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Sinoatrial Block in Lithium Toxicity

TO THE EDITOR: Lithium carbonate is a mainstay in the treatment of mania and bipolar disorder. A serum level between 0.8 mEq/l and 1.2 mEq/l is considered therapeutic, usually obtained with a dose of approximately 900 to 1200 mg/day (1). The drug has a narrow therapeutic index, with progressive toxicity ranging from gastrointestinal complaints to marked neurological impairment that correlate with increasing serum levels beginning at about 1.5 mEq/l (2).

Electrocardiogram (ECG) manifestations, including prolonged QT interval, T wave flattening and inversion, and first-degree atrioventricular (AV) conduction delay, have been reported with lithium toxicity (3–6). In rare cases, ventricular tachycardia and ventricular fibrillation resulting in death have been reported (4).

Sinoatrial block associated with lithium therapy was first reported in 1975 (7). Subsequent reports cite reversible sinus node suppression as a consequence of chronic lithium therapy, even at therapeutic levels (8–10). Although the mechanism is poorly understood, it may be related to lithium's competitive inhibition of calcium in the Na^{+}/Ca^{++} exchange in cardiac cells (11).

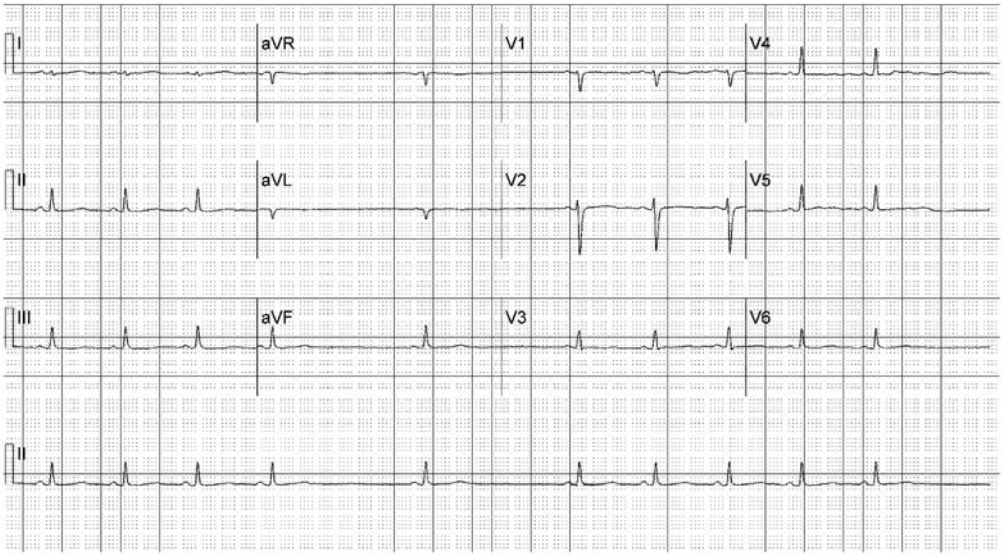
The case report presented here demonstrates prominent bradycardia due to second-degree, type II sinoatrial block that resulted from toxic lithium levels.

A 43-year-old woman with a long-standing history of bipolar disorder was started on lithium at 600 mg twice daily, reportedly a lower dose than her chronic therapy, which she had discontinued 1 year before. She was also prescribed naproxen sodium, amitriptyline, and mirtazapine. One week later, she was found to have a lithium level of 3.2 mEq/l (therapeutic level <1.0) and a creatinine level of 2.3 mg/dl. She immediately was sent to the emergency department, and repeated chemistries revealed a further increase in her creatinine level of 4.2 mg/dl and lithium level of 3.64 mEq/l.

Her initial vital signs were normal—she was afebrile; her heart rate was 72 beats per minute and regular; her blood pressure was 117/70 mmHg; and her respiratory rate was 16 breaths per minute with an oxygen saturation of 97% on room air. However, she quickly developed hypothermia at 34.5°C, bradycardia to 36 beats per minute, and hypotension. Other laboratory values were remarkable for hypokalemia with a potassium level of 2.8 mEq/l (normal range: 3.7–5.2), metabolic alkalosis with a serum bicarbonate of 33 mEq/l (normal range: 22–32), and hypochloremia of 88 mEq/l (normal range: 98–108). She was started on norepinephrine and dopamine infusions and transferred to the medical intensive care unit for hemodynamic support and urgent hemodialysis.

The patient's ECG was remarkable for sinus rhythm/sinus bradycardia consistent with sinoatrial block with an intermittent 2:1 conduction pattern, yielding a variable rate of 78 beats per minute and 39 beats per minute, respectively (Figure 1). Nonspecific T wave flattening was also present with borderline low QRS voltage and a QRS axis of about +90°.

FIGURE 1. Twelve-Lead ECG



In the case described, second-degree (type II) sinoatrial block was present. The prolonged P-P interval was a direct multiple of the shorter P-P cycles. This is in contrast to second-degree type I sinoatrial block (Wenckebach type), characterized by a sinus pause after progressively decreasing P-P intervals. In such instances, the sinus pause duration is less than two P-P cycles.

The patient's ECGs also demonstrated 4:3, 5:4, and 6:5 second-degree type I sinoatrial Wenckebach block during dialysis (tracings not shown).

After dialysis, the patient's lithium level decreased to 0.41 mEq/l. There was no further evidence of sinoatrial block. In this case, renal insufficiency, likely secondary to dehydration in combination with nonsteroidal anti-inflammatory therapy, may have precipitated elevated serum levels of lithium, despite the patient's initially low dose. In the setting of dehydration and vomiting, the lithium ion is selectively resorbed in the renal tubules, sometimes accumulating to toxic levels. Indeed, the triad of hypokalemia, hypochloremia, and metabolic alkalosis observed on admission was consistent with a history of bulimia nervosa, revealed later in the patient's hospitalization. Of note, chronic lithium therapy, by itself, may result in renal insufficiency and other renal toxicity (12).

As the uses of lithium continue to expand with an increasingly larger patient population, clinicians must be mindful of the cardiac risks associated with lithium therapy, including sinoatrial block with resultant bradycardia, which can occur abruptly with chronic therapy.

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Dr. Goldberger reports no competing interests.

Oxcarbazepine in Youths With Autistic Disorder and Significant Disruptive Behaviors

TO THE EDITOR: Disruptive behaviors are a frequent reason for psychiatric visits among autistic individuals. The following case report describes beneficial effects in three consecutive oxcarbazepine-treated autistic youths with disruptive behaviors. All three patients had been conjointly engaged in behavioral therapies provided by local treatment facilities.

"A.B." is a 13-year-old Hispanic male with frequent aggression toward others and property, irregular sleep, and poor ability to follow instructions. Previous effective trials of risperidone and olanzapine were both discontinued because of elevated liver transaminases and excessive weight gain, respectively. Oxcarbazepine was titrated to 300 mg every morning and 600 mg every night over 7 days. Two weeks later, the patient's mother reported improved compliance at home, and school reports showed improved cooperation and attention span. The aggression was decreased in severity and frequency, and regular sleep was established. He has been stable on this regimen for 4 months.

"C.D." is a 19-year-old Caucasian female with dysfunctional compulsive routines, head banging, and frequent violent outbursts. Fluoxetine was titrated to 20 mg daily over 2 months. The compulsive symptoms improved dramatically, but she remained aggressive. Risperidone augmentation failed, so oxcarbazepine was titrated to 600 mg b.i.d. One month later, her tantrums were significantly reduced, and cooperativeness improved. The head banging was reduced from more than 10 spells per day to approximately once per week. The patient has been on this combination of fluoxetine and oxcarbazepine for 6 months.

"E.F." is a 4½-year-old Hispanic child whose symptoms included head banging, property destruction, hitting others, irregular sleep, and hyperactivity. Previous treatments with methylphenidate and amphetamine salts resulted in agitation; trials of guanfacine and risperidone failed. Oxcarbazepine was titrated to 150 mg every morning and 300 mg every night over 2½ months, resulting in normalized sleep schedule, improved cooperativeness, and lessened aggression. The patient has been maintaining these improvements for 3½ months.

Written informed consent was obtained from the legal guardians in all three cases. None of the patients have developed hyponatremia or other untoward outcomes.

To our knowledge, this is the first report of oxcarbazepine use in autism with disruptive behaviors. These symptoms are best managed by combining behavior modification and psychotropic agents (1). While haloperidol and risperidone have solid evidence base supporting their efficacy and effectiveness in this indication, their side-effect profiles (i.e., extrapyramidal symptoms and weight gain, respectively) are equally well documented (2). Controlled trials also support fluoxetine and fluvoxamine, but treatment-emergent behavioral activation (3) limits their clinical applicability. Oxcarbazepine has a more favorable side-effect profile, and it is available in liquid form, which is often more convenient for autistic patients. Hopefully, this report will inspire future research on the effects of oxcarbazepine in autistic individuals.