Does acetazolamide act in intra-axonal flow?
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INTRODUCTION:
Acetazolamide (ACTZ) is a carbonic anhydrase inhibitor used in the treatment of papilledema associated with idiopathic intracranial hypertension (IIH). Its mechanism of action results in decreased production of CSF in the choroid plexus with secondary decompression of the optic nerve in the subarachnoid space and reduction of axoplasmic congestion within the optic nerve axons. The effect of ACTZ on the intra-axonal fluid dynamics is unknown. In this regard, we report three patients with optic nerve edema due to optic nerve sheath meningiomas without evidence of increased intracranial pressure treated with ACTZ.

CASE REPORTS:

Patient #1:
A 51 year-old woman presented with a six-month history of transient visual obscurations (TVO) in the right eye occurring spontaneously or when rising from a chair. The symptoms last up to 1 minute but were increasing in frequency and intensity. She was asymptomatic in the left eye. She had a >20 year history of diabetes requiring insulin for a right cataract. Mild headaches developed in the previous year. Examination disclosed visual acuity of 20/20 eyes. She had an altitudinal papillary defect (APD) on the right. Color plates were readily identified. 15 of 15, bilaterally. Goldmann visual fields were normal except for an enlarged blind spot on the right. Funduscope examination showed moderate to severe edema of the right papilla and a normal optic disc on the left (photo). A 2004 MRI scan showed an empty sella, but was otherwise within normal limits. She underwent a lumbar puncture that showed an opening pressure of 223 mm of water. Subsequently, she was placed on acetazolamide, 250mg three times a day. Over 6 months, her symptoms improved. The right optic disc was mildly swollen, but the positive APD persisted. She had lost 55 pounds. Acetazolamide was tapered and stopped. One year later, she returned with complaints of headaches for six weeks and TVOs lasting several minutes. Visual acuity was 20/25 OD and 20/20 OS. This right optic disc edema worsened (fig.1).

Acetazolamide was resumed. After five months, she had fewer TVOs. However, visual acuity progressively declined to 20/30 OD; she remained 20/20 OS. She now recognized only 4 of 15 color plates with the right eye and developed visual field defects (fig.2). MRI scan of the brain now showed a contrast enhancing meningioma (fig.8). The TVOs stopped. In 2005, he complained of decreased peripheral vision in the left eye. A MRI scan of the brain showed bilateral meningiomas about the proximal optic canals (fig.4) and two small meningiomas on the falx cerebri. In 2005, visual acuity was 20/20 OD and 20/15 OS with correction. Goldmann visual fields showed a normal field on the right and inferior and superior arcuate scotomas on the left (fig.5). There was no APD. Color plate testing showed correct identification of 13/5 OD and 14/15 OS. Intraocular pressures were 11 OD and 15 OS. Funduscope examination showed cup-to-disc ratios of 0.1, elevation of both discs and an optociliary shunt vessel at 3 o’clock on the left (fig.6). He continued acetazolamide. Repeated fundus exam and Goldmann visual fields in 2006 showed significant improvement following fractionated radiation therapy (fig.7).

Patient #2:
A 43 year-old man presented with an insidious history of visual complaints. He suffered a left sixth nerve palsy in 1982 spontaneously resolving within 3 months. A right fourth nerve palsy occurred in 1989 and also spontaneously resolved. MR scans of the brain and spinal fluid studies at that time were normal. In 1996, he developed TVOs for ten seconds that increased in frequency. Bilateral optic disc edema was found. Despite an opening pressure of 160mm of water, HH was suspected. He was given 500 mg of acetazolamide twice a day. Interestingly, an optociliary shunt was also observed over the left optic nerve. The TVOs stopped. In 2004, he complained of decreased peripheral vision in the left eye. A MRI scan of the brain showed bilateral meningiomas about the proximal optic canals (fig.4) and two small meningiomas on the left optic nerve. In 2005, visual acuity was 20/20 OD and 20/15 OS with correction. Goldmann visual fields showed a normal field on the right and inferior and superior arcuate scotomas on the left (fig.5). There was no APD. Color plate testing showed correct identification of 13/5 OD and 14/15 OS. Intraocular pressures were 11 OD and 15 OS. Funduscope examination showed cup-to-disc ratios of 0.1, elevation of both discs and an optociliary shunt vessel at 3 o’clock on the left (fig.6). He continued acetazolamide. Repeated fundus exam and Goldmann visual fields in 2006 showed significant improvement following fractionated radiation therapy (fig.7).

DISCUSSION:

CSF formation is directly proportional to the transport of Cl- and Na+ ions across the choroid plexus into the ventricles. There is more than one type of transport in the cellular membranes of the choroid plexus. NaCl co-transport and Cl-/HCO3- exchange represent mechanisms in the basolateral membrane for moving Cl- into the choroid cell for eventual transport into CSF (1-3). ACTZ interferes with extrusion of Cl- and HCO3- via apical channels. ACTZ also decreases choroid cell-to-CSF transport of Na+ ions and subsequently CSF secretion. In addition, ACTZ acts to increase choroid cell pH and slows basolateral Na+ exchange for cell H+ (fig.12).

The patients presented here have a different pathological process causing optic disc edema. All of them presented with meningiomas compressing the proximal optic nerve in and about the optic nerve canal. The two with intracranial tumours did not have increased intracranial pressure by lumbar puncture. The third patient’s tume was intraorbital. In all three patients, acetazolamide improved symptoms or signs of optic nerve edema due to optic nerve compression. The mechanism possibly involves changes in intra-axonal fluid dynamics. A role for acetazolamide in the treatment of unilateral disc edema is warranted by the response to treatment observed in these three patients.

REFERENCES:

Supported in part by Research to Prevent Blindness