

Sick sinus syndrome associated with topical timolol maleate instillation

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ABSTRACT

A 70-year-old black woman presented with intermittent palpitations and dyspnea was found to be bradycardic with a normal sinus rhythm. She had instilled her topical timolol maleate approximately 30 minutes prior to each of these episodes. Topical timolol was discontinued and the conduction abnormality resolved. She was diagnosed as having intermittent sinus bradycardia with intermittent atrioventricular block, likely induced by topical beta-blocker therapy. Topical timolol maleate is an effective treatment for ocular hypertension, acting by reducing aqueous fluid production. However, it can induce systemic side effects and should be used with caution in patients with, or predisposed to, cardiac or respiratory depression.

Key words: Beta blocker, sick sinus syndrome, timolol

INTRODUCTION

Topical timolol maleate is a nonselective beta-adrenergic receptor blocker that is commonly used for treatment of open-angle glaucoma. It has been frequently used as first-line therapy for reduction of associated ocular hypertension. While systemic concentration after administration of topical beta-blockers is low in comparison to that achieved with oral beta-blockers, it is well known that topical therapy can induce cardiovascular, respiratory, central nervous system, and metabolic side effects.^[1] We report an interesting case of a sinus bradycardia with intermittent atrioventricular block induced by topical timolol maleate.

CASE REPORT

A 70-year-old black woman with a history of dyslipidemia, diabetes, hypertension, obesity, depression, and primary open-angle glaucoma presented to her cardiology appointment complaining of intermittent palpitations and dyspnea. At the time of examination at 9:00 AM, she was found to be bradycardic, with a normal sinus rhythm of 44 beats per minute; her cardiopulmonary examination was otherwise unremarkable. She had no history of structural or acquired cardiac disease. Her medications included hydrochlorothiazide, lisinopril, simvastatin, bupropion, topical timolol, and topical brimonidine.

She was admitted to the telemetry unit for further monitoring and evaluation of bradycardia. A serum electrolyte panel, complete blood count, and cardiac marker panel were drawn and all were within normal limits. Initial management consisted of inpatient telemetry monitoring with collection of serial cardiac enzymes and potential cardiac catheterization the following day. While on telemetry, she returned to normal sinus rate and rhythm until 9:45 PM, when her heart rate dropped to 41 beats per minute. An EKG at that time revealed

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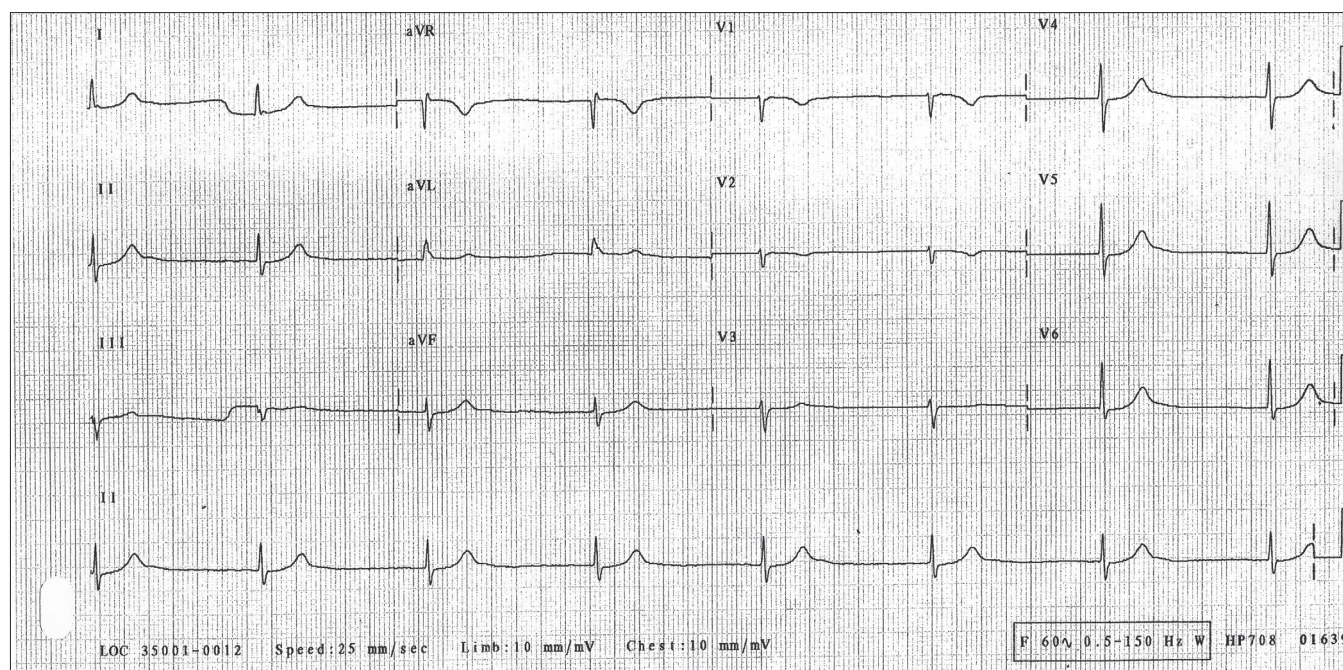


Figure 1: EKG demonstrating atrioventricular block

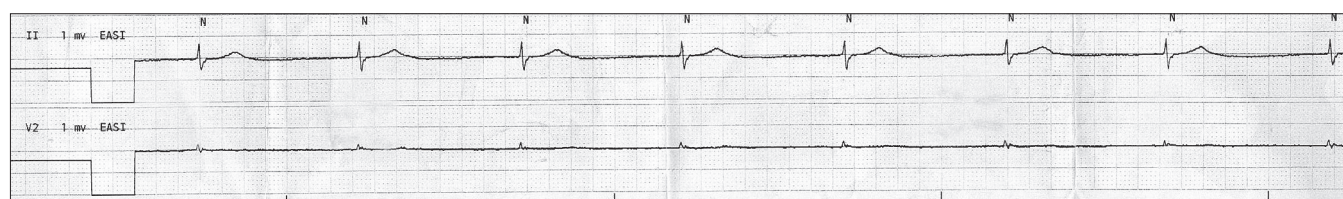


Figure 2: Telemetry recording demonstrating atrioventricular block

atrioventricular block [Figure 1]. She was asymptomatic and after approximately 14 minutes spontaneously converted back to a regular rate and rhythm. The next morning at 8:50 AM, the same phenomenon occurred, where she transiently went into an episode of asymptomatic atrioventricular heart block with a rate of 44 beats per minute [Figure 2]. Upon questioning we discovered that she had instilled her topical timolol maleate approximately 30 minutes prior to each of these episodes. Topical timolol was discontinued and the conduction abnormality resolved. She was diagnosed as having intermittent sinus bradycardia with intermittent atrioventricular block, likely induced by topical beta-blocker therapy. Subsequently, topical timolol was substituted with topical dorzolamide and a permanent pacemaker was placed.

DISCUSSION

Topical timolol maleate has long been known to be effective in the treatment of ocular hypertension.^[2] It typically lacks direct myocardial depressant activity.^[3] Timolol maleate like most topical ophthalmic agents is absorbed into the conjunctival, nasal, oropharyngeal, and gastrointestinal mucosal capillaries.^[1] After administration, onset of action

is in 20 minutes, with peak effect in 4 hours; the total effect usually lasts 24 hours.^[3] Peak plasma levels following topical administration have been shown to vary from undetectable to 9.6 ng/ml, but on average is accepted to be approximately 1 ng/ml. Although this is significantly lower than plasma concentrations following oral administration, it is sufficient to induce some degree of systemic beta-adrenergic blockade.^[1]

With regard to cardiac side effects, topical timolol has been shown to induce a decrease in heart rate and diastolic blood pressure.^[4] This effect has been shown to be synergistic with oral beta-blockers. A recent randomized controlled trial showed that in the subset of glaucoma patients not using either topical or oral beta-blockers, the mean resting pulse was 76 beats per minute (bpm); in comparison, patients using topical beta-blockers had a resting pulse of 70.3 bpm, patients on oral beta-blockers had a resting pulse of 64.7 bpm, and patients using both topical and oral beta-blockers had a resting pulse rate of 58 bpm.^[5] Our patient was not using oral beta-blockers. However, this information is important in the management of patients with both ocular and systemic hypertension.

Numerous reports exist of various cardiac and respiratory

disturbances occurring as a result of topical timolol. Third-degree atrioventricular block has been reported as a consequence of topical administration.^[6] However, our case report is the first to describe sinus bradycardia with intermittent atrioventricular block.

CONCLUSIONS

Topical timolol maleate is an effective treatment for ocular hypertension, acting by reducing aqueous fluid production. However, it can induce systemic side effects and should be used with caution in patients with, or predisposed to, cardiac or respiratory depression. More recently, topical prostaglandin E2 has emerged as a first-line therapy in glaucoma owing to its effect of increasing aqueous outflow while avoiding the systemic effects of topical beta-blockade.^[2] Additionally, a variety of medications and therapeutic options exist for both systemic hypertension and ocular hypertension associated with open-angle glaucoma. The clinician treating patients with coexisting ocular and systemic hypertension should be aware of these options, especially since topical beta-blockers

can induce severe systemic effects in patients without known cardiac or pulmonary dysfunction.

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