Benzodiazepine toxicity with profound suppression of the electroencephalogram

JASON P. STABLEY, DO
EDWARD J. FREAR
MARVIS WINE
MILIND J. KOTHARI, DO

The authors report the case of a 60-year-old man with respiratory distress secondary to exacerbation of chronic obstructive pulmonary disease, right lower lobe pneumonia, and severe bronchospasm. High doses of lorazepam were given intravenously after failure to control bronchospasm and agitation with bronchodilators and mucolytic agents; the patient was unresponsive to all stimuli while receiving lorazepam. Electroencephalography revealed a profoundly suppressed pattern without accompanying low-voltage fast activity—this was reversible following withdrawal of the lorazepam.

(Key words: toxicity, benzodiazepines, lorazepam, electroencephalography)

Benzodiazepines are widely used in clinical practice as anxiolytics, anticonvulsants, anesthesia inducers, hypnotic agents, and antispasmodics.1 As a class, they are well known to cause central nervous system depression. Electroencephalographic changes associated with use of benzodiazepines have also been described. The authors report profound reversible suppression of the electroencephalographic record in a patient receiving large doses of lorazepam (Ativan).

Report of case

A 60-year-old Caucasian man was transferred to the Milton S. Hershey Medical Center for respiratory distress secondary to exacerbation of chronic obstructive pulmonary disease, right lower lobe pneumonia, and severe bronchospasm. He was started on intravenous corticosteroid and antibiotic therapy several days before transfer to our facility. One day before transfer, he had acute onset of right upper extremity weakness. On the patient’s admission to our facility, computerized tomography revealed two small subcortical hypodensities in the left frontotemporal region that were believed to represent subacute cerebral infarcts.

Past medical history was positive for chronic obstructive pulmonary disease secondary to alpha-1-antitrypsin deficiency, diverticulitis, multiple rectal polyps, and heavy tobacco smoking.

Physical examination initially revealed an intubated man who was mildly drowsy. Vital signs were stable. General physical examination was positive for diminished breath sounds throughout both lung fields, with a moderate amount of inspiratory and expiratory wheezing. Neurologic examination revealed moderate right-sided weakness involving mainly the upper extremity. Findings of the cranial nerve examination were unremarkable. Reflexes were mildly brisk on the right. Plantar responses were extensor on the right and flexor on the left. Sensory, cerebellar, coordination, and gait examinations could not be adequately assessed.

Hospitalization was initially complicated by severe bronchospasm and mucous plugging of the airways. This was treated with aggressive pulmonary toilet, bronchodilators, and mucolytic agents without success. Large doses of lorazepam were administered intravenously via drip infusion (variable doses up to 20 mg/h) after failure to control bronchospasm and agitation with the bronchodilators and mucolytic agents. The patient was unresponsive to all stimuli while receiving lorazepam. Before and during lorazepam administration, there was no evidence of hypoxia, hypercapnia, or significant metabolic disturbances.

Electroencephalography revealed a profoundly suppressed pattern without accompanying low-voltage fast activity (Figure 1). Within 72 hours after withdrawal of lorazepam, the patient began to arouse. Five days after discontinuing lorazepam, electroencephalography revealed significant return of baseline activity with mild focal slowing on the left, believed to be secondary to the recent left hemispheric infarcts (Figure 2).

Discussion

The most common electroencephalographic change noted with the use of benzodiazepines is excessive low-voltage fast activity,2-4 which is most prominent anteriorly,5-7 but may spread posteriorly.8 A decrease in slow activity has also been shown to accompany the increase in low-voltage fast activity.9 Others have noted that in acute benzodiazepine intoxication, prominent fast activity is followed by coma patterns similar to those seen in barbiturate intoxication.9 Other reports have described alpha coma, delta slowing with superimposed beta activity, and rarely, isoelectric coma. Spindle coma associated with benzodiazepine intoxication has also been reported.10
This particular patient was receiving large doses of lorazepam to control agitation and bronchospasm. The electroencephalogram showed significantly suppressed background activity similar to that seen with other causes of severe diffuse brain injury. After withdrawal of the lorazepam, there was a gradual return to a baseline encephalographic record with evident focal slowing of the left hemisphere, believed to be related to the recent ischemic insult.

References


