Clinical Imaging 40 (2016) 1286–1290

Contents lists available at ScienceDirect

Clinical Imaging

journal homepage: http://www.clinicalimaging.org

Original Article

Evaluation of aqueductal cerebrospinal fluid flow dynamics with phase-contrast cine magnetic resonance imaging in normal pediatric cases☆

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ARTICLE INFO

Article history:
Received 1 May 2016
Received in revised form 21 August 2016
Accepted 8 September 2016

Keywords:
Phase-contrast cine MRI
Cerebrospinal fluid
Normal pediatric cases
Cerebral aqueduct

ABSTRACT

Purpose: This study aimed to determine differences according to age groups and gender in the parameters of aqueductal cerebrospinal fluid (CSF) flow in childhood using phase-contrast cine magnetic resonance imaging (MRI) method.
Materials and methods: This prospective study included 47 boys and 36 girls for a total of 83 healthy children. The cases were divided into three groups depending on age as infants (1–12 months), children (12–120 months), and adolescents (120–204 months). To quantitatively evaluate CSF flow, images in the transverse plane were taken at the cerebral aqueduct level using the phase-contrast MR angiography technique in a 1.5-T MR unit. Peak and average velocity (cm/s), cranial direction, caudal direction and net volume (ml), and aqueduct area (mm^2) were calculated. To assess differences between the groups, a one-way analysis of variance and least significant difference tests were used.
Results: A statistically significant difference was determined between children and adolescents in peak velocity and caudal direction volume (P=.012 and P=.039, respectively) and between infants and children in cranial direction volume (P=.036). Peak velocity, cranial direction, and net volume were higher in boys (P=.050, P=.016, and P=.029, respectively). There were no differences by age and gender in the aqueduct area.
Conclusion: In conclusion, this study determined the normal values for the CSF flow parameters of velocity, volume, and aqueduct area using phase-contrast MRI in healthy children. Velocity and volume parameters varied according to age and sex and were not affected in the aqueductal area.

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1. Introduction

The evaluation of cerebrospinal fluid (CSF) flow physiology and pathology with cine phase-contrast magnetic resonance imaging (MRI) methods has become more widespread in recent years. Studies related to this method, which is extremely sensitive even in a very slow flow, have focused on structures such as the cerebral aqueduct, which shows the most regular course of the flow in addition to the spinal canal, the subarachnoid space, and the ventricular system [1–4]. Before beginning to define the flow on the aqueduct with numerical parameters, the normal flow patterns were first understood and then the changes in flow in different pathologies were examined. These pathologies included normal pressure hydrocephaly, idiopathic intracranial hypertension, Chiari malformation, and arachnoid cysts [5–8]. With an increase in neuroendoscopic procedures, clinical applications following surgery—such as the evaluation of CSF flow in the aqueduct after endoscopic aqueductoplasty or investigation of the patency of third ventriculostomies—have come into use [9–11]. To evaluate pathological CSF flow, it is necessary to know the normal data. To the best of our knowledge, there are very few insufficient studies that include normal aqueductal CSF flow data of a pediatric population [12–14].

The aim of this study was to determine the normal values of CSF flow dynamics with cine phase-contrast MRI and any differences according to the age group or gender.

2. Materials and method

2.1. Patients

This prospective study was conducted over a 12-month period. Approval for the study was granted by the Local Ethics Committee, and informed consent was obtained from each participant. The study

☆ Conflict of interest: The authors declare that they have no conflict of interest.

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http://dx.doi.org/10.1016/j.clinimag.2016.09.005
0899-7071/Published by Elsevier Inc.

included a total of 83 cases, comprising 47 (56.6%) males and 36 (43.4%) females, aged 5–204 months, who were free from neurologic disease and had no cerebrovascular risk factors, none of whom had any brain pathology or were using any medication. To reduce the movement artifact in children, 50 mg/kg chloral hydrate was administered orally to make them sleep. No sedative was used in older children who cooperated. All MRI examinations of the day, the same hour, were made in the morning. Phase-contrast MR images were of diagnostic quality in all cases, and no cases were excluded from this study. In the neonatal age group, MRI cases in which brain pathology was detected and continuous drug users were excluded from the study. The cases were separated into three age groups: infants (1–12 months, n=21, 25.3%), children (12–120 months, n=46, 55.4%), and adolescents (120–204 months, n=16, 19.3%). The mean age of each group was 9.6±2.1 months, 39±20 months, and 150.5±24 months.

2.2. MRI technique

The images were taken with a 1.5-T MR device (Siemens Somatom, Erlangen, Germany) using a standard head coil in a neutral position. Routine cranial, axial, and sagittal fast spin echo T2-weighted images were taken [repetition time (TR)/echo time (TE)/number of excitations (NEX)/flip angle (FA), 5540/97/2/150°; slice thickness, 5 mm; field of view (FOV), 250; matrix, 189×256]. Cardiac gating was applied to all cases with MR compatible electrodes (Kendall, Arbo, Tyco International, Neustadt, Germany). For each patient, taking the phase-contrast MRI lasted approximately 5 min, with sagittal, coronal, and axial T2-weighted advance images taken first from the midline. The rephase image, magnitude of complex difference, and directional phase difference images were obtained in the half axial plane with the cerebral aqueduct ampulla vertical over the sagittal plane. For the images in the axial plane, depending on the heartbeat, between 14 and 30 slices were obtained in the cardiac phase at TR: 31.25 ms, TE: 8.06 ms, slice thickness 5.5 mm, number of signal averages: 1, FOV: 16×10 cm, matrix 128×256, and a 10° deviation angle. Cardiac trigger finger plethysmography was applied prospectively. Flow sensitivity (velocity encoding) was determined as 20 cm/s [9,12].

2.3. Image analysis

The images obtained with FLASH through-plane and in-plane sequences were transferred to an ARGUS image analysis program on a Leonardo Workstation (Magnetom Avanto, Siemens), and phase, rephase, and magnitude images were obtained in the half axial and sagittal plane. The CSF flow was first evaluated visually in all cases. Whereas the flow within the cerebral aqueduct on phase and magnitude images was observed at a high signal on all slices, on phase images, the signal intensity of the flow was observed as high in the cranial direction and low in the caudal direction. The region of interest (ROI) measurement was performed by two researchers (A.S. and M.Ö. with 10 and 5 years of experience in pediatric neuroradiology) together, in all cases, until the optimum CSF velocity curve was obtained. The images were enlarged to provide an optimal view of the aqueduct ampulla. As the flow within the aqueduct and the contrast with surrounding brain tissue were more evident on phase and magnitude images, a circular ROI was placed separately on each slice in a manner not to overlap the aqueduct borders on one of each of these two series types (Fig. 1a and b). In this way, data tables and graphics were obtained, including all the flow values and the changes with time throughout the cardiac cycle of the CSF flow parameters. In the graphics, the section above the value of zero represents the flow toward the cranial direction, and the section below represents the caudal flow. A comparison was made between the three groups according to age and in all the age groups according to gender, peak and average velocity, cranial direction, caudal direction, and net volume with the aqueduct area.

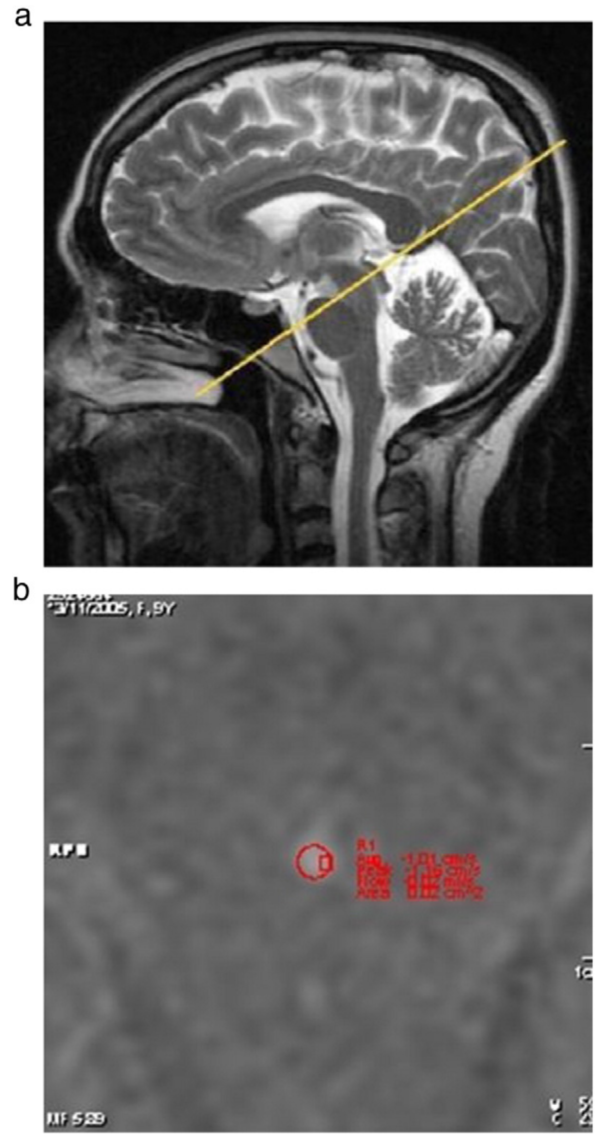

Fig. 1. (a) Midline sagittal T2-weighted image demonstrates the positions of the localizers for the velocity map at the level of the cerebral aqueduct. The yellow line indicates the position of the localizers of the oblique axial images set perpendicular to the aqueduct of Sylvius. (b) Axial phase-contrast MR images obtained at the levels of the cerebral aqueduct. Appropriate drawing of the ROI on the cerebral aqueduct.

2.4. Statistical analysis

Statistical evaluation was made with SPSS v. 13 software. To define the direction of negative rate values, absolute values were taken. Normal distribution was determined with the Shapiro–Wilk normality test. Evaluations between the groups were made with a one-way analysis of variance (P=.05) and the least significant difference test (P=.05).

3. Results

The values calculated for all the cases in all age groups for peak and mean velocity in cranial and caudal directions, net volume, and aqueduct area are shown in Table 1. A statistically significant difference was determined between children and adolescents in respect to peak velocity and caudal direction volume values (P=.012 and P=.039, respectively) and between infants and children in respect to cranial direction volume (P=.036). No statistically significant difference was determined between the groups in respect to average velocity, net volume, and aqueduct area values.

Table 1
The mean CSF flow parameter values according to age groups.

Group	Peak velocity (cm/s)	Average velocity (cm/s)	Cranial volume(ml)	Caudal volume (ml)	Net volume (ml)	Aqueductal area (mm^2)
Infants n=21	5.28±2.88	0.74±0.90	**0.01±0.008**[c]	0.012±0.021	0.005±0.005	1.9±1
Children n=46	**6.57±3.41**[a]	0.87±0.69	**0.02±0.013**[c]	**0.015±0.022**[b]	0.010±0.015	1.8±1.5
Adolescents n=16	**4.12±2.07**[a]	0.85±0.62	0.015±0.02	**0.008±0.013**[b]	0.007±0.008	1.8±1.5
Total N=83	5.77±3.18	0.83±0.73	0.015±0.014	0.013±0.02	0.008±0.013	1.8±0.9

[a] P=.012.
[b] P=.039.
[c] P=.012.

The values calculated for all the cases according to gender in respect to peak and mean velocity, cranial and caudal direction, net volume, and aqueduct area are shown in Table 2. The values of peak velocity, cranial direction, and net volume were found to be statistically significantly higher in boys than girls (P=.050, P=.016, and P=.029, respectively). No statistically significant difference was determined between the other flow parameters in respect to gender.

4. Discussion

In this study, the velocity, volume, and area parameters for CSF flow were measured using phase-contrast MRI in the pediatric age group, and significant results were obtained. The first is that the data obtained are important as they reflect the normal values for healthy children according to age group. The second is that, of these parameters, caudal direction volume varied according to age, net volume varied according to sex, and peak velocity and cranial direction volume varied with age and sex. The third conclusion is that no variation was observed in aqueduct area according to age and sex.

Demonstration of CSF flow dynamics is crucial especially in children who will undergo MRI since their evolving brain results in a changing volume of CSF in relation to the brain parenchyma. The absence of flow-void signal intensity on sagittal MR images may imply CSF pathway obstruction. Time spatial labeling inversion pulse (SLIP) is a noninvasive unenhanced direct visualization of CSF flow, and it can be beneficial for understanding CSF hydrodynamics, diagnosis, and treatment choice for patients with hydrocephalus. Time SLIP allows the labeling of a certain volume of CSF in any place in the central nervous system. The acquisition time to obtain a series of two-dimensional images is short, and repetitive studies can be performed to evaluate CSF movements under normal circumstances or in pathological conditions to observe the efficacy of a treatment modality. On the other hand, restrictions of this method include nonquantitative movement of CSF and limited ability for observing CSF flow with satisfactory contrast definition. This technique can be particularly useful for confirming if two CSF containing spaces are in communication, such as patients with syringomyelia associated with Chiari I malformation [15].

Phase-contrast can quantitatively evaluate the stroke volume in selected regions, particularly the aqueduct of Sylvius. Fine-tuning of the technique is essential to improve maximal temporal resolution since visualization of CSF motion is limited for many CNS regions. Phase-contrast is utilized for patients with suspected normal pressure hydrocephalus and a Chiari I malformation. Correlation with successful treatment outcome has been troublesome. Time–spatial labeling inversion pulse, with a high signal-to-noise ratio, assesses linear and turbulent motion of CSF for any location in the CNS. Time–spatial labeling inversion pulse can qualitatively visualize whether there is CSF flow between two compartments and determine whether flow occurs through the aqueduct of Sylvius or a new surgically created stoma. Cine images demonstrate linear and turbulent flow patterns of CSF [16].

Appropriate evaluation of CSF dynamics is crucial in disorders involving the intracranial hemodynamic/CSF regulatory system. Evaluation of CSF dynamics is crucial in disorders as hydrocephalus, hydrocephalus linked with achondroplasia, Chiari I malformation, confirmation of aqueductal stenosis and determination of the patency of a third ventriculostomy that are likely to interfere with the perfusion of the brain parenchyma and CSF dynamics [11,16]. Recent publications support that many pathological conditions such as cerebrospinal venous insufficiency, multiple sclerosis, leukoaraiosis, and vascular dementia are associated with alteration of CSF flow dynamics [16–21]. In these circumstances, reduction of the cerebrospinal blood flow is not uniformly necessary. Increased hydraulic resistance of the cerebral vascular bed and altered hydrodynamic features of periventricular veins may give rise to ischemia and plaque formation. Venous hypertension in the dural sinuses may adversely affect intracranial compliance. Evaluation of CSF dynamics by means of contemporary imaging modalities such as phase-contras-MRI and Time-SLIP may not only provide a better understanding of pathophysiological basis of these diseases, but new diagnostic and therapeutic implications can be possible [15,16].

Developments in phase-contrast MRI examinations have led to an increase in studies that quantitatively evaluate CSF flow. Several parameters are used in the examination of CSF flow dynamics, and these can be classified as velocity, volume, and aqueductal area. The cine phase-contrast MRI is a noninvasive test that takes less than 15 min to perform. It also does not require the use of X-rays, patient preparation, or contrast dye injections. The most significant disadvantage to using cine phase-contrast MRIs is the need to administer anesthesia when they are applied to young children. With age, two main changes can be observed in the physiology of CSF: reductions in the production of CSF and increases in resistance to CSF flow. It has been suggested that Alzheimer's disease develops when a decrease in CSF production is dominant, and normal pressure hydrocephaly develops when resistance to flow is dominant. However, the course of this disease increases the risk for others to form [22,23]. Currently, no existing studies have evaluated changes in CSF flow parameters caused by gender and aging in healthy children. As the first of its type to cover this topic, this study will prove to be an especially valuable reference for related studies that examine the various disease groups affected by CSF flow in children.

Various studies have reported different values related to cranial, caudal, and net volumes in adults. Lee et al. [24] reported a net volume

Table 2
The mean CSF flow parameter values of both sexes.

Sex	Peak velocity (cm/s)	Average velocity (cm/s)	Cranial volume (ml)	Caudal volume (ml)	Net volume (ml)	Aqueductal area (mm^2)
Boys n=47	**6.11±3.25**[a]	0.98±0.86	**0.018±0.016**[b]	0.014±0.022	**0.01±0.016**[c]	1.8±1
Girls n=36	**5.34±3.09**[a]	0.63±0.43	**0.011±0.009**[b]	0.01±0.019	**0.04±0.03**[c]	1.8±0.8
Total n=83	5.77±3.18	0.83±0.73	0.015±0.014	0.013±0.02	0.008±0.013	1.8±0.9

[a] P=.050.
[b] P=.016.
[c] P=.029.

of 0.03±0.01 ml, Brinkmann et al. [25] reported 0.04±0.02 ml, and Enzmann et al. [26] reported 0.06±0.034 ml. In studies by Schroeder et al. [9], cranial volume of 0.06 ml and caudal volume of 0.06–0.07 ml were reported, whereas Barhof et al. [5] found cranial volume to be 0.16±0.10 ml and caudal volume to be 0.29±0.19 ml. In a study by Unal et al. [12], which included an adolescent age group, the cranial, caudal, and net volumes were determined as 0.013±0.008, 0.022±0.011, and 0.008±0.005 ml, respectively, in the whole patient group and as 0.016±0.008, 0.026±0.012, and 0.010±0.007 ml, respectively, in the adolescent age group. No difference was found between the age groups in that study. In the current study, a statistically significantly higher value was found in the caudal volume of adolescents compared to children. In respect to cranial volume, the values of children were determined to be higher than those of infants. However, no statistically significant difference was found in net volume between the groups. These findings may have been due to physiological variations between age groups. It is noteworthy that there are a variety of physiological boundaries related to the parameters of velocity, flow, and time. These normally accepted variations are associated with many different factors, such as heart rate, respiration, jugular venous flow, the dimensions of blood vessels, systolic and diastolic blood pressure, compliance of surrounding brain tissue, and the anatomy and dimensions of CSF distances [27,28].

Unal et al. [12] reported cranial, caudal, and net volume values of 0.011±0.009, 0.019±0.010, and 0.007±0.004 ml, respectively, in males and 0.015±0.007, 0.023±0.014, and 0.010±0.008 ml, respectively, in females, with no difference determined according to gender. In the current study, the cranial, caudal, and net volume values were determined to be 0.018±0.016, 0.014±0.22, and 0.010±0.016 ml, respectively, in boys and 0.011±0.001, 0.011±0.018, and 0.004±0.003 ml, respectively, in girls. The cranial and net volume values were found to be higher in boys.

In studies related to adult peak velocity, different values have been reported varying from 1.5 to 12.7 cm/s related to physiological variation regardless of age [5,7,17,18]. In a study of adolescents by Unal et al. [12], peak velocity was found to be 7.89±2.57 cm/s, and mean velocity was 0.74±0.55 cm/s. Although these values are high compared to the adult group, no statistically significant difference was found. Iskandar et al. [13] reported measurements taken at the level of the foramen magnum in 10 pediatric cases aged 3–16 years as peak velocity varying from 2.2 to 19.9 cm/s and average velocity of 6.9 cm/s. Peak velocity was found to decrease with an increase in age. In the current study, the statistically significant difference in peak velocity between children and adolescents was consistent with the literature, which shows a decrease in peak velocity with increasing age. No difference was observed between the groups in respect to average velocity. Of these velocity parameters, peak velocity was found to be higher in boys than girls. Recent studies have revealed that CSF flow parameters can be used to diagnose and monitor responses to the treatment of normal pressure hydrocephaly and idiopathic intracranial hypertension in adults [8,29]. In this respect, the numerical values that have emerged may serve as vital references during the diagnoses and follow-up treatments of similar diseases that affect children.

Despite the current use of high-resolution imaging units, errors may occur in CSF flow rate data. Reasons for this include nonlinear gradients, eddy current, partial volume effect, and incorrect placement of ROI [30,31]. In addition, the difficulty of ROI placement in cases with a narrow aqueduct may result in errors. It has been reported that it is necessary to take the measurement on an area of 1.5 mm^2 over the aqueduct for a reliable measurement [25,32]. In studies by Unal et al. [12], the aqueduct areas were determined to be 2.33 mm^2 in adolescents and 2.67 mm^2 in all age groups, and no difference was determined according to gender. Similar to previous reports in the literature, in the current study, the aqueduct area values were between 1.71 and 1.89 mm^2, and no differences were determined according to age or gender. Although an aqueduct diameter can reveal different values depending on age and gender, as in cases where micro/macrocephaly and Chiari malformation are structurally affected, these values can also serve as valuable references for future clinical studies.

There are some limitations of our study. The first is that as measurements at the aqueduct level are technically difficult, the newborn age group was not included in the study. The second is that in the adolescent age group, the number of cases was slightly low. Finally, in cases with narrow aqueduct area, the error margin may increase due to difficulties locating the ROI.

In conclusion, the normal values for the CSF flow parameters of velocity, volume and aqueduct area using phase-contrast MRI in healthy children according to the age and gender groups were determined. Velocity and volume parameters varied according to age and sex. In clinical pathologies related with CSF flow, we consider our findings should take into account to evaluate the differences in these parameters.

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