

Pregabalin Intoxication-Induced Prolonged PR Interval on Electrocardiogram

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ABSTRACT

Pregabalin is a lipophilic analogue of gamma-aminobutyric acid (GABA) and has a similar chemical structure to gabapentin and is more potent than gabapentin. This report documents the case of a 28-year-old male presenting with suicidal attempt by pregabalin intake. The patient had an abnormal PR interval (reversible AV-block). He was managed with general supportive care and symptomatic approach such as discontinuation of the drug, hydration with IV fluids, oxygenation, gastric lavage and activated charcoal administration.

Key words: Pregabalin, intoxication, AV-block

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INTRODUCTION

Pregabalin has been used increasingly in recent years in the treatment of neuropathic pain, epilepsy and anxiety disorders. It has been reported in the literature with suicidal attempt and its side effects [1,2]. Pregabalin is a lipophilic analogue of gamma-aminobutyric acid (GABA) and has a similar chemical structure to gabapentin and is more potent than gabapentin. Pregabalin does not bind to plasma proteins and thus readily penetrates the blood-brain barrier. It is primarily cleared unchanged by renal excretion with an elimination half-life of approximately 6 hours but is increased in patients with renal impairment and depends on creatinine clearance [3].

We report here a case of isolated pregabalin toxicity that was successfully managed with conservative treatment only.

Case report

A 28-year-old man admitted to our emergency department (ED) who had taken 16 Lyrica 150 mg (Pregabalin) for suicide attempt. On presentation to the ED, he was alert with Glasgow Coma Score (GCS) of 15 points, his vital

parameters were stable with a heart rate of 75 per minute and blood pressure of 120/70 mmHg, afebrile with a body temperature of 37.0 °C and had good respiratory effort with a respiratory rate of 18 per minute. His initial laboratory tests were normal except for creatine phosphokinase (CPK: 878 U/L). But on his electrocardiogram (ECG), PR interval was longer than normal (350 msec). He was hospitalized in emergency observation unit with the diagnosis of 1 st degree AV block. Initially, he was managed with general supportive care and symptomatic approach such as discontinuation of the drug, hydration with IV fluids, oxygenation, gastric lavage and activated charcoal administration via nasogastric catheter and enhanced elimination techniques. He was monitored in the emergency observation unit. On the second day, his PR interval was a bit shorter than the baseline ECG but still over 200 msec. On the third day of observation, finally PR interval returned to normal limits (120-200 msec). The patient was treated with general supportive care and symptomatic approach for 3 days. At the end of 3 days his serum CPK level and ECG findings became normal. He was discharged home after following up for 3-days at hospital.

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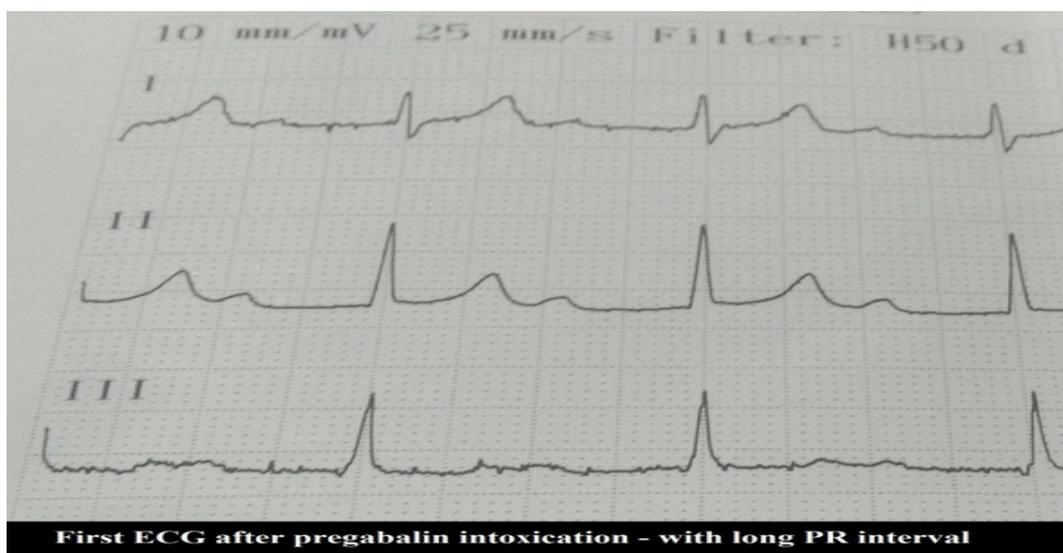


Figure 1. First electrocardiogram of the patient

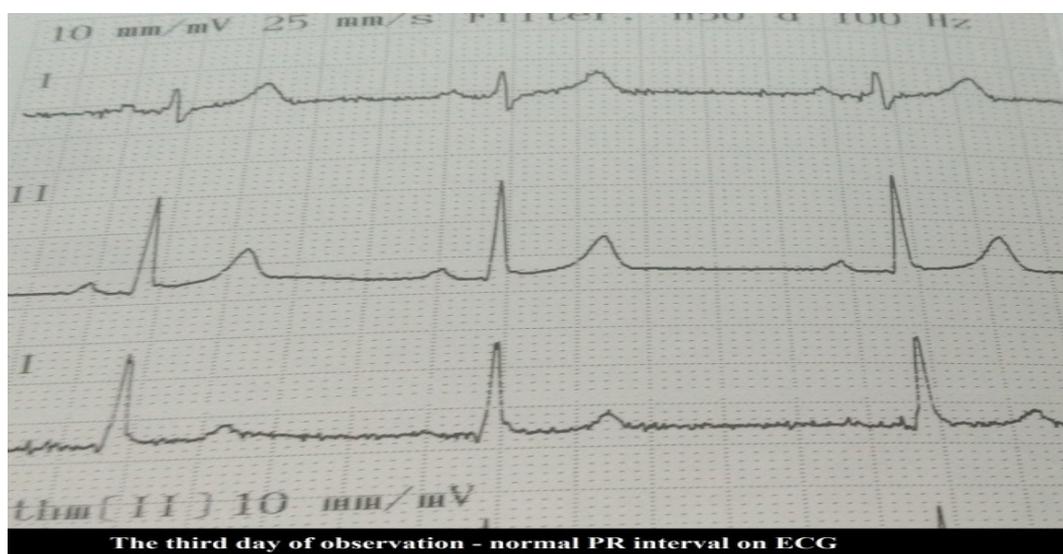


Figure 2. Electrocardiogram of the patient at the third day

DISCUSSION

Pregabalin is a synthetic derivative of GABA, an inhibitory neurotransmitter. It is used commonly in many chronic pain syndromes, especially in diabetic neuropathic pain. Its main advantages are its safety, ease of use, and lack of interaction with other medications [4].

Pregabalin is a selective and high affinity ligand for the $\alpha 2$ - δ subunit of voltage-gated L-

type calcium channels. Pregabalin reduces calcium flux to the nerve terminals, decreases neurotransmitter release and thus results in an inhibitory neurological response. The $\alpha 2$ - δ subunits of L-type sodium channels are well described for the heart and brain. L-type calcium channels play a key role in calcium entry

into cardiac cells; excitation-contraction coupling. Dihydropyridine group calcium channel blockers similarly act via L-type calcium channels [5].

The most common adverse events associated with pregabalin intoxication are fatigue, sleepiness, mouth dryness and peripheral edema. Cardiac effects of pregabalin overdose have also been reported in the literature. Due to pregabalin overdose, changes in PR distance, complete AV conduction-block, and decompensated heart failure may develop [6]. In our patient, PR interval was prolonged on admission and measured as 350 msec on ECG.

Despite the considerable increase in the use of pregabalin in recent years, there is insufficient information about its side effects. Our report has revealed the possible alteration on ECG following pregabalin use for suicidal attempt. Although we could not

determine the blood level of pregabalin in laboratory, we had the opportunity to clinically observe the patient for 3 days. During this period, we managed the patient conservatively with supportive and symptomatic treatment. In a report by Belli et al., supportive and symptomatic therapy was revealed to be sufficient in patients with pregabalin abuse. Additionally, the importance of being in contact with a center capable of hemodialysis was underlined. Hemodialysis may be beneficial to reduce the half-life of pregabalin approximately three-fold [7]. We identified two abnormalities in our follow-up; increase in serum CPK level and conduction abnormalities on ECG. We also monitored urine output, urine color and serum creatinine, since elevated serum CPK levels could lead rhabdomyolysis, and eventually acute renal failure. In the follow up laboratory tests, serum CPK levels tended to decrease. Besides, the ECG change we detected was in the form of isolated PR prolongation, defined as type I AV block. We aimed to share this side effect, which is rare in high doses of pregabalin.

Conflict of Interests: The authors declare that they have no conflict of interest.

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