Mianserin Cardiotoxicity with First Degree AV Block: Case Report and Review of the Literature

Birinci Derece AV Blokla Seyreden Mianserin Kardiyotoksisitesi: Olgu Sunumu ve Literatürün Gözden Geçirilmesi

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Geliş Tarihi/*Received:* 31.08.2015
Kabul Tarihi/*Accepted:* 19.03.2016

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ABSTRACT Mianserin, which has a tetracyclic structure, is frequently used in depression, sleep disorders, and anxiety treatment in clinical practice. Although mianserin is considered to be more safely than other anti-depressant agents in terms of fewer side effects and cardiotoxicity, results of the studies and case reports on effects of mianserin in the literature are controversial. In this paper, we reported that case of a woman who was admitted for self-poising with mianserin and detected first-degree AV block on electrocardiogram without clinical findings such as hypotension, bradycardia, and arrhythmias. Although mianserin is known as a safe drug terms of cardiotoxicity, physicians should be aware that overdosing of these drugs can cause changing from non life-threatening situations to life-threatening situations.

Key Words: Mianserin; poisoning; atrioventricular block; cardiology

ÖZET Mianserin tetrasiklik yapıya sahip olup, klinik pratikte genellikle depresyon, uyku bozuklukları ve anksiyete tedavisinde kullanılan bir ajandır. Diğer antidepresanlara göre mianserinin kardiyotoksisite ve yan etkiler açısından daha güvenilir olduğu düşünülmesine rağmen bu konudaki çalışmaların ve vaka sunumlarının sonuçları çelişkilidir. Bu yazıda, mianserin ile intihar girişiminde bulunma şikayeti ile başvuran ve hipotansiyon, bradikardi ve aritmi gibi herhangi bir klinik bulgusu olmayan ancak elektrokardiyografisinde birinci derece AV blok saptanan kadın hasta raporlanmıştır. Mianserinin kardiyotoksisite açısından güvenli bir ilaç olarak bilinmesine rağmen, klinisyenler bu ilaçların yüksek alımlarında basit semptomlar kadar yaşamı tehdit edebilecek durumlara da yol açabileceklerinin farkında olmalıdırlar.

Anahtar Kelimeler: Mianserin; zehirlenme; atriyoventriküler blok; kardiyoloji

Turkiye Klinikleri J Case Rep 2016;24(2):197-200

Mianserin, which has a tetracyclic structure, is frequently used in the clinical treatment of depression, sleep disorders, and anxiety. When it is compared to tricyclic antidepressants, it has a good clinical safety profile due to fewer side effects and a lower risk of cardiotoxicity. However, some experimental studies and case reports have shown that cardiovascular and arrhythmogenic side effects have occurred due to mianserin usage or overdosage.[1-3] We report the case of a woman who was admitted for self-poisoning with mianserin, in which a first-degree AV block was detected via electrocardiogram (ECG).

doi: 10.5336/caserep.2015-47726

CASE REPORT

A 29-year-old woman was admitted for attempted suicide by taking 13 tablets of 30 mg mianserin, and she had also taken an unknown dosage of alcohol one hour before admission. The patient's anamnesis revealed that she had been taking mianserin 30 mg/day for depression for the past year. Upon initial evaluation, she was alert and oriented, and her Glasgow coma score was 15. She had no other clinical complaints. Her vital signs were as follows: temperature of 36.6°C, heart rate of 110 beats per minute, blood pressure of 120/70 mmHg, respiratory rate of 14 breaths per minute, and oxygen saturation of 99% on room air. An initial ECG revealed sinus tachycardia and a PR interval of 0.16 seconds. The durations of QRS complex and the QT interval were normal (Figure 1). When the patient's blood alcohol level was analyzed via breathalyzer, it was detected at 30 promill. Orogastric lavage was administered using 1 gr/kg of active charcoal, and intravenous normal saline was started. Laboratory results were normal. Urine toxological analysis showed no other toxic agents.

Eight hours later, control ECG detected prolongation of the PR interval (0.26 seconds) without clinical findings of hypotension, bradycardia, or arrhythmia, but the QRS complex and QT interval were normal (Figure 2). Twenty-four hours after admission, the patient's ECG and vital signs were normal, and she was discharged.

DISCUSSION

Mianserin is a tetracyclic piperazinoazepine; the major effects of this agent are blocking presynaptic alpha-2 receptors and 5-hydroxytriptamin receptors in the central nervous system. Therefore, it can be used to treat depression, sleep disorders, and anxiety.[4,5] In addition, these agents have anti-histaminic properties, and mianserin was initially designed to be an anti-allergic drug due to these features.[6]

Although these drugs are considered to be safer than other anti-depressant agents (such as tricyclic anti-depressants, serotonin re-uptake inhibitors, and mirtazapine) due to fewer side effects and reduced risk of cardiotoxicity, the results of studies on the effects of mianserin are controversial. The first experimental studies in the 1970s showed that in vivo, mianserin can cause prolongation of the PR interval, widening of the QRS complex, ventricular arrhythmia, and ventricular tachycardia.[1,7] Other animal studies in the 1970s showed that rapid intravenous infusion of mianserin can cause transient hypotension.[8] How-

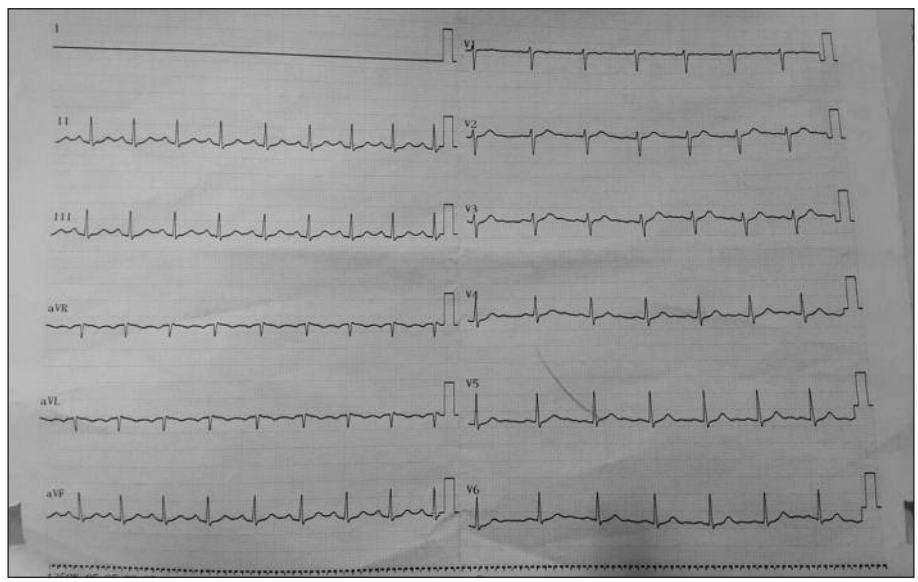

FIGURE 1: Patient's initial ECG, PR interval was normal (0.16 sec).

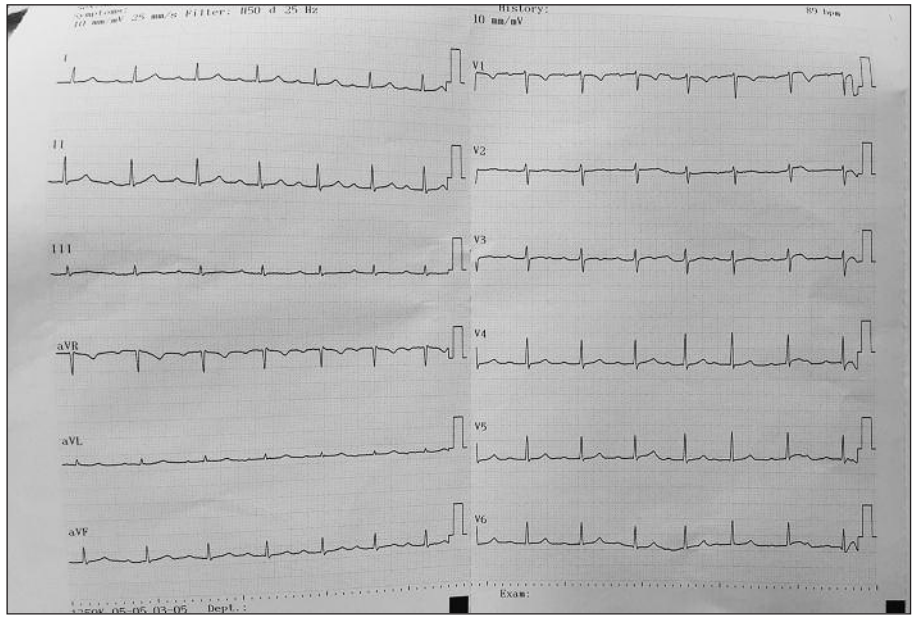

FIGURE 2: Patient's control ECG eight hours later, PR interval was prolongation (0.26 sec).

ever, clinical studies in the 1970s and 1980s showed that mianserin had no cardiotoxic side effects, such as prolongation of the PR interval, widening of the QRS complex, changes in T wave amplitude, or changes in QT duration.[9,10] However, in 1978, Burgess et al. reported that mianserin could cause reversible prolongation of the QT interval.[11]

Although there are no more recent clinical studies, there are some case reports on the side effects of mianserin use or overdose. Deutsch et al. reported the case of a 24-year-old woman who was diagnosed with non-sustained polymorphic ventricular tachycardia due to using mianserin 30 mg/day for depression for six weeks.[3] Similarly, Haefeliet al. reported a 61-year-old man who was admitted for self-poisoning with a large, unknown dose of mianserin and diagnosed with ventricular tachycardia and ventricular fibrillation 28 hours after the poisoning.[2] Although these arrhythmias are thought to be related to blockage of the human ether-a-go-go related gene (hERG) channels—which is the alpha subunit of a potassium ion channel—by mianserin, Scherer et al. have reported that mianserin is a low-affinity antagonist of hERG potassium channels, and it has not been found to cause prolongation of QT duration or ventricular arrhythmias.[12] Overall, although Hughes et al. explained that the cause of PR prolongation in mianserin intoxication is the lowering effect of mianserin on the heart rate, it is unclear how mianserin could cause prolongation of the PR interval.

Although there are no case reports of lethal self-poisoning with mianserin alone, in a study conducted by Ohberg et al., which analyzed suicide mortality due to antidepressant drugs in Finland from 1990 to 1995, they reported that there were only two cases (1.9%) resulting from overdose with mianserin alone.[13] In addition, Isabelle et al. reported a fatal case of a patient who was admitted for attempted suicide with large and unknown doses of mianserin and disopyramide, which is an oral anti-arrhythmic drug that reduces cardiac conduction velocity.[14] However, according to the study authors, it is most likely that the cause of death in this case was disopyramide.

Koseoglu et al. reported that a 37-year-woman was admitted for attempted suicide with 30 mianserin 10 mg tablets. In this case, although her initial examination was normal, hypotension and sinus bradycardia occurred after four hours, but the PR interval, duration of the QRS complex, and the QT interval were normal.[6] Similar to our case, a study by Green et al. reported the case of a patient

admitted for attempted suicide with 58 tablets of 10 mg mianserin and diagnosed with a first degree AV block. The QRS complex, ST segment, and QT interval on the ECG of the patient were normal.[15] In our case, we detected a transient first degree AV block without clinical findings, such as hypotension, bradycardia, or arrhythmias.

In conclusion, we believe that in our case, the cause of the transient prolongation of the PR interval was mianserin overdose. In addition to the effects of mianserin, it has been suggested that alcohol consumption may be responsible for PR prolongation. However, as shown in previous studies, this effect of alcohol occurs only after heavy alcohol consumption.[16,17] Although mianserin is known as a safe drug in terms of cardiotoxicity, physicians should be aware that overdosing on this drug can cause various clinical situations, from non-life-threatening situations such as first degree AV block, hypotension, and sinus bradycardia to life-threatening situations such as ventricular tachycardia and fibrillation.

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