

# Complete Atrioventricular Block Caused By Timolol Eye Dropping: Case Report

## Atriyoventriküler Tam Bloğa Neden Olan Timolol Göz Damlası

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**ABSTRACT** Beta adrenergic receptor blockers are widely used medications for various clinical indications such as hypertension, acute coronary syndromes, heart failure and atrial fibrillation. Beta blockers that are locally administered like timolol, carteolol and betaxolol are widely used in ophthalmology. Locally administered beta adrenergic receptor blockers may rarely cause systemic effects that necessitates hospitalization such as asthma attack and symptomatic bradycardia. Beta blockers used in the management of intraocular hypertension and glaucoma may rarely be the reason for atrioventricular complete block. In this elderly patient admitted to hospital with symptomatic bradycardia, her electrocardiogram showed atrioventricular complete block. Past medical history revealed the patient was on timolol eye dropping for glaucoma. Atrioventricular complete block resolved after suspending the eye dropping.

**Key Words:** Atrioventricular block; timolol; glaucoma

**ÖZET** Beta adrenerjik reseptör blokerleri, hipertansiyon, akut koroner sendrom, kalp yetmezliği ve atrial fibrilasyon gibi değişik klinik endikasyonlarda yaygın olarak kullanılırlar. Timolol, karteolol, betaksolol gibi lokal uygulanan beta blokerler oftalmolojide sıklıkla kullanılmaktadır. Lokal kullanılan beta adrenerjik reseptör blokerlerinin, nadiren, astım atağı, semptomatik bradikardi gibi hastaneye yatış gerektiren, sistemik yan etkileri olabilmektedir. İntraoküler basınç yüksekliği ve glokom tedavisinde kullanılan beta adrenerjik reseptör blokerleri, nadiren atriyoventriküler tam blok nedeni de olabilirler. Semptomatik bradikardi nedeni ile hastaneye başvuran ileri yaşlı bu olgunun, elektrokardiyografisinde atriyoventriküler tam blok izlendi. Hastanın geçmiş tıbbi hikayesinde glokom nedeni ile timolol göz damlası kullandığı öğrenildi. Hastanın göz damlası kesildiğinde atriyoventriküler tam bloğun çözüldüğü izlendi.

**Anahtar Kelimeler:** Atriyoventriküler blok; timolol; glokom

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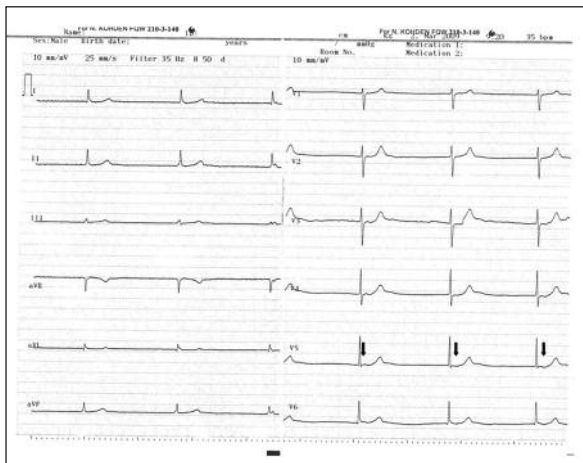
**B**eta adrenergic receptor blockers are widely used medications for various clinical indications. Ocular beta adrenergic receptor blocker preparations in the management of ocular hypertension and glaucoma can rarely cause systemic sympatholytic effects necessitating hospitalization despite local administration. We present a case of an elderly patient on topical timolol maleate therapy for glaucoma, diagnosed with complete AV block which resolved subsequently with the cessation of the offending topical drug.

## CASE REPORT

Seventy-eight year old female patient was referred for evaluation of dizziness and near-syncope which were present for two weeks. She denied palpitations and any other complaints. Her past medical history was not significant other than glaucoma, for which she was prescribed timolol (timolol aqueous solution 0.5%) eye dropping for the last month. She was not on any other medications. She had a regular heart rate of 35 beats per minute and her blood pressure was 120/85 mmHg. Cardiac auscultation was normal other than a variable S1 intensity. Electrocardiogram showed complete AV block (Figure 1). Transthoracic echocardiography demonstrated normal valvular and left ventricular function. The patient was hospitalized and her rhythm was closely monitored. Her medication for glaucoma was withheld and replaced with latanoprost after ophthalmology consultation. On the third day of her admission, patient was in sinus rhythm with a heart rate of 60 to 65 beats per minute (Figure 2) and her complaints were completely resolved. She was discharged home and being followed without any symptom and recurrent AV block.

## DISCUSSION

Non-selective beta receptor antagonist, timolol, was once used orally in cardiovascular therapy,<sup>1</sup> however, it is currently one of the options recog-



**FIGURE 1:** Complete AV block caused by topical timolol aqueous 0.5% solution (Arrows indicate p waves).



**FIGURE 2:** Normal sinus rhythm third day after cessation of the ocular timolol aqueous solution.

nized for the topical treatment of increased intraocular pressure, among with other therapies such as prostaglandin analogs, carbonic anhydrase inhibitors and  $\alpha$ 2-agonists.<sup>2,3</sup> Although locally used, due to the absorption from the eye, nasal mucosa or gastrointestinal epithelium, timolol can lead to systemic sympatholytic effects, such as a decrease in heart rate, and asthmatic attacks due to beta-2 receptor antagonism. There are reports regarding the heart-rate lowering effects of locally administered timolol, both for aqueous (0.5%) and gel (0.1%) formulations, that demonstrated the correlation between plasma concentration of timolol and heart rate, both at resting and especially during exercise.<sup>4,5</sup> The formulation of the drug could also have different effects on heart rate.<sup>5</sup> There could be individual discrepancies in the heart-rate lowering effect of timolol among subjects. Timolol is metabolized through CYP2D6 enzyme, and one of the underlying mechanisms of various negative chronotropic effects of timolol among patients is thought to be due to the differences in metabolizing the drug.<sup>6</sup> That is, poor metabolizers are more prone to sympatholytic effects of timolol, particularly in individuals with high adrenergic tonus.

The prevalence of chronic glaucoma increases with age and beta blockers such as levobunolol and timolol are widely used for this indication. Falls are

found mostly due to beta blocker eyedrops in elderly glaucoma patients.<sup>7</sup> There are very few cases of complete AV block caused by topical timolol reported in the literature.<sup>8</sup> Therefore, before imple-

menting a permanent device therapy for complete AV block, one should always carefully inquire any offending medication, including ocular beta blockers.

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