CASE REPORT

CYPRUS
JOURNAL OF MEDICAL SCIENCES

DOI: 10.4274/cjms.2021.2546
Cyprus J Med Sci 2022;7(5):698-700

An Unexpected Cause of Symptomatic Bradycardia: Anti-glaucoma Eye Drops

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Abstract

Non-selective beta adrenergic blockers of which pharmaceutical form is eye drops are generally used for the treatment of glaucoma. Although applied topically, systemic side effects of these eye drops may occur. Here, a case of symptomatic bradycardia due to brinzolamide/timolol eye drops is presented. A 65-year-old woman with vertigo and dizziness was admitted to our hospital. Her electrocardiogram (ECG) revealed sinus bradycardia (heart rate 50/min). She was not using any oral negative chronotropic drugs. She was further questioned regarding her use of eye drops. She was using eye drops containing brinzolamide/timolol. She was told to stop using the eye drops. Two weeks later she was asymptomatic and her heart rate had increased to 65/min. When a patient presents with bradycardia, drug history should include topically administered drugs such as eye drops before performing further tests.

Keywords: Timolol, bradycardia, dizziness

INTRODUCTION

A topically administered fixed combination of brinzolamide and timolol is used for glaucoma treatment when intraocular pressure cannot be reduced sufficiently with monotherapy. Brinzolamide is a strong inhibitor of human carbonic anhydrase-II and inhibition of this isozyme decreases aqueous humor secretion. Timolol, on the other hand, is a non-selective beta blocker without intrinsic sympathomimetic activity which mainly decreases the formation of aqueous humor and increases outflow facility slightly. Although applied topically, these drugs may have severe systemic side effects. Here, we present a case of symptomatic bradycardia due to the use of topical brinzolamide and timolol combination.

CASE PRESENTATION

A 65-year-old woman with known ischemic heart disease and type-2 diabetes was admitted to our hospital with fatigue and dizziness. Her blood pressure was within normal limits (120/62 mmHg) but her pulse rate was 50/min. Initial physical examination did not reveal orthostatic hypotension. Further physical examination, including neurological examination, showed no pathological findings. Electrocardiogram (ECG) revealed sinus bradycardia with a heart rate 50/min (Figure 1). Transthoracic echocardiogram was normal. She was on aspirin (100 mg od), atorvastatin (40 mg od), amlodipine (5 mg od) and gliclazide (30 mg od). She had no history of taking any oral beta-blockers, non-dihydropyridine calcium channel blockers, antiarrhythmics, digitalis glycosides or parasympathomimetics. She was further questioned regarding the use of any eye drops and her answer was "yes". The name of the drug was Azarga® (Alcon Inc, Fort Worth, TX, USA) which is a topical ophthalmic solution consisting of brinzolamide 1.0% and timolol maleate 0.5%. She was using it one drop per eye twice daily. Since timolol is a beta-blocker and known to be rarely associated with symptomatic bradycardia, she was advised to stop using these eye drops and to see her ophthalmologist. Two weeks later, the patient was free of any symptoms and ECG revealed normal sinus rhythm with a heart rate of 65/min (Figure 2) after the discontinuation of the eye drops. Her symptomatic bradycardia was attributed to the use of these topical eye drops. Informed consent was obtained.

To cite this article: Baha RM. An Unexpected Cause of Symptomatic Bradycardia: Anti-glaucoma Eye Drugs. Cyprus J Med Sci 2022;7(5):698-700

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Received: 25.07.2020
Accepted: 28.02.2021

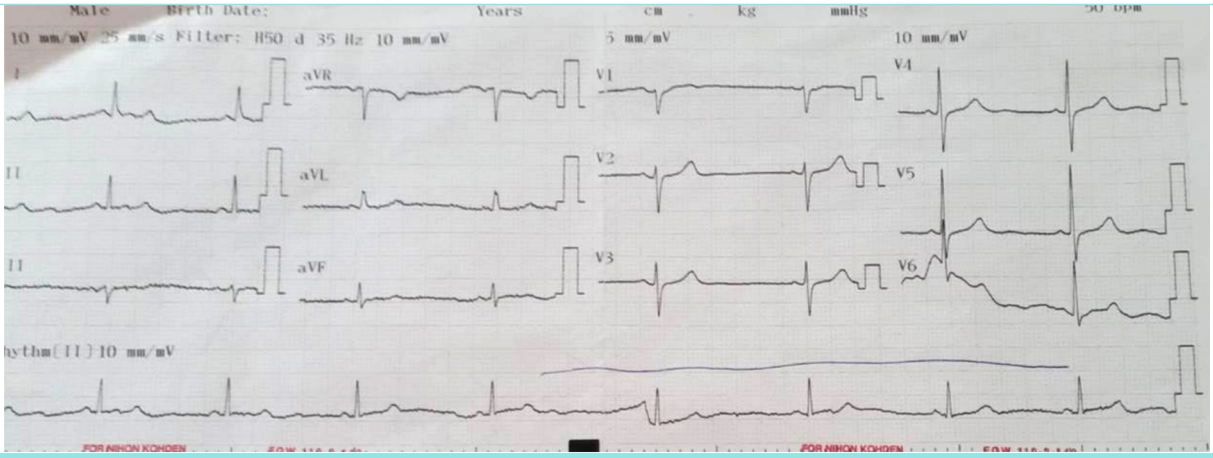

Figure 1. Initial resting ECG revealing sinus bradycardia while using eye drops.
ECG: electrocardiogram.

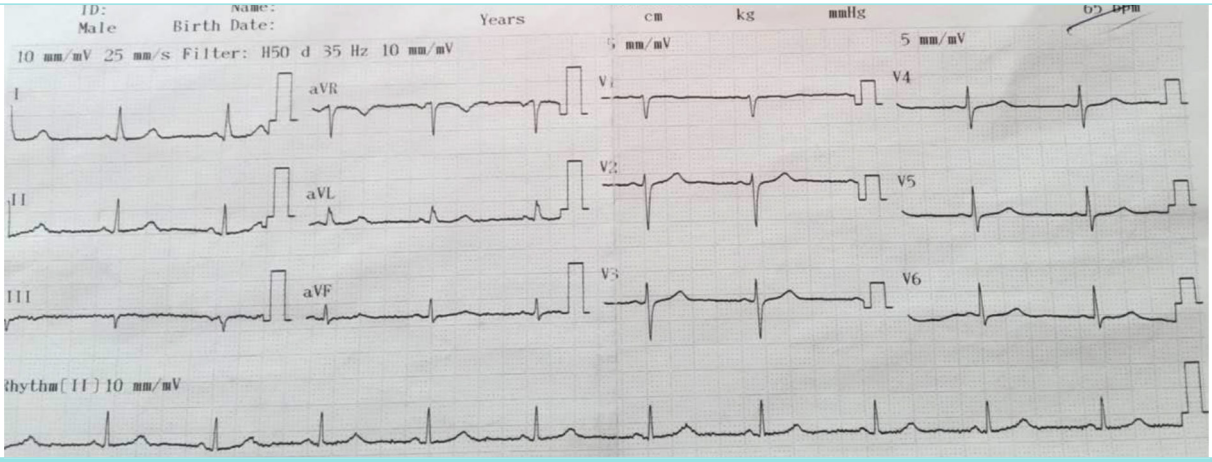

Figure 2. Resting ECG taken 2 weeks later showing normal sinus rhythm after the discontinuation of the eye drops.
ECG: electrocardiogram.

DISCUSSION

In our case, the responsible drug for the bradycardia was thought to be timolol because there is no evidence regarding systemic side effects associated with brinzolamide in the literature.[1]

Timolol is a non-selective beta-adrenergic blocking agent without intrinsic sympathomimetic activity and it has been on the market since 1978. Approximately 80% of topically applied timolol is absorbed from both conjunctival and nasal mucosa and directly enters systemic circulation, thus bypassing the pre-systemic metabolism of the liver.[2,3] This is why even when applied at small doses topically, it can cause systemic beta-adrenergic blocking effects.[2] Initial reports about timolol included only a slight decrease in heart rate.[4] On the other hand, nowadays, there are many reported adverse cardiovascular effects including arrhythmias (tachycardia and bradycardia), anginal chest pain, acute myocardial infarction, hypotension, heart failure, low blood pressure, orthostatic hypotension, heart and syncope.[4-7] A study including 14 patients treated with ophthalmic timolol showed only a minor decrease in pulse rate.[8] In another study, Dickstein et al.[9] reported similar results with a decrease in daytime mean heart rate of about 6 beats per minute (bpm) in patients with topically administered timolol eye drops. In our patient, timolol reduced the heart rate by 15 bpm which was more than expected indicating inter-individual variabilities regarding the effect of this drug. This possible exaggerated response to the drug may be associated with the age of our patient. It was shown that bradycardia associated with topical timolol may be more profound when used concurrently with oral negative chronotropic drugs. In 2006, a randomized controlled trial including 205 patients showed that in a group of glaucoma patients who were not on either topical or oral beta-blocking agents, average resting heart rate was 76 bpm, however, average resting heart rates were 70.3 bpm in those patients on topical beta-blocking agents, 64.7 bpm in patients on oral beta-blocking agents and 58 bpm in patients on both topical and oral beta-blocking agents.[10] The interaction of topical timolol with oral verapamil was also reported.[11] However, our patient had not been on any oral negative chronotropic drugs.

As shown in asthmatic patients, lacrimal occlusion may almost completely inhibit the systemic absorption of topical timolol, thus

preventing the systemic adverse events (e.g. bronchoconstriction) associated with this drug.[12]

We present this case in order to highlight the importance of careful history taking in the setting of bradycardia. Eye drops with beta-adrenergic blocking effects can have profound and sustained systemic effects, predominantly in old and fragile patients. Therefore, they should be prescribed with caution in the elderly population and in those patients with accompanying cardiovascular diseases. If such patients present with bradycardia, a thorough drug history should include topically applied medicines such as eye drops in order to avoid unnecessary further tests.

MAIN POINTS

- Eye drops, even when used as topical medicines, can have profound systemic effects.
- Beta-blocker eye drops should be prescribed with caution in older patients especially with cardiovascular co-morbidities.
- A clinician should take the patient's history carefully including all medicines with different pharmaceutical forms in order to avoid unnecessary tests.

ETHICS

Informed Consent: It was obtained.

Peer-review: Internally peer-reviewed.

DISCLOSURES

Financial Disclosure: The author declared that this study had received no financial support.

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