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Editorial

Hydrocephalus: Current trends and future perspectives in management

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1. Introduction

Hydrocephalus, a condition first documented by Hippocrates and later named by Celsus, is a brain disorder caused by abnormal accumulation of cerebrospinal fluid (CSF). It can be attributed to genetic mutations or idiopathic origins and is often associated with congenital malformations. Secondary hydrocephalus results from pathological events such as infections, hemorrhages, or trauma.[1,2] In neonates, intraventricular hemorrhage due to prematurity is a predominant cause of post-hemorrhagic hydrocephalus, while in low-resource settings, infections like meningitis remain a leading contributor. Post-traumatic hydrocephalus is increasingly recognized as a complication of traumatic brain injuries, particularly among military personnel and individuals with a history of severe head trauma.[3]

Traditional treatment approaches for hydrocephalus have primarily relied on CSF diversion techniques, most notably the surgical implantation of shunts. However, emerging advancements have introduced alternative therapeutic strategies, including endoscopic third ventriculostomy (ETV) with choroid plexus cauterization, as well as promising biological and pharmacological interventions aimed at modifying CSF dynamics and neuroinflammation.[4]

1.1. Pathophysiology and molecular mechanisms of hydrocephalus

Hydrocephalus is caused by disturbances in cerebrospinal fluid (CSF) dynamics, often due to impaired absorption at the arachnoid granulations. Genetic mutations, blood-brain barrier (BBB), and glymphatic system regulate CSF composition and clearance, with dysfunctions contributing to hydrocephalus, especially in aging and neurodegenerative conditions. Inflammation significantly contributes to hydrocephalus pathogenesis, with cytokines such as IL-1β and TNF-α altering choroid plexus permeability and CSF secretion. Experimental therapies targeting TLR4, NF-κB, and MCP-1 have shown promise in reducing inflammation and CSF imbalance.[5,6]

1.2. Current management and interventions in the pipeline

Future research on genetic and molecular mechanisms may lead to targeted therapies for hydrocephalus management. Current management strategies include Ventriculoperitoneal (VP) shunt surgery, endoscopic third ventriculostomy (ETV), and Choroid Plexus Coagulation (CPC) and lumbar-peritoneal shunt surgery.

Pharmaceutical therapeutic approaches for hydrocephalus remain a significant challenge due to the restrictive nature of the blood-brain barrier (BBB). Recent studies suggest that targeting ion channels involved in cerebrospinal fluid (CSF) secretion offers a promising therapeutic avenue, particularly through inhibition of the NKCC1 co-transporter, which is regulated by inflammatory pathways in the choroid plexus epithelium. Evidence indicates that inflammatory pathways, especially those mediated by TLR4-regulated cytokines and immune cells, play a crucial role in post-hemorrhagic hydrocephalus pathogenesis. Although ventriculoperitoneal (VP) shunt

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placement remains the standard surgical intervention, emerging pharmacological strategies show potential to enhance treatment outcomes and minimize surgical complications.[7]

Historically, pharmacological interventions for hydrocephalus date back to 1924, with the advent of shunt therapy in the mid-20th century. Drugs aimed at reducing CSF production or dehydrating the brain were explored, often based on positive responses observed in animal models. Current pharmacological interventions include anti-inflammatory agents such as corticosteroids, neuroprotective compounds targeting oxidative stress, and experimental therapies like recombinant human hepatocyte growth factor, pirfenidone, losartan, and decorin.[8]

Bioengineered approaches have introduced innovative solutions for hydrocephalus management, including programmable shunt valves with adjustable pressure settings, hydrogel-coated shunt catheters, and nanotechnology advancements such as Slippery Liquid-Infused Porous Surfaces (SLIPS). Mesenchymal stem cells (MSCs) represent another promising avenue for hydrocephalus treatment, exhibiting immunomodulatory and regenerative properties.[9]

Recent advances in diagnostics have led to promising non-invasive assessment techniques, such as fundus videography for intracranial pressure estimation and pupillometry. Advancements in biomaterials and nanotechnology have paved the way for innovative drug delivery systems capable of circumventing the BBB. Preclinical studies have demonstrated the potential of stem cell therapy in regenerating damaged brain tissue and restoring CSF flow.[10,11]

Precision medicine is also emerging as a key approach in hydrocephalus management, leveraging genetic, biomarker, and clinical data to tailor individualized treatment strategies.

2. Conclusion

Hydrocephalus is a neurological disorder caused by genetic mutations, choroid plexus dysfunction, and hemorrhage. Despite traditional surgical treatments, they are associated with high failure rates and financial burdens. Recent research explores pharmacotherapy, modern surgical techniques, gene therapy, and nanotechnology-based interventions. Enhancing BBB permeability is crucial for non-surgical treatment. Interdisciplinary collaboration and translational research are essential for improving hydrocephalus management.

3. Conflict of Interest

None.

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