Propranolol in the Treatment of Rage and Violent Behavior Associated With Korsakoff’s Psychosis

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Propranolol controlled the rage and violent behavior of a man with alcohol withdrawal, Korsakoff’s psychosis, and seizures. The authors present evidence linking Korsakoff’s psychosis and alcohol withdrawal to pathophysiologic alterations in CNS adrenergic amines and receptors.


Recent reports (1–3) in the scientific literature have demonstrated that high-dose propranolol is effective in the treatment of disinhibited rage and violent behavior in patients with acute and chronic brain disease. In addition to disturbances of memory, cognition, perception, and orientation, patients with Korsakoff’s psychosis are often affected with agitation and belligerent behavior, which are socially disabling and highly refractory to treatment (4). Therefore, when we evaluated a patient with Korsakoff’s psychosis associated with severe rage outbursts, agitation, and violent behavior not responsive to traditional psychopharmacologic and behavioral interventions, we initiated high-dose propranolol treatment.

CASE REPORT

Mr. A, at the time he came to the emergency room, was a 40-year-old man with a 20-year history of alcohol abuse, several prior admissions for delirium tremens, and a longstanding major motor seizure disorder, which had been treated with phenytoin and phenobarbital. He was admitted to the inpatient medical service because of his exposure-induced blepharitis, fever, delirium, and visual and auditory hallucinations associated with alcohol withdrawal, and he received standard medical treatment for delirium tremens. Despite treatment with thiamine, folic acid, multiple vitamins, ferrous sulphate, phenytoin, phenobarbital, and several different classes of major and minor tranquilizers, the anterograde and retrograde memory impairment, disorientation, auditory hallucinations, confabulations, and behavioral dyscontrol persisted. Nevertheless, Mr. A maintained a clear sensorium with no fluctuations in levels of consciousness. His EEG was abnormal: There was epileptiform activity in the right parietal-occipital region and focal slowing in the right hemisphere. The CAT scan showed diffuse atrophy.

Particularly refractory to pharmacologic intervention were Mr. A’s rage outbursts. They occurred more than 10 times a day and were triggered by the most minor frustrations. On several occasions his outbursts were so violent that he inflicted physical injury on the nursing aides, who were required to be present 24 hours per day for weeks. During one outburst of rage, he fractured his tibia by striking his leg against the bed. For the greater part of each nursing shift over 2 months, Mr. A required physical control with either camisoles or ankle and hand restraints. During this time he received haloperidol in doses of up to 14 mg/day for a month, but there was no change in his psychosis, dementia, or rage episodes. At that point, propranolol was added to the haloperidol, and the dose was increased at a rate of 80 mg/day, with monitoring of pulse and blood pressure. The dose was increased to 600 mg/day in four divided doses. Two weeks after this 600-mg dose was attained the frequency and intensity of Mr. A’s rage attacks were markedly reduced and restraints were no longer necessary. Stimuli that would have previously induced a rage attack (e.g., delays in receiving cigarettes) did not result in rage episodes. He showed no adverse effects from the propranolol. Mr. A’s auditory hallucinations and paranoid delusions also diminished, but he remained disoriented and confabulatory and had poor anterograde memory. When attempts were made to reduce his propranolol dose, his rage and violent behavior returned. With the reinstatement of propranolol, the symptoms subsided again, at which time he was accepted for transfer to a state psychiatric hospital. At that time he was maintained on 600 mg/day of propranolol, 14 mg/day of haloperidol, and phenytoin and phenobarbital for his seizure disorder.

DISCUSSION

One may speculate that the combination of Korsakoff’s psychosis and acute alcohol withdrawal rendered this patient particularly susceptible to the development of rage attacks. Many studies have linked Korsakoff’s psychosis and alcohol withdrawal to pathophysiologic alterations in CNS adrenergic amines and receptors. Post-mortem evaluations of patients with Korsakoff’s psychosis (4) have shown a consistent pattern of lesions in the third and fourth...
ventricles and the aqueductal regions, all of which are rich in monoamine-containing neurons. McEntee and Mair (5) reported that the concentration of CSF 3-methoxy-4-hydroxyphenylglycol (MHPG), the primary brain metabolite of norepinephrine, is significantly lower in patients with Korsakoff’s syndrome. One may hypothesize that decreased CSF MHPG in patients with Korsakoff’s syndrome could lead either to denervation supersensitivity of the β-adrenergic receptor sites or to a compensatory increase in the number of sites. In addition, patients undergoing alcohol withdrawal have been shown to have increase in norepinephrine production (6) and number of β-adrenergic receptor sites in the CNS (7). Brown and associates (8) found a positive correlation between aggression and CSF MHPG, and Elliot (9) suggested that catecholamine access to the brain stimulates α- and β-adrenergic receptors to induce dyscontrol of anger and violence. If one accepts Elliot’s suggestion, our patient could be considered particularly vulnerable to organic dyscontrol because of a hypothesized chronic catecholamine-receptor sensitivity secondary to Korsakoff’s psychosis in combination with an acutely increased concentration of catecholamines secondary to alcohol withdrawal.

If increased β-adrenergic receptor supersensitivity or a high number of sites is, in fact, related to dyscontrol of rage and violence, centrally acting β blockers may indeed treat this dyscontrol. Propranolol, a lipidsoluble substance that passes through the blood-brain barrier and concentrates diffusely in the brain, has been shown to decrease the elevated 24-hour urinary epinephrine levels found in alcohol withdrawal (6) and decrease the CSF MHPG levels in psychotic patients (10). Without controlled, double-blind studies with histologic and biochemical assays, these explanations remain speculative. Nevertheless, it is clinically relevant that the previously unmanageable agitation, rage, and belligerence of a patient with Korsakoff’s psychosis were successfully controlled by the addition of high doses of propranolol.

We would like to add two final clinical notes. Open trials using propranolol to treat aggressive symptoms (1–3) have found that effective treatment usually requires higher doses than those used in the treatment of cardiovascular disorders. Specifically, although a dose of 2–4 mg/kg per day of propranolol is used in the treatment of hypertension, up to 20 mg/kg per day have been used to treat aggression and other symptoms related to schizophrenia and manic-depressive disorder (11, 12). In the case of our patient, we increased the dose of propranolol by 80 mg/day until his violent behavior showed evidence of amelioration. In our experience in treating aggression and violence with high doses of propranolol, there have been only negligible reductions in the patients’ blood pressures and heart rates at doses higher than 300 mg/day.

Second, although the auditory hallucinations and paranoid delusions of our patient improved significantly with the addition of propranolol, the haloperidol was not discontinued or reduced. We have found that propranolol reduces aggressiveness but does not have inherent antipsychotic properties. However, propranolol has intrinsic anticonvulsive properties (13), and there was a possibility that the medication could have had a beneficial effect on the patient’s major motor seizure disorder. The discharge of the patient to a chronic care facility precluded trials of reducing his phenytoin and phenobarbital doses.

REFERENCES