Lacosamide-Indcued Brugada! *& SA Exit Block!!*

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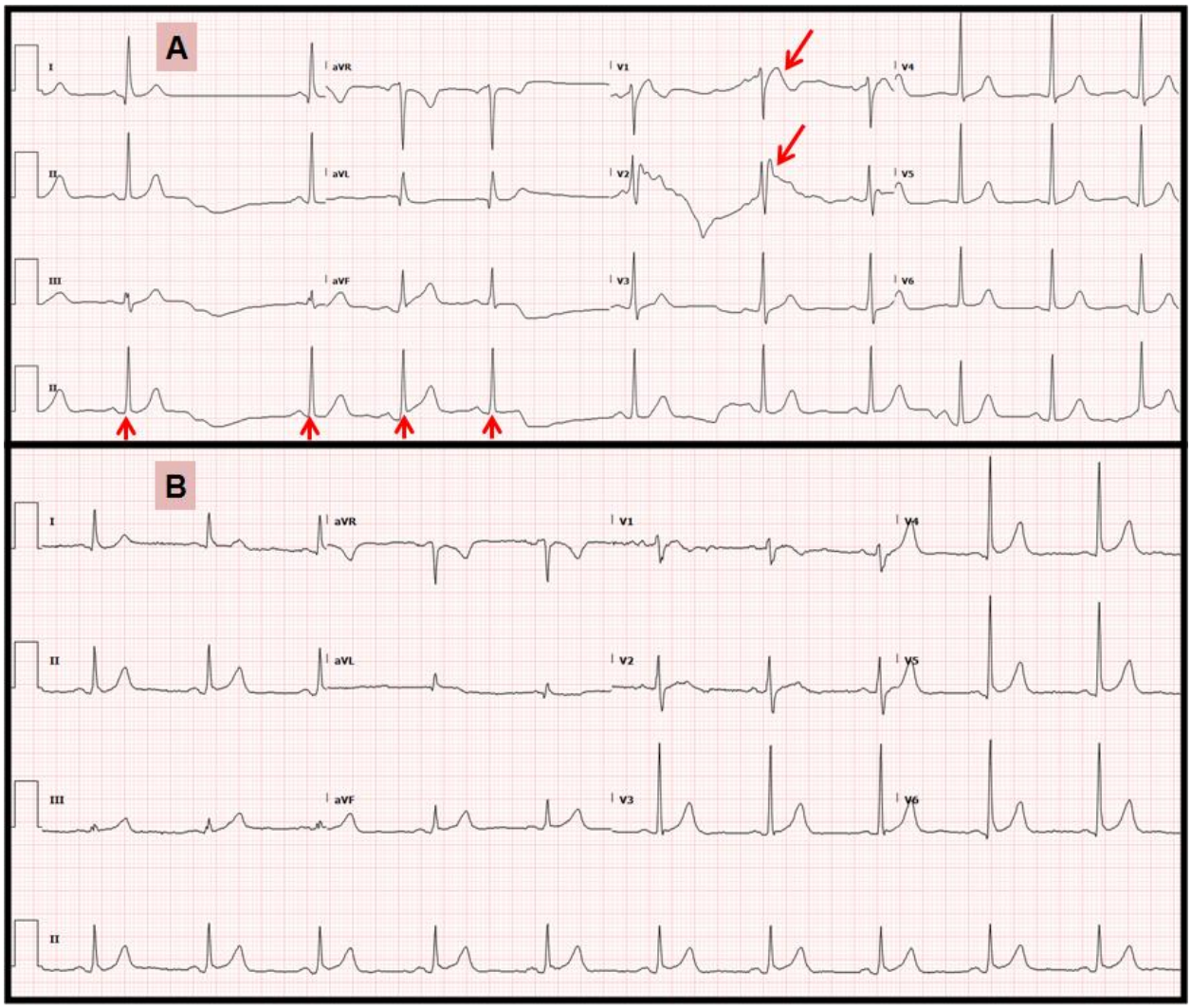

Description

The electrocardiogram shown above reveals Brugada type I pattern in V1 & V2 (large arrows), and sinoatrial exit block (small arrows) while on Lacosamide (A). Changes resolved after stopping Lacosamide (B).

Sodium channel blockers have been used in the treatment of focal and generalized tonic-clonic seizures for more than 70 years [1]. SCB stabilize hyper-excitable neuronal membranes by selectively increasing the slow inactivation of

Manuscript submitted May 20, 2019, accepted May 24, 2019.

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https://cardiofellows.com/newsletter-may-2019.html

ISSN 2689-291X https://doi.org/10.13140/RG.2.2.13611.87847

voltage-gated sodium channels [2]. These drugs reduce the action potential duration and the maximal upstroke velocity (Vmax) in the isolated canine Purkinje fibers, causing unwanted side effects [3].

Lacosamide, carbamazepine, and lamotrigine all inhibit the cardiac sodium channel SCN5A in a concentration-dependent manner [6]. Disruption of the SCN5A channel causes severe arrhythmia, including ventricular tachycardia, in patients with Brugada syndrome, a channelopathy which is associated with an increased risk of ventricular tachycardia and sudden death [6].

Provocation with a sodium channel blocker can unmask latent Brugada syndrome. Brugda syndrome causes arrhythmia in the His-Purkinje system, the right ventricle, the sinus node and atrium, due to ion channel mutations. Sinus node dysfunction may therefore be another cause of syncope in Brugada syndrome [7].

Electrocardiographically characterized by a distinct ST-segment elevation in the right precordial leads, the Brugada syndrome is associated with a high risk for sudden cardiac death in young and otherwise healthy adults. The ECG manifestations of Brugada syndrome are often dynamic or concealed and may be unmasked or modulated by sodium channel blockers [8].

Sudden unexpected death in epilepsy (SUDEP) is the most common epilepsy-related cause of death [9]. While the precise pathophysiological mechanisms underlying SUDEP are still uncertain. The potential role of antiepileptic drugs has been suggested [9].

Drugs which decrease inward currents (fast sodium current) at the end of phase 1 of the action potential can accentuate or unmask ST-segment elevation, similar to that found in the Brugada syndrome, thus producing acquired forms of the Brugada syndrome [10,11]. IV use of phenytoin causes reluctance to its usage due to possible cardiovascular effects. However, there is no reported cardiotoxicity resulting from oral overdose of phenytoin. One patient with post-traumatic epilepsy who received oral phenytoin for five months and developed life-threatening junctional bradycardia, with his serum phenytoin level reaching up to 91 microg/mL. Severe phenytoin overdose should be considered in any patient with dysrhythmia and cardiovascular collapse on oral phenytoin [12].

A case of complete atrioventricular block with ventricular asystole was also reported in a patient receiving intravenous phenytoin [13].

Carbamazepine was suspected of inducing sinus node dysfunction and atrioventricular block. After few months of carbamazepine therapy, patients were reportedly treated in emergency rooms for bradyarrhythmia [14]. A study of the effects of lamotrigine on ECG intervals in healthy volunteer population indicated that the PR interval may be slightly prolonged, especially at high doses of lamotrigine [15].

Lacosamide is a relatively new antiseizure agent approved in the United States and Europe for adjuvant treatment of partial-onset seizures [16], however, experiments examining the mechanism of lacosamide block of neuronal sodium channels have suggested that the interaction of lacosamide with sodium channels is fundamentally different from that of the classic antiepileptic drugs in that lacosamide appears to selectively bind to the slow-inactivated state of the channel [16] suggesting a different binding site and novel mode of action.

Clinical studies have shown a small, dose-related increase in PR interval associated with lacosamide use [17]. There are several case reports which reported cardiac conduction abnormalities in patients with epilepsy while on lacosmaide. A case of second-degree atrioventricular block was reported to be caused by the addition of lacosamide to other antiepilepsy medications known to prolong the PR interval, resulting in hypotension and bradycardia [18].

One patient was reported who experienced ventricular tachycardia during a cardiac stress test [6]. More reported cases in patients taking lacosamide at a higher than approved dosage: one experienced atrial flutter/fibrillation (on 600

mg/day) [19], while the other with low dose had atrial fibrillation [20].

One case was in a child with subclinical seizures, hypoplastic left-heart syndrome, and previously well-controlled atrial tachycardia, who experienced atrial tachycardia coinciding with lacosamide treatment [21]. All patients completely recovered after discontinuing lacosamide.

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KEYWORDS: Lacosamide; Sodium Channels; Seizure Medications; Arrhythmia.

Reference this article as:

Bath K, Akbar A, Tahir H, Rafique M, Omar B. Lacosamide-Induced Brugada! & SA Exit Block!! Cardiofel Newslet 2019 May; 2(5): 17-20.