

# Rivastigmine Adverse Effects: Complete Heart Block

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## Abstract

**Context:** Rivastigmine (Exelon), a brain selective cholinesterase inhibitor, is used in the treatment of Alzheimer's Disease (AD) to improve cognitive functions.

**Case Report:** We report a case in which the addition of rivastigmine to memantine and metoprolol resulted in complete heart block and possibly predisposing a patient to syncope.

**Conclusion:** Rivastigmine should be used with caution, especially in patients with such structural heart diseases as aortic stenosis and those taking other medications that may contribute to bradycardia.

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**Key Words:** rivastigmine, adverse effect, complete heart block, syncope

## Introduction

Of the numerous types of medications studied in the treatment of Alzheimer's Disease, the only class proven to improve cognitive function is cholinesterase inhibitors.<sup>1,2,3</sup> In particular, rivastigmine tartrate, which is typically used in mild and moderate dementia, has the benefit of increased selectivity for brain acetylcholinesterase and butyrylcholinesterase, reducing the peripheral effects of hypotension and bradycardia.<sup>4</sup> Four previous phase-III studies evaluating the electrocardiogram (ECG) effects of rivastigmine did not reveal significant adverse effects with respect to bradycardia, PR, QRS and QT intervals.<sup>5</sup> This report illustrates complete heart block induced by rivastigmine.

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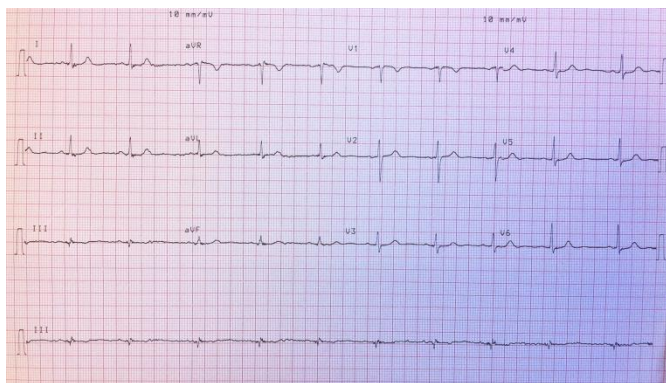
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## Case Report

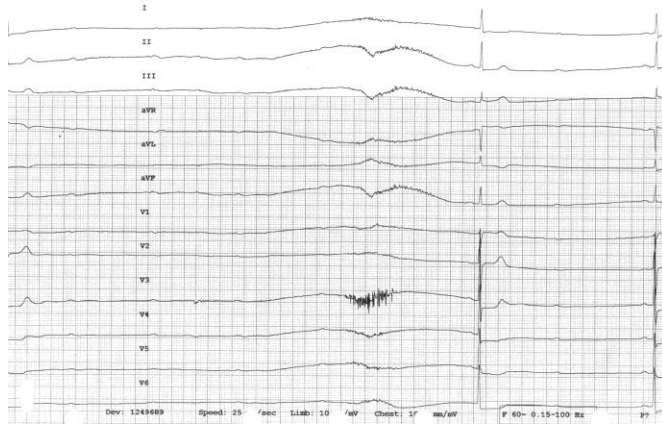
An 82-year old female with a past medical history of hypertension, dyslipidemia and dementia presented to the emergency room with a chief complaint of "not feeling well". Her husband stated that while at home, she suddenly became pale, diaphoretic, and her eyes rolled back as she became unresponsive. This lasted for several minutes until she returned to baseline. Although she experienced nausea, she denied chest pain, palpitations, dyspnea, fever, dysuria, limb weakness, abdominal pain, vomiting or seizure-like activity. She stated she had started a rivastigmine patch two days prior to the date of admission.

The patient's last visit with a cardiologist was five years prior to admission, at which time an ECG and stress test reportedly yielded normal results. She had been taking memantine and metoprolol succinate for approximately two years. She had a drug allergy to cephalosporins. She worked as a saleswoman previously, and lived at home with her husband. She had never smoked and denied alcohol use.

Physical exam revealed a 3/6 crescendo-decrescendo systolic murmur at her right second intercostal space, radiating to her carotid arteries bilaterally, with a normal first and second heart sound. Her neurological exam was normal. Laboratory studies, including cardiac enzymes, were negative. Her chest x-ray revealed no acute cardiopulmonary disease. Her ECG showed sinus bradycardia at 51 beats per minute (bpm), with no Q wave, ST segment, or T wave ischemic changes. Her baseline ECG showed normal PR and QTc (**Figure 1**).



**Figure 1. The baseline ECG.** An elderly patient had been taking medications including memantine and metoprolol succinate. Normal sinus rhythm, normal QRS morphology, PR is 160 ms and QTc is 402 ms.



**Figure 2. Rivastigmine patch associated with complete heart block.** An elderly patient had been taking medications including memantine and metoprolol succinate. Recently the patient added rivastigmine patch for dementia. The patient presented with syncope and her ECG showed complete heart block as above. P waves are subtle findings, but they are present.

While in the emergency room, telemetry monitoring revealed a transient third degree atrial ventricular block ( AVB) with a narrow QRS complex (**Figure 2**). She was admitted to the cardiac intensive care unit. Her rivastigmine patch and metoprolol succinate were discontinued. Within 24 hours, her telemetry monitoring revealed normal sinus rhythm with heart rate of 60-70 bpm. No further transient episodes of complete AV block occurred. Her echocardiogram showed severe aortic stenosis (the area was  $0.6\text{cm}^2$ ). A His bundle study was performed to evaluate her for infra-Hisian block. This study showed no abnormalities in the sinoatrial node, atrioventricular node or His Bundle. She remained stable and discharge was planned. Prior to discharge, she had an episode of syncope with hypotension and bradycardia at 58 bpm noted by the nursing staff. An ECG taken at that time showed sinus rhythm at 60 bpm. A carotid duplex was performed the following day, which revealed mild disease bilaterally. Her EEG was non-remarkable. Cardiothoracic surgery recommended aortic valve replacement for her severe aortic stenosis. Her ECG continued to show sinus rhythm.

## Discussion

In recent years, more elderly people are taking acetylcholinesterase inhibitors like rivastigmine for AD. Rivastigmine has been shown to improve cognition scores in patients with Alzheimer's dementia.<sup>5</sup> Four previous double blinded, placebo controlled, multicenter phase III clinical trials of rivastigmine analyzed the ECG effects, and complete AV block was not reported.<sup>6</sup>

Our patient had been taking metoprolol succinate for years and began rivastigmine treatment with a transdermal patch at the lowest available dose of 4.6mg/24h. Within two days of

starting rivastigmine, she presented with a history suggesting syncope at home, with complete AV block seen on telemetry only hours later. Normal sinus rhythm with heart rate of 60-70 bpm returned shortly after discontinuing her rivastigmine patch. Rivastigmine has a synergistic effect with beta blocker which can lead to complete AVB. Her critical aortic stenosis may have contributed to her second episode of syncope since no AV block was revealed at that time.<sup>7</sup> The first syncope episode at home could be associated with AV block related to rivastigmine in addition to AS.

A literature review showed only one documented episode of complete AV block associated with rivastigmine.<sup>8</sup> Recently, increased hospitalizations due to syncope and symptomatic bradycardia have been associated with rivastigmine, especially in the elderly taking multiple medications for different medical conditions. One case reported rivastigmine associated with prolonged QT interval.<sup>9</sup>

Acetylcholinesterase inhibitors are commonly administered in elderly patients. They may enhance a patient's quality of life, but like any treatment, risks may be associated with their use, including complete heart block and syncope. Careful consideration of patient co-morbidities is needed before starting treatments with rivastigmine and physicians must be alert to potential adverse cardiac effects, including complete heart block.

## Conclusion

This report illustrates a rare case of rivastigmine associated with complete heart block possibly predisposing a patient to syncope. Rivastigmine should be used with caution, especially in patients with aortic stenosis and those taking beta blockers.

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