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Some Therapeutic Aspects in Pediatric Hydrocephalus

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Abstract

We carry out a review about some therapeutic aspects of childhood hydrocephalus. This description has been divided into the following groups: surgical treatment, pharmacological treatment, and spontaneous improvement based on self-compensated criteria: cerebrospinal fluid dynamics, clinical and radiological, cerebrospinal biochemical, and hemodinamical parameters. We conclude with some reflections about its prognosis.

Keywords: Acetazolamide; CSF absorption; CSF pressure; Hydrocephalus; Neuroendoscopic; oxypurines; Shunt; Transcranial Doppler

Introduction

Table 1: Diagnostic test in hydrocephalus

Cranial circumference measurements
Transcranial illumination
Eye examination-papilla
Prenatal infections testing
Electroencephalography
Cranial X-Ray
Neuroradiology: Transfontanelar ulrasound; CT head (Computed axial tomography); MRI of the brain; MRI-angiography; brain Angiography
CSF pressure registration
CSF dynamics and reabsorption (isotopic cisternography)
CSF oxipurines level (HPLC)
Cerebral blood flow (Doppler)

Hydrocephalus represents a relatively common chapter in pediatric neurology pathology, specially, during the neonatal and infant period. This critical time for brain maturation makes early diagnosis and optimal therapy a real need to prevent severe and permanent consequences [1]. Nowadays, its etiological, pathogenic and functional diagnosis is easy and safe. It is based on anamnesis and clinical data at first and confirmed by specific diagnostic test (Table 1) [2-6]. Transcranial illumination, a classical and simple test, feasible anywhere you work, can sometimes inform about the degree of ventricular dilatation or even the type of fluid collection (arachnoid or porencephalic cysts, cystic dilatation of the fourth ventricle "Dandy-Walker syndrome", etc). Transcranial ultrasound usually allows diagnosis and follows up in the newborn and infant patient. It is critical to make the differential diagnosis with other entities presenting with macrocephaly, especially benign subdural effusion or benign external hydrocephalus, which occurs during infancy and includes macrocephaly associated to frontal, parietal and temporal subarachnoid space dilatation and normal ventricular size, evolving with spontaneous resolution over time [5,7].

Treatment

Surgical management

Surgical pediatric hydrocephalus management has progressed including many techniques, ranging from

choroid plexus coagulation, translaminar ventriculostomy, Torkildsen and plexectomy to cerebrospinal fluid (CSF) shunt devices [2-5]. The treatment advocated sixty years ago is still valid and is probably the most effective treatment in most of the children with noncompensated hydrocephalus: to place a shunt [2-5,8,9]. However, it is not free of complications, some of them severe. (Table 2) [2-5,10-12]. Today, most noncompensated hydrocephalic patients must be placed on a ventriculoperitoneal shunt, remembering that if it is working by pressure gradient it is necessary to adjust its opening pressure to intraventricular CSF pressure [13]. If tumor or every space-occupying lesion is

the etiology, hydrocephalus can be solved by surgery of the mass, but sometimes a valve will be need in addition [3,4]. In Dandy-Walker Syndrome surgical opening the roof of fourth ventricle to the cistern magna can be the treatment. A double system or two intracranial catheter linked in "Y" can be used when for example, there is a non surgical cyst not draining to ventricular system [3,4].

Table 2: Shunts complications, only in ventriculo-atrial shunt.

Early complications	Surgery mortality
	CSF leak
	Insufficient drainage
	Infections
	Subdural hemorrhage
Delayed complications	The effect of child growth over the shunt
	Thromboembolism*
	Infections
	Shunt nephritis*
	Seizures
	Microcephaly
	Craniosynostosis
	Ventricular catheter blockage
	Cardiac perforation*
	Overdrainage
	Distal catheter obstruction
	Slit-ventricle syndrome
Abdominal complicationss	Detachment of distal catheter
	Ascites
	Intestinal perforation
	Abdominal distension
	Intestinal obstruction
	Peritoneal cyst
	Catheter externalization
	Hydrocele/hernia
	Pneumoencephalus

Repetitive ("daily") lumbar puncture is considered the initial therapy for newborn hydrocephalus due to ventricular bleeding. It removes blood and proteins from CSF and improves intracranial hypertension. Efficacy of this method has been questioned and controversy exists. The indication would be when ventricular dilatation (ultrasound controlled) is evolving slowly. If it is fast, an external ventricular drain, "ventriculostomy", is the first option and if it is ineffective, to place a shunt. [2-5,9,14]. Debated alternatives are lumbar puncture associated to drugs affecting CSF production and/or absorption and the use of intraventricular fibrinolytic treatment ("tissue plasminogen activator") combined with drain and ventricular irrigation [14]. Endoscopic neurosurgery has appeared over the last years to treat obstructive hydrocephalus and those with multiple septums in children and teenagers. It is less effective for toddlers and infants [3,4, 15-18].

Drug treatment

There are drugs decreasing CSF production, such us acetazolamide and isosorbide. This one also acts increasing its re absorption but it is contraindicated in newborn because of adverse effects. Its efficacy is considered if hydrocephalus is near self compensation because if cerebral mantle thickness is less than 15mm resolution with this therapy is uncommon. The main indication is in temporal control of hydrocephalus when a CNS infection exists or in case of high CSF protein concentration, when a shunt is temporally contraindicated [1-4,9]. Therapeutic strategy would be acetazolamide (25-100mg/kg/day) associated to furosemide (1mg/kg/day). This combination is not free of adverse effects, such as renal damage ("nephrocalcinosis") or severe neurological consequences, when treating ventricular dilatation after preterm intracranial bleeding [19].

Expectant management: "self-compensation criteria"

Some children with communicating hydrocephalus progress with a self compensation, so not always a shunt is the first option. Those children have a progressive slowing in cranial perimeter growth until they reach a normal percentile or above maximum percentile but growing in parallel. The ventricular dilatation doesn´t progress and the psychomotor development is normal. In the past, Hagberg and Naglo [20] justified a hands-off management during the first months of life only if no regression nor neurological disturbances were observed, no increase in the ventricular dilatation and when cranial circumference is going to normal percentile. Zachary [21], studying hydrocephalus in spinal dysraphism, used the CSF pressure and cerebral mantle thickness as a guide. When cerebral mantle thickness was more than 35mm y and CSF pressure less than 300mm3 he waited. The important thing is when to apply this option at diagnosis, in this sense we elaborated in the last thirty-seven years several criteria of self-compensating communicating hydrocephalus based on CSF dynamics, clinical and radiological, CSF biochemical, and hemodinamical parameters.

a) CSF dynamics criteria: they consider CSF pressure and re absorption combination, evaluated by radio-isotope cisternography. If a child with communicating hydrocephalus has CSF pressure and reabsorption in normal values it is probably progressing to self compensation, while if one or both parameters are incorrect, it is not [22].

b) Clinical and neuroimaging criteria: mean weekly increase in cranial circumference combined with Evans´ index ("ratio of maximum width of the frontal horns to the maximum width of the inner table of the cranium"). So if the mean weekly increase is equal or less than 0.4cm and Evans index equal or less than 0.5, it will probably progress to self compensation [23].

c) Biochemical criteria: Xanthine and hypoxanthine level in CSF increase in case of neuronal hypoxia or ischemia. Tissue hypoxia is a known cause of adenine nucleotide

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depletion and its intermediate metabolites appearance in extracellular matrix and corporal fluids. They are used as metabolic markers of ATP depletion [24,25]. This energy deficiency in hydrocephalus could be related to several factors (interrelated as well) such as increase in intracranial pressure, CSF dynamics alteration, decrease in brain blood flow, periventricular edema, [26,27]. The oxipurines "hypoxanthine and xanthine" are the last product of ATP degradation, just before uric acid formation. Hypoxanthine is also the substrate in the recovery of purine nucleotides through hypoxanthine-guanine-phosphoribosyltransferase (HGPRT) enzyme [24,25]. CSF oxipurines usually rise when hydrocephalus is not compensated [26,27]. If both purinic metabolites are in the normal CSF range (hypoxanthine=5.94±0.74, xanthine=5.20±0.87) then hydrocephalus is self compensated but if they rise it will be necessary to place a shunt (Table 3). These metabolites are also useful to know evolution of the hydrocephalus after 15 day of placing the shunt (Table 4) [28,29]. When shunt dysfunction is suspected, it could be confirmed measuring CSF hypoxanthine and xanthine because they rise in this clinical situation [30].

Table 3: CSF Xanthine, hypoxanthine and total oxipurines level (nmol/L) in pediatric hydrocephalus and normalcontrol. Differences between non compensated and other two groups are statistically significative (p<0.001) Castro-Gago and Rodríguez et al. [29].

Group	(n)	Xanthine	Hypoxanthine	Total oxipurines
Control	(8)	5.20±0.87	5.94±0.74	11.29±1.11
Self-compensated	(13)	5.17±1.53	5.71±1.72	10.79±3.02
Non compensated	(15)	9.90±2.44	9.91±1.90	19.82±4.14

Table 4: CSF oxipurines level (nmol/L) in non compensated hydrocephalus, before and after shunt Differences are statistically significant (p<0.001) Castro-Gago et al. [29].

	Xanthine	Hypoxanthine	Total oxipurines
Pre-shunt	9.90±2.44	9.91±1.90	19.82±4.14
After-shunt	4.22±1.76	4.67±1.36	8.80±2.69

d) Hemodynamic criteria: It is based on brain blood flow values calculated with transcranial Doppler in middle cerebral artery (systolic velocity, mean flow velocity, Gosling pulsatility index, Pourcelot resistance index) [31]. If these parameters are normal it is probably that hydrocephalus is self compensated and if not, a shunt is needed [32]. This criterion is also used to know how hydrocephalus progresses and for diagnosis of shunt malfunction [32].

In conclusion there is a narrow relation between the four criteria and statistical significance is similar for everyone [22,23,28,29,32], so the most practical criteria is the last one (transcranial Doppler) because it is a non invasive technique, well tolerated, affordable, feasible, with real time results, and can be repeated when needed.

Prognosis

In general, when a child is diagnosed of hydrocephalus and properly treated, his prognosis is good (exceptions exist) but it is needed periodic control of neurological status and if placed, shunt functionality [3,5,33]. Some children with hydrocephalus had significantly impaired learning, memory and executive functions [34]. If self compensation is achieved the prognosis is better than those requiring a shunt [3,5]. In the recent past, some authors believe that intellectual quotient is less likely affected, even in great hydrocephalus [35-38]. However, other authors observed that there is a correlation between cerebral mantle thickness or brain volume at diagnosis and their psychomotor future. If cerebral mantle thickness is less than 2cm or brain volume is less than 60% psychomotor progression may not be achieved as normal, apart from etiology [3,5,39-42].

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