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Article Author: Gupta BK, Fish DN, Yerevanian BI
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Notes:

Carbamazepine for Intermittent Explosive Disorder in a Prader-Willi Syndrome Patient

Sir: In 1956, Prader, Labhart, and Willi[1] described a syndrome of obesity, short stature, mental retardation, cryptorchidism, and hypotonia at birth. In the Prader-Willi syndrome, patients' behavioral problems, including temper tantrums, self-abuse, and physical and verbal aggression, have been frequently observed.[2] To our knowledge, the diagnosis of intermittent explosive disorder has not been suggested for these patients. We report a case of a Prader-Willi syndrome patient with intermittent explosive disorder who was successfully treated with carbamazepine.

Case report. Ms. A, a 39-year-old, obese, moderately retarded (IQ=58) white woman with previously undiagnosed Prader-Willi syndrome, was referred to the psychiatry service for evaluation of behavioral problems. She was a resident of a group home for the mentally retarded, where there was concern regarding her episodes of loss of temper, slamming doors, verbal and physical aggression, and self-abusive behavior. These conduct problems were reported to have been present for over 25 years and were always associated with a mild precipitating stressor. While at the home, Ms. A was treated with lithium, chlorpromazine, and a token-reward system for good behavior with limited success.

Ms. A's history is poorly documented, although it is known that she was developmentally delayed as a child. She was first institutionalized at 14 years of age because of difficulties with her care secondary to her behavior.

On physical examination, the patient was a hirsute, white female weighing 251 lb (113 kg), with a height of 5′4″ (162.6 cm). The right hand measured 17.5 cm (50th percentile), and the right foot was 20.5 cm (3rd percentile). The examination was otherwise remarkable for absent deep tendon reflexes in the extremities and upgoing Babinski's reflexes.

Additional workup yielded normal results of an EEG and CT scan of the head. Values of complete blood counts, urine analysis, and SMA profile were within normal limits except for a moderately elevated creatinine level. Values of thyroid studies were normal. A glucose tolerance test was not performed. Total testosterone level was elevated at 70 ng/100 ml (normal, adult female, 20–80 ng/100 ml). A genetics and dysmorphology consultation confirmed the clinical diagnosis of Prader-Willi syndrome on the basis of obesity, short stature, and mental retardation.

During the hospitalization, Ms. A had several outbursts that were frequently related to limitations placed on food consumption. Behavior modification measures were continued as instituted in her group home. Because of borderline renal function, lithium was discontinued, carbamazepine therapy was started, and plasma levels of 6.8 μg/ml (adult therapeutic level, 8–12 μg/ml) were achieved. After 3 weeks of carbamazepine therapy, Ms. A was discharged with marked objective improvement in behavior manifested by decreased frequency and severity of temper outbursts.

At the group home this patient was treated with behavioral therapy, lithium, and chlorpromazine with limited success. Carbamazepine treatment markedly improved this patient's behavior and virtually eliminated her outbursts. These results suggest that further application of carbamazepine for the treatment of intermittent explosive disorder in Prader-Willi syndrome patients is indicated.

Tunks and Demer[3] described a 24-year-old woman with episodic dyscontrol syndrome characterized by periodic outbursts of violence toward herself and others. Carbamazepine totally eradicated her aggression; its discontinuation on two occasions resulted in the reemergence of outbursts that disappeared when drug treatment was resumed. Folks et al.,[4] describing 10 patients responsive to carbamazepine, cited one 23-year-old man with cerebral palsy and depressive personality whose violent outbursts ceased in response to carbamazepine. These findings show a marked improvement of aggression in response to carbamazepine in a small number of patients with brain damage and/or mental retardation.

The apparent antiaggressive effectiveness of carbamazepine in humans is mirrored by its ability to inhibit a characteristic rage reaction in cats induced by electrical stimulation of the perifornical area of hypothalamus.[5] This apparent antiaggressive effectiveness requires further systematic clinical study, focusing on the use of controlled methodologies and the issue of whether antiaggressive effects are related to treatment of an associated underlying brain syndrome or whether carbamazepine has selective antiaggressive effects on specific brain syndromes.

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Bhupendra K. Gupta, M.D.
Daniel N. Fish
Boghos I. Yerevanian, M.D.
Rochester, New York

Trazodone-Induced Mania

Sir: Only four cases of mania have been previously reported with trazodone.[1,2] Trazodone is an antidepressant that is chemically distinct from others currently in use.[3] A patient who developed mania when switched from doxepin to trazodone is described.

Case report. Mr. A, a 53-year-old white man with a chronic history of alcohol abuse, was admitted for alcohol detoxification. There was no clear-cut history of manic episodes, but he did report depressive bouts. He was successfully detoxified. The only abnormalities were moderate elevations of serum alkaline phosphatase and SGOT. After 1 week, Mr. A complained of severe, unspecific depression and was treated with doxepin 150 mg/day. He showed no improvement 10 days later, and doxepin was discontinued. Trazodone therapy was initiated at 50 mg t.i.d., and 3 days later he appeared talkative, less depressed, and more energetic. In the next 24 hours, however, he showed a progressive picture of hypomania, with insomnia, restlessness,