Letters to the Editor

Mirtazapine for Treatment of Nausea Induced by Selective Serotonin Reuptake Inhibitors

Dear Editor: Nausea appears to be a dosage-related side effect in as many as 26% of patients treated with selective serotonin reuptake inhibitors (SSRIs) (1,2). SSRIs increase the concentration of serotonin (5-HT) at neuronal synapses. Emesis may result from subsequent activation of central or peripheral 5-HT3 receptors (2,3). Antagonism of 5-HT3 by drugs like ondansetron is known to reduce emesis in chemotherapy patients and may have some application in SSRI-induced nausea, but the effect is short-lived and the cost is prohibitive (2,3).

The 5-HT antagonist cyproheptadine may have some efficacy for SSRI-induced nausea, but it has been associated with worsening of depressive symptoms when used to treat SSRI-induced sexual dysfunction (4). The antidepressant mirtazapine, an antagonist at presynaptic alpha 2 adrenergic inhibitory autoreceptors and heteroreceptors (where it enhances noradrenergic and serotonergic activity), is also a potent antagonist of 5-HT2 and 5-HT3 receptors (5). We report a case of SSRI-induced nausea successfully treated with mirtazapine.

Case Report

Ms K, aged 46 years, is a single white woman who has suffered for 10 years from a recurrent unipolar major depressive disorder associated with insomnia; she also suffers from obsessive–compulsive disorder (OCD). For the last 3 years, her symptoms have been partly controlled with sertraline 300 mg daily, bupropion slow release 150 mg twice daily, and trazodone 100 mg at bedtime. During treatment, she experienced recurring episodes of nausea associated with the administration of SSRIs. With sertraline, the nausea was partly controlled by her taking the dosage in 100 mg increments 3 times daily, approximately one-third of the way into a meal. Despite these efforts, her symptoms were occasionally sufficient to cause projectile vomiting, which forced her to reduce her total daily dosage. Attempts to decrease the sertraline dosage permanently increased her OCD symptoms.

To control her nausea, mirtazapine 15 mg at bedtime was substituted for trazodone. Nausea symptoms decreased the day after starting mirtazapine and completely disappeared within 4 days. However, she had difficulty sleeping and had to restart her trazodone. The combination of mirtazapine and trazodone left her with excess daytime sedation plus restless legs when falling asleep. Mirtazapine was subsequently discontinued, and her nausea returned within 4 days.

Resumption of mirtazapine 15 mg at bedtime once more relieved all nausea. Replacement of trazodone with clonazepam 0.5 mg at bedtime allowed her to have a good sleep with no daytime sedation and no restless legs.

Discussion

We describe a patient who experienced resolution of SSRI-induced nausea with low-dosage mirtazapine. The use of this agent to control nausea associated with SSRIs was first discussed by Pedersen and others in 1997 (6). In their report, 3 patients experienced relief of nausea approximately 2 to 3 days after the addition of mirtazapine 15 mg daily. In 2 patients, nausea resumed when mirtazapine was discontinued and lessened when it was restarted. We observed a similar pattern in our case.

References


Estratios V Caldis, MB, ChB, FRCPCP Robert D Gair, BSc (Pharm)

Vancouver, British Columbia

Effects of Propofol on Electroconvulsive Therapy Seizure Duration

Dear Editor: Propofol is an anesthetic agent alternative to methohexital. It is widely used because it is associated with smaller hemodynamic response during electroconvulsive therapy (ECT) (1). Studies have shown that propofol reduces seizure duration, and reports of reduced seizure duration with ECT under propofol anesthesia have led to concerns that propofol may diminish the efficacy of this treatment (2,3). However, although propofol has been associated with shorter seizures when given for ECT anesthesia, the reduced seizure duration has not been associated with smaller therapeutic effect when compared with methohexital anesthesia (4,5).

We compared the effects of propofol on seizure duration with ECTs performed without anesthesia. We retrospectively studied 26 patients consecutively referred for ECT. All patients were hospitalized and treated in Trakya University Psychiatry Clinic, Edirne, Turkey, between January 1, 2001, and December 31, 2003. Until March 2002, ECT treatments in this clinic were performed without anesthesia. Of the 26 patients, 15 had ECT treatments under anesthesia, and 11 had treatments without anesthesia. Propofol was used as an anesthetic agent and succinylcholine was used as a muscle relaxant in the 15 patients who received anesthesia. Patients in both groups were treated with the same ECT machine (Thymatron TM DGx, Somatics Inc, Lake Bluff, IL). Bilateral electrode placement was applied for all patients. Seizure duration measurements were based on the machine’s automated seizure duration determinations. The groups were compared without taking into consideration the patients’ diagnosis, the drugs that they used, or their psychiatric outcomes.

Results

The groups were similar in terms of sex and mean age. Major depression was the most frequent diagnosis in both groups. The number of ECT treatments in the propofol anesthesia group (mean 9.67, SD 2.99) did not differ significantly from the nonanesthesia group.
When the seizure durations were compared, seizure duration was longer in the propofol anesthesia group (mean 44.38, SD 14.52) than in the nonanesthesia group (mean 39.45, SD 3.47). However, this difference was not significant ($t = 1.26, P = 0.22$). Mean (SD) propofol dosage was 98.68 (4.48) mg. We found no linear correlation between the propofol dosage and seizure duration ($r = 0.24, P = 0.41$). We assessed the effect of both the number of ECTs and having anesthesia on seizure duration; no effects for ECT number ($F_{1,11} = 1.80, P > 0.05$) or patient group ($F = 0.81, P < 0.05$) were revealed, nor was there any significant interaction between the number of ECTs and the patient group ($F_{1,11} = 1.55, P < 0.05$).

**Discussion**

Contrary to previous studies (6–8), we did not find that propofol had any considerable effect on seizure duration. Our study design was different from other studies in that they compared 2 different induction agents (9–11); in our study, seizure durations of patients who received propofol anesthesia were compared with seizure durations of patients who received ECT treatments without anesthesia. Current standards, especially for research purposes, would preclude the use of ECT without anesthesia, but because our study was retrospective, we must assume that this ethical concern was not an issue.

Our study found that propofol did not shorten seizure duration. Although anesthesia with propofol has been associated with shorter ECT seizures, other anesthetic agents used for comparison with the propofol may have affected earlier results. Our study suggests the importance of the control group who received ECTs without anesthesia for comparing the effects of anesthetic agents on seizure duration: results that are more reliable could be obtained and controversial conclusions minimized.

**References**


Okan Caliyurt, MD
Erdal Vardar, MD
Cengiz Tuglu, MD
Ercan Abay, MD
Edirne, Turkey

**Deliberate Ingestion of Peanut as a Suicide Attempt**

**Dear Editor:** I report the case of a man, aged 24 years, with an established history of severe anaphylaxis to peanuts, who deliberately ingested peanut butter as a suicide attempt while admitted to hospital.

The patient was admitted to the psychiatry service for severe depression but had not revealed overt suicidal ideation. His medical history was significant for severe anaphylactic reactivity to peanuts. During his admission, he prepared himself a sandwich that he later admitted was intentionally contaminated with peanut butter. Within 5 minutes of consuming the sandwich, he developed shortness of breath and swelling of the lips and throat, followed by an erythematous, pruritic rash involving his entire body. He was admitted to the emergency department, where he was noted to be tachycardic and hypoxic, with an oxygen saturation of 91% on room air. Immediate treatment included subcutaneous epinephrine 0.3 cc at 1:1000 dilution, intravenous diphenhydramine 50 mg, and intravenous solumedrol 125 mg. His symptoms resolved within 30 minutes, after which he was observed for another 3 1/2 hours.

Later, he acknowledged that the peanut butter ingestion was a deliberate suicide attempt. He was subsequently placed on a suicide watch and denied access to all peanut-containing products.

While there are rare reports of patients with asthma who use their disease as a modality for suicide (either through deliberate avoidance of medications or deliberate induction of a severe attack) (1), no cases are thus far reported of deliberate induction of anaphylactic reactivity.

This is the first reported case of a patient exploiting allergic sensitivity in this manner, demonstrating a possible avenue of suicidal attempt. Upon admission to a psychiatric ward, food allergies should be well-documented; foods with anaphylactic potential should not be accessible to patients.

**Note**

An abstract of this case was previously presented at the Canadian Society of Allergy and Clinical Immunology Meeting; 2002; Quebec (QC).

**References**


Anne K Ellis, MD
Kingston, Ontario

**Postoperative Manic Outburst: A Case Report**

**Dear Editor:** Immediate postoperative psychosis is common after coronary artery bypass grafting (CABG). It is usually short-lived. A clinical profile akin to mania is less common, as most acute postoperative psychoses are hallmarkled either by purposeless agitation or by paranoid features. The following clinical report aims to break some ground on these transient psychic processes to foster better understanding of the psychological issues faced by patients in the immediate postoperative period.

**References**


Case Report
A man, aged 84 years, underwent a scheduled CABG without incident. There was no history of personal or familial psychiatric problems and no history of excessive alcohol intake. On day 1 after surgery, the psychiatric consultant was called to see the patient because he asserted that he was to be filmed. When first seen, the patient was calm and cooperative, the sensorium was clear, and he denied any worries. He displayed a euphoric affect and felt himself to be extraordinarily well. He reported that, when he awoke from anesthesia, he was convinced that he had not been operated upon because he felt no pain and “everything appeared so smooth.” He then said that television crews could film him and that the marvelous medication he had been given should be publicized.

Toward nighttime, he became demanding, wished to leave for home, and was irritable when given instructions to follow regarding his care. He was sleepless the whole night, and his agitation in regard to going home mounted, despite his having received 12 mg of haloperidol. The next day, he opposed any attempts to talk him down, requested that he be discharged, and was more irritable and expansive. He said he could not believe he was still alive and that the operation was such an easy matter that it was almost a miracle. He said that his father had died from heart disease without the benefit of such an operation and that he had known friends that had refused CABG and had died. He denied any worries. He was not sure that he was not dreaming and rambled about someone during the night wanting to set a fire to cover a murder. Within an hour, he was given 20 mg intravenous haloperidol and during the rest of the day received another 18 mg intravenously. Stimulation was kept to a minimum, light was dimmed, and he recovered some sleep. The next morning he awoke rested, was calm, and requested that he be shaved and groomed. He had almost no recall of the previous day, remembering only a strange, dreamy state. He again said how easy it was to go through such an operation. He was transferred to ward care. Later, he admitted that he had had some fear of passing away and was so happy that his surgery went well that he could hardly believe it. His subsequent hospital stay was eventful, and he was discharged home less than a week after surgery.

This report stresses the manic aspect of the short postoperative psychotic flare-up. Such a clinical syndrome should be distinguished from both toxic-organic mania occurring frequently secondary to cerebrovascular lesions (1,2) and secondary mania as described by Krauthammer and Klerman (3), wherein a true manic episode occurs some time after surgery (4,5), physical illness, or drug use, usually after discharge from hospital. The case presented here focuses on the importance of the manic defense in the configuration of immediate postoperative psychosis.

Such a symptomatic pattern meets the clinical aspects of the manic presentation. The clinical triad of elated mood, expansive talking, and increased behavioral activity was present in this case along with a clear sensorium and the absence of significant confusion, purposeless agitation, or important paranoid features accompanied by mistrust. The patient’s elated mood was expressed in the wish to have a television crew film him to publicize the event. The psychiatric consultant equated this to an “anti-necrologic notice”—a major defense against denied death anxiety. Such massive anxiety, experienced soon after awakening from anesthesia, can rarely be expressed as such so early in a patient’s postoperative course; it is either acted upon or formulated in a deluded fashion. The psychological uselessness of such a transient and benign psychotic flare-up can be conceptualized as a kind of fast-track metabolic pathway to reduce excessive anxiety until postoperative experience reassures the patient.

References

François Sirois, MD
Sainte Foy, Quebec

Road Rage: Old Wine in a New Bottle

Dear Editor: In driving research, the debate about the relevance of temperamental factors and psychopathology has a long history. Tillman and Hobbs’ classic 1949 article, “The Accident Prone Automobile Driver,” is the first in the psychiatric literature to describe a link between psychiatric illness and driving problems (1). These researchers recruited 96 drivers who had 4 or more accidents and compared them with accident-free drivers. Clinical evaluation showed that the accident repeaters were “more aggressive, impulsive, resentful of authority and lacking in social responsibility.” The authors coined the phrase, often repeated in the literature, that “a man drives as he lives.” The debate continues.

Smart and others’ timely article “Psychiatric Distress Among Road Rage Victims and Perpetrators” (2) raises several important points regarding underlying psychopathology in this condition. Intermittent explosive disorder is a condition that falls within the impulse-control disorder spectrum. One of the most common categorical diagnoses that underlie impulse-control disorder in adults is attention-deficit hyperactivity disorder (ADHD)—often unrecognized. A good developmental history would usually reveal a childhood diagnosis of this condition. This is significant: the best-documented evidence for psychiatric illness and impulsive driving relates to ADHD (3,4). This differential diagnosis of impulsivity is very important with regard to clinical management. We now have evidence from Cox and others that, in driving simulator studies, stimulant medication significantly improves driving performance by subjects with uncontrolled ADHD, as well as preliminary evidence that stimulants may also improve driving behaviour on the road (5). Jerome and Segal reported on 100 consecutively presenting patients with ADHD (6). Some 80% of these had ADHD, including a combination of both inattentive and hyperactive and impulsive symptoms (combined type). Self-report and collateral data collected with a structured interview questionnaire, the Jerome Driving Questionnaire, indicated that subjects with ADHD, combined type, experienced high levels of frustration and impulsive behaviours in relation to other drivers on the road. Their reported driving behaviours fulfilled the criteria for road rage described by Smart and others (2). Cloninger’s Temperament and
Character Inventory was used to establish personality profiles from this group and a similar group of patients with ADHD, combined type, attending an outpatient clinic at the Centre for Addiction and Mental Health. These profiles showed a high prevalence of externalizing personality disorder (7; personal communication, Dr Umesh Jain, 2003). When treated with stimulants, these patients described a parallel improvement on the JDQ and resolution of ADHD symptoms.

Impulsivity also occurs in a range of unconnected categorical conditions that have their common pathway of expression through deficits in executive function (8). For example, impulsivity as a chronic intermittent condition may well reflect chronic emotional lability, which often is seen as part of chronic dysthymia or borderline personality organization or, less often, reflects a frank mood disorder. Stimulant medication would not be expected to improve emotionally based impulsivity; it would more likely worsen it.

The current Canadian Medical Association guidelines on driving safety include road rage as a subcategory of emotional disorder (9). The latest edition includes ADHD as a reportable condition if it is uncontrolled and associated with impulsive driving. Impulsive road rage may reflect separate orthogonal variables of cognitive impulsivity and emotional lability, which may require quite different treatment modalities. Further careful research into this nonspecific syndrome, which appears to be presenting with increasing prevalence, seems to have merit, both for public health measures and, possibly, for psychiatric practice.

References


Laurence Jerome, MB, ChB, FRCPC
London, Ontario

Reply: Ancient Wine but Still Potent?

Dear Editor: We are grateful for Dr Jerome’s contribution to the debate about road rage and its relation to psychiatric distress. He makes the important point that a significant literature exists on psychiatric issues and driving and correctly notes how several different psychiatric problems—such as explosive disorders, attention-deficit hyperactivity disorder (ADHD), and impulsive behaviour—may relate to road rage (for example, 1,2).

Road rage is sometimes portrayed as a new phenomenon, but as Dr Jerome points out, it has a long history. There are literary and historical references to road rage that point to a relation with psychiatric distress. In Sophocles’ play Oedipus the King, written about 420 BC, a road rage incident is the ostensible reason for which Oedipus kills his father (3). Oedipus is characterized as impulsive and easily provoked to violence. Sophocles based his Oedipus story on a folk tale, and he may have included the road rage incident because his audience would believe and accept it. The poet Lord Byron was involved in a serious road rage case in 1822 (4). It concerned a dispute over the right-of-way on a road, lasted several hours, and resulted in a serious injury to the supposed perpetrator. Lord Byron was subject to depression at many times during his life, but it is not clear whether this contributed directly to the road rage incident. Byron was also subject to irritation and sudden bouts of violence (4).

We have used the General Health Questionnaire (GHQ) in our own research (5). The GHQ, a general psychiatric screening instrument for identifying people experiencing psychiatric distress, has proved very useful in survey research (6). However, it does not assess impulse-control disorders, explosive behaviours, or aggression. Virtually all its items deal with depression, anxiety, and feelings of stress. No questions probe aggression, hostility, or impulse control. Future research in this area would therefore profitably consider these potentially important factors.

Much remains to be done in research on road rage and psychiatric distress. Both victims and perpetrators of road rage should be examined with psychiatric instruments that allow for the identification of ADHD and impulse-control disorders as well as depression and anxiety. As Dr Jerome suggests, mood disorders may underly impulsivity. At present, we also know nothing of how road rage behaviour in young people may relate to various psychiatric problems. It is also important to note that our work does not allow the disentanglement of cause–effect relations; thus we must keep in mind the importance of considering road rage as a cause of such problems as depression and posttraumatic stress disorder (PTSD) (for example, 7).

Available evidence makes it clear that motor vehicle collisions wherein road rage may have played an important role (8) are a major source of injuries and premature death in Canada and also a major source of psychiatric problems such as PTSD (9,10). Additional efforts to understand the role of psychiatric problems as both precursors to and results of motor vehicle collisions should be considered as a research priority. We completely agree with Dr Jerome that further understanding of road rage may have important implications for public health and psychiatric practice.

References

Dear Editor: Approximately one-half of all patients with schizophrenia abuse or depend on psychoactive substances at some point during their lives (1), but few studies to date have proposed an integrated pharmacologic treatment for this schizophrenia–addiction comorbidity. Because of their strong dopamine D2 receptor antagonism, conventional antipsychotics such as haloperidol should in theory be the treatment of choice for comorbid schizophrenia and substance abuse. In practice, however, such treatment has not been demonstrated to be consistently effective and has only controlled drug abuse in special cases (2). A few pilot studies suggest that, among the conventional antipsychotics, fluphenixol may reduce cravings in schizophrenia patients with cocaine addiction (3). To date, the most promising results have been obtained with clozapine, a prototype of the atypical antipsychotics (4). Sharing certain key properties with clozapine (for example, 5-HT2–D2 ratio) (5), quetiapine may also reduce drug cravings in psychosis patients with addictions. A pilot study of 12 patients suffering from bipolar disorder (BD) and cocaine addiction appears to support this hypothesis (6). To expand on this promising result, we report case histories for 8 psychosis patients whose cannabis use habits significantly improved after treatment with quetiapine.

Case Report
The group of patients (5 men and 3 women) included 4 patients with schizophrenia and 4 with affective BD. All patients had cannabis dependency, and 2 also had a cocaine use disorder, according to DSM-IV criteria. Their mean age was 38.5 years (range 25 to 46 years). Before quetiapine was initiated, they received antipsychotics (5 patients), antidepressants (2 patients), lithium (2 patients), clonazepam (2 patients), and procyclidine (1 patient). All 8 patients were given quetiapine for an average of 5.8 months, at dosages ranging between 100 and 1200 mg daily. Concomitantly, 4 patients received antidepressants, 2 received gabapentin, and 1 was on methadone maintenance treatment. Overall, an average 97.3% reduction in their weekly cannabis use was observed with an average quetiapine dosage of 388 mg daily. When interviewed, patients reported consuming an average of 35.6 g weekly of cannabis (range 18 to 56 g) before quetiapine introduction. After quetiapine treatment, patients reported an average cannabis consumption of 1.1 g weekly.

Like clozapine, quetiapine has proven benefits when compared with conventional antipsychotics (7,8). First, clozapine and quetiapine have a beneficial effect on mood. Showing mesolimbic selectivity, these agents do not appear to cause extrapyramidal symptoms. Further, these medications produce little or no neuroleptic-induced dysphoria. Last, it is possible that these atypical antipsychotics (mainly clozapine) alleviate the negative and cognitive symptoms of schizophrenia more than do conventional antipsychotics. To the extent that some patients with schizophrenia may take substances as a form of self-medication, the clinical data presented here suggest that quetiapine, like clozapine, could form the basis of an integrated pharmacologic treatment for the psychosis–addiction comorbidity. Further controlled research is needed to validate the preliminary data collected to date.

Acknowledgement
The authors would like to pay tribute to Jean-Yves Roy, a pioneer psychiatrist in dual diagnosis in Montreal, who passed away in April 2004.

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Note
This report was previously presented at the annual meeting of the International Society of Addiction Medicine; October 2002; Reykjavik (Iceland).

References