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Evaluation of aqueductal CSF flow dynamics with phase contrast cine MR imaging in idiopathic intracranial hypertension patients: preliminary results

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Abstract. – OBJECTIVE: We aimed to evaluate dynamic cerebrospinal fluid (CSF) flow in idiopathic intracranial hypertension (IIH) patients with new MRI technology phase contrast cine (PCC) MRI.

PATIENTS AND METHODS: Nineteen patients diagnosed with idiopathic intracranial hypertension and 11 healthy volunteers were included in this study. Nine of the IIH cases had been previously diagnosed and had been on drug treatment and 10 cases were diagnosed with IIH recently and had not been put on drug treatment yet. All CSF flow datas were evaluated by phase contrast-MRI using a 1,5 T MRI. The CSF flow was calculated in the equidistant MRI sequence which was taken through a cardiac cycle.

RESULTS: Mean aqueduct area in the IIH group was 3.04 ± 1.14 mm², mean peak rate was 3.29 ± 1.77 cm/sec, mean average rate was 0.35 ± 0.33 cm/sec and mean flow was 0.67 ± 0.95 ml/min. In the control group mean aqueduct area was 2.87 ± 1.01 mm², mean peak rate was 4.20 ± 1.40 cm/sec, mean average rate was 0.37 ± 0.18 cm/sec and mean flow was 0.64 ± 0.40 ml/min. A statistically significant difference was found for the PCC MRI parameter of mean rate value (*p*: 0.007) between the control group and IIH patients. A statistically insignificant (*p*: 0.058) but marked difference was found for mean flow value.

CONCLUSIONS: To our knowledge this study is the first CSF flow study in the idiopathic intracranial hypertension patients. We found a difference between the IIH groups and controls in mean rate and flow parameters. It was interesting that the mean rate and flow values of the untreated group that were higher than the controls. CSF flow analysis may be a marker to follow up IIH patients.

Key Words:

Cerebrospinal fluid, Idiopathic Intracranial hypertension, Phase contrast-cine magnetic resonance imaging.

Introduction

Idiopathic intracranial hypertension (IIH) is a disorder of unknown etiology that predominantly affects obese women of childbearing age. The most common IIH symptoms are headaches, visual problems, and pulsatile tinnitus and the most important complication is permanent vision loss. The incidence of IIH is 1-2/100,000 and it is more common in females[1,2]. The pathogenesis of IIH remains unclear. Several underlying mechanisms have been proposed, such as parenchymal edema, increased cerebral blood volume, excessive cerebrospinal fluid (CSF) production, venous outflow obstruction, and compromised CSF resorption[3]; however, no single theory has fully explained the exact cause of IIH.

Magnetic resonance imaging (MRI), the imaging method with the highest soft tissue resolving power, can display brain tissue without contrast agents. Moreover, vascular investigations can be carried out with phase contrast cine MRI techniques without the need for invasive procedures such as catheterization or the use of contrast agents. CSF flow physiology and pathology have been investigated with the phase contrast cine (PCC) MRI method over the last 15 years. PCC is extremely sensitive, even to very slow flows, and has been used to study the ventricular system, the subarachnoid space, the spinal canal, different pathologies including Chiari malformations and arachnoid cysts, and the cerebral aqueduct, where CSF pressure is most regular[4-9].

We investigated whether there was a difference between CSF flow dynamic parameters at the aqueduct level in IIH patients using PCC MRI, and whether drug treatment in these patients caused a change in PCC MRI findings.

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Patients and Methods

A total of 19 patients diagnosed with IIH based on the modified Dandy criteria at Inonu University Turgut Ozal Medical Center's Neurology Department were enrolled. Nine of these cases had been previously diagnosed, were on drug treatment, and were followed by our clinic for the last 2-4 years. The other 10 cases were patients who presented to the clinic during this study and who had been diagnosed with IIH recently but had yet to start a drug treatment. The control group consisted of 11 healthy volunteers of similar age and gender. The detailed history, neurological examination, neuro-imaging, and other laboratory findings of the patients who were included in the study were obtained from the Hospital Information Management System of our hospital, as well as from patient interviews. The study received approval from the Inonu University Medical Faculty Ethics Committee. All patients were informed about the investigation to be performed before PCC MRI and signed informed consent was obtained. All patients underwent a detailed neurological examination before the investigation.

MRI Investigation

The quantitative evaluation of CSF flow was performed with images obtained in the axial plane with the two-dimensional (2D) Q FLOW phase-contrast MR angiography technique using a 1.5 Tesla MR device (Magnetom Avanto, Siemens, Erlangen, Germany) available in the radiology department of our hospital, using the standard "head coil". The PCC MRI duration for each patient was approximately 5 minutes. Midline sagittal, coronal, and axial T1A preliminary images were first obtained. "Mean modulus", 'magnitude of complex difference', and 'directional phase difference' images perpendicular to the cerebral aqueduct in the sagittal plane were then obtained at the semi-axial plane. For images in the axial plane, the parameters used for the 14 to 30 cardiac phase sections according to heart rate were: repetition time, 31.25 ms; echo time, 8.06 ms; section thickness, 5.5 mm; number of signal averages, 1; field of view, 16 × 10 cm; matrix, 128 × 256; and deviation angle, 10°. Cardiac triggering was performed prospectively with finger plethysmography. Flow sensitivity (venc) was determined as 20 cm/sec. Flow in the caudocranial direction was identified as negative and flow in the craniocaudal direction was identified as positive.

MRI Analysis

The images were evaluated by two separate radiologists using the Siemens user console (Argus software, Siemens, Erlangen, Germany). Regions of interest contained the entire aqueduct in axial phase images obtained during one cardiac cycle. Peak rate (cm/s), mean rate (cm/s), advanced flow volume (mL), back flow volume (mL), net advanced flow volume (mL), flow (mL/s) values, and the rate-time and flow-time curves of the flow passing through the aqueduct were obtained. CSF flow values were multiplied by 60 and converted into mL/min. The investigation was evaluated by the same radiologist at two different time points and the results were subsequently compared.

Statistical Analysis

All statistical analyses were performed using the SPSS for Windows software (ver. 13.0; SPSS Inc., Chicago, IL, USA). Quantitative data were presented as means ± standard deviation and qualitative data were presented as numbers and percentages. The Kruskal-Wallis variance analysis test, the Connover test and analysis of variance were used for group comparison of the aqueduct area, peak rate, mean rate, and back flow volume variables that did not show normal distribution. The Mann-Whitney U-test was used for the comparison of lumbar puncture results in the untreated and treated IIH patient groups. A p-value < 0.05 was accepted as statistically significant.

Results

The 19 IIH patients included in the study ranged in age from 21 to 54 years. Ten (8 females, 2 males) IIH patients were recently diagnosed and were not receiving treatment; these patients ranged in age from 22 to 53 years (mean age = 35.30 years). Nine cases (8 females, 1 male) had been previously diagnosed with IIH and were receiving drug treatment; these patients ranged in age from 21 to 54 years (mean age = 39.88 years). The control group consisted of 11 healthy volunteers aged from 21 to 46 years (mean age = 32.36 years). The demographic characteristics of all patients are presented in Table I. The presenting symptom was headache in both the untreated and treated patients. Headache was accompanied by blurred vision in 70% of the patients.

Table I. Demographic characteristics of untreated and treated IIH patients and the control group.

Patient characteristics	Untreated IIH patients (n: 10)	Treated IIH patients (n: 9)	Control group (n: 11)	*p*-value
Gender (M/F)	8/2	8/1	7/4	0.370*
Age	35.30 ± 10.25	39.88 ± 11.15	32.36 ± 7.83	0.244**

The mean lumbar puncture CSF opening pressure value was 28.36 cm H_2O (range: 25-35 cm H_2O) in untreated patients and 34.20 cm H_2O (25-54 cm H_2O) in treated patients. There were no significant group differences in CSF pressures ($p = 0.146$).

For the control group, the mean aqueductal area was 2.87 ± 1.01 mm^2, the mean peak rate was 4.20 ± 1.40 cm/s, the mean average rate was 0.37 ± 0.18 cm/s, and the mean flow was 0.64 ± 0.40 mL/min. For the IIH group, the mean aqueduct area was 3.04 ± 1.14 mm^2, the mean peak rate was 3.29 ± 1.77 cm/s, the mean average rate was 0.35 ± 0.33 cm/s, and the mean flow was 0.67 ± 0.95 mL/min. The comparison of CSF flow parameters measured with PCC MRI in the untreated and treated IIH patients and the control group are listed in Table II.

For the treated patient group, the mean aqueduct area was 3.35 ± 1.17 mm^2, the mean peak rate was 2.97 ± 1.27 cm/s, the mean rate was 0.15 ± 0.13 cm/s, and the mean flow was 0.26 ± 0.39 mL/min. A statistically significant difference was found between the mean rate value ($p = 0.007$) of the control group and the untreated and treated patient groups. A trend ($p = 0.058$) toward a difference was found between the mean flow values of the IIH and control groups. The mean rate on Fisher's least significant difference (LSD) test was significantly lower in the treated group than in the untreated group ($p = 0.003$) and post hoc analysis of the three groups showed a trend toward ($p = 0.055$) a decreased mean rate compared to the control. The mean flow value evaluated with the LSD test was found to be significantly lower in the treated group than in the untreated group ($p = 0.032$) and post hoc analysis of the three groups showed a trend toward ($p = 0.254$) a decreased mean flow value compared to the control group.

Comparison of the PCC MRI values of the three groups revealed that peak rate, mean rate, and mean flow were higher in the untreated group than in the control group; moreover, these values were lower in the treated group compared with the control group. PCC MRI parameters were evaluated in terms of gender but no statistical evaluation was performed because the number of males was low in all groups. In general, peak rate, average rate, and average flow values were higher in males than in females in the IIH group. However, no such difference was seen in the control group. The comparison of mean rate between the three groups is shown in Table III.

Discussion

The investigation of CSF flow physiology and pathology has attracted increasing interest over the last 15 years[4,6-8,10]. Studies using the PCC MRI method, which is extremely sensitive

Table II. The comparison of CSF flow parameters measured with FK-MRI in the acute and chronic IIH patient group and the Control group.

	Control group	Acute patients	Chronic patients	*p*-value
Aqueduct area (mm^2)	2.87 ± 1.01	2.76 ± 1.08	3.35 ± 1.17	0.402
Peak rate (cm/sec)	4.20 ± 1.40	3.58 ± 2.15	2.97 ± 1.27	0.135
Mean rate (cm/sec)	0.37 ± 0.18	0.52 ± 0.35	0.15 ± 0.13	0.007
Advanced flow Volume (ml)	0.020 ± 0.009	0.019 ± 0.018	0.014 ± 0.008	0.667
Back flow Volume (ml)	0.012 ± 0.007	0.009 ± 0.007	0.011 ± 0.006	0.238
Net advanced flow volume (ml)	0.007 ± 0.003	0.010 ± 0.012	0.03 ± 0.05	0.112
Mean flow (ml/min)	0.64 ± 0.40	1.03 ± 1.15	0.26 ± 0.39	0.058

Table III. The comparison of mean rate between the three groups.

	Mean rate (cm/sec)	*p*-value
Control group/acute patients	0.37 ± 0.18 / 0.52 ± 0.35	> 0.005
Control group/chronic patients	0.37 ± 0.18 / 0.15 ± 0.13	< 0.005
Acute patient/chronic patients	0.52 ± 0.35 / 0.15 ± 0.13	< 0.005

to very slow flow, have focused on the ventricular system, the subarachnoid space, and the spinal channel, as well as on the cerebral aqueduct where the flow shows the most regular course[7,8]. Normal flow patterns have previously been studied, expressing flow in the aqueduct with numerical parameters, and flow changes have been investigated in different pathologies, such as normal pressure hydrocephalus (NPH), Chiari malformations, arachnoid cysts, and multiple sclerosis[11-14]. Based on these studies, we hypothesized that there may be a difference in CSF flow dynamics in patients with IIH at the aqueduct level. To the best of our knowledge, there are no other studies in the literature concerning this subject. We investigated whether there were differences in PCC MRI parameters between IIH patients and controls, and between untreated IIH patients and those undergoing long-term treatment.

Nitz et al[15] demonstrated the fundamental characteristics of CSF flow dynamics in detail with the cardiac triggered 2D fast imaging with steady-state precession sequence. In a study by Kadowaki et al[16], cine MRI showed additional function in aqueductal stenosis on conventional sequences. Moreover, Hoffmann et al[17] reported a flow-void jet flow in CSF-connected arachnoid cysts using the PSIF sequence; the flow-void jet flow shape has been accepted as the most significant finding related to the CSF connection of an arachnoid cyst. The sensitivity of the cardiac triggered PSIF sequence in showing the connection of arachnoid cysts and adjacent CSF areas has been reported as 90% in several studies[15-17].

NPH is the disorder for which PCC MRI is most commonly used, and aqueductal CSF flow is very significantly increased in NPH patients[11,12,18]. Based on this, we investigated the CSF flow dynamics in treated or untreated IIH patients at the aqueduct level by using the PCC MRI method. There were differences in the peak rate value between the IIH patient group and the control group, with a lower peak rate in the IIH patients. We did not find any significant differences between the patient and control groups for any of the other parameters.

Conclusions

We compared the PCC MRI parameters of the IIH patients who were recently diagnosed and who were untreated to those with improved symptoms after long-term treatment. We found a difference between the IIH groups and controls in terms of mean rate and flow with this comparison. This difference was due to a marked decrease in the mean rate and flow values in the patient group with improved symptoms following treatment compared to both the control group and the recently diagnosed untreated group. It is interesting to note that the mean rate and flow values of the untreated group were higher than those of the controls; however, this difference was not significant. All treated IIH patients in our study were using the carbonic anhydrase enzyme inhibitor acetazolamide as a medical treatment, and two patients were also using the anti-epileptic drug and weak carbonic anhydrase enzyme inhibitor topiramate in addition to acetazolamide treatment. The low rate and flow passing through the aqueduct in the patient group may be related to decreased CSF production following medical treatment. The peak rate, average rate, and average flow values were generally higher in males than in females in the IIH group; no such difference was found in the control group. This difference indicates a more aggressive course of the disorder in males in clinical practice.

As this study was conducted with a limited number of patients, further, larger-scale studies should be repeated in patients treated with the carbonic anhydrase enzyme inhibitor acetazolamide and other similar drugs. Overall, PCC-MRI may be a new marker for following IIH patients.

Conflict of Interest

The Authors declare that there are no conflicts of interests.

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