ACETOLAZAMIDE USING IN IDIOPATHIC INTRACRANIAL HYPERTENSION

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Abstract. *The management of patients with idiopathic intracranial hypertension (IIH) has been guided primarily by informed opinion, clinical experience, and a small number of primarily retrospective studies. Given the results of the IIH Treatment Trial (IIHTT), there is now evidence supporting the use of acetazolamide for patients with IIH, especially with visual loss. Acetazolamide, a compound developed in the 1950s as a diuretic drug and presently used as an antiglaucoma, antiepileptic and diuretic agent, is effective in the treatment of IIH. is a low nanomolar inhibitor of Carbonic anhydrase(CA) isoforms involved in cerebrospinal fluid (CSF) secretion. Inhibition of brain/choroid plexus CA II, IV, VA and XII leads to a decreased CSF fluid secretion and control of the intracranial pressure.*

Keywords: *acetazolamide, carbonic anhydrase, intracranial hypertension, cerebral fluid secretion, pressure, convoluted tubule.*

ИСПОЛЬЗОВАНИЕ АЦЕТОЛАЗАМИДА ПРИ ИДИОПАТИЧЕСКОЙ ВНУТРИЧЕРЕПНОЙ ГИПЕРТЕНЗИИ

Аннотация. *Лечение пациентов с идиопатической внутричерепной гипертензией (ИВГ) в первую очередь основывалось на информированном мнении, клиническом опыте и небольшом количестве преимущественно ретроспективных исследований. Учитывая результаты исследования лечения ИВГ (IIHTT), в настоящее время имеются доказательства, подтверждающие применение ацетазоламида у пациентов с ИВГ, особенно с потерей зрения. Ацетазоламид, соединение, разработанное в 1950-х годах как диуретическое средство и в настоящее время используемое как противоглаукомное, противоэпилептическое и диуретическое средство, эффективно при лечении ИВГ. является низконаномолярным ингибитором изоформ карбоангидразы (КА), участвующих в секреции спинномозговой жидкости (СМЖ). Ингибирование мозгового/хориоидального сплетения КА II, IV, VA и XII приводит к снижению секреции СМЖ и контролю внутричерепного давления.*

Ключевые слова: *ацетазоламид, карбоангидраза, внутричерепная гипертензия, секреция мозговой жидкости, давление, извитой каналец.*

Introduction: Acetazolamide is a carbonic anhydrase inhibitor, hence causing the accumulation of carbonic acid. In short, under normal conditions, the net effect of carbonic anhydrase in the urinary lumen and cells of the proximal convoluted tubule is to acidify the urine

and transport bicarbonate (HCO_3^-) into the body. Another effect is excretion of Cl^- as it is needed to maintain electroneutrality in the lumen, as well as the reabsorption of Na^+ into the body.

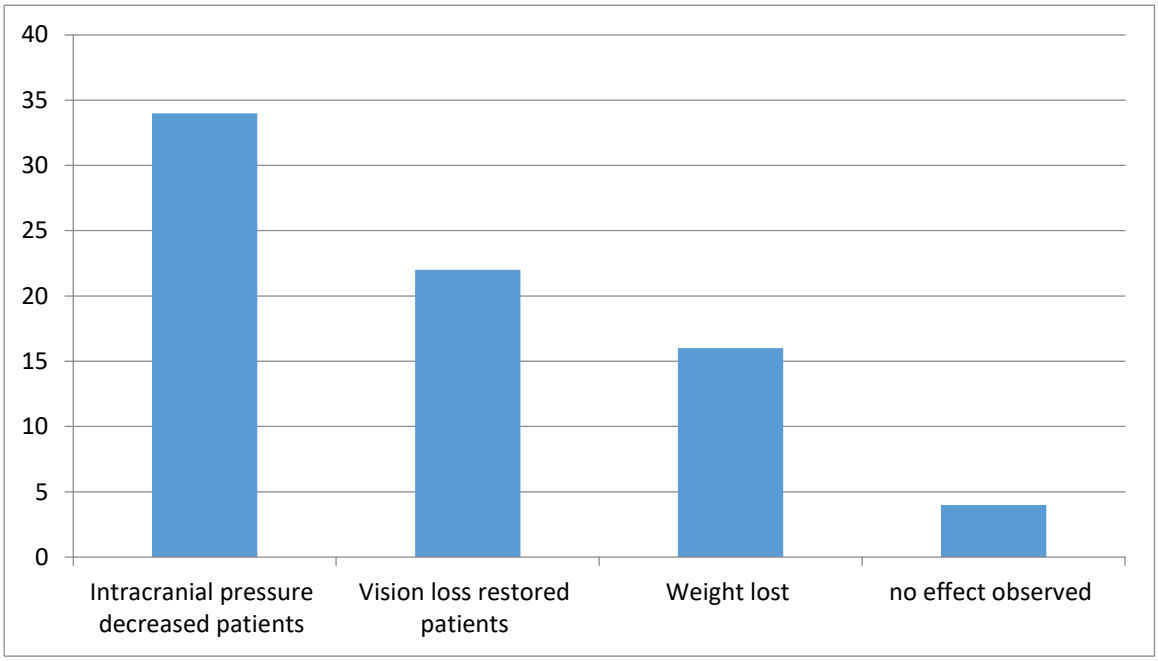
Mechanism: Under normal conditions in the proximal convoluted tubule of the kidney, most of the carbonic acid (H_2CO_3) produced intracellularly by the action of carbonic anhydrase quickly dissociates in the cell to bicarbonate (HCO_3^-) and an H^+ ion (a proton), as previously mentioned. The bicarbonate (HCO_3^-) exits at the basal portion of the cell via sodium (Na^+) symport and chloride (Cl^-) antiport and re-enters circulation, where it may accept a proton if blood pH decreases, thus acting as a weak, basic buffer. The remaining H^+ left over from the intracellular production of carbonic acid (H_2CO_3) exits the apical (urinary lumen) portion of the cell by Na^+ antiport, acidifying the urine. There, it may join with another bicarbonate (HCO_3^-) that dissociated from its H^+ in the lumen of the urinary space only after exiting the proximal convoluted kidney cells/glomerulus as carbonic acid (H_2CO_3) because bicarbonate (HCO_3^-) itself can not diffuse across the cell membrane in its polar state. This will replenish carbonic acid (H_2CO_3) so that it then may be reabsorbed into the cell as itself or CO_2 and H_2O (produced via a luminal carbonic anhydrase). As a result of this whole process, there is a greater net balance of H^+ in the urinary lumen than bicarbonate (HCO_3^-), and so this space is more acidic than physiologic pH. Thus, there is an increased likelihood that any bicarbonate (HCO_3^-) that was left over in the lumen diffuses back into the cell as carbonic acid, CO_2, or H_2O.

Thus, by disrupting this process with acetazolamide, urinary Na^+ and bicarbonate (HCO_3^-) are increased, and urinary H^+ and Cl^- are decreased. Inversely, serum Na^+ and bicarbonate (HCO_3^-) are decreased, and serum H^+ and Cl^- are increased. H_2O generally follows sodium, and so this is how the clinical diuretic effect is achieved, which reduces blood volume and thus preload on the heart to improve contractility and reduce blood pressure, or achieve other desired clinical effects of reduced blood volume such as reducing edema or intracranial pressure.[

Methods: For studying of acetozalamide effect 40 participants with IIH wa selected and mild visual loss who received a low-sodium weight-reduction diet. Participants were enrolled in 4 clinis in Bukhara and followed up for 3 months (january 2025 - march 2025).Prospective evaluation and data collection of high intracranial pressure CSF leaks was performed. Subjects underwent CSF diversion and postoperative assessment of pressure changes via a standard protocol. Lumbar drains or ventriculostomies were clamped on postoperative day 2 for 4 hours prior to assessment with a manometer. Acetazolamide (500 mg) was administered orally immediately following the recording and CSF pressure was measured after 4 hours. Data regarding demographics, etiology of CSF leak, body mass index (BMI), location and size of

defect, and clinical follow-up were also collected.

Outcomes and measures.



Conclusion

This study provides some of the first direct evidence of decreased intracranial pressure associated with the oral administration of acetazolamide, especially symptom with vision loss. In combination with the excellent endoscopic repair outcomes noted in a high risk population, this evidence supports the routine use of acetazolamide in patients with high intracranial pressure CSF leaks.

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