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Case Study

BRONCHOCONSTRICTION SECONDARY TO USE OF TOPICAL TIMOLOL IN A NON-ASTHMATIC PATIENT

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ABSTRACT

Ophthalmic application of a non-selective beta blocker like timolol maleate is known to produce bronchoconstriction in asthmatic individuals or patients with obstructive lung diseases. Timolol-induced bronchoconstriction in a previously healthy young adult without any pulmonary disease is rare. We report a case of a young adult who developed bronchoconstriction following ocular instillation of timolol maleate ophthalmic solution when he was treated for open-angle glaucoma.

Keywords: Topical beta blocker, Asthma, Timolol maleate, Glaucoma

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INTRODUCTION

Timolol, a non-selective beta-adrenergic blocker is commonly used as an ophthalmic solution for the treatment of glaucoma. It blocks the beta adrenergic receptor in the ciliary body, resulting in the reduction of aqueous humour formation, by decreasing cyclic adenosine monophosphate (cAMP). It possesses the therapeutic advantage of lowering intraocular pressure without changing the pupillary size or causing a diminution of vision and has no significant intrinsic sympathomimetic, direct myocardial depressant or local anesthetic (membrane-stabilizing) activity [1].

Timolol ophthalmic administration into conjunctiva will drain down the nasopharyngeal mucosa through nasolacrimal duct to the systemic circulation, bypass the liver, where it is normally metabolized [1]. Here, we present a case of timolol-induced bronchospasm in a patient without a history of respiratory disorders and resolved following drug withdrawal.

CASE REPORT

A 36-year-old male farmer (consent obtained from the patient for publication of case report) was admitted with a history of high-grade, intermittent fever, and conjunctival congestion. There was no previous history of bronchial asthma or exertional breathlessness. He was not a smoker. There was no family history of bronchial asthma. Physical examination of the patient showed conjunctival suffusion with subconjunctival hemorrhage. Respiratory system examination was normal. His laboratory parameters during admission were normal, except for leukocytosis (14,600 cells/cu. mm). His chest x-ray showed prominent perihilar broncho vascular markings.

In view of conjunctival suffusion and hemorrhage, an ophthalmology consultation was sought for. The evaluation showed raised intraocular pressure and patient was diagnosed to have primary open angle glaucoma. He was prescribed a combination of brimonidine with 0.5% timolol ophthalmic solution, to be instilled twice a day. The patient was also started on piperacillin-tazobactam with doxycycline as empirical therapy for leptospirosis, pending serology.

The patient developed a dry cough on the 3rd day after starting timolol eye drops. Auscultation of the chest revealed bilateral polyphonic rhonchi. However, his fever and other systemic symptoms subsided. Repeat chest X-ray showed clearing of perihilar shadow. He was started on nebulised salbutamol and ipratropium bromide for his respiratory complaints. His cough is increased on subsequent days and rhonchi worsened. We worked up for the etiology of bronchospasm, however no known cause could be established. Timolol was discontinued and plain brimonidine (α2-adrenergic receptor agonist) was continued. After discontinuation, the patient improved symptomatically, and rhonchi completely cleared up in 2 d. At follow-up after 2 w, the patient was asymptomatic and had a normal intraocular pressure.

DISCUSSION

Timolol has been found to cause bronchospasm based on a few reports documented previously, which were either in mild asthmatic patients or in healthy elderly individuals [2]. The present case is important to note because this young patient had no respiratory disorder during or prior to admission. He is neither a smoker nor does he give a history of bronchial asthma or bronchitis. In our case, timolol was found to be a "probable" cause of bronchoconstriction (based on Naranjo's algorithm for causality). We did not rechallenge our patient with timolol as any other drug was found to be responsible for the bronchospasm and the temporal relationship between the timolol dose and the subsequent occurrence of cough strongly implicated timolol as the inciting agent. Also, rechallenge is not necessitated as bronchoconstriction could be potentially life-threatening [3].

Assessment of adverse drug reaction was performed by using Naranjo scale and Hartwig scale [4, 5]. According to the Naranjo scale, the adverse drug reaction was found to be "probable" (score of 7 was obtained). As per Hartwig scale, it was moderately severe (level 4(a), i.e. adverse drug reaction requires the discontinuation of suspected drug, and treatment is required which increases the length of stay by at least one day).

CONCLUSION

The authors are reporting this case to stress on the fact that local use of a beta blocker even in non-asthmatic individuals can produce significant bronchoconstriction and hence, caution should be exercised even when using a topical beta blocker [6].

CONFLICT OF INTERESTS

Declared none

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