Intranasal Ketamine for Intermittent Explosive Disorder: A Case Report

Sir: Ketamine is an *N*-methyl-D-aspartate blocker. Nasal administration has been used successfully to abort one type of paroxysmal neurologic disorder, namely migraine.[1,2] This case describes successful use to abort rage episodes refractory to multiple medical and behavioral interventions.

Case report. Mr. A, a 20-year-old man, has a lifelong history of rages following denial of perseverative requests. There was often postictal regret of severe intensity, e.g., holding a knife to himself. Although the frequency of these episodes remained constant with age, perhaps 2 to 3 times daily, as the patient's physical strength increased with age he could no longer be contained by parental physical restraint. At age 18, parental injury was common and the police were called to the house as often as twice a week.

Medical history is suggestive for metabolic encephalopathy given prenatal stroke, focal epilepsy, one block exercise tolerance with hyperthermia, and unexplained hospitalization at 14 years of age with elevated creatine phosphokinase levels. Family history is germane as Mr. A's father has a history of severe medically refractory migraine and his sister has a history of episodes of confusion. Diagnostic review reveals magnetic resonance imaging evidence for prenatal stroke in the left middle cerebral artery distribution, negative surface video electroencephalogram monitoring during 2 rages, positron emission tomography evidence for corresponding left frontal-parietal hypoperfusion with possible medial temporal lobe involvement, and multiple negative serologic tests for classical metabolic disorder.

Failed medical interventions for anger include 7 anticonvulsants titrated to toxicity (phenobarbital, divalproex, topiramate, gabapentin, lamotrigine, clonazepam, and topiramate), 6 antidepressants (paroxetine, sertraline, clomipramine, imipramine, fluvoxamine, and buspirone), 4 antipsychotics (haloperidol, olanzapine, quetiapine, and risperidone), and clonidine, propranolol, lithium, and tamoxifen. Vagal nerve stimulator implantation was declined by 1 neurologist citing an absence of current epilepsy.

After an emergency room visit at 18 years of age resulted in involuntary treatment referral, Mr. A's family provided consent to use ketamine. Ketamine was considered given the density of his father's migraine. Reasoning from analogy with observed variable phenotypic expression in the channelopathies, it seemed reasonable to try an agent shown to be effective in migraine to abort a distinctly different neuropsychiatric event. In the following 16 months, as-needed doses of intranasal ketamine up to 60 mg over 4 hours generally kept rages under control. Tolerability was excellent, with initial prompting by parents replaced by requests for use with time. Cumulative doses greater than 200 mg daily, however, produced hallucinosis.

Ketamine is the most widely used anesthetic in the world. Previous reports only describe intramuscular or oral use to acutely manage agitated or explosive patients.[3–6] The intranasal route, as shown in this report, offers additional advantage in terms of speed of action and ease of use by the general public.

Use of ketamine remains relatively unexplored in rage episodes or other paroxysmal events such as panic, catatonia, or surface null electroencephalogram eye closure seizures. Risks of hallucinosis, addiction, or posterior cingulate damage need to be considered with each individual case.

Dr. Berner reports no financial or other relationships relevant to the subject of this letter.

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Jon E. Berner, M.D., Ph.D.
Private Practice
Woodinville, Washington

Cognitive Facilitation and Behavioral Disinhibition With Benzodiazepine: A Case Report

Sir: Although paradoxical effects of γ-aminobutyric acid (GABA)-ergic medications (excitation instead of sedation) are well-known, they have received no satisfactory explanation. We report the case of a 54-year-old woman with schizophrenia, in which we were able to observe this clinical pattern and its neural correlates.

Case report. The patient was in her forties, working as an assistant professor at a university, when she developed mostly negative symptoms. She did not engage in any new professional endeavors and became careless and apathetic. Following benzodiazepine intake, she enjoyed an increase of her wakefulness, and recovered some abilities to have a conversation and to make plans. Her benzodiazepine intake became uncontrolled, and 8 years ago, after taking bromazepam, she killed her husband with a chopper.

She had spent 2 years in prison when she came to our psychiatry department in November of 2001 with a probation order. The neuropsychological assessment showed a minor dysexecutive syndrome, and the single-photon emission computed tomography (SPECT) showed frontotemporal hypoperfusion. Both neuropsychological status and SPECT hypoperfusion were stable over the next 4 years, a pattern that ruled out frontotemporal dementia. Therefore, she received the diagnosis of late-onset schizophrenia (DSM-IV criteria). Various antidepressant treatments, including electroconvulsive therapy, and antipsychotic medications, including clozapine, provided no major improvement.

On 2 occasions, she was hospitalized for acute excitation without confusion, and benzodiazepine metabolites were

