gabapentin, and in 3 of the 5 patients, we stopped it completely.

Chronic PTSD is now commonly treated with combination therapy. Atypical antipsychotics seem very popular as adjunctive agents in this disabling disorder (4). Still, there are few controlled data to support this practice.

In several case reports, risperidone has shown efficacy in treating flashbacks and other intrusive symptoms that relate to traumatic events, as well as in treating irritable aggression (5–8). One controlled study with risperidone targeted psychotic features in combat veterans with chronic PTSD. In this trial, positive and negative psychotic symptoms improved, compared with the placebo group, but core PTSD symptoms measured by total Clinician Administered PTSD Scale (CAPS) score did not differ from those in the placebo group (9).

Another small controlled trial with olanzapine (15 civilians randomized to monotherapy or placebo), did not differentiate the active drug from the placebo, although an open-label study suggested benefits for olanzapine in 48 veterans with chronic PTSD (10,11). In this last study, however, one-third of subjects failed to complete the trial, largely because of adverse events or noncompliance (11).

A case report found clozapine useful in a treatment-refractory patient with combat-associated PTSD and psychosis (12).

With respect to using quetiapine as an adjunctive treatment, Hamner and others completed an open-label trial in 20 refractory patients with PTSD, and the results are encouraging. The average dosage of quetiapine was 100 mg daily, with a range of 25 mg to 300 mg daily. Patients experienced improved sleep and a reduction in the frequency and intensity of nightmares. The total CAPS rating and the symptom clusters were also significantly improved by quetiapine (13).

In our experience, quetiapine adjunctive treatment has reduced flashbacks in 5 chronically affected PTSD patients—flashbacks being one of the core and most painful symptoms in PTSD.

Use of quetiapine as adjunctive treatment and monotherapy for PTSD needs assessment in well-designed clinical trials with larger samples, because it may represent an interesting treatment option in PTSD.

References

Marie-Josée Filteau, MD, FRCPC; Jacinthe Leblanc, Pharm, BCPP; Roch-Hugo Bouchard, MD, FRCPC Quebec City, Quebec

Behaviour Therapy for Dizziness?

A woman in her mid-30s presented with recurrent, unexplained dizziness. Two years prior to presentation, she had a 3- to 4-hour period of dizziness, nausea, and vomiting. She saw her family doctor and was told that she had a viral illness, but since then, she has become fearful of further episodes of dizziness. When she felt dizzy, she immobilized her head and neck for several hours until the feeling of dizziness disappeared. She saw numerous physicians who performed many investigations to rule out medical conditions. She was quite distressed about these episodes and had significant anticipatory anxiety with respect to the dizziness. She had decreased functioning at her work because of dizziness. However, she did not meet criteria for panic attacks. Otherwise, she was healthy and had no other psychiatric or medical comorbidity. She did not take any medications. There was no family history of anxiety problems.

The diagnosis of limited-symptom panic disorder was the best explanation for this presentation. Although pharmacotherapy (that is, a serotonin reuptake inhibitor [SRI]) was considered, this treatment modality was avoided, owing to the sensitivity of patients with panic disorder to side effects of antidepressants and to this woman’s limited-symptom panic attacks.

She was treated with 4 individual sessions, using exposure and response prevention. In the first 2 sessions, it was explained to the patient that she had developed fear of the dizziness sensation through classic conditioning. The more she tried to avoid the sensation, the more sensitive she had become to any head movement that resulted in slight dizziness sensations. She was asked to gradually expose herself to the dizziness sensation by spinning around for 30 to 60 seconds daily. She responded well to the systematic desensitization, with no further episodes of dizziness. She was followed for 6 months and maintained her improvement.

Dizziness that is unrelated to a medical condition is a common problem in the population (1–3) and is associated with significant disability and high rates of medical services use (4,5). Recent studies have demonstrated that a significant proportion of persons with unexplained dizziness have an underlying anxiety disorder diagnosis (6,7). Recognition and treatment of this problem is likely to reduce disability and costs to society. A recent open-label trial confirmed that most people with psychogenic dizziness respond to treatment with an SRI antidepressant (8). Of the sample in this study, however, 25% stopped the antidepressant because of adverse effects (8). With respect to nonpharmacologic strategies, data support behaviour therapy and vestibular rehabilitation as similar and
effective in treating psychiatric dizziness (9–11). The problem with cognitive-behavioural therapy is the lack of availability of trained clinicians to conduct this treatment.

This case highlights 2 important issues: 1) individuals presenting with dizziness who do not meet the full criteria for panic attacks may be underrecognized and undertreated or delayed in receiving treatment, and 2) the feasibility of applying brief behavioural interventions in primary care and otolaryngology clinics should be further explored (12).

References

Case Report
FD is a 35-year-old single, childless white woman on social assistance. Her extensive psychiatric history began at age 14 years with the diagnosis of panic disorder. Anorexia nervosa was diagnosed 2 years later but soon revised to bulimia nervosa. At age 17 years, bipolar affective disorder type I was added. FD also engages in polydipsia, consuming as much as 84 cans of cola during a weekend. This has been manifested independently of bulimia. A borderline level of integration underlies her histrionic and narcissistic behaviour.

FD’s family is highly enmeshed. Her father retired early from farming, owing to his rheumatoid arthritis and his struggle with alcoholism. Her mother was a nurse and worked night shifts so she could “babysit” FD’s father. Prestigious awards for academic brilliance and ballet dancing marked FD’s early development. However, she pursued high marks as an end. FD once admitted that, in Grade 3, she injured her foot deliberately to be excused from a rare slip in her marks. Corresponding documentation indicates that the orthopedic surgeon found FD had changing symptoms, which he attributed to chronic ankle strain. She was unable to complete the second year of university or maintain employment for more than a few months. Clinical records aside, FD’s charts are littered with writings that discuss her engrossment with the pursuit of youth, beauty, and prestige. They reflect frequent resort to denial, to acting out, to externalization, and to intellectualization, as well as to erotic transference to male psychiatrists. Subtle suggestions of deception abound. In fact, in one letter, she detailed reasons for maintaining her bulimia, one of which was the freedom from responsibility.

Her medical records show 91 hospitalizations between 1981 and 2001. FD was certified for at least part of 30 admissions. There were numerous examples of noncompliance and of premature discharges against medical advice, many of which were facilitated by her mother. Hospital fees alone totalled $1.6 million, overshadowing the costs of other health care use, including her 175 emergency room visits that did not lead to admission. Inconsistencies on several levels insinuate a factitious component in FD’s presentation: 1) her frequent calls for attention to her symptoms contrast sharply with her habitual defences; 2) rarely does one encounter a patient with bulimia who frequents the emergency room demanding specific blood work and intravenous therapy; and most informative, 3) mental status examinations contradicted her complaints on many occasions.

It seems paradoxical to apply long-term certification in treating a patient with factitious disorder. FD’s case, however, is complicated by comorbidity with Axis I diagnoses. Periods of relative stability followed previous involuntary hospitalizations. Lasting gains are likely possible only in a setting where her treatment cannot be sabotaged by her impulsivity and her mother’s interference. The outcome remains to be evaluated.

Bienia Lau, Resident
Saskatoon, Saskatchewan

Eugene Marcoux, Consultant
Saskatoon, Saskatchewan