

Idiopathic Normal Pressure Hydrocephalus Controversy of Diagnosis and Management

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Abstract:

Background: Normal pressure hydrocephalus is a chronic steadily progressing disease, characterized by an expansion of the ventricles of the brain with normal (ICP). The aim of this study was to study the importance of completing the clinical triad in the diagnosis, clarify the rule of MRI Flowmetry in the decision of V-P shunt insertion in patients with NPH **Methods:** This study has been done on 25 patients who were suspected to have (iNPH). Patients were divided into two groups; group A included 12 patients with stroke volume above 42 microliter/cycle in MR-CSF Fflowmetry and group B included 13 patients with stroke volume below 42 microliter/cycle. These patients have been subjected to clinical examination, radiological, and laboratory investigations. **Results:** There is a highly statistical significance between these two items as following; Dementia: All cases improved after tapping (11 cases), improved after shunting and 12 cases out of 14 did not show improvement in the test and shunting with a highly significant P value, Gait disturbance: 11 cases improved after tapping in comparison to 10 cases improved after shunting and 13 cases out of 14 did not show improvement in the test and shunting with a significant P value. Urinary incontinence: 11 cases improved after tapping in comparison to 13 cases improved after shunting and 11 cases out of 14 did not show improvement in the test and shunting with a highly significant P value. **Conclusions:** CSF Tapping and clinical FU after tapping is the most important test in the decision of shunting.

Keywords: Idiopathic Normal Pressure Hydrocephalus; Cerebrospinal fluid ; Management

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Introduction

Cerebrospinal fluid (CSF) is a clear, colorless fluid found within the tissue that surrounds the brain and spinal cord, it serves as a protective fluid to the brain and spinal cord, cushioning them from mechanical injury. It acts to reduce the brain's effective weight as well as providing CNS with both nutrition and immunoglobulins [1].

The CSF has a physiologic volume of about 150 ml with a daily turnover ranges from 300-450 ml, the fine balance between the secretion, composition, volume and turnover of CSF is strictly regulated. However, this balance can be disrupted during certain neurological diseases including Hydrocephalus, idiopathic intracranial hypertension (IIH), edema, traumatic brain injury (TBI), and stroke [2]. For the first time NPH was described by the Colombian neurosurgeon Salomon Hakim Doe (1922–2011) in 1964, followed by a detailed and expanded analysis conducted by S. Hakim in collaboration with the American neurosurgeon Raymond Delesy Adams (1911–2008) in 1965 [3]. The disease is usually observed in adults over 60 years of age. The highest incidence of cases is between 70 and 80 year-old, and it could be under-diagnosed in over 80 year-olds. Its incidence varies between 1.36 and 1.58 per 100,000 persons per year [4].

History and neurological examination is the base of the diagnosis. The classic triad comprises gait disturbance, cognitive deterioration and urinary incontinence. The course is usually slowly progressive and the symptoms most commonly occur in that order, during a minimum period of three month. The triad is not always completely present, especially in the early stages of the disease, and is not necessary for diagnosis [5].

Even though CT can help us in visualizing some anatomical changes in the brain, it is not possible to diagnose normal pressure hydrocephalus with this imaging modality alone, while MRI is the investigational

imaging of choice for NPH to image the structural changes, it provides findings may be suggestive of NPH as Evans index, Callosal angle which should be between 40 – 90 degrees and the flow rate of greater than 24.5 mL/min is 95% specific for NPH [6].

The international guidelines recommend tests of CSF hydrodynamics (tap test, external lumbar drainage, and infusion testing) to demonstrate either that the patient has the potential to respond to shunt surgery or that the patient has abnormal CSF hydrodynamics that are consistent with hydrocephalus. The tap test, also known as Miller Fisher test [7].

V-P shunts can improve symptoms, especially gait dysfunction, in up to 74% of patients. Early treatment within 3 months of symptoms is associated with better outcomes [7].

The aim of this study was to study the importance of completing the typical clinical triad of symptoms in the diagnosis of the disease, Clarify the role of MRI Flowmetry in the decision of Ventriculo-peritoneal shunt insertion in patients with NPH.

Patients and Methods

This prospective cohort study has been done on 25 patients admitted to the outpatients' clinic and the inpatients' of the Neurosurgery Department Benha University hospitals who are suspected to have idiopathic normal pressure hydrocephalus (iNPH) during the period from start of March 2023 to March 2024.

Informed written ethical consent is taken from patients included in this study or their relatives after explaining the study measures in details. The study was done after approval from the Ethics Committee on research involving human subjects of Benha faculty of Medicine

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Inclusion criteria were patients with ventriculomegally and two of the three symptoms of the clinical triad of iNPH, or patients with all the three symptoms of

Adam Hakim triad & operated for V-P Shunt.

Exclusion criteria were patients with a known cause of hydrocephalus, patients with only one symptom of the classical triad of iNPH & patients with high opening pressure of LP above 25 Cm.H₂O.

Grouping

Group A :12 patients with stroke volume above 42 microliter/cycle in MR-CSF Flowmetry is subdivided into 2 categories:(7 Patients who had ventriculomegally and all the three symptoms of the clinical triad, 5 Patients who had ventriculomegally and only two out of three of the symptoms of the clinical triad

Group B: 13 patients with stroke volume below 42 microliter/cycle in MR-CSF Flowmetry.

These patients have been subjected to the following: History taking (Especially history of gait disturbance, Urinary incontinence and cognitive abnormalities “dementia”),Clinical Examination: General (Vital Signs,Fundus examination), Neurological including (Glasgow coma scale (GCS), Motor Power, Gait, Reflexes), Radiological including (CT brain/MRI for detection of ventriculomegally, MRI Flowmetry), Laboratory: As regarding(CBC including deferential counting,Blood coagulation profile especially PT, PTT and INR), Ancillary tests for NPH including (Visual Field, Lumbar puncture (LP) as a tap test in the diagnosis and for determination of opening pressure in the left lateral decubitus position)

Surgical management

Surgery is done by members of Neurosurgery Department in Benha University Hospital.

Ventriculo-peritoneal Shunt inserted as follows: An area of hair on the head is shaved. This may be behind the ear or on the top or back of the head. The surgeon makes a skin incision behind the ear. Another small surgical cut is made in the

belly. A small hole is drilled in the skull. One end of the catheter is passed into a ventricle of the brain. A second catheter is placed under the skin behind the ear. It is sent down the neck and chest, into the belly area. A valve is placed underneath the skin, usually behind the ear. The valve is connected to both catheters.

Postoperative follow up

Clinical follow up: Has been done in the 1st day post-operative for dementia, urinary incontinence, gait disturbance, CSF leakage & fever, Late follow up (3-6 months) for post-operative persistence of symptoms.

Radiological follow up: Immediate Post-operative (2nd day) CT brain showing the ventricular end inside the lateral ventricle, Late follow up (3-6 months) CT brain.

Statistical analysis:

Statistical analysis was done by SPSS v26 (IBM Inc., Armonk,NY,USA). Quantitative variables were presented as mean and standard deviation (SD) and compared between the two groups utilizing unpaired Student's t- test. Qualitative variables were presented as frequency and percentage (%) and were analysed utilizing the Chi-square test or Fisher's exact test when appropriate. A two tailed P value < 0.05 was considered statistically significant.

Case 1

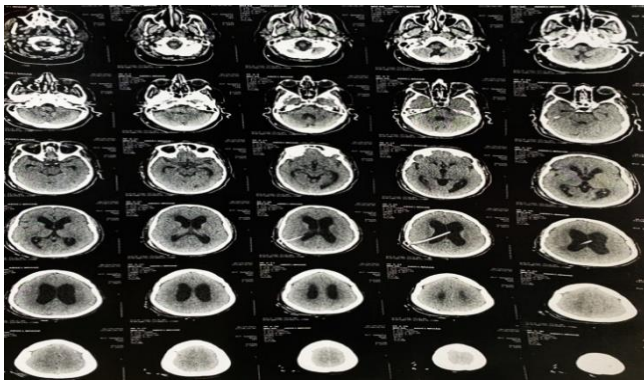
Female patient 59 years old, known to be diabetic and hypertensive, was complaining of gait disturbance 2 years ago, dementia 2 years ago & urinary incontinence 9 months ago. Brain MRI shows ventriculomegally, MR-CSF Flowmetry shows a systolic stroke volume 37 microliter/cycle. Tap test is done, the pressure of CSF was 15 cm.H₂O, pt showed no improvement after tapping. The patient is operated upon by insertion of a V-P shunt. The patient showed no signs of improvement regarding gait, urinary incontinence or dementia, in the late follow up in outpatient clinic (3 months post op). Patient was complaining of

repeated vomiting and positional headache, Follow up CT brain was done and showed a widening in the subdural

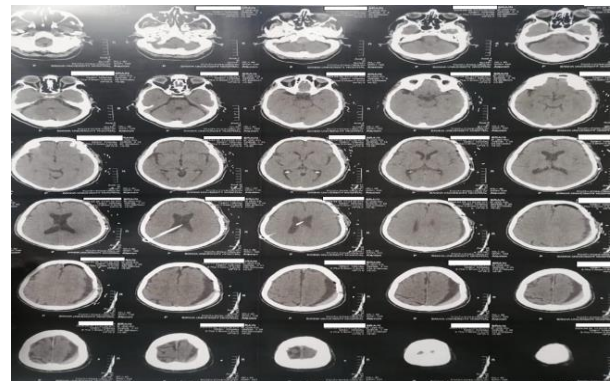
space, patient is re-operated for shunt removal. **Figure 1**



A



B



C

Figure 1: Pre operative T2 Sagittal MRI brain showing ventriculomegaly, Immediately post-operative Axial CT brain showing the Ventricular end of the shunt draining the lateral ventricle and Three months post-operative Axial CT brain showing left fronto-parietal SDH.

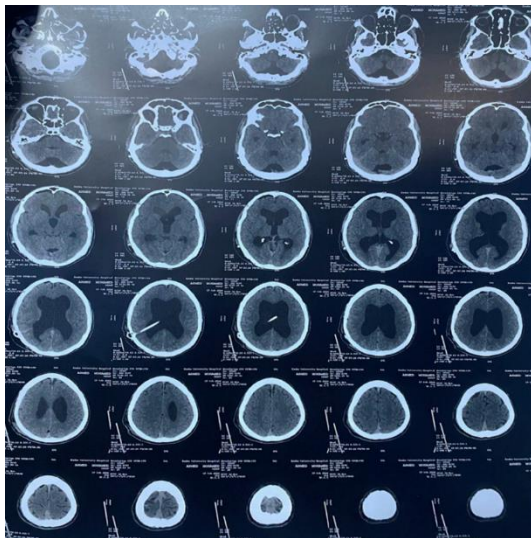
Case 2

Male patient 42 years old, was complaining of gait disturbance 6 months ago and newly developed urinary incontinence with no complaint from dementia. Brain MRI shows ventriculomegaly and acute Callosal angle (80°), MR-CSF Flowmetry shows a systolic stroke volume 70 microliter/cycle. Tap test is done, the pressure of CSF was

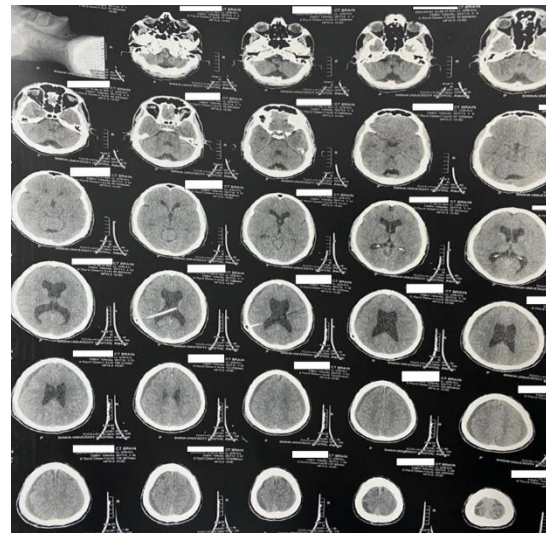
20 cm.H₂O and the gait movement improved for 2 days. Patient is operated upon by insertion of a V-P shunt. He improved regarding gait immediately post-operative & urinary incontinence improvement appeared in the late follow up in outpatient clinic (3 months post op). Follow up CT brain was done 2nd day post-operative. **Figure 2**



A



B



C

Figure 2 : Pre operative T2 Sagittal MRI brain showing ventriculomegaly, Immediately post-operative Axial CT brain showing the Ventricular end of the shunt draining the lateral ventricle. And Three months post-operative Axial CT brain Follow up.

Results

There was a significant difference between the two studied groups regarding post-operative complications after inserting the VP shunt as the percentage of complicated cases in the first group equals 16.7% in comparison to the 61.5% in the second group.

It also shows that the main complication after VP shunt insertion was over drainage which is 6:1 between the two groups.

As regard complications such as intra parenchymal hemorrhage, superficial wound infection, post-operative incisional hernia, CSF Leakage and seizures they didn't occur in our study, while DVT (1 (4%)) was present only in group A due to being bed ridden for a prolonged time. CSF infection (2 (8%)) occurred only with group B which was managed by broad spectrum antibiotics and removal of shunt hardware for a month. **Table 1**

The percentage of presence of the clinical triad in the two groups as well as the improvement of symptoms immediately post op & after 3 months of surgery, there

was no statistically significant value between the two groups in spite of the obvious difference in improvement noticed by the clinical follow up. **Table 2**

Table 1: Comparison between the two studied groups according to basic Clinical data, preoperative measured CSF pressure, complications

	Total (n = 25)		Stroke Volume				Test of p	
	No.	%	Group A More than 42 (n =12)		Group B Less than 42 (n = 13)		Sig.	p
	No.	%	No.	%	No.	%		
Complications							χ^2	^{FE} p
No	15	60.0	10	83.3	5	38.5	5.235*	0.041*
Yes	10	40.0	2	16.7	8	61.5		
Over drainage	7	28.0	1	8.3	6	46.2	4.427	0.073
DVT	1	4.0	1	8.3	0	0.0	1.128	0.480
Infection	2	8.0	0	0.0	2	15.4	2.007	0.480

X²: Chi square test, MC: Monte Carlo, *: Statistically significant at p ≤ 0.05

Table 2: Comparison between the two studied groups according to the presence & improvement of the clinical triad after V-P Shunt insertion

		Total (n = 25)		Stroke Volume				χ^2	p
				Group A More than 42 (n = 12)		Group B Less than 42 (n = 13)			
		No.	%	No.	%	No.	%		
Dementia	Pre-operative	23	92.0	10	83.3	13	100.0	2.355	^{FE} p=0.220
	Post-operative	0	0.0	0	0.0	0	0.0	—	—
	After 3 months	11	44.0	7	58.3	4	30.8	1.924	0.165
Gait disturbance	Pre-operative	23	92.0	10	83.3	13	100.0	2.355	^{FE} p=0.220
	Post-operative	8	32.0	5	41.7	3	23.1	0.991	^{FE} p=0.411
	After 3 months	11	44.0	6	50.0	4	30.8	1.924	0.165
Urinary incontinence	Pre-operative	24	96.0	11	91.7	13	100.0	1.128	^{FE} p=0.480
	Post-operative	9	36.0	4	33.3	5	38.5	0.071	^{FE} p=1.000
	After 3 months	13	52.0	8	66.7	5	38.5	1.989	0.158

X²: Chi square test, FE: Fisher Exact, p: p value for comparing between the two studied groups

The correlation between the improvement after performing the tab test and the improvement of symptoms after inserting the V-P shunt.

There is a highly statistical significance between these two items as following; Dementia: All cases improved after tapping (11 cases), improved after shunting and 12 cases out of 14 did not show improvement in the test and shunting with a highly significant P value. Gait disturbance: 11 cases improved after

tapping in comparison to 10 cases improved after shunting and 13 cases out of 14 did not show improvement in the test and shunting with a significant P value.

Urinary incontinence: 11 cases improved after tapping in comparison to a 13 cases improved after shunting and 11 cases out of 14 did not show improvement in the test and shunting with a highly significant P value. **Table 3**

Table 3: correlation between the improvement of symptoms after performing the tap test and the improvement of symptoms after inserting the V-P shunt.

	Total (n = 25)		χ^2	FE p
	No.	%		
Symptoms after Tapping				
Not improvement	14	56.0	21.280*	<0.001*
Improvement	11	44.0		
Post op Symptoms after 3 months				
Dementia				
Not present pre op	2	8.0	16.520*	MC p <0.001*
Not improvement	12	48.0		
Improvement	11	44.0		
Gait disturbance				
Not present pre op	2	8.0	11.360*	MC p = 0.002*
Not improvement	13	52.0		
Improvement	10	40.0		
Urinary incontinence				
Not present pre op	1	4.0	19.571*	MC p <0.001*
Not improvement	11	44.0		
Improvement	13	52.0		

χ^2 : Chi square test, MC: Monte Carlo, p: p value for comparing between the two studied groups, *: Statistically significant at $p \leq 0.05$

Discussion

NPH is a chronic, steadily progressing disease that significantly reduces the quality of life, especially in the absence of timely diagnosis and treatment, due to its disabling character. The NPH is characterized by a gradual development of the classical Hakim–Adams triad: Disorders of gait, dementia and urinary incontinence [3].

Regarding our clinical data there was no statistical difference between Group A and B in the diagnosis of the disease in spite of the clinical triad in group A was not completed in 5 cases out of all the 12 cases with a P value in the presence of preoperative dementia, gait disturbance & Urinary incontinence equals 0.220, 0.220 & 0.480 respectively while it is completed in all cases of group B. Kiefer M et al. study reported the same observation as following; In the past, NPH was only diagnosed and treated when all three cardinal symptoms (the so-called "Hakim triad") were demonstrably present; the current recommendation, however, is that NPH can be diagnosed and treated in the presence of only two cardinal symptoms, or even just one. This change in attitude

resulted from the recognition that the prognosis worsens the longer NPH remains untreated, with the complete Hakim triad always representing an advanced stage of the disease [8].

Regarding the clinical outcomes of shunting in NPH patients resulted in the following clinically relevant conclusions: An accurate and uniform protocol is needed to accurately select patients and achieve a correct diagnosis of NPH, Surgery with V-P shunt improves gait, balance, continence and memory with an impact on quality of life and daily activities of the patients. The most important investigation in the decision of shunting statistically is the improvement of symptoms after tapping CSF with a highly significant P value in the improvement of dementia, gait disturbance and urinary incontinence as $<0.001^*$, 0.002 , $<0.001^*$ respectively, MRI-CSF Flowmetry shows no statistically significant value between the two groups in the improvement of the symptoms in spite of the obvious difference in improvement noticed by the clinical follow up.

These results agree with the German Neurological Society Guidelines,

Nakajima M et al & Trungu S et al studies as following; The measurement of CSF dynamics has not yet become established in the German centers. It is nonetheless recommended in the current guidelines of German Neurological society (Deutsche Gesellschaft für Neurologie), The CSF drainage test (tap test) is the most useful for diagnosing iNPH and predicting the therapeutic effect of a shunt intervention [9], Surgical treatment by VPS for NPH improves symptoms in most patients, when accurately selected. Follow-up with stroke volume measurement is a valuable tool for the need for valve adjustment [10]. As regard complications such as intra parenchymal hemorrhage, superficial wound infection, post operative incisional hernia, CSF Leakage and seizures didn't occur in our study. DVT (1 (4%)) was present only in group A due to being bed ridden for a prolonged time. CSF infection (2 (8%)) occurred only with group B which was managed by broad spectrum antibiotics and removal of shunt hardware for a month. However over drainage is seen in (7 (28%)) in both groups with statically significant P value for the CSF Flowmetry as P value was 0.041 between the two groups.

Conclusion

It is not necessary to wait for completing the clinical triad to establish the diagnosis of the disease and start the optimal treatment. CSF Tapping and following the improvement of clinical symptoms after tapping is the most important test in the decision of shunting. MRI-CSF Flowmetry shows no statistically difference in the decision of shunting, however MRI-CSF Flowmetry is statistically significance in decreasing the complications after shunting especially over-shunting complications.

Limitation: this study had certain limitation as a small sample size, single center study and short follow up duration.

Recommendation: further larger multicenter coharts are recommended to validate our finding.

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Conflict of Interest: Nil

List of abbreviation :

CSF Cerebro-spinal fluid
CT Computed tomography
GCS Glasgow coma scale
ICP Intracranial pressure
IIH Idiopathic intracranial hypertension
LP Lumbar puncture
MRI Magnetic resonance imaging
NPH Normal pressure hydrocephalus
TBI Traumatic brain injury
CNS Central nervous system
SD Standard deviation
IQR Inter quartile range

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