Outcomes of Endoscopic Third Ventriculostomy in Cases of Congenital Hydrocephalus Based on MRI CSF Flowmetry and Transcranial Doppler in Infants

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ABSTRACT

Background: Endoscopic Third Ventriculostomy (ETV) is considered an alternative to ventriculo-peritoneal (VP) shunt insertion to avoid the shunt complications. To improve the outcome of the infants with congenital hydrocephalus (HCP) through using adjuvant tools with endoscopic third ventriculostomy, which are transcranial Doppler and CSF flowmetry to assess the flow through the ventriculostomy.

Objectives: Primary objective was to assess the clinical and radiological outcomes of endoscopic third ventriculostomy in cases of hydrocephalus below two years. Secondary objective was to assess the early and late complications associated with ETV during follow up study.

Subjects and methods: This uncontrolled clinical trial included children with congenital HCP attended the Outpatient Neurosurgery Clinics, Suez Canal University Hospitals. Twenty patients, divided into 2 groups: Group I included congenital aqueductal stenosis patients and group II that included patients with Chiari II malformations, using Transcranial Duplex, CT brain and MRI CSF Flowmetry.

Results: Patients of hydrocephalus with aqueductal stenosis, after ETV, had statistically higher stroke volume than those suffered from Chiari II pathology (p=0.008) and elicited a statistically reduction in peak systolic velocity (p=0.001), pulsatility index (p=0.001) and mean maximum velocity (p=0.005). Patients with congenital hydrocephalus of Chiari II pathology had higher rate of complications than that of aqueductal stenosis (p=0.015). Success rate was higher among cases with aqueductal stenosis than in Chiari II pathology (p=0.007).

Conclusion: ETV is a safe and effective technique for managing infants with congenital hydrocephalus due to aqueductal stenosis. MRI CSF flowmetry is a reliable method for evaluating the patency of a third ventriculostomy. **Keywords:** Aqueductal stenosis, Chiari II malformations, Macrocephaly.

INTRODUCTION

Congenital hydrocephalus is a condition in which there is dilatation of the ventricular system due to Cerebrospinal Fluid (CSF) accumulation associated with increased head size at birth ⁽¹⁾.

Common causes of congenital hydrocephalus include aqueductal stenosis, which obstructs the passage of CSF between third and fourth ventricles, neural tube defects commonly known as spina bifida, which results in CSF leakage followed by downward herniation of the cerebellum and fourth ventricles causing obstruction and Dandy Walker malformations that are associated by posterior fossa cysts and arachnoid cysts ⁽²⁾.

The most common symptoms are the increased head size and the bulging fontanelles due to increased intracranial pressure. Decreased motor and mental milestones like delayed crawling, teething and increased somnolence are other symptoms. Seizures may be a sign of congenital hydrocephalus. If caused by spina bifida, back sac will be visualized early postnatal in spine region either intact or ruptured sac ⁽³⁾.

Diagnosis is mainly made by regular computed tomography imaging of the brain. Magnetic resonance of the brain with cinematic flowmetry of the CSF gives idea about the pressure and flow at obstruction level ⁽⁴⁾.

Cranial ultrasound imaging also is considered as a great tool in diagnosis of the hydrocephalus with identifying the cause of obstruction. Also, it is used to measure the pressure inside major cerebral veins to reflect the state of hydrocephalus and intra cranial pressure ⁽⁵⁾.

Ventricular-peritoneal (VP) shunting of CSF is considered the common and traditional method of managing the increased intracranial pressure. VP shunts have potential risks and complications especially in the first year of life such as infection and shunt obstruction that results in shunt failure requiring another surgery for revision or new shunt insertion ⁽⁶⁾.

Endoscopic Third Ventriculostomy (ETV) is considered an alternative to VP shunt insertion as a small opening is made in the floor of third ventricle allowing CSF to pass through a different route to interpeduncular cistern thus bypassing the obstructed area ⁽⁷⁾. After ETV, transcranial Doppler and MRI CSF flowmetry MRI are used as an assessment tool of success of the procedure.

SUBJECTS AND METHODS

This Prospective interventional study was conducted in the period between August 2016 to March 2019, at the Neurosurgery Department, Suez Canal University Hospital, Ismailia, Egypt. This study included children with congenital HCP attending the Outpatient Neurosurgery Clinics of Suez Canal University Hospitals.

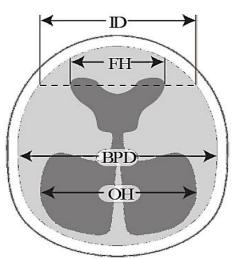
Inclusion criteria: Age below 2 years. Patients with congenital aqueductal stenosis suggested by imaging. Chiari Malformations type Π . Patients with previous CSF diversion procedures.

Exclusion criteria: Communicating hydrocephalus suggested by imaging. History of CNS infection. Coagulopathies (Defective bleeding disorders). Very poor general condition. Multiple congenital anomalies that are life threatening.

All patients with a diagnosis of noncommunicating hydrocephalus during this period were included in the study. The number of patients included in this study was 20 patients. They were classified according to the cause of hydrocephalus into two groups: hydrocephalus due to congenital aqueductal stenosis and hydrocephalus with myelomeningocele. The patients were examined generally and neurologically. The patients were investigated radiologically by transcranial duplex (TCD), CT and/or MRI for diagnosis of hydrocephalus and the cause of obstruction. The patients were admitted to the hospital one or two days before operation for laboratory investigation and examination for fitness for surgery. The patients were operated on the regular operative schedule. For the patients with hydrocephalus and myelomeningocele, the patients were managed firstly with myelomeningocele repair followed by ETV.

Investigations required pre-operatively including:

- 1. CT and/ or MRI Brain that displayed:
 - a. Enlargement of temporal horns.
 - b. Trans-ependymal flow.
 - c. Dilated third ventricle ≥ 1 cm.
 - d. Normal or collapsed fourth ventricle.
 - e. Thinned or absent corpus callosum.
 - f. Evan's index (figure 1): Ratio between maximum width of frontal horns compared to maximum internal width of cranial vault > 0.3 is diagnostic for hydrocephalus.





FH: Frontal horns, **ID:** Internal diameter from inner table to inner table , **BPD:** Biparietal diameter, **OH:** Occipital horns ⁽³⁾.

2. Trans-Cranial Duplex:

Spectral analysis to obtain blood flow velocity of major cerebral vessels as well as characteristics of the flow. Peak systolic velocity (Vs), end diastolic velocity (Vd), systolic upstroke/acceleration time, pulsatility index (PI) and mean maximum velocity (V_{mean}).

Operative technique:

After general anesthesia, the patient was positioned supine with the head in neutral position at a head rest and flexed 15° , no Mayfield is used to fix the head.

The scalp at the site of surgery was shaved. Then the site of the burr hole was determined according the standard measures; 2.5 cm from the midline and 1 cm anterior to the coronal suture. In newborns and infants of widened sutures, the burr hole was positioned at the same 2.5 cm from the midline and at the frontal bone just in front of the widened coronal suture. Then the skin was draped and infiltrated with adrenaline of 1/200.000 concentration. Then small C-shaped flap was done.

Rt. Frontal burr hole was done with careful hemostasis of any bone bleeding. The dura was opened, and orientation of the camera and focus is done. The ventricle is then punctured either with the sheath with its stylet. Then orientation of the anatomy and the anatomic landmarks as the foramen of Monro, the choroid plexus, the septum pellucidum, the thalamosteriate and septal veins was done. After that, proceeding into the third ventricle and also orientation of the anatomic structures the mammillary bodies, the infundibular as pigmentation, the site of perforation in between, and the position of the basilar artery was attained. The site of perforation was mostly in the midline, in front of the basilar artery and behind the infundibulum.

The fenestration was done either by the closed scissors and dilatation if needed by Fogarty balloon catheter of 3 or 5 French. Only one time the bipolar is used to coagulate the floor because it was thick, and bleeding happened with trial to open it. The fenestration size was usually sufficient to pass with the endoscope to the interpeduncular cistern and to see the basilar artery and if there were another membrane. This size of fenestration at any condition is bigger than the transverse diameter of the sheath 4.7 mm. In some cases, the membrane was completed with the forceps to prevent supposed overlap and closure of the ostium.

After fenestration the irrigation was stopped and movements of the edges of the fenestration were moving which was considered a sign of success of the technique. Then the endoscope was withdrawn from the third ventricle, the fornix was observed for any trauma, and the track of the endoscope through the cerebral mantle was observed also to see if there is any bleeding or not. The opening was packed with a small piece of gel foam and the wound is closed in two layers; the subcutaneous and the skin.

Intra-operative irrigation was done using warm lactated ringer solution to clear the view and to stop

bleeding if happened. Intra-operative monitoring of the heart rate through the anesthiologist was done for reporting about any change of the heart rate. The patients were kept under observation at the recovery room for any changes in the conscious level and for any neurological deficits. CT was done immediately post-operatively in case of neurological deficits. Patients then were observed for neurological condition, the state of the wound, CSF leak, and fever. Patients with persistent CSF leak with the same clinical condition and CT post-operatively was the same, are considered failure cases and prepared for ventriculoperitoneal (VP) shunts.

Post operatively clinical and radiological evaluation:

Within first week post-operative:

- Follow up of the possible complications: (CSF leakage, convulsions, vomiting ... etc.).
 Head circumference.
 Trans-cranial Duplex.
 CT brain.
 MRI CSF flowmetry.
- ➤ 3 months:
- CT brain. Head circumference.
- ➢ 6 months:
- CT brain. Head circumference.
- > 9 months:
- Head circumference.

MRI CSF flowmetry was repeated if the head is markedly enlarged.

Ethical Considerations: The participants provided written informed permissions to participate in the trial. Permission to conduct the study was received from the Department of Neurosurgery, Suez Canal University, Ismailia, Egypt. For the purpose of conducting research involving human subjects, this study has been carried out in conformity with the Declaration of Helsinki, which is the Code of Ethics of the World Medical Association

RESULTS

Our study included 20 patients who were attending to Neurosurgery Outpatient Clinic at SCU hospitals with congenital aqueductal stenosis or Chiari malformations. Patients underwent endoscopic third ventriculostomy where the CSF flow was assessed postoperative. Table (1) summarized the baseline characteristics of the studied sample. The mean age of the participants was 7.3 ± 3.26 months. The most frequent complaint among the patients was enlarged head (45%) and bulging fontanelles (30%). About 30% of the patients had other congenital anomalies.

Variables	n=20
Age (months), mean ± SD	7.3 ± 3.26
Gender, n (%)	
Male	12 (60)
Female	8 (40)
Complaint	
Enlarged head	15 (75)
Disturbed Consciousness	3 (15)
Convulsions	2 (10)
Other congenital anomalies	
Absent	14 (70)
Present	6 (30)
Data are presented as mean \pm SD or	
frequency (percentage)	

Table (2) showed pre-operative clinical assessment of the studied sample, which showed that the mean head circumference of the patients was 44.5 ± 5.16 cm. Only two patients had flattened occiput and three patients had affected 6th cranial nerve. No other sensory or motor affection was found. Trans-Cranial duplex showed that the mean peak systolic velocity was 34.29 ± 15.83 and end diastolic velocity was 5.91 ± 4.82 . The mean resistance index, pulsatility index and maximum velocity were 0.63 ± 0.29 , 1.63 ± 0.67 and 17.01 ± 8.45 . On the other hand, all patients showed enlargement of temporal horns, dilated third ventricle ≥ 1 cm, collapsed 4th ventricle and Evan's index < 0.3 by CT/ MRI brain.

Table (2): Pre-operative investigations of the infants

 have congenital hydrocephalus

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Variables N =20			
Trans-Cranial Duplex, mean ± SD			
Peak systolic velocity (Vs)	34.29 ± 15.83		
Resistance index (RI)	0.63 ± 0.29		
End diastolic velocity (Vd)	5.91 ± 4.82		
Pulsatility Index (PI)	1.63 ± 0.67		
Mean maximum velocity (Vmean)	17.01 ± 8.45		
CT and/ or MRI Brain, n (%)			
Enlargement of temporal horns	20 (100)		
Dilated third ventricle ≥ 1 cm.	20 (100)		
Collapsed fourth ventricle	20 (100)		
Thinned or absent corpus callosum	3 (15)		
Evan's index <0.3	20 (100)		
$\mathbf{D}_{\mathbf{r}}$			

Data are presented as mean \pm SD or frequency (%)

Table (1): Baseline characteristics of the - infants have hydrocephalus

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Table (3) showed a comparison between both pathological types of congenital hydrocephalus, aqueductal stenosis and Chiari II, in the Post-operative investigation parameters. It was found that patients with aqueductal stenosis had statistically significant higher stroke volume (29.67 \pm 13.57) than those who suffered from Chiari II pathology (13.80 \pm 6.41) (p=0.008).

Variables	Total	Congenital hyd	rocephalus	p-value
	(n=20)	aqueductal stenosis	chiari II	_ •
		(n=13)	(n=7)	
Head circumference (cm), mean ± SD				
1 st week	44.50 ± 5.16	44.77 ± 5.99	44 ± 3.46	0.87 a
3 months	45.65 ± 4.76	46.08 ± 5.38	44.86 ± 3.58	0.59 a
6 months	46.7 ± 4.38	47 ± 4.95	46.14 ± 3.34	0.64 a
9 months	47.15 ± 4.18	47.54 ± 4.7	46.43 ± 3.21	0.54 a
Trans-Cranial Duplex, mean ± SD				
Peak systolic velocity (Vs)	19.74 ± 7.53	17.74 ± 6.56	23.45 ± 8.31	0.14 ^a
Resistance index (RI)	0.42 ± 0.17	0.45 ± 0.19	0.38 ± 0.1	0.21 ^a
End diastolic velocity (Vd)	6.06 ± 4.77	5.93 ± 4.74	6.31 ± 5.21	0.88 ^a
Pulsatility Index (PI)	0.94 ± 0.56	0.95 ± 0.65	0.94 ± 0.35	0.53 ^a
Mean maximum velocity (Vmean)	10.57 ± 4.93	10.03 ± 5.59	11.57 ± 3.55	0.54 ^a
CT Brain, n (%)				
Widened subarachnoid spaces				
Absent	2 (10)	1 (7.7)	1 914.3)	0.98 ^b
Present	18 (90)	12 (92.3)	6 (85.7)	_
Reduction of lateral ventricular dilatation				
Absent	9 (45)	8 (61.5)	1 (14.3)	0.7 ^b
Present	11 (55)	5 (38.5)	6 (85.7)	_
MRI CSF flowmetry				
CSF flow direction, n (%)				
Bi-directional	11 (55)	9 (69.2)	2 (28.6)	0.21 ^b
Uni-directional	8 (40)	4 (30.8)	4 (57.1)	
No flow detected	1 (5)	0	1 (14.3)	
Peak systolic velocity (ml /s), mean ± SD	7.60 ± 4.37	8.52 ± 4.25	5.89 ± 4.37	0.21 ^a
Stroke volume, mean ± SD	24.12 ± 13.77	29.67 ± 13.57	13.80 ± 6.41	0.008 ^a

Table (4) showed that regarding aqueductal stenosis, it was found that the intervention with endoscopic third ventriculostomy had elicited a statistically significant reduction in peak systolic velocity (p=0.001), pulsatility index (p=0.001) and mean maximum velocity (p=0.005). Similarly, the intervention with endoscopic third ventriculostomy had elicited a statistically significant reduction in peak systolic velocity (p=0.028), pulsatility index (p=0.018) and mean maximum velocity (p=0.020) in cases with Chiari II pathology.

Table (4): Comparison of trans-cranial duplex parameters before and after the intervention amon	g
each pathological type of congenital hydrocephalus	

Variables	Trans-Cranial Duplex Pre-operative Post-operative		n voluo
_			p-value
Aqueductal stenosis			
Peak systolic velocity (Vs)	29.27 ± 12.47	17.74 ± 6.56	0.001 ^a
Resistance index (RI)	0.64 ± 0.26	0.45 ± 0.19	0.1 ^a
End diastolic velocity (Vd)	5.58 ± 4.75	5.93 ± 4.74	0.51 ^a
Pulsatility Index (PI)	1.65 ± 0.77	0.95 ± 0.65	0.001 ^a
Mean maximum velocity (Vmean)	13.98 ± 6.95	10.03 ± 5.59	0.005 ^a
Chiari II			
Peak systolic velocity (Vs)	43.63 ± 18.07	23.45 ± 8.31	0.028 ^a
Resistance index (RI)	0.62 ± 0.36	0.38 ± 0.1	0.063 ^a
End diastolic velocity (Vd)	6.53 ± 5.28	6.31 ± 5.21	0.39 ^a
Pulsatility Index (PI)	1.61 ± 0.48	0.94 ± 0.35	0.018 ^a
Mean maximum velocity (Vmean)	22.61 ± 8.54	11.57 ± 3.55	0.020 ^a
p-values are based on Wilcoxon Signed I	Ranks test. Statistical	significance at p < 0	0.05

Table (5) showed the complications encountered after the intervention in cases with congenital hydrocephalus both pathologies. 8 patients had CSF leak, three cases had post-operative infections and only one case suffered convulsions. Moreover, patients with congenital hydrocephalus of Chiari II pathology had significantly higher rate of complications than that of aqueductal stenosis (p=0.015). Success rate of the intervention was significantly higher among cases with aqueductal stenosis than in Chiari II pathology (p=0.007).

 Table (5): Association between adverse outcomes and pathological types of congenital hydrocephalus

Variables		Congenital hy	drocephalus	p-value
	Total (n=20)	Aqueductal stenosis (n=13)	Chiari II (n=7)	
Complications, n (%)				
Absent	8 (40)	8 (61.5)	0	0 015 a
Present	12 (60)	5 (38.5)	7 (100)	0.015 ^a
CSF leak	8 (40)	3 (23.1)	5 (71.4)	
Infection	3 (15)	2 (15.4)	1 (14.3)	
Fits	1 (5)	0	1 (14.3)	
Failure, n (%)			. ,	
Absent	14 (70)	12 (92.3)	2 (28.6)	0.007 ^a
Present	6 (30)	1 (7.7)	5 (71.5)	
VP shunt	5 (25)	0	5 (71.4)	
EVD	1 (5)	1 (7.7)	0	

DISCUSSION

Endoscopic third ventriculostomy is increasingly used in the treatment of hydrocephalus. It is considered the treatment of choice in obstructive hydrocephalus. It is also now advocated in some communicating hydrocephalus, such as normal pressure hydrocephalus by some authors ⁽¹⁾. There should be adequate space between the basilar artery and the clivus under the floor of the third ventricle to allow for a safe ventriculostomy ⁽²⁾.

In the study, the mean age of the participants was 7.3 ± 3.26 months. 60% of the sample came from rural areas. Similarly, a study done at Sohag University hospital reported that sociodemographic factors may play a role in congenital hydrocephalus ⁽³⁾. Sociodemographic factors affect the educational levels and financial ability of the parents. Parents in rural areas usually have less educational levels and poor financial abilities so they are less likely to notice the problem and less likely to seek medical advice ⁽⁴⁾.

We also found that the most frequent complaint was increased head size (45%) and bulging fontanels 30%. Because at this young age sutures of the head are not closed yet, which allow an increase in the size of the head and bulging of fontanels. These results are similar to the results found by **Tully** *et al.* ⁽⁵⁾, which stated that the most common presentation in their population was enlargement of the head. Another study in Sudan reported the relation between hydrocephalous and other congenital anomalies ⁽⁶⁾. This is consistent with our results, which found that about 30% of the participants had other congenital anomalies. As most congenital anomalies have similar origins such as exposure to radiation during pregnancy, low folic acid, and gene defects that may cause a cluster of defects ⁽⁷⁾.

Regarding the prenatal characteristics of the studied sample, we found that the mean maternal age of patients was 24.85 ± 4.79 years. About half of them had maternal insult (45%). Similarly, **Mahmoud** *et al.* ⁽⁶⁾ found that maternal insult during pregnancy was significantly associated with congenital hydrocephalus. While, maternal age is not significantly associated with congenital hydrocephalus.

To assess the outcomes of ETV in our study sample we assessed Trans-Cranial Duplex, CT brain, and MRI CSF flowmetry. Pre-operative Trans-Cranial Duplex showed that the mean peak systolic velocity was 34.29 ± 15.83 and end diastolic velocity was 5.91 ± 4.82 . The mean resistance index, pulsatility index, and maximum velocity were 0.63 ± 0.29 , 1.63 ± 0.67 and 17.01 ± 8.45 respectively. On the other hand, all patients showed enlargement of temporal horns, dilated third ventricle \geq 1 cm, collapsed 4th ventricle and Evan's index <0.3 by CT/MRI brain. **Kolarovski** *et al.* ⁽⁸⁾ reported that Trans-Cranial Duplex showed the improvement of cerebral circulation after the drainage procedure of pediatric hydrocephalus. After Endoscopic Third Ventriculostomy there were widened subarachnoid spaces in 90% of patients and the reduction of lateral ventricular dilatation was present in about 45% of patients. This indicates the importance of ETV in improving radiological outcomes in congenital hydrocephalous patients less than two years. Similarly, **Nowoslawska** *et al.* ⁽⁹⁾ have found that ETV is usually radiologically effective. They stated that The ETV was clinically and radiologically successful in 30 (71.4%) of 42 procedures during a mean follow up period of 45.0 ± 4.8 months (range 12–127 months).

We also found that the peak systolic velocity was decreased after the operation probably due to the decrease in the CSF pressure after the operation. **Bakker** *et al.*⁽¹⁰⁾ found that postoperative cerebral blood flow velocities and pulsatility index were lower compared to their preoperative values in the whole group.

Post-operative assessment of CSF flow showed bidirectional flow in 55% of patients (69% of congenital aqueductal stenosis patients and 28% of Chiari II syndrome patients), and uni-directional flow in 40% of patients (30% of congenital aqueductal stenosis patients and 57% of Chiari II syndrome patients) indicating that ETV resulted in better CSF flow after the surgery, which can be assessed by MRI CSF flowmetry. Similarly, **Abdelhameed** *et al.* ⁽¹¹⁾ reported that all patients showed no flow through the aqueduct of Sylvius on systole and diastole, with normal flow through the foramen magnum. Three of the patients underwent surgical ETV, with all of them showing positive flow through its site ⁽¹¹⁾.

It was found that patients with aqueductal stenosis had statistically significant higher stroke volume (29.67 \pm 13.57) than those who suffered from Chiari II pathology (13.80 \pm 6.41) (p=0.008), which may represent the importance of the Endoscopic Third Ventriculostomy procedure in cases of aqueductal stenosis. Similarly, **Hopf** *et al.* ⁽¹²⁾ reported that the best results of ETV treatment have been demonstrated for patients with primary aqueductal stenosis.

Also, it was found that the intervention with endoscopic third ventriculostomy had elicited a statistically significant reduction in peak systolic velocity, pulsatility index and mean maximum velocity. Similarly, the intervention with endoscopic third ventriculostomy had elicited a statistically significant reduction in peak systolic velocity, pulsatility index and mean maximum velocity in cases with Chiari II pathology.

The complications encountered after the intervention in our study was 40% of the patients had CSF leak, three cases had post-operative infections and only one case suffered convulsions. This is consistent with **Bouras and Sgouros** ⁽¹³⁾.

Limitations of Study:

Multi-centric larger studies across the country are needed in order to have a better understanding of the outcomes of ETV in Egypt.

CONCLUSION

Patients with aqueductal stenosis benefitted more from ETV and were less prone to complications than patients with Chiari II syndrome. Pre-operative MRI for the patients with hydrocephalus should be done for planning of the surgery, and for detection of abnormal anatomy. We believe that our findings confirmed that MRI CSF flowmetry is a reliable method for evaluating the patency of a third ventriculostomy.

Minor flow in the third ventricle should be considered an early sign of obstruction. It is possible that CSF flow studies may detect obstruction before symptom recurrence or clinical deterioration. ETV gave unfavorable outcome in infants of congenital hydrocephalus due to Chiari II Malformations.

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- Availability of data and material: Available
- **Competing interests:** None
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