An Unusual Cause of Syncope Due to Topical Carbonic Anhydrase Inhibitor Prescribed for Glaucoma

Matlooba Al-Zadjali

Ministry of Health, Directorate of Hospital Affairs, Department of Curative Services Development, Oman

Abstract  Introduction: To report a case of vasovagal syncope due to topical carbonic anhydrase inhibitors (Brinzolamide) this is one of the option used for treatment of glaucoma. Methods: Case report. Results: A 74 year old man was referred for tilt table testing for syncope. Symptoms coincided with commencement of brinzolamide eye drops and resolved with its cessation. Conclusion: To the authors' best knowledge, this is the first report of carbonic anhydrase inhibitor eye drops causing syncope.

Keywords Vasovagal Syncope, A Topical Carbonic Anhydrase Inhibitor, Glaucoma

1. Background

Topical treatments are the preferred treatment option for glaucoma, as they avoid the systemic side effects with oral drugs. Topical carbonic anhydrase inhibitors have been shown to have very low absorption into the systemic circulation with red blood cell assays of carbonic anhydrase activity demonstrating levels insufficient to produce clinically-relevant side effects [1].

The following case of syncope induced by brinzolamide highlights the importance of consideration of systemic side effects of topical agents, despite the widely-accepted safety and tolerability profile of these agents.

2. Case Presentation

A 74 year old man with a history of hypertension on low dose of ACE inhibitors Lisinopril 5mg OD for more than 7 years and his blood pressure is well controlled. Recently was diagnosed with glaucoma presented to his general practitioner with a 12 month history of worsening pre-syncopal and syncopal symptoms. Pre-syncopal symptoms included dizziness, blurred vision and nausea, occurring 2-3 times a week with a single episode of syncope that occurred after he had returned home from a 20 minute walk. He had never previously had episodes of syncope prior to 12 months ago. There is no history of taking other medications a part from brinzolamide eye drops which was started for his glaucoma.

3. Investigations

He was referred to the tertiary hospital, (Department of Cardiology) where he underwent tilt table testing, confirming a diagnosis of vasovagal syncope with a VASIS type 1 (mixed vasodepressor and cardioinhibitory) collapse pattern [2] (Figure 1). Holter monitoring demonstrated sinus rhythm throughout and echocardiogram showed normal biventricular function with only mild aortic and mitral regurgitation.
Top trace shows the systolic and diastolic blood pressure curves; bottom trace shows heart rate curve, plotted against duration (minutes). The first 5 minutes of trace is when the patient is lying down on the tilt table in the preparatory phase, before upright tilt to 60 degrees is performed. There appears to be only a minor increase in heart rate and blood pressure initially on upright tilting to 60 degrees at 5 minutes, following which both parameters appear to stabilise over the next 20 minutes. At 25 minutes, the patient is given sublingual glyceryl trinitrate (GTN), which leads shortly after to a rapid decrease in heart rate and blood pressure, reaching a low of 50/30, at which time the patient loses consciousness. The patient is rapidly returned to the supine position, with prompt recovery of consciousness, and blood pressure and heart rate to baseline values.

4. Outcome and Follow-up

He was seen in the cardiology clinic following tilt table testing where a careful history was taken. He revealed that prior to developing these pre-syncopal and syncopal episodes; he had been started on brinzolamide 1% (Azopt) twice daily topical eye drops for glaucoma. His Ophthalmologist had therefore stopped this drug. Since this change in topical treatment for glaucoma, he has had no further symptoms of pre-syncope or syncope in the 1 year follow up period.

5. Discussion

To our knowledge, this is the first description of syncope induced by topical carbonic anhydrase inhibitors. Dorzolamide was the first topical carbonic anhydrase inhibitor to be introduced in the early 1990s, followed after by the newer agent brinzolamide. Both agents are commonly used to treat patients with glaucoma by lowering intraocular pressure by reducing the rate of aqueous humour formation [4-6]. Oral carbonic anhydrase inhibitors, such as acetazolamide, are known to cause many potential side effects, with the potential for blood pressure changes due to disturbances in acid-base balance [5-6]. To-date, there has been no systemic side effects reported with brinzolamide [3-4], with the reported side effects being confined to localised eye irritation, burning, stinging and blurred vision, which were fully reversible with cessation of the drug. This case report highlights the potential for topical agents to cause systemic side-effects, and the need to consider iatrogenic causes in evaluation of patients who present with syncope. Additionally, decrease the risk of systemic side effects with topical medications for glaucoma.

6. Learning Points

- Systemic side effects of topical agents for glaucoma should be considered, despite the widely-accepted systemic safety profile of these agents.
Always establish a clear history, including a drug history, in any patient presenting with episodes of syncope.

Declaration of Interest: Non

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