Tiagabine for Rage, Aggression, and Anxiety

SIR: Few studies have examined the effects of pharmacologic augmentation in patients with treatment-resistant rage and aggression. Gamma-aminobutyric acid (GABA) may be critical in the neurochemical control of aggressive behavior.[1] Agents that modulate GABA-ergic activity have been shown to significantly reduce aggressive symptoms.[1]

Management of behavioral complications of psychiatric disorders, such as rage and aggression, presents a clinical challenge. When faced with patients who continue to exhibit these symptoms, despite otherwise adequate treatment, clinicians will often augment therapy, rather than switch medications. However, few studies have examined the effects of pharmacologic augmentation in patients with treatment-resistant rage and aggression.

Gamma-aminobutyric acid (GABA), the primary inhibitory neurotransmitter, may be critical in the neurochemical control of aggressive behavior.[1] Agents that modulate GABA-ergic activity, including valproic acid, topiramate, and gabapentin, have been shown to significantly reduce aggressive symptoms.[1]

Tiagabine, a selective GABA reuptake inhibitor (SGRI), increases synaptic GABA availability via transporter inhibition.[2] Preliminary reports suggest that tiagabine may be effective in the treatment of a variety of anxiety disorders, including generalized anxiety disorder in an open-label study and posttraumatic stress disorder (PTSD) and panic disorder (PD) in case-series reports.[3–5]

We conducted a retrospective chart review of 36 consecutive patients (aged 15–54 years), with symptoms of rage, aggression, or anxiety in association with one or more of the following disorders: bipolar, intermittent explosive, major depression, PD, attention deficit hyperactivity disorder, or substance abuse. All patients had previously tried a variety of medications (including antidepressants, anxiolytics, antipsychotics, anticonvulsants, mood stabilizers, and central nervous system stimulants), yet they continued to display excessive anxiety, anger, rage, abuse, or irritability. In addition to existing treatment regimens, patients initially received tiagabine 4 mg/day (2 mg bid) and then were titrated on an individual basis. Treatment response was graded by the physician using a 4-point categorical scale (none, minimal, good, or excellent). A patient with a rating of "good" or "excellent" was defined as a responder.

Twenty-nine patients were eligible for analysis; the remaining seven patients were lost to follow up or were noncompliant. Of these, 20 patients (69%) demonstrated a good or excellent response to tiagabine (responder), with reduction or elimination of the symptoms of rage, aggression, or anxiety. Symptomatic improvement was noted as early as 2 weeks after initiating treatment, and sustained for a period of up to 52 weeks. Tiagabine dosage ranged from 4 to 32 mg/day (dosed hs, bid, tid, or qid), with 75% of responders receiving doses ≤16 mg/day, taken mainly bid. One patient discontinued due to lack of efficacy. Tiagabine treatment was well tolerated. Of the 29 patients, 8 discontinued treatment because of the following adverse events: cognitive dysfunction (N = 4) and acne, depression, fatigue, and panic attacks (N = 1 for each).

These preliminary findings indicate that tiagabine augmentation may be effective in reducing the symptoms of rage, aggression, and anxiety. Further evaluation in controlled clinical trials is warranted.

Daniel A. Hoffman, M.D.
Medical Director,
Neuro-Therapy Clinic,
Denver, CO

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Tardive Dyskinesia After Long-Term Veralipride Treatment

SIR: Veralipride (VRD) is a benzamide derivative that is effective in the treatment of menopausal syndrome. A double-blind study[1] indicated a total elimination of the