Point of View: Exit ventriculoperitoneal shunt; enter endoscopic third ventriculostomy (ETV): contemporary views on hydrocephalus and their implications on management

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Abstract

Hydrocephalus has been known to affect humans since the birth of human medicine as it is described by Hippocrates. The management of this condition is however still dodged by challenges due to a poor understanding of its pathophysiology. The ventriculoperitoneal shunt presents considerable problems especially with respect to infection and shunt malfunction. Low income countries, that currently face the greater burden of paediatric hydrocephalus. experience an increased challenge with ventriculoperitoneal shunts due to a shortage of qualified personnel to handle shunt complications. Recent advances in neuro-endoscopic surgery have presented opportunities for alternative treatment options for hydrocephalus such as endoscopic third ventriculostomy (ETV). This paper explores the alternative views in the pathophysiology of hydrocephalus and how they explain the effectiveness of ETV in treating hydrocephalus arising from a variety of causes.

Introduction

Hydrocephalus is a common neurosurgical condition affecting humans of all ages with variable effects. The earliest scientific description of hydrocephalus is ascribed to Hippocrates (466–377 BC), who mentioned such symptoms as headache, vomiting, visual disturbance, and diplopia, and explained the illness as a "liquefaction of the brain caused by epileptic seizures"[1]. The Hippocratic corpus also contains the first reference to the term, "hydrocephalus", which is constructed from the Greek words hydro, which means water and kefalé, head[1]. Since that time, the condition has accumulated a very rich scientific and treatment history. Scanty data exists on the global incidence of hydrocephalus. Studies have reported variation in the incidence rate and this could be due to differences in both the definition of aetiology and study designs (including inclusion and exclusion criteria, and study populations) in different geographical areas[2]. Hospital-based studies only estimate the burden of hydrocephalus in populations who seek health care whilst community-based studies mainly describe the incidence of congenital hydrocephalus[2,3]. A review of data involving 639 children with hydrocephalus identified some of the common causes of hydrocephalus in children including intracranial hemorrhage (20%), brain tumors (26%), and craniospinal congenital malformations, like myelomeningocele (MMC), Dandy Walker malformation and others, in 36% of patients, and central nervous system (CNS) infections (<10%)[2].

The History and Burden of Hydrocephalus in Malawi

The early history of hydrocephalus in Malawi is poorly documented. Just before the turn of the millennium however, Professor Adelola Adeloye, who was the founding Professor and Head of Surgery at the inception of the College of Medicine in 1991, raised the profile of hydrocephalus in Malawi in the regional literature[4–8]. Within a few years of his stay in Malawi, he had documented that two major aetiological varieties of hydrocephalus existed in Malawi which he named "the congenital" and "the meningitis"[5]. His finding was later confirmed in Malawi by Waluza and Borgstein in 2005[9]. During his period in Malawi, Adeloye devised the Malawi shunt as a treatment of hydrocephalus, which he applied in over 100 patients until it was replaced, in 2001, by the Chhabra shunt. The adoption of the Chabbra shunt arose from collaboration with the International Federation for Hydrocephalus and Spina Bifida (IFSBH), and remains in use until this day[4, 6, 7, 9].

The epidemiology of hydrocephalus in Malawi remains largely unknown. Waluza and Borgstein, in 2005, reported 223 cases of hydrocephalus in 2 years at Queen Elizabeth Central Hospital (QECH)[9]. In their report, 90% of the patients were children with an open fontanelle. In the same report, the researchers observed that, in half of the children that they treated for hydrocephalus, there was a prior history of meningitis. In the same year (2005), Warf also reported a high proportion (60%) of post-infection hydrocephalus in 300 new cases of hydrocephalus in children treated with endoscopic third ventriculostomy (ETV) in Uganda[10]. Using flexible neuro-endoscopy, he was able to demonstrate evidence of inflammatory changes within the ventricles, which is characterised by hemosiderin deposits, inflammatory exudates and intraventricular septations, among others features.

Since Waluza and Borgstein's report in 2005, there are indications that the burden of hydrocephalus at QECH is on the increase (personal observation). This may be due to increased awareness of the condition by clinicians and society at large, and may also be related to the positive impact of the hydrocephalus programme that was set up by Adeloye and that is currently supported by the IFHSB. It is estimated that over the past 2 years approximately 4 new patients with hydrocephalus are treated are QECH each week representing a patient load of around 200 new cases per year. This is more than what was reported previous by Borgstein and Waluza in 2005.

Currently in Malawi, hydrocephalus is also managed in 3 other central hospitals located in each of the main cities of Mzuzu, Lilongwe, and Zomba, where approximately 30 to 40 VP shunt operations are conducted in each hospital annually (Borgstein E, 2012, personal communication). Thus, although no studies have been conducted to estimate the burden of hydrocephalus in Malawi, it would appear that hydrocephalus is a considerable problem in Malawi.

Motivation for this Special Communication

Cure International, a not-for-profit organization providing orthopedic and neurosurgical care in over 11 countries, has, over the past 3 years, been championing a new method in the treatment of paediatric hydrocephalus which combines ETV and choroid plexus cauterization (ETV-CPC). This follows their 10 year experience of hydrocephalus work at the Cure International Children's Hospital in Mbale, Uganda[4,10,11]. Over the past 3 years, the hospital has been providing training to general surgeons and neurosurgeons from low income countries (LICs) on the ETV-CPC technique which uses a flexible neuro-endoscope to fenestrate the floor of the third ventricle and cauterizes the choroid plexus in both lateral ventricles. Malawi has recently joined the list of the few countries in Africa that have expertise in treating patients with this new technique, using equipment donated to QECH

by Cure International in September 2012.

The aim of this paper is threefold

1. To introduce ETV-CPC to clinicians and readers of the Malawi Medical Journal;

2. To discuss the scientific basis of ETV-CPC;

3. To stimulate debate and research in the field of hydrocephalus

Details of the generic aspects of hydrocephalus and VP shunt complications will not be discussed and the reader is referred to the work of Black, Sante-Rose and others[12–15].

Defining Hydrocephalus

Despite the very rich and long history of hydrocephalus in human kind, there is no consensus on the definition of this condition to date. This is a result of poor understanding of the mechanisms of ventricular dilatation in hydrocephalus. Two theories have been proposed to explain ventricular enlargement which are: the cerebrolspinal fluid (CSF) bulk flow theory and the hydrodynamic theory. The lack of consensus in the definition has also been propagated by the fact there has been little communication between the proponents of the theories in present times, and also, neither side has considered incorporating the opposing views[16,17]. It is likely that both theories have a role to play in our understanding of the pathophysiology of hydrocephalus and there is need to move towards describing a combined theory. The importance of appropriately defining hydrocephalus cannot be overemphasized since clarifying the pathophysiologic mechanisms underlying the condition will assist in the development of optimal management options.

The starting point towards developing a combined theory is the fact that the proponents of each theory in present-day discourse concur that the fluid accumulation in hydrocephalus is a result of a hydrodynamic disorder (i.e. pressure-driven). This rules out conditions like cerebral atrophy and focal destructive lesions which are also characterized by an abnormal increase in CSF volume. In such cases, the increase in CSF is a result of passive flow of CSF to fill spaces created by the loss of cerebral tissue (hydrocephalus ex-vacuo)[13, 18, 19]

The CSF Bulk Flow Theory and Classification of Hydrocephalus

The present-day understanding of hydrocephalus was inspired by the work of Dandy at the beginning of the 20th century. Dandy and Blackfan, in 1914, classified hydrocephalus, in terms of the CSF bulk flow theory[1, 18–20]. They argued that ventricular enlargement is caused by a backup of CSF flow, caused by obstruction either within the ventricles (non-communicating hydrocephalus) or beyond the ventricles (communicating hydrocephalus). Although their definition states that each type is due to obstruction, this differentiation, into non-communicating hydrocephalus and communicating, has been a source of confusion among clinicians, with some assuming that the first is due to obstruction and the latter, not. This has also led to the thinking that the two types should be managed differently[19–21].

In 1960, Ransonhoff and colleagues suggested a modification to Dandy's classification while still maintaining the CSF bulk flow theory. They classified hydrocephalus as intraventricular obstructive hydrocephalus and extraventricular obstructive hydrocephalus[17,18]. Intraventricular obstruction results from partial or complete occlusion of any of the ventricles, the foramen of Monroe, the cerebral aqueduct (of Sylvius) and outlets of the fourth ventricle; whilst obstruction of the basal cisterns, arachnoid villi and cranial venous system draining to the heart cause extraventricular obstruction[17,18]. A wide spectrum of conditions cause such obstruction ranging from congenital to acquired causes such as infections, tumors, and the presence of blood in CSF. Rekate, recently, has expanded on Rasonhoff's perception and he concludes the CSF bulk flow theory by stating that "with the rare exception of hydrocephalus associated with overproduction of CSF in patients with choroid plexus papillomas (CPPs), all cases of hydrocephalus are as a result of CSF flow obstruction"[18].

Thus Dandy, Rasonhoff and Rekate are proponents of the CSF bulk flow theory which supposes that, in hydrocephalus, ventricular enlargement is caused by a backup of CSF flow, caused by obstruction either within the ventricular or the extraventricular systems.

The Hydrodynamic Theory and Development of Ventricular Enlargement in Hydrocephalus

The CSF bulk flow theory presupposes a passive dilatation of the ventricles proximal to an obstructed pathway within or outside of the ventricles. In order to understand this theory better, Greitz compares ventricular dilatation in the CSF bulk flow theory to what would happen if a river were obstructed[19]. In such a case, the water would dam up proximal to the point of obstruction, which is the same broad consequence observed in intraventricular obstruction leading to ventricular enlargement in the acute phase of obstructive hydrocephalus, according to Greitz[19].

However, such is not the case in extraventricular obstructive hydrocephalus. If CSF absorption takes place at the arachnoid villi (in keeping with the CSF bulk flow theory), and once again applying the simplistic analogy of a blocked river, blockage at the arachnoid villi, would cause an initial dilatation of the subarachnoid space immediately adjacent to the arachnoid villi[16,19,21]. It is known, however, that in extraventricular obstructive hydrocephalus the ventricles dilate, whilst the cortical subarachnoid space is, in fact, narrowed[19,20,22].

Greitz, therefore, proposes an alternative to the CSF bulk flow theory, which he calls the hydrodynamic theory[19]. This theory propounds that ventricular enlargement in extraventricular obstructive hydrocephalus is caused by decreased intracranial compliance, which increases the systolic pressure transmission into the cerebral parenchyma thereby generating a transmantle pulsatile stress.

The hydrodynamic theory can be explained as follows. Each systolic flow of arterial blood into the cerebral arteries results in brain pulsation and an increase (transient and pulsatile) in both the blood component of the brain and intracranial pressure. According to the Monroe-Kelly doctrine the skull is rigid and the sum of the volumes of brain, CSF, and intracranial blood is constant[23]. Any increase in the components of the brain would therefore result in raised intracranial pressure unless some component was to compensate. Therefore, the transient, pulsatile and systolic expansion of the intracranial arteries described above has been shown to be offset by a commensurate expulsion of CSF through the foramen magnum into the thecal sac, and expulsion of blood from the veins into the dural venous sinuses[19]. The efficiency of this intracranial pressure or volume regulation mechanism depends on the compliance of

the subarachnoid space. According to Greitz's hydrodynamic theory, in the presence of extraventricular obstruction, the capacity of the subarachnoid space (and the dural venous system) to accommodate the pulsatile increase in volume of CSF and venous blood (and hence increase in intracranial pressure), is compromised, and this results in an increase in the effective systolic pulsation of the brain[19].

Ventricular enlargement in turn is explained by the difference in the physical property of brain tissue and CSF within the ventricles. The brain is compressible (visco-elastic), whereas the CSF within the ventricles is not[19,24]. Therefore, when there is decreased compliance of the subarachnoid space in extraventricular obstruction, a higher than normal systolic pressure is transmitted through the ventricles and, since the CSF (and the ventricles) are incompressible, the ventricles push into the cerebral cortex toward the skull. This, Greitz calls transmantle (that is trans-cerebral cortex mantle) pressure, which results in the ventricles progressively ploughing into the brain (or the brain is moulded around the ventricles) consequently enlarging the size of the ventricles, and narrowing the cortical subarachnoid space between the cerebral cortex and skull[19,21]. For a more detailed understanding the reader is referred to the work of Greitz but also Bateman[16,19–21,25].

In summary, the hydrodynamic theory explains ventricular enlargement in extraventricular obstruction but not in intraventricular obstruction. Greitz's explanation of the latter, which he calls acute obstructive hydrocephalus, seems to be based on the CSF bulk flow theory[19]. Thus, we need both the CSF bulk flow theory and the hydrodynamic theory to explain (ventricular dilatation in) hydrocephalus in its broad sense. This forms the basis for my proposal for a unified theory of hydrocephalus whereby the bulk theory explains intraventricular obstructive (non-communicating) hydrocephalus and the hydrodynamic theory, extraventricular obstructive (communicating) hydrocephalus.

Management of Hydrocephalus

There are several approaches to the definitive management of hydrocephalus, but, in principle, these involve treatment of the cause whenever possible in case of a mass lesion, and CSF diversion. Most patients require CSF diversion where a shunt is used to divert CSF from the ventricles to an alternative site outside the brain. In most patients the shunt is inserted usually into one of the lateral ventricles to drain CSF into either the peritoneal cavity (VP shunt). In cases where the peritoneal cavity is not able to absorb CSF (for example - a frozen abdomen), the right atrium of the heart or the pleural cavity may be used[1]. Shunts have been associated with a number of serious complications, which include shunt infection, mechanical shunt blockage (acute or sub-acute), over-drainage or under-drainage, among others[1,14, 26,27]. In countries with low income status there exist unique problems with VP shunts which include poor access to neurosurgical services in the event of a blocked shunt and shunt erosion through skin of malnourished children[11, 28].

Although shunts have greatly improved the prognosis of hydrocephalus, the nefarious complications associated with their use have led neurosurgeons to explore alternative treatment methods. ETV has emerged as a plausible alternative to VP shunting. Third ventriculostomy is a procedure which involves creation of a small perforation (stoma) at the floor of the third ventricle to allow flow of CSF from the third ventricle into the pre-pontine subarachnoid space thereby bypassing a distal blockage beyond the third ventricle in distal intraventricular obstruction or increasing the compliance of the subarachnoid space in extraventricular obstruction (according to the hydrodynamic theory)[19, 20]. Over the past 3 decades this procedure has been done endoscopically (hence ETV) using either a rigid or flexible neuro-endoscope. Since there is no implantation of a foreign body, ETV avoids most of the complications of VP shunting.

The history of ventriculostomies dates back to the era of Dandy when he did open ventriculostomies, but he met serious safety challenges which stalled progress into these types of procedures[1]. Interest in ventriculostomy has been revived over the past 25 years with the widespread use of neuro-endoscopy. Indications for ETV are still being elucidated[29]. Traditionally ETV has been reserved for intraventricular obstructive hydrocephalus. In such cases, a small perforation of about 3 to 6 mm diameter is made at the floor of the third ventricle bypassing a distal blockage and re-establishing flow into the pre-pontine subarachnoid space to the arachnoid granulations for absorption (thereby satisfying the CSF bulk flow theory). ETV has also been demonstrated to be successful in patients who have previously had VP shunts, for whatever indication, with about two thirds of such patients attaining shunt independence[30]. Infections cause hydrocephalus through blockage of the subarachnoid spaces (extraventricular obstruction or communicating hydrocephalus), and by possible scarring of the arachnoid granulations (the supposed site of CSF absorption according to CSF the bulk flow theory). A number of authors have also reported success in patients with hydrocephalus due to bacterial infections or tuberculous meningitis[31]. Whilst it is not fully understood why ETV works in these non-traditional indications, the proponents of the hydrodynamic theory suggest that ETV should work in communicating hydrocephalus since CSF flow through the stoma into the pre-pontine subarachnoid space improves compliance[19, 20].

In the early literature on ETV, effective control of hydrocephalus was mainly reported in adults and children above 6 months old. Most clinicians refrain from doing ETV procedures in infants less than 6 months due to reports of high failure rates in the early literature on ETV, but Jadvadpour et al noted that the success of ETV is aetiology-, and not age- dependent[32,33]. Fritsch et al reported a 10% success rate in infants with communication hydrocephalus and a 50% success in infants with hydrocephalus related to myelomeningocele (MMC-hydrocephalus)[34].

Combined Endoscopic Third Ventriculostomy and Choroid Plexus Cauterization

Over the past decade, the work by Warf in Uganda has shown that ETV procedures, combined with choroid plexus cauterization (ETV-CPC) in selected groups of children with hydrocephalus, are an effective treatment[10,11,35]. The choroid plexus is the structure that produces most of the CSF in the brain, accounting for 80-90% of total CSF production. Destruction of the choroid plexus has been known for a long time to have some positive impact on hydrocephalus but long-term efficacy has been low with about two thirds of the patients ultimately requiring a VP shunt[1,36]. As had Javadpour et al and other researchers, Warf, in his initial work, observed a success rate of 50% or less in infants of less than 1 year old with open aqueducts, congenital aqueductal stenosis and MMC-hydrocephalus[10,37]. In a prospective study published in 2005, with a mean follow up of 19 months for the ETV cohort;

and 9.2 months for the ETV-CPC cohort, he demonstrated a 66% overall success rate of ETV–CPC compared to that of ETV alone (47%) amongst infants younger than 1 year of age ($p = 0.0001$)[37]. This result included a 76% success rate in ETV–CPC procedures performed in infants with MMC-hydrocephalus compared to 35% in infants with the same condition who had had ETV only ($p = 0.0045$).

These findings suggest a superiority of ETV-CPC in avoiding shunt dependency in children, as compared to ETV alone, and have proffered a paradigm shift in the management of hydrocephalus in the low income countries. Although there are no prospective randomized trials to compare this new approach with shunt management, the prospect of minimizing shunt dependency within the inherent constraints existing in low income countries makes ETV-CPC an option worthy of urgent consideration. More importantly, subsequent research conducted in Uganda has demonstrated that, for children with MMC-hydrocephalus treated with ETV-CPC, the neurocognitive development was not different from those treated with VPS[38]. This finding was confirmed in 2006 by Takahashi, who also reported adequate neurological development in children with hydrocephalus undergoing ETV when their cerebral cortex was still normal[39].

Conclusion

The scientific basis for application of ETV-CPC in hydrocephalus is plausible, based on both the historical perspective and the clinical experiences in Uganda. Historically, ETV and CPC have each been shown to control hydrocephalus to some extent. It is therefore understandable that a combination of the two methods ought to improve outcome, relative to application of each method in isolation. Although the long term outcomes and complications of ETV-CPC are not yet known, the results from Uganda are promising[35]. Evidence to date also indicates that children undergoing ETV are not disadvantaged in terms of neurocognitive development, when compared to those treated with VP shunts.

Malawi is fortunate to be involved in the development of this new technique whilst it is in its infancy. A window of opportunity exists to conduct research to validate the success of the procedure, through well-designed prospective studies, but also to elucidate why, contrary to accepted understanding of its mechanism of action, ETV seems to be effective in non-traditional indications. Such validations and clarifications will have a great impact on the management of children with hydrocephalus not only in low income countries but also in middle and high income countries who also face significant challenges with VP shunts (14, 15, 18, 40). The burning question, at this point, is whether, in the near future, VP shunts will be relegated to the back seat as ETV-CPC becomes the first line management in paediatric hydrocephalus.

Conflict of interest

Dr Kamalo has undergone 3-month training in ETV/CPC at CURE International Hospital in Uganda.

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