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Original Research Paper

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PRE- AND POST- SHUNT CEREBRAL PERFUSION MEASURED BY DYNAMIC SUSCEPTIBILITY CONTRAST MRI IN PATIENTS WITH NORMAL PRESSURE HYDROCEPHALUS.

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ABSTRACT

Background: NPH-related dementia is the only surgically manageable dementia. Response to ventricular shunting in NPH is variable. This study aims to establish a possible correlation between the changes in cerebral perfusion with clinical response to shunting. **Methods:** The study group consisted of 20 patients with NPH diagnoses who underwent ventricular shunting. Pre- and 3-month post- shunt DSC-MRI was done to assess the change in relative cerebral blood flow (rCBF). **Results:** Mean ± SD values of rCBF in frontal grey matter, frontal periventricular white matter, parietal periventricular white matter and hippocampus were 0.91 ± 0.11, 0.61 ± 0.09, 0.47 ± 0.11 and 0.93 ± 0.06 before shunt surgery and 0.98 ± 0.06, 0.70 ± 0.07, 0.54 ± 0.07 and 0.98 ± 0.06 after shunt surgery in NPH patients who responded to shunt surgery; and 0.78 ± 0.17, 0.37 ± 0.14, 0.41 ± 0.11 and 0.89 ± 0.10 before shunt surgery and 0.79 ± 0.14, 0.37 ± 0.19, 0.38 ± 0.09 and 0.84 ± 0.07 after shunt surgery in NPH patients who did not respond to shunt surgery. Therefore, regional rCBF in these regions increased in responders after shunt surgery, with a significant statistical difference (p-value < 0.05) while no significant change was seen in shunt non-responders (p-value > 0.05). **Conclusion:** There is a correlation between a significant increase in regional rCBF and clinical improvement after shunt surgery.

KEYWORDS : Normal pressure hydrocephalus, relative cerebral blood flow, DSC MRI, shunt response

INTRODUCTION

In 1965, Hakim and Adams[1] were the first to describe Normal Pressure Hydrocephalus (NPH) as a condition characterized by the clinical triad of gait disturbance, urinary incontinence, and memory impairment; the presence of normal CSF pressure on lumbar puncture; the radiologic finding of enlarged cerebral ventricles; and improvement after ventricular shunting. Many patients have since undergone CSF shunt surgeries for the treatment of NPH, with a great variation in response to surgery, with improvement lasting from a few months to years.[2] Perfusion measurements by dynamic susceptibility contrast magnetic resonance imaging (DSC MRI) utilize very rapid imaging (most commonly echo-planar imaging – EPI) to capture the first pass of intravenously injected paramagnetic contrast agent (bolus tracking).[3] The gadolinium contrast upon entering the circulation induces susceptibility changes due to its paramagnetic properties that cause shorter T2* values and a significant signal loss. Suitable software is used to generate curves displaying intensity changes depending on gadolinium concentration over time. Researchers are increasingly deploying MRI Perfusion as a diagnostic and research technique to provide valuable information about the regional variability in cerebral microvasculature of normal and pathological brains.[4] Compared to most other perfusion techniques (such as SPECT, Xenon-CT, [^{15}O]H2O PET), DSC MRI perfusion has the advantage of greater spatial resolution, sensitivity for deep structures, easier availability, and reduced acquisition times.[5]

MATERIALS AND METHODS

The study was conducted at a tertiary care institute in North India over a period of two years.

This study involved 20 patients.

Detailed informed consent was taken from the patients before inclusion in the study.

Study Design: Prospective study

Selection of subjects:

Inclusion Criteria:

1. All patients clinically suspected of NPH i.e., presence of one or more symptoms of the triad
2. Age ≥ 60 years
3. Conventional MRI findings suggestive of NPH including ventriculomegaly with Evans' index of ≥ 3, callosal angle of < 90°, disproportionately enlarged subarachnoid spaces, and CSF flow void through the aqueduct and fourth ventricle.

Exclusion Criteria:

1. Age < 60 years
2. Obstructive hydrocephalus
3. Dementias other than NPH that could cause similar clinical symptoms or radiological findings
4. History or evidence of conditions that might cause secondary NPH
5. Patients with general contraindications to MRI

All Magnetic Resonance Imaging (MRI) studies were performed using a 1.5 Tesla MR system (Magnetom Avanto, Siemens Medical Systems, Erlangen, Germany), with a standard head coil, in neutral supine position.

The following protocol was used:

Table 1: MRI protocol

Sequence	FOV (mm/%)	Slice thickness (mm)	TR/TE (ms)	NEX	Flip angle (degrees)
ep2d_perf	230/100	5	1430/30	1	70

FOV = field of view, TR = time to repeat, TE = time to echo, NEX = number of excitations, ep2d = echo planar two dimensional, perf = perfusion, mm = millimetre , ms = millisecond

DSC-MRI was done twice to assess relative cerebral blood flow (rCBF) in the frontal grey matter, frontal and parietal periventricular white matter, and hippocampus in patients with NPH, once before shunt surgery and the second time at 3 months follow-up after the shunt surgery.

The study was done using a bolus of 0.2 mmol/kg Gadodiamide (0.5 mmol/ml Omniscan, GE Healthcare) immediately followed by a 10 ml saline flush, administered in the antecubital vein.

Post-processing was done on the Siemens workstation using the perfusion application. rCBF was measured using circular ROIs of the same areas throughout of 0.16 sq.cm, placed in the frontal grey matter, frontal and parietal periventricular white matter, and hippocampi. ROIs were placed symmetrically in both hemispheres and the mean of the two corresponding ROIs was computed. The cerebellum was used as reference. Therefore, the rCBF was expressed as the ratio of regional to cerebellar level.

All patients were assessed pre- and 3-month post- shunt surgery using clinical NPH score as well as DSC MRI findings.

Table 2: Clinical NPH score [6]	
Gait evaluation:	
Patient is bedridden or not able to ambulate	1
Ambulation is possible with help	2
Independent walking is possible but unstable or the patient falls	3
Abnormal but stable gait	4
Normal gait	5
Cognitive function:	
Patient is vegetative	1
Severe dementia	2
Important memory problems with more or less severe behaviour disturbances	3
Memory problems reported by patient or family	4
Cognitive disturbances are only found by specific tests	5
Sphincter disturbance:	
Urinary and faecal incontinence	1
Continuous urinary incontinence	2
Sporadic urinary incontinence	3
Urinary urgency	4
No objective or subjective sphincter dysfunction	5

Total NPH score = gait evaluation score + cognitive function score + sphincter disturbance score.

A patient with ≥ 1 increase in clinical NPH score 3 months after shunt surgery was defined as a shunt responder.

Statistical Analysis:

Data was fed into Microsoft Excel. Continuous variables were summarized as mean and standard deviation and represented as Box plots showing mean (x), 25th, median and 75th percentiles (box) and ±95th percentiles (whiskers). A two-sided p-value was reported and a p-value of < 0.05 was considered statistically significant.

OBSERVATIONS AND RESULTS

The study was conducted on 20 patients with NPH diagnoses who underwent CSF shunt operation. Subsequently, at 3 months follow-up, symptoms of 14 patients lessened (shunt responders), whereas no changes were observed in the symptoms of 6 patients (shunt non-responders).

The mean values ± SD of regional rCBF in NPH responders before and after shunt operation was as shown in Table 3 & Figure 1.

Table 3: Comparison of regional rCBF in NPH responders before and after shunt operation			
ROI	Pre-op	Post-op	P-value
Frontal grey matter	0.91 ± 0.11	0.98 ± 0.06	0.04
Frontal periventricular white matter	0.61 ± 0.09	0.70 ± 0.07	0.007
Parietal periventricular white matter	0.47 ± 0.11	0.54 ± 0.07	0.04
Hippocampus	0.93 ± 0.06	0.98 ± 0.06	0.03

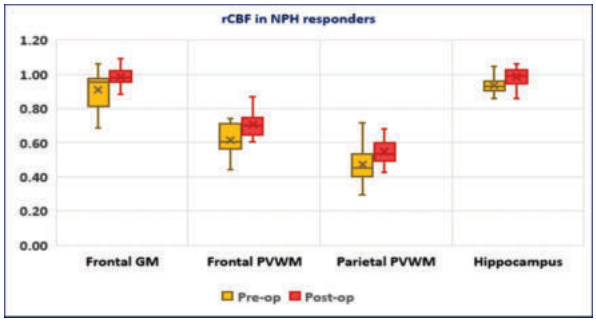

Figure 1. *Box plots showing the comparison of regional rCBF in NPH responders before and after shunt operation*

The mean values ± SD of regional rCBF in NPH non-responders before and after shunt operation was as shown in Table 4 & Figure 2.

Table 4: Comparison of regional rCBF in NPH non-responders before and after shunt operation			
ROI	Pre-op	Post-op	P-value
Frontal grey matter	0.78 ± 0.17	0.79 ± 0.14	0.9
Frontal periventricular white matter	0.37 ± 0.14	0.37 ± 0.19	1.0
Parietal periventricular white matter	0.41 ± 0.11	0.38 ± 0.09	0.6
Hippocampus	0.89 ± 0.10	0.84 ± 0.07	0.3

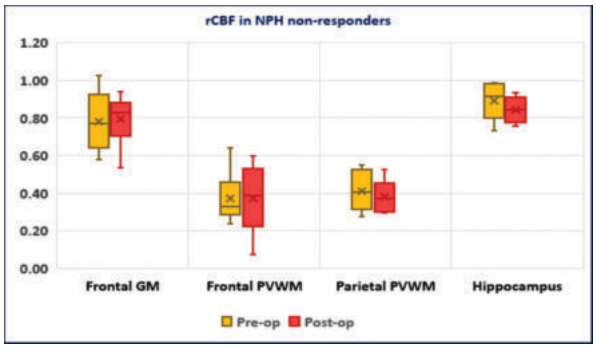

Figure 2. *Box plots showing the comparison of regional rCBF in NPH non-responders before and after shunt operation*

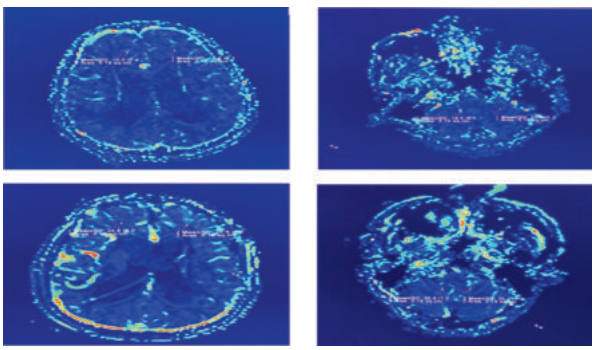

Image 1: *Pre- and post- op frontal periventricular white matter/cerebellar ratio of rCBF on DSC MRI images.*

DISCUSSION

There is a generally held consensus that the symptoms of NPH are produced due to the expanded lateral ventricles applying excessive tangential shearing forces on periventricular white matter fibers associated with gait.[7] The continuing ventricular expansion exposes the cortex to increased radial shearing forces which leads to dementia. Many researchers have implicated compromised cerebral blood flow due to compression of cerebral microvasculature by enlarged ventricles as the chief contributing factor to these changes.[8-12] The purpose of shunting in such patients is not to decrease the mean CSF pressure (which is already normal), but instead to provide additional capacitance. Therefore, as the brain expands during systole, some of the CSF goes out via the shunt which restricts the maximum pressure rise and the resultant shearing forces on the periventricular fibers.[7]

In our study, the regional rCBF in frontal grey matter, frontal periventricular white matter, parietal periventricular white matter and hippocampus increased in responders after shunt surgery, with a significant statistical difference (p-value < 0.05), while no significant change was seen in shunt non-responders (p-value > 0.05). Our study indicates that there is a correlation between a significant increase in rCBF in these regions and clinical improvement after shunt surgery. Our results correlate with the study by Ziegelitz et al.[13] which found that in shunt responders, the post-operative rCBF increase in cortical, subcortical & periventricular regions was significant. Similar results were found by Tanaka et al.[14] who stated that in shunt responders, CBF improved, while in non-responders CBF deteriorated; and in two studies by Lying-Tunnel et al.[15,16] in which CBF improved with successful shunting. Our results are in contrast to the studies by Kushner et al.[17] which measured CBF around 3 months after shunting and found it not to be significantly different from the preoperative CBF levels; and by Meixenberg et al.[18] who were also unable to find an increase in CBF after shunting.

CONCLUSION

DSC MRI perfusion is a potentially useful tool in NPH. Regional rCBF in frontal grey matter, frontal and parietal periventricular white matter, and hippocampus increases after shunt surgery in shunt responsive NPH patients, while no significant change is seen in shunt non-responders. Therefore, there is a strong indication of a correlation between a significant increase in rCBF in these regions and clinical improvement after shunt surgery.

Strengths And Limitations

The primary strengths of this study are the clinically well-characterised patient groups and the use of a single MRI scanner with identical protocols for both pre- and post-operative examination of the patients. In addition, the use of a 1.5T machine minimized shunt artefacts making it possible to obtain perfusion estimates postoperatively.

There are some limitations too. The main one is a limited number of study subjects. This can potentially be due to the widespread hesitancy of the local population to any kind of "brain surgery" and to the COVID-19 pandemic.

Conflicts Of Interest: Nil

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