International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2022): 7.942

# New Aspects in the Treatment of Intracranial Hypertension Syndrome

**Golban Lidia Valentin**

6th Year student, USMF "Nicolae Testemițanu", Republic of Moldova

**Abstract:** ***Introduction: There are numerous pathologies that affect the central nervous system (CNS) with the onset of intracranial hypertension syndrome (IHC), so the quality of life of these patients largely depends on drug treatment. The purpose of the article was to study and analyze the specialized literature with the argumentation of the groups of preparations administered in SHIC, the principles of action of each group and their effectiveness. Material and methods: It is a review of articles from the last 10 years, using medical sites such as PubMed, Medscape, NCBI, Med bullets. Results: SHIC is a pathology that triggers various functional disorders, manifested by headaches, visual disturbances, nausea and vomiting. Drug treatment in SHIC is poor and mostly dependent on the triggering factor of intracranial hypertension (ICH), thus the first place in the treatment of SHIC is occupied by diuretics such as: acetazolamide, furosemide, topiramate, mannitol, etc. The administration of these preparations is justified by the effects obtained after administration (diuretic, antiepileptic, antiglaucoma, carbonic anhydrase inhibitors from the choroid plexus). Conclusions: The results of this study confirm that diuretic therapy is clearly superior in the treatment of SHIC. Indications for treatment depend on the morphological substrate that is the basis of SHIC, on the patient's comorbidities, this requires an individualized approach, according to international standards aimed at correlating the risk/benefit ratio.***

**Keywords:** Nervous system, intracranial hypertension syndrome, intracranial pressure, diuretics

## 1. Introduction

The central nervous system (CNS) represents the highest level of regulation and control of all important body functions [2].

CNS pathology means damage to the brain tissue, its structure and function, thus the incidence of diseases has an important place in the healthcare system, being among the pathologies with a high risk of lethality. Intracranial hypertension syndrome (IHC) occurs as a result of an anatomical - physiological imbalance between two major components, the cranial contents and the cranial box, manifesting itself in headaches, visual disturbances and vomiting [3, 14]. Etiopathogenetic SHIC is determined by cerebral edema, expansive intracranial processes (tumor, hematoma, abscess), cerebrovascular accidents, infections (meningitis, encephalitis), hydrocephalus, etc.

## 2. Material and Methods

It is a review of articles from the last 10 years, using medical websites (recognized worldwide for the latest information on scientific research) such as PubMed, Medscape, NCBI, Medbullets.

## 3. Results

Drug treatment in SHIC is poor and mostly dependent on the triggering factor of intracranial hypertension (ICH), thus the first place in the treatment of SHIC is occupied by diuretics such as: acetazolamide, furosemide, topiramate, mannitol, etc.

**Acetazolamide** is one of the most used preparations for the treatment of idiopathic intracranial hypertension (IIH), which has as its mechanism the inhibition of carbonic anhydrase in the choroid plexus, thus reducing the production of cerebrospinal fluid (CSF) with a subsequent decrease in intracranial pressure (ICP) [10]. Acetazolamide has a moderate diuretic effect of medium duration that decreases when used for several days, the antiepileptic effect it possesses is also important, as well as the antiglaucomatous, gastric antisecretory effect [4]. In many patients, HII headache responds well to management of ICP by decreasing CSF production following acetazolamide administration, with the best effect being determined within the first month of treatment. Immediate headache relief is usually seen after diagnostic lumbar puncture with CSF removal. In a small prospective study it was found that the prevalence of headache was reduced from 68% to 43% in patients treated with acetazolamide [14]. It is important to emphasize the fact that, in addition to the decrease in CSF production, acetazolamide also has other indications such as: the treatment of glaucoma, epilepsy, acute forms of climbers' disease, someforms of hypocalcemicperipheral paralysis, metabolicalkalosis, etc. [4].

Side effects associated with acetazolamide include dysgeusia, paresthesia, fatigue, nausea, diarrhea, and polyuria. May producemildhypokalemia and metabolicacidosis. Lesscommon but more severe adverse effects anaphylaxis, Stevens - Johnson syndrome, kidney stones, and blood dyscrasias [4; 12]. It is important that the treatment strategy in HII with acetazolamideis stratified according to the severity of the disease [6].

**Topiramate** is most commonly used for the treatment of headache disorders and may also be considered for the treatment of SHIC. Topiramate is a weak carbonic anhydrase inhibitor and often causes some weight loss as a side effect, suggesting that it may be more suitable for the treatment of HIC than other agents used to prevent headache [13]. The main side effects of topiramate include paresthesia, difficulty concentrating, drowsiness and decreased appetite.

Patients should be aware of the increased risk of acute angle – closureglaucoma secondary to topiramate therapy. Topiramate is contraindicated in patients with liver failure and has a relative contraindication in patients with a history of kidney stones [8].

**Furasemide** is a powerful oopdiuretic used in the treatment of edematous conditions associated with heart, kidney and liver failure and for the treatment of hypertension. and has as its mechanism of action [4]: - blocks the thiol groups (SH) of the enzymes of the epithelial cells of the ascending part of the loop of Henle with the inhibition of energy processes (oxidative phosphorylation and glycolysis) that decrease the active reabsorption of Na, Cl and partially K ions; - relaxes the smooth muscles of the vessels with the intensification of prostaglandin synthesis (I2, E2) with the increase of renal flow and glomerular filtration; - inhibits carbonic anhydrase (secondary mechanism); - inhibits the active reabsorption of Mg and subsequently of Ca.

It is effective in the treatment of SHIC, the effect due to the diuretic action of the drug, its ability to inhibit the production of CSF, or in combinations of both effects. SHIC treatment aims to reduce intracranial pressure, relieve headache and protect patients' vision [7].

Currently, hyperosmolar therapy with mannitol or hypertonic saline is the main therapeutic strategy for the management of SHIC. Hyperosmolar agents reduce brain volume and ICP through multiple mechanisms. During the first few minutes of infusion, mannitol and hypertonic saline expand plasma volume, decrease blood viscosity, and reduce cerebral blood volume. Once the plasma osmolarity increases, a gradient is established along the blood - brain barrier that causes the mobilization of water from the tissue into the vessels with the increase in circulating blood volume. (Figure 1) This effect can last up to several hours, until the osmotic balance is restored [1; 9; 15].

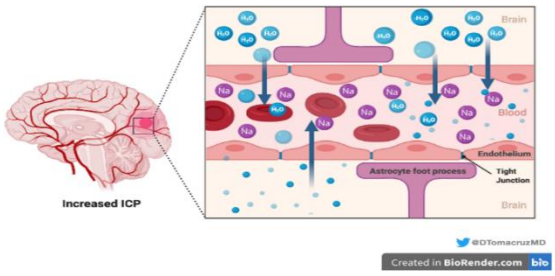


**Figure 1:** Mechanism of action of osmotic diuretics [16].

Intravenous bolus administration of mannitol lowers ICP within 1 to 5 minutes, with a maximal effect at 20 to 60 minutes and lasting 1.5 to 6 hours. The administration dose differs depending on the time of installation of the effect, in case if an urgent decrease of the PIC is required, it is necessary to administer in a dose of 1g/kg of body weight, and when a long – term reduction of the PIC is required, 0, 25 to 0.5 g/kg may be repeated every 2 to 6 hours. It is important to maintain serumos molarity less than 320 mOsm to avoid side effects such as hypovolemia, hyperosmolarity and renal failure [5].

The reflection coefficient for sodium approaches 1.0, making it an ideal agent for inducing an osmotic gradient between blood and brain tissue [1]. The effect of 3% hypertonic saline in reducing ICP is satisfactory, the difference with the effect of mannitol is not significant, but the effect of 3% hypertonic saline in reducing ICP was more sustained and easy to obtain clinically [11]. At the base of SHIC treatment are two preparations, mannitol and saline solution, this requires a comparative analysis to assess the effectiveness and estimate the benefits of each individual preparation (Table 1).

**Table 1:** Comparative analysis of hyperosmolar therapy [17]

| Mannitol | | Saline solution |
|---|---|---|
| • increases the gradient of the blood - brain barrier<br>• quickly reduces PIC<br>• the duration of the effect up to 6 hours | **Primary mechanism** | • increases the blood - brain barrier gradient<br>• immediate reduction of PIC<br>• the duration of the effect up to 4 hours |
| • cerebral vasoconstriction<br>• blood viscosity decreases<br>• increases cerebral blood flow | **Secondary mechanism** | • mixed immunomodulatory and anti - inflammatory effects |
| • the transient expansion of the intravascular volume<br>• rapid osmotic diuresis hypovolemia and hypotension | **Effect on hemodynamics** | • expansion of the intravascular volume<br>• increases mean arterial pressure |
| • may cause tolerance<br>• produces sustained hyperosmolarity | **Efficacy upon repeated administration** | • does not cause tolerance<br>• maintains tolerance when tolerance to mannitol has developed |
| • acute renal failure<br>• dehydration<br>• hypotension<br>• electrolyte imbalance<br>• the rebound effect | **Adverse effects** | • osmotic demyelination syndrome<br>• fluid overload/pulmonary edema<br>• hyperchloremic metabolic acidosis<br>• hyperoncotic hemolysis |

Following the comparative analysis of hyperosmotic therapy in the treatment of SHIC, the superiority of the saline solution compared to mannitol was determined, it has an immediate effectiveness in reducing ICP, does not cause tolerance, has a higher refractive index and a mixed immunomodulatory and anti - inflammatory effect as a secondary mechanism.

In addition to the higher degree of effectiveness of the saline solution, we cannot deny the effectiveness of mannitol, which also has more beneficial effects in SHIC.

## 4. Conclusion

SHIC is a pathology that triggers various functional disorders at the level of the body, manifested by headaches, visual disturbances, nausea and vomiting, resulting from the imbalance between the cranial box and the intracranial contents. Diuretic therapy in SHIC is clearly superior in the treatment of SHIC. Indications for treatment depend on the morphological substrate that is the basis of SHIC, on the patient's comorbidities, this requires an individualized approach, according to international standards aimed at correlating the risk/benefit ratio.

## References

[1] Allan H. Ropper, M. D., Hyperosmolar Therapy for Raised Intracranial Pressure, The New England journal of medicine, 08/2012, Volume 367, Issue 8
[2] Catereniuc Ilia, LupașcuTeodor, Batîr Dumitru, Bendelic Anastasia, ZorinaZinovia, Certan Galina, Globa Lilian, Angela Babuci. Vol. II. Sistemulnervos central. Splanhnologie (culegere de cursuri). Chișinău, 2015
[3] Galina Valova, Olga Bogomyakova, Andrey Tulupov, Alexander Cherevko, Influence of interaction of cerebral fluids on ventricular deformation: A mathematical approach, PLOS ONE, 2022, Volume 17, Issue 2
[4] Ghicavîi V. Bacinschi N. GușilăGh. Farmacologie (revizuitășicompletată) Ed. a 3 - a, Chișinău. Prinț Caro, 2019. pp: 431
[5] H. Richard Winn MD, Hyperosmolar Therapy: Mannitol versus Hypertonic Saline, Youmans and Winn Neurological Surgery, 2017
[6] Jensen RH, Radojicic A, Yri H. The diagnosis and management of idiopathic intracranial hypertension and the associated headache. Therapeutic Advances in Neurological Disorders.2016; 9 (4): 317 - 326.
[7] Kalyvas, A., Neromyliotis, E., Koutsarnakis, C. et al. A systematic review of surgical treatments of idiopathic intracranial hypertension (IIH). Neurosurg Rev 44, 773–792 (2021).
[8] Linde M, Mulleners WM, Chronicle EP, et al. Topiramate for the treatment of episodic migraine in adults. Cochrane Database Syst Rev.2012
[9] Rafael Badenes, Brian Hutton, Giuseppe Citerio, Chiara Robba, Gerardo Aguilar, Adolfo Alonso - Arroyo, Fabio Silvio Taccone, Carlos Tornero, FerránCatalá - López, Hyperosmolar therapy for acute brain injury: study protocol for an umbrella review of meta - analyses and an evidence mapping, BMJ OPEN (FEB 2020), Volume 10, Issue 2
[10] Raoof N, Hoffmann J. Diagnosis and treatment of idiopathic intracranial hypertension. Cephalalgia.2021; 41 (4): 472 - 478.
[11] Shi J, Tan L, Ye J, Hu L. Hypertonic saline and mannitol in patients with traumatic brain injury: A systematic and meta - analysis. Medicine (Baltimore).2020 Aug
[12] ten Hove, Martin W. MD; Friedman, Deborah I. MD; Patel, Anil D. MD; Irrcher, Isabella PhD; Wall, Michael MD; McDermott, Michael P. PhD for the NORDIC Idiopathic Intracranial Hypertension Study Group. Safety and Tolerability of Acetazolamide in the Idiopathic Intracranial Hypertension Treatment Trial. Journal of Neuro - Ophthalmology 36 (1): p 13 - 19, March 2016.
[13] Thurtell MJ, Wall M. Idiopathic intracranial hypertension (pseudotumor cerebri): recognition, treatment, and ongoing management. Curr Treat Options Neurol.2013 Feb;
[14] Y. Contreras - Martin, J. H. Bueno - Perdomo, Idiopathic intracranial hypertension: descriptive analysis in our setting, Neurología (English Edition), Volume 30, Issue 2, March 2015, Pages 106 - 110
[15] Yri H., Ronnback C., Wegener M., Hamann S., Jensen R. (2014b) The course of headache in idiopathic intracranial hypertension: a 12 - month prospective follow - up study. Eur J Neurol 21: 1458–1464.
[16] https: //www.renalfellow. org/2020/06/22/dealing - with - hypertonic - saline - in - the - neuro - icu/
[17] https: //slideplayer. com/slide/10205408/