Evaluating the Postoperative Results of Endoscopic Third Ventriculostomy in Triventricular Hydrocephalus by Correlation of Clinical Outcome and Magnetic Resonance Dynamic Cerebrospinal Fluid (CSF) Flowmetry

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Authors’ contributions
This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: Endoscopic third ventriculostomy is a surgical procedure that is operated for management of obstructive hydrocephalus and regained popularity with large number of promising results.

Aim: To evaluate the outcome of Endoscopic Third Ventriculostomy by correlation between clinical outcome and MRI cerebrospinal fluid flowmetry postoperatively.

Patients and Methods: This study was conducted in Department of Neurosurgery at Tanta University from January 2018 to January 2020. It included 25 patients with triventricular hydrocephalus with different etiologies. All patients were subjected to history taking, complete
physical, neurological examination, routine preoperative laboratory investigations, radiological investigations e.g. non contrast CT and MRI of the brain. Patients underwent surgery according to the exact cause of hydrocephalus, which was known and identified by neuroimaging and endoscopic third ventriculostomy. Outcome assessment was done by neurological evaluation for resolution of their clinical symptoms and a shunt free stable clinical status. Patients were evaluated once weekly for the first month then monthly for the first 3 months and the patients were finally evaluated at the end of the 6th month postoperatively.

**Results:** Of 25 patients, 9 patients (36%) with Aqueduct stenosis, 1 patient (4%) with Brain stem glioma, 1 patient (4%) with Brain stem tumor, 5 patients (20%) with PF tumor, 6 patients (24%) with Pineal tumor, 1 patient (4%) with Thalamic glioma, 1 patient (4%) with Tectal glioma and 1 only one patient (4%) with Chiari 1 malformation. 92% had Patent ETV stoma with adequate flow: OFA value >75 μL, 8% had Patent ETV stoma with low flow: OFA value from 25 up to <75 μL. The mean Headache VAS Preoperative was 6.08 (±1.04 SD). the baseline mean Evan's Ventricular ratio was 0.34 ± 0.02 and 60% of cases had papilledema. Blurring of vision was present in 60% of cases, headache in 100% of cases, and vomiting was present in 60% of cases.

**Conclusions:** Dynamic MRI of CSF flow provides reliable and immediate information on the efficacy of ETV, in addition to the flow-void presence at the level of the 3rd ventricle floor fenestration in both midsagittal and perpendicular plane, even in the absence of phase-contrast techniques which is significantly correlated with clinical signs and symptoms improvement in the patients.

**Keywords:** Endoscopic third ventriculostomy; hydrocephalus; MRI cerebrospinal fluid flowmetry.

1. INTRODUCTION

Hydrocephalus, the pathological CSF accumulation in the brain affecting children and adults [1]. This typically causes increased pressure inside the skull [2].

There is no effective treatment for hydrocephalus. Since the 1950s, extracranial CSF shunting to another body cavity, most frequently the peritoneum, heart atrium, or pleura, has been the standard therapy for hydrocephalus [3].

It was accompanied by high complications and high mortality rates because of technical problems as insufficient illumination, poor lenses and scopes weren’t provided with cameras, so this procedure was replaced by shunting [2].

Endoscopic third ventriculostomy is a surgical procedure that is operated for management of obstructive hydrocephalus; it was first done in 1922 by Dandy [1].

It was preferred for management of non-communicating hydrocephalus as more normal physiological solution for avoiding complications of shunting as infection and over drainage of cerebrospinal fluid [3].

"In addition to clinical outcome, many radiological imaging parameters have been evaluated for assessment of the permeability and patency of the 3rd ventriculostomy stoma, beginning with monitoring of reduction of ventricular size, using of isotope or contrast ventriculography, detection of flow voids on conventional MRI imaging studies, and concluding with examination with cine phase-contrast MRI techniques imaging, which is considered the most reliable and accurate method used for post operative follow-up of the patient and providing valuable information on hydrodynamics of CSF" [4].

"MRI cerebrospinal fluid approach can qualitatively display pulsatile CSF motion and allows the quantitative evaluation of the amplitude CSF flow, As CSF flow is pulsatile, synchronous with the cardiac cycle, Therefore, cardiac gating is necessary for the synchronization of CSF flow with the cardiac cycle to improve resolution" [5].

2. PATIENTS AND METHODS

This study included 25 patients with triventricular hydrocephalus with different etiologies has been performed at the period from January 2018 to January 2020. Patients have been operated in neurosurgical department of Tanta University Hospital. Patients underwent surgery according to the exact cause of hydrocephalus, which was known and identified by neuroimaging.

All patients were subjected to history taking, complete physical, neurological examination,
routine preoperative laboratory investigations, CSF sample of 2-3 ml was obtained either through lumbar puncture, tapping shunt reservoir or tapping through anterior fontanel. Cytological and bacteriological analysis was done for the sample obtained if CSF infection was suspected. Radiological investigations e.g. non contrast CT and MRI of the brain were obtained for every case and postcontrast films were only done in patients with suspected intracranial space occupying lesions.

Patients underwent surgery according to the exact cause of hydrocephalus, which was known and identified by neuroimaging and endoscopic third ventriculostomy. All procedures were performed using only rigid endoscopes. The third ventricle was entered and the following structures were identified: paired mammillary bodies, dorsum sellae, infundibular recess and pulsating basilar artery. Generally, the stoma was placed in the tuber cinereum midway between infundibular recess and mammillary bodies just behind the dorsum sellae and avoiding the basilar artery. Blunt perforation was always the rule (even with tough floor) using monopolar forceps or Fogarty catheter. Following perforation, the stoma was dilated using size 3 French Fogarty catheter to achieve a fenestration size of at least 5 mm. The interpeduncular and prepontine cisterns were then inspected for any second membrane which if present was also perforated and dilated applying the same principles. On completion of the procedure the operating sheath is withdrawn with the endoscope inside to look for any active bleeding. A gel foam sponge is used to pack the burr hole.

2.1 Outcome Assessment

Outcome assessment was done by neurological evaluation for resolution of their clinical symptoms. Evaluation of the general state and a shunt free stable clinical status. Patients were evaluated once weekly for the first month then monthly for the first 3 months and the patients were finally evaluated at the end of the 6th month postoperatively for recurrence of their symptoms. And presence of any complication.

2.2 Postoperative Imaging

Postoperative imaging in the form of CT brain was obtained in every patient at the end of the first week or if the patient showed any clinical deterioration. MRI CSF flowmetry of the brain was obtained at the end of the first month postoperatively in every patient and at the end of third month postoperatively for patient in whom their previous neuroimages didn't reveal significant change in spite of their clinical improvement. CT brain was also done immediately in any patient presented with recurrence of their symptoms during the follow up period.

2.3 Statistical Analysis

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp) Qualitative data were described using number and percent. The Kolmogorov-Smirnov test was used to verify the normality of distribution. Quantitative data were described using range (minimum and maximum), mean, standard deviation, median and interquartile range (IQR). The significance of the obtained results was judged at the 0.05% level.

3. RESULTS

Of 25 patients, fifteen patients were males (60%), and ten patients were females (40%) their ages ranged from 5 years to 55 years with a mean age of 19.4 years. Sixteen patients (64/100; 64%) were under the age of twenty years, 9 patients were above the age of twenty up to 55 years, Table 1.

Table 1. Demographic distribution of cases

<table>
<thead>
<tr>
<th>Gender</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>15</td>
<td>60.0</td>
</tr>
<tr>
<td>Female</td>
<td>10</td>
<td>40.0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;20</td>
<td>16</td>
<td>64.0</td>
</tr>
<tr>
<td>≥20</td>
<td>9</td>
<td>36.0</td>
</tr>
<tr>
<td>Min. – Max.</td>
<td>5.0 – 55.0</td>
<td></td>
</tr>
<tr>
<td>Mean ± SD.</td>
<td>19.48 ± 13.72</td>
<td></td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>14.0 (9.0 – 27.0)</td>
<td></td>
</tr>
</tbody>
</table>

As regard Preoperative manifestations there were 16 patients (64%) with disturbed gait (ataxia), 5 patients (20%) with cranial nerve dysfunction (Abducent nerve palsy), 15 patients (60%) with papilledema, 15 patients (60%) with nausea and vomiting, only one patient (4%) with disturbed consciousness, while two patients (8%) with Memory disturbance and 2 patients (8%) with Neck pain, Fig. 1.
The mean VAS of preoperative HA was 6.08 (±1.04 SD) with range (4-8) while the mean VAS of postoperative HA was 2.04 (±1.46 SD) with range (0-6). That concludes that headache improved postoperatively. There was high statistically significant difference between preoperative and postoperative as regard Headache Visual Analogue Scale, Fig. 2.

The mean Papilledema grade Preoperative was 1.44 (±1.42 SD) with range (0-4) and the mean Papilledema grade Postoperative was 0.24 (±0.66 SD) with range (0-3). There was high statistically significant difference between preoperative and postoperative as regard papilledema grade.

The overall flow of CSF through the ventriculostoma was markedly improved up to more than 75 μL. That was reported from MRI CSF Flowmetry that was done one month postoperative.

The mean Diameter 3rd ventricle in mm Preoperative was 9.92 (±1.14 SD) with range (7.9-12.4) and the mean Diameter 3rd ventricle in mm Postoperative was 5.72 (±1.82 SD) with range (3-17). There was a high statistically significant difference between preoperative and postoperative Diameter 3rd ventricle in mm, Fig. 3.

There was high statistically significant difference between preoperative and postoperative as regard Evan's index. This table shows that the mean Evan's index Preoperative was 0.39 (±0.02 SD) with range (0.37-0.43) and the mean Evan's index Postoperative was 0.34 (±0.02 SD) with range (0.29-0.38), Table 2.
Table 2. Comparison between preoperative and postoperative according to Evan’s index

<table>
<thead>
<tr>
<th>Evan’s index</th>
<th>Preoperative</th>
<th>Postoperative</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Min. – Max.</td>
<td>0.37 – 0.43</td>
<td>0.29 – 0.38</td>
<td>12.254</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean ± SD.</td>
<td>0.39 ± 0.02</td>
<td>0.34 ± 0.02</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>0.39 (0.38–0.40)</td>
<td>0.33 (0.33–0.35)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Fig. 3. Pre and post operative scenario for 3rd ventricle

Of 25 patients, there were 8 (32%) with Intraoperative abnormal finding and the findings were one case (12.5%) with absent septum pellucidum, three cases (37.5%) with Tough Liliequest membrane, one case (12.5%) with Ependymal wall pigmentation, three cases (37.5%) with non tough Liliequest membrane, Fig. 4.

Of 25 patients, there were 23 (92%) postoperative clinical improved and 2 (8%) didn’t improve.

Fig. 4. Intraoperative abnormal finding

That there were 4 (16%) without postoperative imaging changes while there were 21 (84%) with postoperative imaging changes among those cases there were 19 (90.5%) with Opening SA spaces, 8 (38.1%) with anatomical defect floor, 11 (52.4%) with Resolved permeation, 15 (71.4%) with reduced 3rd Ventricle size and 12 (57.1%) with Reduced 4th Ventricle size, Table 3.

Of 25 patients, there were 16 (64%) without complications while there were 9 (36%) with complications among those cases there were 3
(33.3%) with Fever, 1 (11.1%) with Fever and wound infection, 1 (11.1%) with Diabetes insipidus (medical ttt), 1 (11.1%) with Transient postop urinary incontinence, 1 (11.1%) was Dizziness improved, 1 (11.1%) with Increased ataxia, spontaneous and 1 (11.1%) with CSF leakage, wound revision, Table 4.

Table 3. Distribution of the studied cases according to postoperative imaging changes

<table>
<thead>
<tr>
<th>Postoperative imaging changes</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>No change</td>
<td>4</td>
<td>16.0</td>
</tr>
<tr>
<td>Yes</td>
<td>21</td>
<td>84.0</td>
</tr>
<tr>
<td>Opening SA spaces</td>
<td>19</td>
<td>90.5</td>
</tr>
<tr>
<td>Anatomical defect in the floor of the third ventricle</td>
<td>8</td>
<td>38.1</td>
</tr>
<tr>
<td>Resolved trans-ependymal permeation</td>
<td>11</td>
<td>52.4</td>
</tr>
</tbody>
</table>

Table 4. Distribution of the studied cases according to complications and management

<table>
<thead>
<tr>
<th>Complications and management</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>16</td>
<td>64.0</td>
</tr>
<tr>
<td>Fever</td>
<td>3</td>
<td>11.1</td>
</tr>
<tr>
<td>Fever, wound infection</td>
<td>1</td>
<td>11.1</td>
</tr>
<tr>
<td>Diabetes insipidus (medical ttt)</td>
<td>1</td>
<td>11.1</td>
</tr>
<tr>
<td>Transient postop urinary incontinence</td>
<td>1</td>
<td>11.1</td>
</tr>
<tr>
<td>Dizziness</td>
<td>1</td>
<td>11.1</td>
</tr>
<tr>
<td>Increased ataxia, spontaneous</td>
<td>1</td>
<td>11.1</td>
</tr>
<tr>
<td>CSF leakage, wound revision</td>
<td>1</td>
<td>11.1</td>
</tr>
</tbody>
</table>

4. DISCUSSION

“Endoscopic third ventriculostomy (ETV) has been considered as the treatment of choice for the patients with non-communicating hydrocephalus. As alternative to ventriculo-peritoneal shunting, ETV provides an anatomical internal pathway for drainage of CSF from the third ventricle to the interpeduncular and pre-pontine subarachnoid cisterns. It can, therefore, bypass any obstruction at the level of the cerebral aqueduct or the fourth ventricular outlet foramina” [6].

“Cine phase contrast magnetic resonance imaging (PC MRI) is a non-invasive technique that uses a bipolar gradient pulse to impart net phase change as CSF moves along the gradient, thus sensitizing MR images to velocity changes in a specific direction while canceling signals from stationary protons and motion in other directions. It is also sensitive to areas of slow flow, allows flow direction to be appreciated, and permits quantification” [7].

“This technique can display pulsatile CSF motion qualitatively and allows the quantitative assessment of the CSF flow amplitude. Since CSF flow is pulsatile, synchronous with the cardiac cycle, so cardiac gating is essential for synchronization of the CSF flow with cardiac cycle to improve resolution” [8].

The main objective of this study was to evaluate the outcome of endoscopic third ventriculostomy by the correlation between clinical outcome and an MRI cerebrospinal fluid flowmetry postoperatively.

A prospective study was carried out including 25 patients with aqueduct stenosis either congenital or acquired as in cases of third ventricles tumor or tectal gliomas and patients with posterior fossa tumors and cyst with hydrocephalus. The mean age of the current studied cases was 19.48 years with range of (5-55) years, 40% were females and 60% were males. An age of 6 months was used as a cut-off below which no ETV procedures were performed.

Kulkarni et al. [9] analyzed 618 ETVs performed consecutively on children at 12 international institutions to identify predictors of ETV success in children. The authors proposed ETV Success Score that closely approximates the predicted probability of ETV success”. The found three main items could predict success; age, etiology and previous shunt. The least success rate expectation is seen in post hemorrhagic/infectious hydrocephalus and age 1- 6 months with no previous shunt history. Better success rate is noted in age more than 10 years with primary or tumor induced aqueductal stenosis.

The present study shows that headache was the most frequently reported in all cases, blurring of vision was present in 60% of cases, nausea and vomiting were present in 60% of cases.

Hassanien et al. [10] as they reported that “according to the main patient complains there were, (4 patients; 20%) complaining from headache, (2 patients; 10%) complaining from some blurred vision, (2 patients; 10%) complaining from confusion & diplopia, (1 Patient; 5%) complaining from ataxia & behavior changes,
and (1 Patient; 5%) suffering from lethargy, confusion & coma”.

The current study shows that the baseline mean Evan's Ventricular ratio was 0.39 ± 0.02 and 60% of cases had papilledema.

Hassanien et al. [10] measured “the diameter of third ventricle and also calculate the Evan’s ratio, which is the ratio of frontal horns largest width to that of the maximal bi-parietal diameter, ratio more than 30% is suggestive for hydrocephalus”.

Our results are in agreement with study of Hassanien et al. [10] as they observed that the main cause of obstructive hydrocephalus in our cases was aqueductal obstruction by different pathological conditions as 25% had congenital aqueductal stenosis, 10% had Colloid cyst of 3rd ventricle, 10% had Pineal body tumor and 10% had thalamic glioma.

Our results are in agreement with (Qiguang Wang, Jian Ching, Si Zhang, Qiang Li, Xuhui Hui, Yun Ju) as they observed that all the patients underwent ballooning of the floor of the third ventricle, the most common etiologies were brain tumors and aqueduct stenosis.

Lucic et al. [11] showed “patients included in their study hospitalized for the treatment of obstructive hydrocephalus due to the non-tumorous stenosis/obstruction of cerebral aqueduct”. Zohdi et al. [12] reported that their patients had obstructive hydrocephalus due to congenital aqueductal stenosis.

In the study in our hands, there is a statistically significant decrease in the amount of headache, degree of papilledema evaluated following surgery. There is also a significant difference between preoperative and postoperative Evan's Ventricular ratio. A substantial decline in the transverse diameter of the third ventricle was also detected. All of these patients were shunt independent.

Bargallo et al. [13], “found most of ETV cases, the lateral ventricular size reduction is often slow and, in some cases, little or no change was observed. They emphasized on postoperative follow-up and assessment of the efficacy of third ventriculostomy to be judged by resolution of clinical symptoms”.

In the study of Hassanien et al. [10]; “(13 cases, 65%) of the ETV cases showed no ventricular size changes, while (7 cases, 35%) showed a little reduction of ventricular size; although with successful ETV evidenced by clinical improvement”.

Lev et al. [14], “in their study to evaluate ETV patency had used the flow void that seen on T2 weighted images at the floor of the third ventricle as an indicator of patency, indicating functioning ventriculostomy and they observed it in most of their patients who had clinical improvement. However, they found that the absence of a flow void was not necessarily indicating impaired ETV function as the pulsation of the basilar artery is producing a flow void in the pre-pontine cistern that may interfere with the interpretation”.

Kulkarni et al. [15] showed that “successful clinical response was associated with a more significant reduction in ventricular volume after the procedure. Direct measurement of improvements in CBF resulting from ETV is an attractive candidate as a surrogate outcome measure because a chronic decrease in CBF is likely to reflect chronic severe effects resulting from hydrocephalus or failure of the procedure to reduce cerebral interstitial pressure”.

However, Javadpour et al. [16] reported “an ETV success rate of 33% (continued patency during follow-up in 7 of 21 patients) and found that success depended on etiology rather than on patient age”.

We reported two unsuccessful ETV out of 25 patients (8%). One patient aged 9 years with primary aqueductal stenosis (out of total nine cases with the same etiology) failed to improve end eventually required VP shunt insertion. Eleven patients had a tumor-related aqueductal obstruction; one of them (pineal tumor) also needed VP shunt insertion.

Baldauf et al. [17] reported that “ETV was successful in nine patients, with a mean follow-up period of 26.2 months. The procedure was successful in four patients with idiopathic aqueductal stenosis - success rate with such etiology was 50%. In two with other congenital anomalies, in one posthemorrhagic, and two with tumor-related hydrocephalus. In 12 patients, the ETV was unsuccessful after a mean follow-up of 3.3 months. These patients required a shunt. Ten of them were less than one year old when ETV was performed”.

Fritsch et al. [18] “reporting a 39% ETV success rate, present ETV as an effective alternative for
the treatment of obstructive hydrocephalus in infants younger than one year. The authors note that age does not present a contraindication for ETV or increase the perioperative risk. They conclude that the success of ETV is determined by the cause of hydrocephalus.

We did not report significant morbidity or mortality among patients of the current study. Transient postoperative fever was reported in 4 patients (16%). Other complications included; wound infection, diabetes insipidus, transient postop urinary incontinence, dizziness, ataxia, CSF leakage, and wound revision. Each of them had one per 25 patients (4%) incidence and resolved without a morbid impact.

According to Mohanty et al. [19], "reclosure of the stoma because of gliosis and scarring has been observed in 6-15% of ETV failures. They reported ETV failure in 13 of 72 patients, with 8 of the 13 being infants. Repeated endoscopic surgery was performed in 7 infants. In 3 of these 7, the stoma was found to be closed and was reopened".

Hassanien et al. [10] used “the overall flow amplitude (OFA) as the standard variable for follow up of the patients after surgery together with correlation with clinical outcome. They found that patients with bad outcome had lower stroke volume values, while the patients with higher values usually had no or minor complains, such as mild, tolerable headache", and this in agreement with previous studies done by Bargallo et al. [13]

Bargallo et al. [13], also demonstrated that “OFA was a better test than the other variables to predict the response to surgery in the postoperative studies. When OFA value is ≥75 µL, the sensitivity and specificity of this technique to determine which patient will improve were 76.7% and 87.5%, respectively".

5. CONCLUSION

Dynamic MRI of CSF flow provides immediate and reliable information on the ETV efficacy, in addition to the flow-void presence at the level of the third ventricle floor fenestration in both midsagittal and perpendicular plane, even in the absence of phase-contrast techniques which is significantly correlated with clinical signs and symptoms improvement in the patients. Quantitative assessment of functional status of ETV stoma by OFA stroke volume was the best indicator for evaluation and the higher OFA stroke is a predictor of favorable clinical outcome, while the ventricular size is not a good indicator of ventriculostomy patency.

6. RECOMMENDATIONS

➢ Further studies on large geographical scale and on larger sample size to emphasize our conclusion.
➢ Emerging techniques, such as 4D-phase contrast are promising methods for multidirectional assessment of flow. Knowledge about the physical background of this technique is essential to provide repeatable and comparable results.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES
