

Acetazolamide responsive episodic ataxia treated with methazolamide

CASE REPORT

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Abstract

Acetazolamide-responsive ataxia is a rare episodic ataxia (EA) disorder characterized by paroxysmal cerebellar ataxia. Many of the symptoms with EA can be treated with the carbonic anhydrase inhibitor acetazolamide. EA is a family of channelopathies each with its own unique mutation. We report a case of EA treated with methazolamide in a 37 year old man who experienced dysguesia with acetazolamide. Methazolamide has higher rates of diffusion into the tissue and a longer half-life compared with acetazolamide. It should be considered for episodic ataxia.

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Introduction

Acetazolamide-responsive ataxia is a rare hereditary episodic ataxia (EA) disorder which is characterized with symptoms of paroxysmal cerebellar ataxia. The condition was first described by Parker in 1946 at the Mayo Clinic in a case series of 11 patients [1]. The patients had ataxic episodes with minimal to no symptoms between attacks. Such episodes could be brought on by overexertion both physically and mentally and trigger attacks.

EA is most commonly treated with a carbonic anhydrase inhibitor, which prevents the interaction of $H_2O + CO_2 \leftrightarrow H_2CO_3$ [2]. This inhibition leads to a state of acidosis within the CSF. The reduction of pH using acetazolamide, a well-known carbonic anhydrase inhibitor, is believed to cause the therapeutic benefits when treating episodic ataxia. Studies do show that patients experiencing episodic ataxia have an abnormal high cerebellar pH level causing regional alkalosis.

There are several subtypes of EA. While the symptoms remain relatively constant throughout all subtypes, it's the duration and

genetic factors that differentiate them. Episodic ataxia type 1 (EA1) has been mapped to a specific brain channelopathy and shows less of a treatment response to acetazolamide, as opposed to episodic ataxia type 2 (EA2). Acetazolamide has been used as a successful therapy in EA2 for 50% to 75% of patients it [3].

Case Report

A 39 year old right-handed Caucasian man with EA presented to our neurology clinic. The patient has a 10 year history of ataxic spells deemed acetazolamide-responsive ataxia. Episodes tend to reach their peak in 10 minutes lasting from 1 hour up to 4 hours requiring multiple emergency department visits. The patient describes that these episodes start with numbness and tingling in his feet, progressing to his neck and head also associated with light-headedness, dizziness, blurry vision and sensation of heaviness throughout his body, reporting a feeling of "drunkenness". Stumbles while walking and must hold onto someone while walking. His wife states that his eyes are "jerky" during these episodes, and his speech becomes very slurred; although at baseline he does have a speech impediment per his wife and father. The patient has no family history of any neurological disorders and no one else in his family has experienced similar symptoms. Although EA is usually hereditary and seen throughout a family sporadic cases do appear.

The patient was having episodes on average once a week in the winter and 3-4 times a week during the summer. The patient reported that 2-3 years previously he was prescribed acetazolamide for his ataxic spells with great relief of symptoms in terms of frequency and severity. However, the patient discontinued acetazolamide due to dysgeusia, a disorientation of taste often producing a sour taste.

On the patient's initial exam, he showed prominent saccade and nystagmus, however, without other cerebellar findings. He was prescribed metha-

zolamide, another carbonic anhydrase inhibitor, at 50 mg twice a day later up-titrated to 100 mg twice a day. He denied dysgeusia while on methazolamide and reported efficacy in terms of attacks of ataxia even greater than acetazolamide.

Discussion

We present a sporadic case of acetazolamide-responsive ataxia that was successfully treated with methazolamide. Treatment with methazolamide is believed to be completely unique and never used before in treating EA. The patient was on acetazolamide with good clinical efficacy but discontinued due to dysgeusia. This adverse-effect is well published. For example, acetazolamide is known to be used by hikers to counter the effect of altitude sickness. A group of hikers took 500 mg of acetazolamide to ascend between 12,000-14,000 feet and reported a change in taste with carbonated beverages [4].

Treatment with acetazolamide in cases of EA are well documented, however, to our knowledge, never reported with methazolamide. However, generally heterocyclic compound such as methazolamide are more active than homocyclic compounds such as acetazolamide [5]. Maren in his article comparing the pharmacology between methazolamide and acetazolamide states that methazolamide is superior in almost all domains. Methazolamide has higher rates of diffusion into the tissue with lower plasma binding and a longer duration of activity. The half-life of methazolamide is 14 hours compared to 5 hours with acetazolamide [5]. Further, Maren goes as far as saying "I do not recommend acetazolamide for any medical use or any experimental use either" [5].

Conclusion

We demonstrate the clinical efficacy of methazolamide for acetazolamide-responsive ataxia in our patient. Comparing the effectiveness of acetazolamide versus methazolamide in the treatment of EA (and other conditions such as glaucoma and idiopathic intracranial hypertension) may be warranted.

Competing Interests

The authors declare that they have no competing interests.

Authors' Contributions

All authors participated in the preparation of the manuscript, and read and approved the final manuscript.

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