Update in of Hydrocephalus Research

Abstract:

Hydrocephalus is a common neurological disease caused by imbalance in the production and absorption of cerebrospinal fluid (CSF) or obstruction of its circulation pathways. The etiology of the disease is complex, often accompanied by a variety of complication. In recent years, hydrocephalus has been intensively studied. In this paper, the etiology, epidemiology, diagnosis and treatment of hydrocephalus in study on traditional Chinese and western medicine treatment were reviewed in order to provide reference for clinical diagnosis and treatment of hydrocephalus in the future.

Key words: Hydrocephalus Research New progress

UNDER PEER REVIEW

Introduction

Hydrocephalus is caused by unbalanced production and absorption of cerebrospinal fluid (CSF) or its blocked circulation pathway, which can lead to ventriculomegaly and increased intracranial pressure [1]. Cerebrospinal fluid is a transparent, colorless fluid produced by choroid plexus, corticodiencephalic and meninx, circulating from ventricle to spinal subarachnoid space along head and tail direction, and then discharged through lymph-vessel and venous systems. The volume is about 150ml, updated 3-5 times a day [2]. In the classical CSF circulation model, CSF is mainly absorbed into the blood through the arachnoid

villus, with a small amount absorbed into the spinal cord. With the development of molecular and cellular biology and neuroimaging, the physiological mechanism of CSF production and absorption has become more complex. CSF circulation not only includes the directional flow of CSF, but also the pulsating reciprocating movement of the whole brain, as well as the local liquid exchange between blood, interstitial fluid and CSF [3]. The clinical manifestations of this disease depend on the etiology and hydrodynamics of hydrocephalus [4]. Acute, rapidly developing hydrocephalus is a life-threatening condition that requires immediate neurosurgical treatment. A sharp rise in intracranial pressure can lead to temporal lobe passing transtentorial herniation, known as transcerebellar tentorial hernia, and/or cerebellar tonsillar hernia. This can lead to disturbance of consciousness, disturbances of pupil movement function and oculomotor nervous system, autonomic nervous dysfunction, loss of brainstem reflexia, and even coma. In contrast, slow-progressing chronic hydrocephalus usually presents with nonspecific symptoms such as headache, dizziness, decreased vision, setting sun- alike eye, and difficulty in concentrating. Other typical clinical symptoms are vomiting in the morning and papilledema on eye examination [5].

Pathogenesis

Hydrocephalus is a common symptom after craniocerebral injury and can be caused by a variety of diseases. Active, progressive dilatation of ventricular system due to an obstructed passage of cerebrospinal fluid (CSF) from its point of production to its point of absorption, evident in secondary hydrocephalus associated with cerebral tumor, infection or hemorrhage. Currently, hydrocephalus in infants is classified as primary

UNDER PEER REVIEW

or congenital hydrocephalus (CH) when it occurs without a known antecedent (Congenital hydrocephalus，CH) [6]. Recent human genome analyses have highlighted important differences between congenital and acquired hydrocephalus, with data showing that up to 25% of sporadic congenital hydrocephalus are caused by newborn mutations and impaired neural stem cell development processes [7].

Congenital hydrocephalus (CH) is characterized by the significant enlargement of the ventricle, which is considered to be caused by the imbalance of cerebrospinal fluid (CSF) circulation, and treated by lifelong surgical CSF shunt. The incidence of Congenital hydrocephalus occurs in 1 case of every 1000 neonates [8]. The pathogenesis of CH is poorly understood.

Furey et al. used data from the largest CH exome sequencing study to date to identify four genes not previously involved in CH (TRIM71, SMARCC1, PTCH1 and SHH). Notably, all four genes regulate the development of neural stem cells in the ventricular region and together explain about 10% of CH cases. These findings suggest that neurogenesis impairment in the pathogenesis of a large number of CH patients has potential diagnostic, prognostic and therapeutic implications [7].

Normal pressure hydrocephalus can be divided into two distinct entities —— Idiopathic (iNPH) and secondary (sNPH), the potential etiology of the former is still unclear, while the latter may be the result of various pathologic factors, such as subarachnoid hemorrhage, trauma, meningitis, malignant tumor, cerebral stroke and hemorrhage [8].

Epidemiology

Isaacs et al. noted 88 cases of hydrocephalus per 100,000 people

UNDER PEER REVIEW

under the age of 18, 11 cases per 100,000 people between the ages of 19 and 64, and 175 cases per 100,000 people over the age of 64. Interestingly, the morbidity of hydrocephalus also varies across income countries, with both analyses reporting significantly higher rates in low - and middle-income countries [9,10]. Thus, Isaacs et al. found that in nearly 30 cases, the rate of morbidity per 100,000 cases per year was higher in low- and middle-income countries than that in high-income countries [9]. Dewan Dewan et al. also reported that the annual incidence of hydrocephalus in children in low - and middle-income countries was 123 cases per 100,000 people, compared with 79 cases per 100,000 people in high-income countries [10]. Thus, the morbidity of hydrocephalus is largely driven by socioeconomic status. As discussed below, one of the main reasons for this difference is the predominance of postinfection hydrocephalus among children in poorer countries, where neonatal and infant infections are more common.

Although hydrocephalus is a common complication of many central nervous system (CNS) injuries [10,11], hemorrhage and post-infection are the two most common forms of acquired hydrocephalus worldwide. Post-infectious hydrocephalus (PIH) is the most common cause of hydrocephalus in children, with the highest morbidity in Africa, Latin America and Southeast Asia. About 123,000 cases of PIH are reported annually in low- and middle-income countries [10].

In developing countries such as India [12], China [13] and the Philippines [14], secondary hydrocephalus after TB infection accounts for a large proportion, up to 85%. Intrauterine infection is a common cause of pregnancy induced hypertension (PIH) in high-income countries, usually

UNDER PEER REVIEW

caused by toxoplasma gondii and cytomegalovirus (CMV). The postnatal and pediatric cause is usually bacterial meningitis caused by escherichia coli, streptococcus agalactiae and Listeria monocytogenes.

In contrast, post-hemorrhagic hydrocephalus (PHH) is the most common cause of acquired hydrocephalus in high-income countries, with about 38 newborn per 100,000 live births [15]. PHH mainly occurs in infants less than 32 weeks of gestation and infants with very low birth weight, and the bleeding site is mostly choroid plexus, accounting for 60% [16].

Postinfective hydrocephalus is a major global health problem, with the highest prevalence in Africa and Asia. The systematic assessment of the prevalence of bacterial meningitis complicated with hydrocephalus was reported to be 6.90% [17]. While the pathogens may differ, the damaging effects of bacteria-associated hydrocephalus are consistent.

Diagnosis

Hydrocephalus can be divided into three categories:

Obstructive hydrocephalus: This type of hydrocephalus, also known as non-communicating hydrocephalus [6], is caused by an obstruction of the cerebrospinal fluid pathway. Although there is a preference for obstruction of cerebrospinal fluid pathway, it must be considered that, in principle, every intracranial tumors of a certain size may block the cerebrospinal fluid pathway. Subacute cerebellar infarction with continuous cerebral swelling is the most common mass of posterior fossa in adults that can compress the fourth ventricle. Lesions in the interventricular foramen region can lead to bilateral lateral ventricular dilatation, and more rarely, unilateral ventricular dilatation. The most

UNDER PEER REVIEW

common cause of obstruction at this area is colloid cyst. This is a benign cyst with mucoprotein. 1% cerebral tumor and 20% ventricular tumor [18].

Absorptive hydrocephalus: This hydrocephalus is caused by the impaired absorption of cerebrospinal fluid. All ventricles are affected in the same way. Therefore, this type of hydrocephalus is also known as communicating hydrocephalus. It can be caused by subarachnoid hemorrhage (SAB) or hemorrhagic changes following SAB as well as inflammation or post-inflammatory changes. Sab is usually caused by the rupture of arterial aneurysm supplying cerebral artery and is accompanied by typical symptoms such as sudden onset of headache. Subarachnoid hemorrhage showed high density on plain scan in the basilar cistern area [19].

Hypersecretory hydrocephalus: This type of hydrocephalus is caused by an oversecretion of cerebrospinal fluid, which is usually caused by a papilloma of the plexus and is rarely caused by plexus carcinoma [20].

Idiopathic normal pressure hydrocephalus: Idiopathic normal pressure hydrocephalus (iNPH) is a special type of communicating hydrocephalus, the pathophysiology of which is not yet fully understood. The disease usually occurs in adults and morbidity increases with age. Different clinical manifestations, and difficulties in differential diagnosis from other neurodegenerative disease - lead to underdiagnosis of the disease, leading to a significant reduction in patients' quality of life, and even disability.

Imageology plays an important role in confirming diagnosis, finding etiology and making treatment plan. Although magnetic resonance (MR) imaging is the first-line imaging method, computed tomography (CT) is

UNDER PEER REVIEW

usually the first-line imaging test in emergency patients. For patients with clinical manifestations of acute hydrocephalus and acute disturbance of consciousness, cranial computed tomography is the main method of examination for its short time and fast speed. Secondly, MRI is the preferred examination method [21]. If the patient is in intensive care and there are difficulties and potential risks in transferring to CT or MR, craniocerebral B-ultrasound is a better choice for early diagnosis. However, the inferior ventricle of B-ultrasound can only be located by identifying ependyma, namely two parallel pulsating high-echo lines, rather than by visualization of cerebrospinal fluid. Parallel high-echo lines often appear in the cerebral parenchyma and are prone to misinterpretation. Therefore, preoperative CT or MR examination is still recommended [22].

Ventriculomegaly is a typical imaging manifestation of hydrocephalus. A very obvious feature is the dilation of the temporal horn. Currently, there is no relevant standard value, but it is generally considered that the pathological manifestation is the adult temporal horn diameter >2mm. In addition, there is an increase in the width of the third ventricle, which is dilated or laterally curved, and the posterior horn, which is usually slit, is rounded, and the external CSF cavity appears unusually thin compared to the dilated ventricle [5]. In daily clinical diagnosis and treatment, Evans Index (EI) is used for the diagnosis of ventricular dilation, which can be diagnosed when EI > 0.3 [23]. Attention should be paid to the differentiation of neurodegenerative diseases such as encephalatrophy.

However, conventional MR and CT have some limitations. Their

UNDER PEER REVIEW

image resolution cannot clearly display the subtle structures of the craniocerebrum.In recent years, modern medical imaging technologies such as single photon emission computed tomography (SPECT), MRS, MR perfusion, MR diffusion weighted imaging, magnetic resonance three-dimensional steady-state composition interference sequence (3D-CISS), MR phase contrast cine imaging (PC-cine), magnetic resonance three-dimensional fast spin echo sequence with variable turning angle (3D-space), virtual endoscopy (VE) , etc. as supplementary means have made up for the deficiency

By clinically observing 144 patients with hydrocephalus,Tang Yuhui et al. [24] applied SPECT to conduct the evaluation of the cerebrospinal fluid dynamics and judge different types of hydrocephalus (97 cases of communicating hydrocephalus and 47 cases of obstructive hydrocephalus). It was found that communicating hydrocephalus showed enlargement and continuous development of lateral ventricle on cistern imaging, with less or no distribution of radiation on convex surface of brain, while obstructive hydrocephalus showed slow migration of radiation to sagittal sinus and delayed development of convex surface of brain, The lateral ventricle does not develop all the time, which is similar to the research results of Guan Feng et al. [25]

MRS can quantitatively analyze a series of specific nuclei such as material metabolism in living brain tissue and other compounds by using the phenomenon of nuclear magnetic resonance and chemical displacement. Lundin f et al. [26] performed MRS examination on 14 patients with hydrocephalus before operation and 3 months after operation. It was found that the total n-acetylaspartic acid and

UNDER PEER REVIEW

n-acetylaspartic acid in thalamus before and after shunt were significantly lower than those in healthy individuals, while the spectral analysis of deep brain white matter before shunt was not significantly different from that in normal people. After shunt, the total choline in deep brain white matter increased and inositol decreased, which may be related to clinical improvement

MR perfusion reflects the microvascular distribution and blood perfusion of tissues at the molecular level for imaging, intravenous injection of contrast agent to reflect local perfusion and arterial spin label tracer (ASL) perfusion imaging. Virhammar J et al. used ASL perfusion imaging to conduct comparative analysis of cerebral blood flow between idiopathic normal pressure hydrocephalus and normal people, and found that perfusion of periventricular white matter, basal ganglia and thalamus in patients with normal pressure hydrocephalus was less than that in normal people, with statistical significance. This is consistent with the results of pathophysiological studies on hydrocephalus [27].

MR diffusion weighted imaging is performed according to the microscopic motion of water molecules, and its clinical application is more popular than other examination methods. Some Chinese scholars [28] studied MRI and diffusion tensor imaging of early obstructive hydrocephalus in rats, and experiments showed that in patients with hydrocephalus, the micro-structure of cerebral white matter around the ventricle was damaged at the early stage. It is related to the degree of ventriculomegaly, which can show the damage of white matter microstructure in early stage.

3D-CISS focuses on cerebrospinal fluid signals by using heavy

UNDER PEER REVIEW

T_2WI effect, while other brain tissues appear as dark background. In addition, 3D-CISS images can be continuously and dynamically played with MRI dynamic player software, so as to observe the dynamic flow of cerebrospinal fluid. Huang Jianglong et al [29] studied 45 cases of aqueduct of sylviusobstructive hydrocephalus patients who underwent magnetic resonance conventional sequence and sagittal viewCUBE T2 and 3D-FIESTA sequence scans, and analyzed the display of aqueduct obstruction cause by CUBE T2 combined with 3D-FIESTA sequence Compared with the conventional magnetic resonance sequence, the CUBE T2 combined with 3D-FIESTA sequence can significantly improve the diagnostic level of the cause of aqueduct obstruction, and can provide a reliable basis for the selection of surgical methods and the evaluation of postoperative efficacy.

Pc-cine is an MR imaging technology that measures fluid flow velocity by using the phase changes generated by fluid flowing protons. This technology can display the anatomical structure of blood vessels and ventricles and provide fluid flow dynamics information such as flow direction, flow rate and flow of blood and cerebrospinal fluid for diagnosis and prognosis assessment of hydrocephalus [30].

3D-SPACE can realize ultra-thin layer scanning and high-contrast images, and can clearly display dissepiment at interventricular foramen, aqueduct of sylvius, cistern, etc., which is very helpful for diagnosis obstructive hydrocephalus, thereby improving the early diagnosis rate of patients with obstructive hydrocephalus, helping doctors choose the best treatment plan, improve curative effect, and improve prognosis of patient [30].

UNDER PEER REVIEW

Virtual endoscopy technology (VE) is a visualization virtual computer imaging technology used to observe the inner surface of the lumen. Based on 3D-space sequence, 3D reconstruction technology is used to obtain 3D images of the inner surface of the lumen. Due to the complexity of imaging and image processing, this technology is rarely used in clinical applications.

Treatment

Hydrocephalus is a symptom of a disease that, if left untreated, can develop into an independent disease requiring continued treatment after treatment of the primary cause.

Although folic acid fortification is mandatory in many countries, and many reviews support the use of folic acid as a prenatal or continuing supplement, the effect of folic acid supplementation on hydrocephalus has not been well validated. Considering that hydrocephalus occurs in about 80% of infants with neural tube abnormalities, some studies have shown that taking a small dose of folic acid in early pregnancy can reduce the morbidity of neural tube abnormalities by 5%-80% [31], and oral folic acid may reduce the imorbidity of hydrocephalus. Although we did not find any difference in the mobidity of hydrocephalus with or without forced folic acid fortification, we would warn against making any major inferences from these findings.

Regardless of the cause of acquired hydrocephalus, treatment usually involves cerebrospinal fluid shunt via ventriculo-peritoneal shunt or endoscopic third ventriculostomy (ETV). It should be noted that there is an intracranial mass leading to ventricular obstruction. Therefore, surgical resection of the mass lesion should be tried first to restore normal

UNDER PEER REVIEW

cerebrospinal fluid flow However, since pregnancy induced hypertension and PHH are the most common causes of acquired hydrocephalus, shunt may be the most common treatment for hydrocephalus in all age groups. A retrospective study of 40 preterm infants with posthaemorrhagic hydrocephalus evaluated the results of different cerebrospinal fluid shunt procedures (25% continuous lumbar puncture, 37.5% ventriculo-inferior lumen shunt, and 37.5% ventriculo-peritoneal shunt) and found that cerebrospinal fluid shunt was beneficial for younger infants with lower birth weight. Temporary cerebrospinal fluid drainage should be considered as a priority, while permanent ventriculo-peritoneal shunt should be considered for healthier, higher-birth weight newborns [32]. In a meta-analysis of 33 idiopathic normal pressure hydrocephalus shunt studies, 75% of patients improved gait, more than 60% improved cognitive function, and 55% improved urinary incontinence. There was no significant difference between different procedures. Surgery-related complications were significantly reduced [33].

Complications after shunt surgery are common, including shunt blockage, infection, excessive or insufficient shunt, abdominal complications, epilepsy, etc. [34]. At this point, preoperative preparation and postoperative nursing play a crucial role in improving prognosis, reducing complications and death rate. Chi Jieshan, Qiu You et al. [35,36] found that perioperative period and the combination of Chinese and western nursing have certain clinical application value in reducing postoperative complications and improving nursing satisfaction. Postoperative hydrocephalus in children is often accompanied by neurological dysfunction and growth development dysfunction of varying

UNDER PEER REVIEW

degrees. Accurate rehabilitation assessment and early rehabilitation intervention have positive effects on the prognosis of children [37]. Domestic studies [38-40] have found that through early intervention rehabilitation, the morbidity of postoperative complications in children is reduced, Barthel score is significantly increased, and motor function is significantly improved.

It is worth noting that traditional Chinese medicine therapy has unique advantages in conservative treatment of hydrocephalus and shunt postoperative nursing. In recent years, the clinical research and reports on the treatment of this disease with traditional Chinese medicine have gradually increased, with good clinical advantages. Hydrocephalus disease belongs to the category of traditional Chinese medicine ununited skull, there is no clear pathogenesis standard at present, most domestic scholars believe that the disease is caused by deficiency of spleen and kidney, phlegm, blood stasis, fluid retention, a variety of causes intertwined. Professor Zhang Xuewen believes that traditional Chinese medicine syndrome differentiation of cerebral edema is based on kidney deficiency, blood stasis, phlegm turbidity and fluid retention through the "fluid stasis theory".The cause of infantile hydrocephalus is likely to kidney deficiency, while the cause of adult hydrocephalus is tended to domination of pathogen. The key mechanism of the disease is craniocerebrum fluid stasis and brain collaterals congestion. The main treatment principles are promoting blood circulation to remove blood stasis, activate fluid and reduce nephelo andrefreshing and invigorating, which is based on decoction for activating blood circulation and adding some essential items for activating blood circulation so as to refresh and

UNDER PEER REVIEW

invigorating [41]. Feng Hui et al. [42] found in the clinical study that decoction for activating blood circulation can improve the levels of MBP, S-100β and NSE in patients with posttraumatic fluid stasis type hydrocephalus, and increase the protein expression levels of P73 and P38 in cerebrospinal fluid, which improved the clinical symptoms of patients. Qi Xinhua et al. [43] gave decoction for activating blood circulation combined with acupuncture to the patients, and found that the complication rate of the patients was lower than that of the conventional nursing group, which could better improve the neurological function. Xiang Gaobo et al. [44] clinically observed 60 patients with hydrocephalus in the control group who were treated with ventriculoperitoneal shunt, and the treatment group was treated with decoction for removing blood stasis on the basis of the control group. The comparison found that BI, GCS, NIHSS scores and traditional Chinese medicine syndrome scores in the treatment group were improved more significantly, and the hydrocephalus degree in the treatment group was lighter during follow-up. Therefore, the treatment plan of decoction for removing blood stasis combined with ventriculoperitoneal shunt is significantly superior to the conventional measures of ventriculoperitoneal shunt alone, which is beneficial to the absorption and regression of ventricular edema, and can effectively reduce the headache degree, frequency and the risk of complications.

The occurrence of hydrocephalus is related to the metabolism of fluid, and Wu Ling San is the basic prescription of warming Yang and promoting diuresis. All drugs are used together to regulate the metabolism of the Five Zang , and it has the effect of warming Yang and

UNDER PEER REVIEW

transforming Qi and diuresis. Modern pharmacology shows that Wu Ling San has function in diuresis, blood glucose and lipid regulation, kidney protection and other effects, which can improve systemic or local edema [45]. Domestic clinical studies have found that Wu Ling San has a definite curative effect on hydrocephalus after craniocerebral trauma, which can significantly reduce brain fluid volume and the lesions involved area [46,47].

At present, clinical acupuncture combined with acupoint application treatment has been widely recognized to promote the recovery of nerve function. Lin Hai et al. [48] clinically observed 25 patients after hydrocephalus shunting, and found that acupuncture combined with acupoint application treatment was significantly better than western medicine alone for the recovery of neurological function posthydrocephalus. Again, the advantages of acupuncture combined with acupoint application treatment in postoperative rehabilitation were demonstrated. Yu Mengjin et al. [49] proved the efficacy of acupuncture of "warming method" in treating infantile hydrocephalus and its dysfunction through clinical trials. Methods: 12 children with hydrocephalus were treated with acupuncture and warm moxibustion therapy for 6 months, and the improvement of hydrocephalus and its dysfunction was compared before and after treatment. Results: After acupuncture treatment, the anterior fontanelle of all the children began to sink back and narrow, the head circumference no longer increased rapidly, and the state was stable. The emotion, intelligence and movement of 11 children were improved to varying degrees: 2 cases were cured, 5 cases were effective, 4 cases were improved, and 1 case was ineffective. The total effective rate was 91.7%.

UNDER PEER REVIEW

Conclusion: Acupuncture and moxibustion “warming method” is an effective method to treat infantile hydrocephalus and its dysfunction. Liu Shizhe et al. [50] treated 18 cases of infantile hydrocephalus with acupuncture and massage. The treatment period of this group of cases was 2 months as a course of treatment, and the judgment results after 3 courses showed: Thirteen cases were cured, 4 cases were improved, and 1 case was ineffective, the cure rate was 72%, and the total effective rate was 94%. Peng Changlin et al. [51] used heavy moxibustion combined with acupuncture to treat 27 cases of infantile hydrocephalus. The main acupoints were: Bai Hui, GuanYuan, Yong Quan. For children with poor physical activity, active and passive functional exercise should be coordinated. Do this at least 3-4 times a day for about minutes each time. In treatment, acupuncture is usually followed by moxibustion. 3 months is a course of treatment, and the next course of treatment is performed after a 1-month break. After 1-6 courses of treatment, 6 cases were cured, 6 cases were markedly effective, 4 cases were effective, and 11 cases were ineffective. It shows that acupuncture treatment has a significant effect on improving the symptoms and functions of infantile hydrocephalus

As to children hydrocephalus, Professor Wang Songling believes that infantile hydrocephalus is mainly caused by deficiency, that is to say, fluid and blood stasis is the symptom, spleen deficiency is throughout the course of the disease. Children hydrocephalus treatment should be based on harmony method, with invigorating the spleen and kidney, warming Yang and eliminating blood stasis methods, the use decoction and pill in common, and temporary and permanent treatment. The prescription

UNDER PEER REVIEW

mainly focuses on warming and removing blood stasis. Commonly used drugs: Red ginseng, antler gum, dried human placenta, tortoise shell glue, dried lacquer, asarum, dragon's blood, notoginseng and dried rhizome rehmannia have been powdered through a 120-mesh sieve to make water pills, 3 times a day.Each time according to the age of children appropriate quantitative, with noodle soup or 3 meals delivered. It is intended to strengthen the spleen and stomach, assist metabolize Qi and blood, strengthening the body resistance and enhance the power of warming. Very good clinical effects have been achieved [52].

Zhou Zhengxin [53] and others used a comprehensive Chinese medicine scheme to treat fluid stasis type of infantile hydrocephalus, and 60 children diagnosed with fluid stasis typehydrocephalus were randomly divided into a treatment group and a control group with 30 cases in each group. The treatment group was given Chinese medicine and acupuncture traditional Chinese medicine comprehensive therapy, the control group was given oral administration of acetazolamide diamox. The results showed that the total effective rate was 90% in the treatment group and 50% in the control group. The therapeutic effect of the treatment group was significantly better than that of the control group ($P<0.05$). It shows that the comprehensive treatment of traditional Chinese medicine for children fluid stasis typehydrocephalus achieves better therapeutic purposes through the combination of partial and overall syndrome differentiation.

Feng Taozhen et al. [54] adopted integrated traditional Chinese and western medicine to treat 56 cases of infantile hydrocephalus with spleen deficiency fluid syndrome, and randomly divided them into control group

UNDER PEER REVIEW

and treatment group (28 cases in each group). The control group was treated with hydrochlorothiazide plus calf serum proteolytic hydrolysate, and the treatment group was additionally treated with invigorating spleen, warming Yang and promoting diuresis and acupuncture. The clinical efficacy grading and syndrome score of hydrocephalus after 1 course of treatment (28d) were compared. Results after 1 course of treatment, compared with the control group, the clinical efficacy grade of the treatment group was improved, and the syndrome score was decreased. The effective rate of the treatment group was 92.9%, higher than that of the control group (64.3%), and the comparison between the two groups was statistically significant ($P<0.01$). The results showed that the comprehensive program of integrated traditional Chinese and western medicine, regulating internal and external, ameliorated the overall symptoms of the children with hydrocephalus through methods such as warming the spleen and promoting diuresis, dredging the collaterals and inducing resuscitation , tonifing kidney-essence and nourishing the marrow, etc.

The author believes that the key pathogenesis of the disease is "Yang asthenia and Yin sthenia, Yin subjugation Yang, water and blood stasis, brain orifices obstruction", the most common pathogenesis type is fluid stasis type, so the "removing blood stasis and resuscitation, activating yang promote diuresis" should be the principle of treatment. The Trinity comprehensive therapy is the internal and external use of traditional Chinese medicine combined with acupuncture and massage, aiming at eliminating dropsy and improving brain injury. It integrates the characteristics of traditional Chinese medicine [55]. It has been clinically

UNDER PEER REVIEW

verified that trinity comprehensive therapy can significantly improve motor function and intelligence level of children with normal pressure and fluid-stasis type hydrocephalus [56-59].

Conclusion

At present, with the progress of medical technology, more and more in-depth research on the pathogenesis of hydrocephalus, and the development of imaging, which has provided an advantage for the diagnosis of the disease, clear classification, treatment plan. However, there is no literature for standardized quantitative treatment of the temporal horn dilation in imageology. Clinical observation and relevant standards need to be formulated in the future. In addition, due to the limitations of technology, economy, patients' psychological factors and other aspects, various old and new technologies still need to be popularized and improved, and clinical promotion is actively carried out. In terms of treatment, it is particularly important to actively treat the primary disease and control complications. Shunt operation is still the first choice for current treatment. The advantages of traditional Chinese medicine in the treatment of hydrocephalus also deserve attention. The combination of traditional Chinese and western medicine has great clinical value in the treatment of hydrocephalus.

UNDER PEER REVIEW

References

[1] Hodler J, RA Kubik-Huch, GK Von-Schulthess. Diseases of the Brain, Head and Neck, Spine 2020-2023: Diagnostic Imaging[M].

Cham (CH): Springer, 2020.

[2] H Tumani, Huss A, Bachhuber F. The cerebrospinal fluid and barriers - anatomic and physiologic considerations[J]. Handb Clin Neurol, 2017, 14621-32.

[3] T Brinker, Stopa E, Morrison J, et al. A new look at cerebrospinal fluid circulation[J]. Fluids Barriers CNS, 2014, 1110.

[4] K-R Fink, Benjert J-L. Imaging of Nontraumatic Neuroradiology Emergencies[J]. Radiol Clin North Am, 2015, 53(4): 871-890.

[5] S Langner, Fleck S, Baldauf J, et al. Diagnosis and Differential Diagnosis of Hydrocephalus in Adults[J]. Rofo, 2017, 189(8): 728-739.

[6] H-M Tully, Dobyns W-B. Infantile hydrocephalus: a review of epidemiology, classification and causes[J]. Eur J Med Genet, 2014, 57(8): 359-368.

[7] C-G Furey, Choi J, Jin S-C, et al. De Novo Mutation in Genes Regulating Neural Stem Cell Fate in Human Congenital Hydrocephalus[J]. Neuron, 2018, 99(2): 302-314.

[8] B Daou, Klinge P, Tjoumakaris S, et al. Revisiting secondary normal pressure hydrocephalus: does it exist? A review[J]. Neurosurg Focus, 2016, 41(3): E6.

[9] A-M Isaacs, Riva-Cambrin J, Yavin D, et al. Age-specific global epidemiology of hydrocephalus: Systematic review, metanalysis and global birth surveillance[J]. PLoS One, 2018, 13(10): e204926.

[10] M-C Dewan, Rattani A, Mekary R, et al. Global hydrocephalus epidemiology and incidence: systematic review and

UNDER PEER REVIEW

meta-analysis[J]. J Neurosurg, 2018, 1-15.

[11] J-K Karimy, Zhang J, Kurland D-B, et al. Inflammation-dependent cerebrospinal fluid hypersecretion by the choroid plexus epithelium in posthemorrhagic hydrocephalus[J]. Nat Med, 2017, 23(8): 997-1003.

[12] A Aranha, Choudhary A, Bhaskar S, et al. A Randomized Study Comparing Endoscopic Third Ventriculostomy versus Ventriculoperitoneal Shunt in the Management of Hydrocephalus Due to Tuberculous Meningitis[J]. Asian J Neurosurg, 2018, 13(4): 1140-1147.

[13] K Li, Tang H, Yang Y, et al. Clinical features, long-term clinical outcomes, and prognostic factors of tuberculous meningitis in West China: a multivariate analysis of 154 adults[J]. Expert Rev Anti Infect Ther, 2017, 15(6): 629-635.

[14] A-S Kamat, Gretschel A, Vlok A-J, et al. CSF protein concentration associated with ventriculoperitoneal shunt obstruction in tuberculous meningitis[J]. Int J Tuberc Lung Dis, 2018, 22(7): 788-792.

[15] T-N Munch, Rostgaard K, Rasmussen M-L, et al. Familial aggregation of congenital hydrocephalus in a nationwide cohort[J]. Brain, 2012, 135(Pt 8): 2409-2415.

[16] L Afsharkhas, Khalessi N, Karimi Panah-M. Intraventricular Hemorrhage in Term Neonates: Sources, Severity and Outcome[J]. Iran J Child Neurol, 2015, 9(3): 34-39.

[17] J Casado-Flores, Aristegui J, de Liria C-R, et al. Clinical data and factors associated with poor outcome in pneumococcal meningitis[J]. Eur J Pediatr, 2006, 165(5): 285-289.

[18] A-G Osborn, Preece M-T. Intracranial cysts:

UNDER PEER REVIEW

radiologic-pathologic correlation and imaging approach[J]. Radiology, 2006, 239(3): 650-664.

[19] S Langner, Kirsch M. Radiological Diagnosis and Differential Diagnosis of Headache[J]. Rofo, 2015, 187(10): 879-891.

[20] Y-Z Shi, Wang Z-Q, Xu Y-M, et al. MR findings of primary choroid plexus papilloma of the cerebellopontine angle: report of three cases and literature reviews[J]. Clin Neuroradiol, 2014, 24(3): 263-267.

[21] M-G Kartal, Algin O. Evaluation of hydrocephalus and other cerebrospinal fluid disorders with MRI: An update[J]. Insights Imaging, 2014, 5(4): 531-541.

[22] A Caricato, Ioannoni E, Gelormini C. Is It Really Third Ventricle? A Pitfall in the Diagnosis of Hydrocephalus by Brain Ultrasound[J]. Neurocrit Care, 2020, 33(3): 844-846.

[23] D-K Ragan, Cerqua J, Nash T, et al. The accuracy of linear indices of ventricular volume in pediatric hydrocephalus: technical note[J]. J Neurosurg Pediatr, 2015, 15(6): 547-551.

[24] Tang Yuhui, Li Saichun, Guo Hao, et al. Analysis of Cisternal Imaging Value in 144 Patients with hydrocephalus [J]. Biomedical Engineering and Clinical, 2020, 24(05): 570-574.

[25] Guan Feng, Hu Zhiqiang, Wang Zhengwei, et al. The application value of spect in the diagnosis and treatment of hydrocephalus[J]. Neurological Disorders and Mental Health, 2008, 8(06): 433-435.

[26] Fredrik Lundin, Tisell Anders, Leijon Göran, et al. Preoperative and postoperative 1H-MR spectroscopy changes in frontal deep white matter and the thalamus in idiopathic normal pressure

UNDER PEER REVIEW

hydrocephalus.[J]. Journal of neurology, neurosurgery, and psychiatry, 2013, 84(2).

[27] J Virhammar, Laurell K, Ahlgren A, et al. Arterial Spin-Labeling Perfusion MR Imaging Demonstrates Regional CBF Decrease in Idiopathic Normal Pressure Hydrocephalus[J]. AJNR Am J Neuroradiol, 2017, 38(11): 2081-2088.

[28] Li Lulu, Liu Pengfei, Liu Zhilan, et al. MRI and Diffusion Imaging Characteristics of Early Rat model of Obstructive Hydrocephalus [J]. Chinese Journal of Practical Diagnosis & Therapy, 2013, 27(10): 954-956.

[29] Huang Jianglong, Tang Xiaoping, Zhang Ran, et al. Diagnostic Value of Magnetic Resonance CUBE T2 Combined with 3D-FIESTA Sequence in Obstructive Hydrocephalus [J] Journal of Clinical Radiology, 2019, 38(01): 18-21.

[30] Liu Huaxiu, Shi Hao. Imageology Research Progress of Hydrocephalus[J]. Journal of Medical Imageology, 2019, 29(07): 1221-1223.

[31] Min Yuping. Prevention of Neural Tube Malformation by Oral Folic Acid Before Pregnancy and Early Pregnancy in 7582 Patients [J]. Chinese Journal of Reproductive Health, 2011, 22(2): 119.

[32] JRT Melo, Passos R-K, Carvalho MLCM. Cerebrospinal fluid drainage options for posthemorrhagic hydrocephalus in premature neonates[J]. Arq Neuropsiquiatr, 2017, 75(7): 433-438.

[33] E Giordan, Palandri G, Lanzino G, et al. Outcomes and complications of different surgical treatments for idiopathic normal pressure hydrocephalus: a systematic review and meta-analysis[J]. J

UNDER PEER REVIEW

Neurosurg, 2018, 1-13.

[34] Pang Mingyan. New Progress in the Treatment of Hydrocephalus [J] Chinese Community Physician, 2019, 35(16): 6-7.

[35] Chi Jieshan. Perioperative Nursing Observation of Patients with Hydrocephalus Treated By Ventriculoperitoneal Shunt [J]. Heilongjiang Traditional Chinese Medicine, 2020, 49(05): 147-148.

[36] Qiu You. Nursing Observation of Traditional Chinese and Western Medicine After Ventriculoperitoneal Shunt of Hydrocephalus [J]. Journal of Psychology, 2020, 15(03): 115.]

[37] Zhu Denna, Yang Yonghui, Yang Lei. Postoperative Rehabilitation of Hydrocephalus and Cerebral Trauma in Children [J]. Chinese Journal of Practical Pediatrics 2018, 33(08): 589-592.

[38] Ren Lu. Effect of Early Rehabilitation Nursing on Postoperative Neurological Function in Infantile Hydrocephalus[J]. Systems Medicine, 2021, 6(05): 152-154.

[39] Li Ke. Influence Study of Early Rehabilitation Nursing on Postoperative Infantile Hydrocephalus [J]. Journal of Shanxi Health Vocational College, 2019, 29(06): 91-92.

[40] Lee Man. Effect of Early Rehabilitation Nursing on Postoperative Neurological Function in Infantile Hydrocephalus[J]. Journal of Practical Clinical Medicine, 2017, 21(16): 206-208.

[41] Zhang Xiaogang. “Brain Fluid Stasis Theory” of Professor Zhang Xuewen’s Clinical Experience in the Treatment of Adult Hydrocephalus After Craniocerebral Injury [J] Journal of Shaanxi University of Chinese Medicine, 2020, 43(02): 46-49.

[42] Feng Hui, Zang Li, Zhang Dezhong. Effects of Decoction for

UNDER PEER REVIEW

Activating Blood Circulation on Serum Neuro-biology Markers and Cerebrospinal Fluid p73, p38 Factor Expressions of patients with Posttraumatic Fluid- Stasis Type Hydrocephalus[J]. Chinese Journal of Experimental Traditional Medical Formulas, 2017, 23(13): 185-190.

[43] Qi Xinhua, Ji Xiaona. Effect Analysis of Decoction for Activating Blood Circulation Combined with Acupuncture on Nerve Function and Quality of Life in Patients with Hydrocephalus [J]. Sichuan Traditional Chinese Medicine, 2018, 36(10): 135-138.

[44] Xiang Gaobo, Jiang Xingfu, Li Huansong, et al. Clinical Evaluation of Decoction for Removing Blood Stasis Combined with Ventriculo-Peritoneal Shunt in Treatment of Normal Pressure Hydrocephalus [J]. Journal of Liaoning University of Traditional Chinese Medicine, 2019, 21(04): 124-127.

[45] Wang Yulan, Gong Liping, Guo Chaofeng. Research Progress of Pharmacology and Clinical Application of Wu Ling San [J]. Journal of Hubei University of Traditional Chinese Medicine, 2021, 23(02): 118-120.

[46] Jia Xuecang. Clinical Observation of Warming Yang and Promoting Diuresis Method Based on Wu Ling San in the Treatment of Traumatic Communicating Hydrocephalus [J]. Guangming Journal of Chinese Medicine 2019, 34(14): 2176-2178.

[47] Fan Shaoping. Effect of Wu Ling San Combined with Conventional Conservative Western Medicine on Traumatic Communicating Hydrocephalus and on Renal Function [J] Modern Journal of Integrated Traditional Chinese and Western Medicine 2018, 27(04): 424-426.

UNDER PEER REVIEW

[48] Lin Hai, Li Huizhong, Huang Meifei, et al. Acupuncture Combined with Acupoint Application Promotes Neural Functional Recovery after hydrocephalus in 25 Cases [J]. Fujian Chinese Traditional Medicine, 2017, 48(03): 19-20.

[49] Yu Mengjin, Ye Ruixiong, Huang Pinglan, et al. Report of Acupuncture"Warm Method" Treatment of 12 Congenital Hydrocephalus in Children[J]. Chinese Manipulation & Rehabilitation Medicine, 2015, 6(17): 35-37.

[50] Liu Shizhe Zhang Tie Liu Yuhuan. 18 Cases of Infantile Hydrocephalus Treated by Acupuncture and Massage[J]. Journal of Clinical Acupuncture and Moxibustion, 1997, (03): 16.

[51] Peng Changlin Li Peifang. 27 Cases Observation of Curative Effect of Heavy Moxibustion Cooperating with Acupuncture Treatment in Infantile Hydrocephalus [J]. Journal of Anhui Traditional Chinese Medical College, 1997, (04): 49-50.

[52] Liu Fugui, Peng Chaoqun, Liu Ling, et al. Professor Wang Song ling: Experience in Integrated Method of Invigorating Spleen and kidney by Warming Yang and Eliminating Blood Stasis in the Treatment of Infantile Hydrocephalus [J]. Journal of Tianjin University of Traditional Chinese Medicine, 2020, 39(05): 493-496.

[53] Zhou Zhengxin, Song Hujie, Zhao Xiling. Observation of Curative Effect of Traditional Chinese Medicine Comprehensive Solution for Fluid Stasis Type of Infantile Hydrocephalus [J]. Journal of Changchun University of Traditional Chinese Medicine, 2012, 28(05): 876-877.

[54] Feng Taozhen, Song Hujie, Sun Yubo, et al. Treatment of

UNDER PEER REVIEW

Infantile Hydrocephalus with Spleen Deficiency and Fluid Syndrome Type by Integrated Chinese and Western Medicine[J]. Jilin Journal of Traditional Chinese Medicine, 2016, 36(07): 686-688.

[55] Du Xiaogang, Song Hujie. The Clinical Effect of Professor Song Hujie's Trinity Comprehensive Program in the Treatment of Fluid Stasis Type of Infantile Hydrocephalus[J]. Clinical Research and Practice, 2021, 6(28): 125-127.

[56] Zhang Ling, Song Hujie. Clinical Study on the Psychomotor and Intelligence Level of Children with Normal Pressure Hydrocephalus Aged 1-6 by Adopting the Trinity Traditonal Chinese Medicine Comprehensive Program[J]. Acta Chinese Medicine and Pharmacology, 2011, 39(04): 52-54.

[57] Zhang Ling, Song Hujie. Influence of Traditional Chinese Medicine Comprehensive Program on Intelligence and Movement for Fluid Stasis Type Infantile Hydrocephalus[J]. Shaanxi Traditional Chinese Medicine, 2014, 35(11): 1465-1466.

[58] Song Hujie, Zhang Ling, Liu Yongping, et al. Improvement of Intelligence and Movement Function in Children with Normal Pressure Hydrocephalus by Adopting the Trinity Chinese Traditional Medicine Comprehensive Program[J]. China Journal of Traditional Chinese Medicine and Pharmacy, 2013, 28(03): 862-864.

[59] Ruan Guiji, Song Hujie, Yan Bingcang, et al. Sixty Cases of The "Trinity Therapy" in Treatment of Infantile Hydrocephalus[J]. Lishizhen Medicine and Materia Medica Research, 2016, 27(09): 2181-2184.

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