Lacosamide Associated Complete Heart Block in Elderly

Sir,

A case of a 71-year-old female, suffering from hypertension (controlled on metoprolol 25 mg/day and telmisartan 40 mg/day) for the last 4 years, presented to us with a history of three episodes of focal seizures before 5 months. Her magnetic resonance imaging brain at that time revealed small-vessel ischemic changes, and electroencephalogram was normal. Advised antiepileptic with levetiracetam 500 mg twice daily, and later on, the dose increased to 500 mg thrice daily in view of uncontrolled seizures. One month later, she complained another episode of seizure, so she was prescribed second antiepileptic drug, lacosamide (LCM) 100 mg twice daily, the dose of which increased to 100 mg thrice daily in view of recurrence of seizures. After 5 days of escalation of LCM dose, she presented with a complaint of loose, watery stools for 2 days and altered sensorium for 1 day. On admission, she had blood pressure of 90/60 mmHg with pulse rate of 36/min and electrocardiogram (ECG) indicating complete heart block (CHB) [Figure 1]. Hence, a temporary pace maker was implanted. On investigating, she found to have severe metabolic acidosis with raised lactate level. Her serum creatinine level was raised (3.35 mg/dL), and electrolytes were within normal limit. She had raised liver enzymes – serum glutamic pyruvic transaminase (SGPT) 832 IU/L, SGPT 1364 IU/L with normal bilirubin level, normal partial thromboplastin, and activated partial thromboplastin time value. All viral markers for hepatitis were negative. A diagnosis of multifactorial metabolic encephalopathy due to multiorgan failure due to hypotension (gastroenteritis and CHB) was considered. Metoprolol was discontinued due to CHB and LCM was also stopped in view of its cardiac side effect profile and levetiracetam was continued. She was treated with intravenous fluids and antibiotics. Two days later, CHB reverted to sinus rhythm and the temporary pacemaker was removed. Over the period of hospitalization, her hepatic and renal functions normalized.

LCM is a newer antiepileptic drug marketed since 2008. Its mechanism of action is by inactivation of voltage-gated sodium channels and is indicated as an "add-on" drug for partial onset seizures as well as for neuropathic pain modulation. It is reported to have good safety profile and only minimal side effects including nausea, headaches, dizziness, diplopia, and confusion.[1,2] Cardiac side effects are infrequent, but may occur at therapeutic doses or at toxic level. These include mainly cardiac conduction abnormalities including ST-wave and T-wave changes and PR and QRS interval prolongation on ECG,[1] and rarely, it can lead to second- and third-degree atrioventricular (AV) block that is reversible after stopping LCM.[2,3] Second- and third-degree block has rarely been reported at doses higher than 400 mg, with underlying renal disease or concomitant AV blocking drugs and preexisting AV block.[4-7]

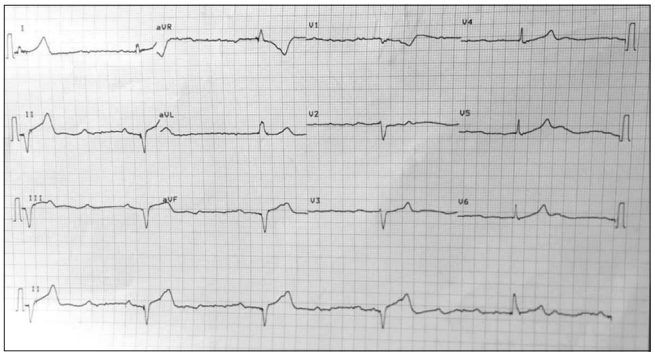

Figure 1: Electrocardiogram showing complete heart block with ventricular rate of 30/min

In our case, we opined that there were mainly three reasons for CHB: first, older age, second, she was on drug that has negative dromotropic effect on AV conduction-metoprolol (although in low dose of 25 mg/day), and third, she developed impaired renal function due to new-onset diarrheal illness, leading to decreased LCM clearance. A dose-dependent accumulation of LCM leading to prolongation of PR interval is a rarely described adverse effect in preclinical and postmarketing studies.[8] A cause–effect relationship could definitely be established in our patient by the occurrence of CHB after dose escalation of LCM as well as its reversal with holding of LCM.

While LCM is being recommended as a relatively safer drug for use in the elderly, with multiple comorbidities, it can rarely be associated with serious adverse events such as CHB, and this needs to be well known to practicing neurologists. We suggest that, in geriatric patients, who frequently have concomitant cardiac dysfunction, are on concurrent polytherapy, LCM should be used at a lower dose and any titration in dose should be closely monitored with ECG and the dose should be reduced immediately in conditions which can alter renal function.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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References

1. Malissin I, Baud FJ, Deveaux M, Champion S, Deye N, Megarbane B, *et al.* Fatal lacosamide poisoning in relation to cardiac conduction impairment and cardiovascular failure. Clin Toxicol (Phila) 2013;51:381-2.
2. Krause LU, Brodowski KO, Kellinghaus C. Atrioventricular block following lacosamide intoxication. Epilepsy Behav 2011;20:725-7.
3. Nizam A, Mylavarapu K, Thomas D, Briskin K, Wu B, Saluja D, *et al.* Lacosamide-induced second-degree atrioventricular block in a patient with partial epilepsy. Epilepsia 2011;52:e153-5.
4. Wittstock M, Benecke R, Johannes Roesche. Transient third degree atrioventricular block following rapid lacosamide titration in a patient with nonconvulsive status epilepticus. Epileptologia 2011;19:165-9.
5. Lachuer C, Corny J, Bézie Y, Ferchichi S, Durand-Gasselin B. Complete atrioventricular block in an elderly patient treated with low-dose lacosamide. Cardiovasc Toxicol 2018;18:579-82.
6. Marin-Gracia M, Cantero-Lozano D, Garces-Anton E, Lopez-Bravo A, Garrido-Fernandez A, Navarro-Perez MP, *et al.* Lacosamide associated with high-degree block in a patient with trigeminal neuralgia. Rev Neurol 2018;66:189-92.
7. Recena Pérez P, Leizaola Irigoyen O, Antuña Braña MT. Complete heart block by lacosamide. Med Clin (Barc) 2018;151:166-7.
8. Husain A, Chung S, Faught E, Isojarvi J, McShea C, Doty P, *et al.* Long-term safety and efficacy in patients with uncontrolled partial-onset seizures treated with adjunctive lacosamide: Results from a phase III open-label extension trial. Epilepsia 2012;53:521-8.

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