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Efficacy Comparison of Ventriculoperitoneal Shunt and Endoscopic Third Ventriculostomy as Treatment of Hydrocephalus in Children in Developing Countries: A Meta-Analysis

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Abstract

Introduction: In Indonesia, cases of hydrocephalus in children are found in 40% to 50% of medical visits or neurosurgical operations. Endoscopic third ventriculostomy was one of choices for treat the patient but efficacy and effects still unknown. Purpose of this study is to broadly assess the outcome of treatments and review evidence that one treatment may have greater efficacy than another.

Method: Researchers develop PICO questions. Demographic information, detailed methods, interventions, and results were extracted from the selected manuscripts. Of the 122 articles identified using optimized search parameters, 52 were withdrawn for full-text review. In total, 6 articles were accepted for inclusion in the evidentiary table and 8 were excluded for various reasons.

Result: The tabulated evidence provides sufficient data to allow our evaluation of the CSF versus ETV shunt.

Conclusion: CSF shunt and endoscopic third ventriculostomy (ETV) are options in the management of hydrocephalus in children

Keyword: Endoscopic third ventriculostomy, Hydrocephalus, Ventriculo-peritoneal Shunt

Introduction

Hydrocephalus is one of the most common diseases in children. In developed countries, the prevalence of congenital hydrocephalus is 0.5-1 per 1000 live births. Meanwhile, the prevalence of hydrocephalus is 3 to 5 per 1000 live births. The prevalence of idiopathic normal pressure hydrocephalus (iNPH) has been reported to be 1.8-2.2 cases per 100,000 and 1,000,000 people, respectively. In Indonesia, cases of hydrocephalus in children are found in 40% to 50% of medical visits or neurosurgical operations. A research showed that the incidence of pediatric hydrocephalus communicants and non-communicants in Dr. Soetomo Surabaya from January 2014 to January 2016 amounted to 35.9% and 51.1% [1].In order to properly understand hydrocephalus, it is first necessary to discuss the production and absorption of cerebrospinal fluid (CSF) and its pathways. CSF is mainly produced by the choroid plexuses in the lateral, third, and fourth ventricles. The ependymal and capillary cells also play a minor role in CSF secretion. Through arachnoid granulation, CSF will flow

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into the venous sinuses and then to the lymphatic system through the Virchow-Robin space. Furthermore, most of it will flow to the craniospinal nerves via the perineural space; while some will flow to the spinal cord. CSF circulates in the cerebral ventricles (lateral, ventricles and third and fourth waterways) and cerebrospinal Subarachnoid Space (SAS). [2] In general, the CSF volume is about 160 mL wherein 25% of this volume circulates in the ventricles and 75% in the spinal and subarachnoid cortical spaces. The average CSF production rate was 0.34 ± 0.13 mL / minute; the average CSF absorption rate in the spinal cord was 0.17 mL / minute. It should be pointed out that under normal physiological conditions, circulating CSF has a constant inflow and pulse. [3]

The most important hydrodynamic parameter that indicates the incidence of hydrocephalus is the CSF Intracranial Pressure (ICP) which refers to the numerical value of the CSF pressure in the upper brain convex in SAS. It should be noted that the ICP wave is different from the Arterial Blood Pressure (ABP) wave. The ICP values in normal infants under one year of age, children, and adults are 3-4 mm Hg, 11 mm Hg, and 10-15 mm Hg, respectively. Many CSF circulation parameters such as CSF flow rate and flow rate diagrams for patients with hydrocephalus and healthy subjects are measured via contrast Cine Magnetic Resonance Imaging (Cine PC-MRI)[4]. Meanwhile, these tools are more useful for understanding patient pathophysiology. The choice of the appropriate surgical method - insertion of a CSF shunt or endoscopic third ventriculostomy (ETV) - for the management of hydrocephalus in children remains a topic of debate. Proponents of ETV cite the low failure rate and the potential to avoid shunt placement and the inherent risks as the main advantages of this procedure, while proponents of ventriculoperitoneal shunt (VP) insertion have questioned the efficacy of ETV in treating hydrocephalus as well as the unknown effects of ETV on neurodevelopment and quality of life. [5]

Although there is a large literature on CSF and ETV shunts, there is a relative dearth of articles describing evaluations of CSF and ETV shunt placement, and no randomized trials comparing the two procedures. ETV may be useful in cases where there is clear obstruction to the CSF stream and ETV provides an alternative pathway. It is less certain that ETV has an advantage over shunts in many other causes of hydrocephalus. There has been much interest in the use of ETV with choroid plexus coagulation (CPC) in the management of infant hydrocephalus. [6]

The Pediatric Hydrocephalus Systematic Review and Evidence-Based Guidelines Task Force anticipates that this topic, together with the effectiveness of ETV compared to shorthand in treating hydrocephalus of specific etiologies, will be discussed in a subsequent publication. In this analysis, we attempted to systematically review the existing literature detailing the efficacy of CSF versus ETV shunts and to produce evidence-based recommendations for the selection of surgical procedures based on the strength of available data. Evidence for ETV and discussion of the procedure in infants under 1 year of age are discussed elsewhere. [7] The main objective of this study is to broadly assess the outcome of treatments and review evidence that one treatment may have greater efficacy than another.

Methods

Researchers develop PICO questions. How to compare the effectiveness of a ventriculoperitoneal shunt and endoscopic third ventriculostomy as a treatment for hydrocephalus in children in developing countries. Based on this, the PICO questions were obtained as follows:

- Patients: Patients aged 0-18 years with hydrocephalus
- Intervention: Ventriculoperitoneal shunt (VPS)
- Comparison: Endoscopic third ventriculostomy (ETV)
- Outcome: The success of the procedure was characterized by postoperative clinical improvement

Researchers applied strict inclusion criteria, selected only RCTs, case-control studies or cohort studies, and pediatric patients with hydrocephalus were treated with these two invasive treatment options. Researchers used the following keywords: *"Hydrocephalus" AND "Shunt" AND "Ventriculostomy"*. Researchers limit the research to only in English languages. Articles published between 2000 and 2020. One reviewer completes all review processes. The following databases were reviewed: Cochrane Library, Medline, Embase, Web of Science, Google Scholar, Scopus, and PubMed.

Demographic information, detailed methods, interventions, and results were extracted from the selected manuscripts for review and recorded on a special data form. The data taken includes:

1. Methods: Research design, description or research flow, sampling technique and the number of respondents included in the study.
2. Patients: Patients aged 0-18 years with hydrocephalus
3. Intervention: Ventriculoperitoneal shunt (VPS)
4. Comparison: Endoscopic third ventriculostomy (ETV)
5. Outcome: The success of the procedure was characterized by postoperative clinical improvement
6. Conclusions from the study

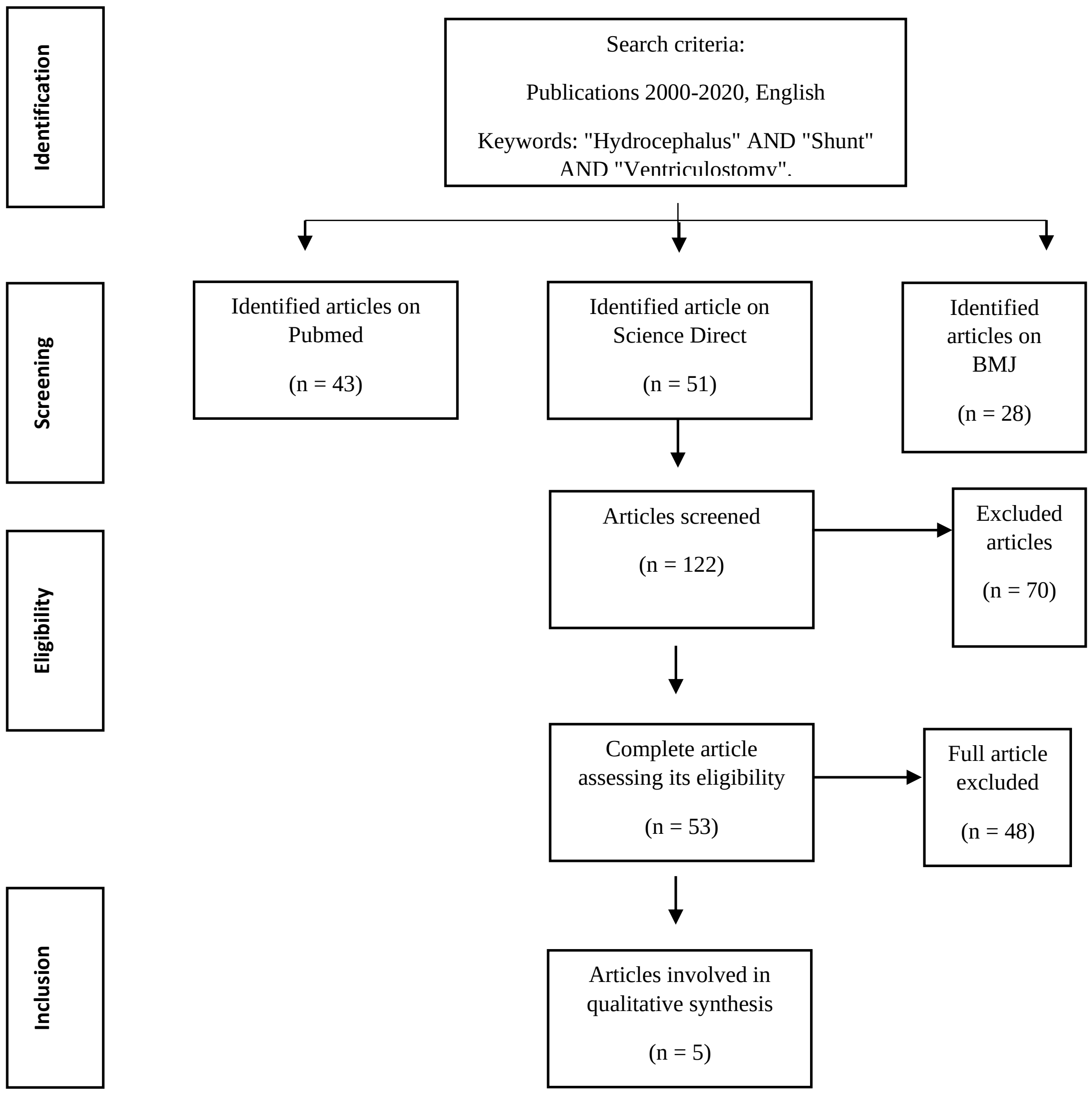

Figure 1. The PRISMA flowchart in identifying the literature included

Results

Of the 122 articles identified using optimized search parameters, 52 were withdrawn for full-text review. The Task Force member assigned to the current topic read and discussed all 52 articles that were recalled for full-text review as well as additional studies who were identified and subsequently disqualified. Since the primary aim of this study was to assess treatment outcomes after CSF or ETV shunt placement, the scope of the evidentiary review was limited to studies reporting quantitative results on both procedures (n = 14). In total, 6 articles were accepted for inclusion in the evidentiary table and 8 were excluded for various reasons as described above. If more than 1 paper addresses the same clinical material or the same subject, only the paper with the largest patient population and current data are included in the evidentiary table.

The tabulated evidence provides sufficient data to allow our evaluation of the CSF versus ETV shunt.

Two articles were excluded because they contained redundant material or were duplicate publications. If more than 1 paper addresses the same clinical material, only the paper with the largest patient population and current data are included in Table 1 as evidence to support the topic. Two other articles by the same research group were also excluded: one because of possible subject redundancy and insufficient data to address the main objective, and the other because it contained different outcome measures. Two articles were excluded because they evaluated the role of ETV or ETV and CSF shunts prior to posterior fossa surgery for tumor excision, a clinical scenario in which hydrocephalus may be expected to resolve in some cases. Finally, 1 article was excluded because the topic was the simultaneous implantation of ETV and CSF shunts, which prohibited the assessment of the outcome of either procedure alone.

Discussion

Cerebrospinal fluid shunts and ETV showed equivalent results in the clinical scenarios studied. All relevant articles, including those planned for inclusion and exclusion, were reviewed before finalizing the evidentiary table. Each article is presented and discussed in detail, and careful consideration is made to determine the data class of each article. Peralo, et al. (2018) reported a retrospective analysis of data obtained prospectively on 98 patients treated with VP shunt (76 patients) or ETV (22 patients). The main result is an operation failure, which is recorded when further operation is required. The failure rates for VP shunt and ETV surgery were 58% and 55%, respectively, with a mean follow-up of 4.7 years. The study group allocation was not controlled, and there was variability in the patient's age at surgery, the etiology of hydrocephalus, and other factors. [8]

Biluts, et al. (2016) reported the results of a retrospective review of 55 procedures (24 ETV and 31 VP shunt placement) performed on 48 patients in the context of a literature review. With a median follow-up of 39 months, the authors noted a trend toward lower failure rates in the ETV group (26% vs 42% in the VP shunt arm), although this was not significant. The authors acknowledged non-significant differences in patient age and sex as well as in the etiology of hydrocephalus between their groups. Shimizu et al. 17 (2012) presents a retrospective, 2-center review of cases in which ETV (9 patients) or VP shunt surgery (36 patients) was performed after removal of the infected shunt. No significant differences were observed between the 2 groups in reinfection rates or length of procedure. Of note, however, 7 out of 9 ETV ultimately failed in the case series of patients treated after shunt infection. [9]

Author, Years	Research description	Research type	Results
Peralo, et al. 2018	Retrospective analysis of a prospective case series of 98 patients treated with VP shunt or ETV. The main result: failure of the procedure for VP shunt or ETV. The timing of failure is also recorded.	Retrospective analysis of uncontrolled prospective case series	Failure rate: 55% ETV group, 58% shunt VP group. Hazard ratios were calculated for shunt failure, patient prematurity, & duration of procedure. Variability was present in patient age, etiology of hydrocephalus & other factors.
Biluts, et al. 2016	Retrospective review of 55 procedures in 48 consecutive patients (ETV: 24 patients; VP shunt surgery: 31 patients).	Retrospective review	The difference in failure rates was not significant (26% with ETV vs 42% with VP shunt operation). There were no differences between groups at 6 months, 1 year, 2 years, or 5 years after surgery.
Gmnelner, et al. 2020	Cohort analysis of ETV vs VP shunts with comparison of cost effectiveness & procedure failure rates with 28 patients in each group	Retrospective cohort study matched to a single institution. Study interval is extended (10 years) & contains variation of application.	The ETV success rate of 54% was not significantly different from VP shunt surgery. However, at 34 months postoperatively, the procedure survival curve preferred ETV. No differences between procedures were observed in cost or efficacy.
Rei, et al., 2017	International multicentre study comparing	A multicenter comparison study with 2 aims: 1)	The unadjusted model shows a lower failure rate for

	retrospective data for ETV & data obtained prospectively for shunts (from the Shunt Design Trial & Endoscopic Shunt Insertion Trial). Main outcome: treatment failure (requirement for subsequent hydrocephalus surgery or hydrocephalus-related death).	retrospective for ETV; 2) data obtained prospectively from 2 previous trials were reanalyzed in this study.	ETV than for shunting. After adjusting for age & etiology of hydrocephalus, ETV had a higher early failure rate than shunting. However, the ETV failure rate was lower than that of shunting at the points after 3 months postoperatively.
Shimizu et al., 2012	Retrospective center 2 study of ETV (n = 9) & VP shunt (n = 36) after removal of infected VP shunt. Compare reinfection rates after each procedure & procedure survival	Retrospective review, simple sample size.	Reinfection rates were not significantly different between the VP shunt (27.8%) & ETV (11.1%) groups. Procedure survival did not differ significantly between VP shunt (658 days) & ETV (929 days).

Table 1. Comparison of hydrocephalus treatment in children with VPS and ETV

Gmeiner, et al. (2020) report a retrospective, single-institution, matched cohort study in which ETV was compared with VP shunt surgery. With 28 patients in each group, no significant differences were noted between the 2 procedures in treatment success rates or in cost-effectiveness parameters such as length of stay, time of operation, or cost per patient. The authors acknowledge several limitations to the study, including simple sample size, long treatment intervals with deviation from practice over time, and the possibility of late ETV failure (there was 1 hydrocephalus-related death in this group). [10]

The largest study included in the evidentiary table was conducted by Rei, et al. (2017). This large multicenter comparison study had 2 arms: a retrospective arm for ETV (n = 489), and an arm where prospectively obtained data for VP shunt was obtained from 2 previous clinical trials and reanalyzed for this study (n = 720). As mentioned earlier, several related studies by the same study group were excluded, because there might be some overlap in the patients included in this study. Rei, et al. describes an analysis of ETV versus VP shunt operation on a large scale. The unadjusted baseline model showed lower failure rates for ETV compared to shunt surgery, but when adjusted for patient age and hydrocephalus etiology, the comparison became more complicated: early failure was higher for ETV than shunt placement, but at points after 3 month, the ETV failure rate is lower than that of shunt operation. Based on these findings, the authors concluded that there may be a survival advantage to long-term treatment for ETV. [11]

Finally, there are a number of limitations to this systematic review. In narrowing the scope of this project to focus specifically on evaluating hydrocephalus management methods - VP shunt or ETV - several key factors known to influence ETV success, namely patient age, hydrocephalus etiology, and previous history of hydrocephalus surgery, were not assessed. [12] The heterogeneity in the subject data we analyze here inherently limits the ability of these recommendations to inform surgical decision making in specific cases. Furthermore, emerging information regarding the role of cauterization of the choroid plexus (CPC) in relation to ETV and alternative indications for ETV with or without CPC (eg, prematurity post-hemorrhagic hydrocephalus) should be evaluated in future iterations of guidelines for the management of hydrocephalus as more information becomes available. Finally, and most significantly, there is an urgent need for large-scale randomized controlled trials to definitively answer the question of optimal surgical technique (VP shunt, ETV, or ETV-CPC) in the etiology of hydrocephalus any case. [13]

Conclusion

CSF shunt and endoscopic third ventriculostomy (ETV) are options in the management of hydrocephalus in children. Cerebrospinal fluid shunts and ETV showed equivalent results in the clinical scenarios studied. However, the results of studies in infants with hydrocephalus suggest that initial treatment with ETV makes more sense than shunt implantation. The results also show that ETV and shunt implantation are the right choices for treating hydrocephalus in children. However, ETV was better during the efficacy time. Computer simulations of hydrocephalus before and after shunt implantation and ETV treatment showed that the maximum CSF pressure was the most relevant and appropriate hydrodynamic index in the analysis of this patient.

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