Original Article Ann Med Res 2022;29(5):496–501

Ann Med Res

Current issue list available at AnnMedRes

Annals of Medical Research

journal page: www.annalsmedres.org

Predictive roles of interpeduncular and pontomesencephalic angle measurements, which are anatomical landmarks in cranial MRI, in the differential diagnosis of pediatric headache

Muhammet Bora Uzuner[a,*], Dondu Ulker Ustebay[b], Oguzhan Ozdemir[c]

[a] *Bandırma Onyedi Eylul University, Faculty of Medicine, Department of Anatomy, Balıkesir, Turkey*
[b] *Dokuz Eylul University, Faculty of Medicine, Department of Children Neurology, İzmir, Turkey*
[c] *Yuksek Ihtisas University, Faculty of Medicine, Department of Radiology, Ankara,Turkey*

ARTICLE INFO

Keywords:
Headache
Children
Cranial
Magnetic resonance imaging
Interpeduncular angle
Pontomesencephalic angle

Received: Sep 24, 2021
Accepted: Nov 02, 2021
Available Online: May XX, 2022

DOI:
10.5455/annalsmedres.2021.09.556

Abstract

Aim: This study aims to comparatively assess the interpeduncular and pontomesencephalic angles in the cranial magnetic resonance imaging (MRI) images of pediatric headache patients. Thus, we think that it will contribute to the studies to be conducted for the objective evaluation of pediatric headache requiring the use of cerebral MRI.

Materials and Methods: This retrospective study was performed using clinical and radiological data extracted from the medical files of 157 patients and 49 controls. Our population consisted of 101 females (49 %) and 105 males (51 %). The patient population was divided into 4 categories as follows: non-specific headache (thought to be of the tension-type), vasovagal syncope, sinusitis, and epilepsy. Interpeduncular (IP) and pontomesencephalic (PM) angles of patients and control groups were compared on MR images.

Results: The population average age in this series was 11.05 $\pm$ 3.78 (range, 5 to 17) years. The comparison of IP angleyielded statistically significant differences between tension-typeheadache-epilepsy, tension type-headache- vasovagal syncope, epilepsy-control, and vasovagal syncope-control groups. Multiple comparisons for PM angle demonstrated remarkable differences between headache-control, epilepsy-control, epilepsy-sinusitis, and control- vasovagal syncope groups.

Conclusion: Our results indicated that measurements of IP and PM angles on the cerebral MRI views of children whose etiology could not be clarified and for whom cranial imaging was required, may yield valuable data in the differential diagnosis. We are of the opinion that by working on larger data sets in the future, more valuable data can be obtained in differential diagnosis.

Introduction

Headache is a frequent complaint in the pediatric population. Due to the popularization and increased availability of brain imaging centers anda growing demand by patients for Computerized Tomography (CT) or Magnetic Resonance Imaging (MRI) studies, brain imaging is being extensively used in the evaluation of headaches, particularly in the clarification of the etiology of those patients who could not have been diagnosed clinically or by physical examination or who are thought to have an organic pathology. However, the value of brain imaging studies in the evaluation of headaches in children without clinical evidence of any underlying structural lesion was reported to be limited [1]. A recent publication indicated that migraine was the most common cause of headaches in children. The lack of any significant hallmarks and diagnostic tips on cerebral MRI images in children with headache constitutes an important challenge in these patients.

Recently, the interpeduncular angle (IPA) was reported as not only a specific, but also a sensitive measure of intracranial hypotension which may yield a reproducible parameter on routine clinical MRI in a reliable way [3]. The pontomesencephalic angle (PMA) is a quantitative metric defined on cerebral MRI views. When compared to the control group, it resulted to be significantly lower in patients who suffered from intracranial hypotension [4]. Even though neurological/physical examination may demonstrate abnormal findings in a considerable number

*Corresponding author:
Email address: borauzuner1@hotmail.com (Muhammet Bora Uzuner)

of pediatric patients with headache, the yield of pathological cerebral MRI seems to be low [5].

We aimed to investigate whether the use of quantitative metrics including IPA and PMA can be useful in the evaluation of children with headache caused by tension-type headache, vasovagal syncope, sinusitis and epilepsy. In this study, we aimed to contribute to the literature by revealing the effects of the angles used in cerebral MRI on headache in pediatric patients with different diagnoses.

Material and Methods

Study design

This retrospective case-control study was performed in the radiology, pediatrics and anatomy departments of our medicine faculty. Permission was obtained from the management of our hospital for the data used in the study. This study was approved by the non-invasive ethics committee with a protocol number of 80576354-050-99/350.

The history, physical examination, neurological and ophthalmological examination, laboratory and clinical investigations were performed on the records of 302 children who were admitted to our hospital between June 2013 and December 2019.Cranial magnetic resonance imaging (MRI) views of children with complaints of tension-type headache, headache accompanied by vasovagal syncope, headache caused bysinusitis and diagnosed epilepsy were retrospectively evaluated for the measurements of IPA and PMA. The medical files and radiological data were extracted from the hospital database. In the study, anatomical measurements were made in the hospital PACS system.

The studies of neuroimaging were conducted based on the recommendations of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society [6]. These included a recent onset of severe headache, changes in the pattern of headaches, abnormal findings of the neurologic examination, signs of increased intracranial pressure, changes in consciousness that could be considered significant, and coexistence of seizures [6].

The study population was comprised of 206 children (101 females, 105 males). The patients' group consisted of 157 children and these patients were categorized as follows: tension-type headache, headache accompanied by vasovagal syncope, headache caused by sinusitis and diagnosed epilepsy. On the other hand, there were 49 children in the control group.

The control group was selected from healthy individuals who applied to our hospital for any reason and underwent cranial imaging but no pathology was detected.

Patients diagnosed with vasovagal syncope were selected among those patients who apart fromshowing some characteristic clinical complaints related to this condition (such as sudden postural changes, staying for a long time on foot, anger, pain, fear and similar triggering conditions),also had a headache and were required to have the cranial MRI. The reason why cranialMRI was required for patients in this group consists in the families' concern that children might have a serious neurological disease andthat doctors who would firstly examine these children might not be able to diagnose a disease that couldbe significant.In addition, patients with a history of syncope lasting more than 2 minutes, unlike expected, and patients with transient focal neurological deficit after fainting were included in the study.

Patients who were diagnosed with generalized tonic chronic epilepsy, and thosewhose headache causes could not be found in their medical history, physical examination and laboratory results were required to have the MRI examination due to suspected cranial pathologies and the epilepsy group was formed by selecting those MRI images where no pathologies were determined. The nonspecific headache group consisted of patients diagnosed with tension headache after their medical history, physical examination and laboratory results had been checked. In this group, cranial MRI was required from those patients whose parents had explicitly requested to due to a need for assurance and who had come to the polyclinic more than three times per month because of thetension-type headache. Inthe patients of this group the headache locations were as follows: in 31 of the patients it was located in the frontal lobe, in 14 of them it was located in the bilateral temporal lobe, in 6 of them it was located in the unilateral temporal lobe, in 19 of them in the occipital lobe, in 5 of them in the vertex and in 7 of them it varied.

The other group was composed of patients who had come to the polyclinic, were diagnosed with sinusitis and for whom no other pathology was defined. It was regarded that all patients in this group were diagnosed with recurrent-chronic sinusitis. In 9 of the patients who were diagnosed with chronic sinusitis, the existence of sinusoidal anomaly was seen (4 sinus cists, 1 hypoplasticsinus, 3 septum deviations, 1 concha hypertrophy). It was regarded that the reason for the cranial imaging was due to detecting any probable additional cranial pathology retraction and sinusoidal pathology.

Interpeduncular and pontomesencephalic angle measurements obtained with the PACS system in the patient groups were compared with the control group.Based on the exclusion criteria, patients older than 18 years of age and those suffering from tumor, subdural empyema, hydrocephalus and congenital Chiari malformation were not included in the groups. After being selected from the same period, age-matched controls underwent MRI for the assessment of nonspecific symptoms.

Following the routine examinations after the initial assessment during the first month, patients were then reviewed every three months and additionally in clinically necessary cases when neurologic symptoms became present, such as a change in the frequency, character or severity of the headache. The patients' diagnosis of sinusitis was determined after their evaluation by an otolaryngologist.

MRI acquisition and evaluation

A 1.5-T MRI device (Siemens MagnetomEssenza; Siemens; Erlangen, Germany) was used to perform the cerebral MRI studies. Quadrature coils were used to obtain cerebral MRI images. The scanning sequence contained Sagittal T1WI (TE (time of echo) 7.8 – 8.5 ms, TR (time of repetition) 450–2000 ms, slice thickness 8 mm), T2WI (TE 92–98 ms, TR 3800– 6000 ms), T1WI (TE 7.5–8.5 ms, TR 400–6000 ms, slice thickness 5 mm), FLAIR (TE 794–109 ms, TR 8500–9000 ms, slice thickness 5 mm), and DWI (TE 75–86 ms, TR 3100–6400 ms, slice thickness 5 mm). Furthermore, the enhancement scanning (contrast agent Gd-DTPA (0.1mmol/kg was applied and following the injection, the scanning of the axial, sagittal and coronal positions took place. Each of the MRI images was read by 2 consultant radiologists with 10 years of experience in neuroradiology and MRI. In case of differing decisions, the MRI scans were reviewed by another senior neuroradiologist with more than 20 years of experience, who could then make a final decision.

Measurement of interpeduncular angle and pontomesencephalic angle

The IPA and PMA were measured by an anatomist and a radiologist, and the average of their measurements was calculated as the true value. For the accuracy of the measurements, statistical accuracy analyzes between measurements and researchers were performed by each researcher.

Based on the median saggital plane, pontomesencephalic angle was defined as the angle between the tangent line of superior border of pons and the leading edge tangent line of the midbrain (Fig.1) [7]. The results show the average of their measurements.

The interpeduncular angle was defined at the level of the mammillary bodies as the angle formed by the posterior half of the cerebral peduncles, based on an axial T2-weighted image (Fig.2) [3].

Outcome measures

The diagnoses of headache were based on the criteria published in the third edition of the International Classi[FB01?]cation of Headache Disorder (ICHD-II) [8].

The baseline descriptions such as sex and age were categorical variables while IPA and PMA were the quantitative variables under investigation.

Statistical analysis

All of the statistical data were analyzed with Statistical Package for Social Sciences 25.0 for Windows software (SPSS Inc., Chicago, Illinois, USA). The normality was tested for IPA and PMA variables. We noted that IPA variable did not display normal distribution. Kruskal-Wallis test was used to compare IPA values between groups. One-way ANOVA test was utilized for PMA, which exhibited normal distribution between groups.

The comparison of IPA values demonstrated significant differences between groups ($x{=}13{,}656 p < 0{,}05$). The comparative analysis between subgroups was performed with Mann-Whitney U test.

The variance homogeneity test indicated that the variance of PMA values was different in various subgroups ($F(4,201) = 2{,}598$; $p < 0{,}05$). Therefore, Tamhane test (post-hoc) was used to compare PMA values. A $p < 0.05$ was considered as statistically significant.

Figure 1. Shows pontomesencephalic angle (PMA) measurement

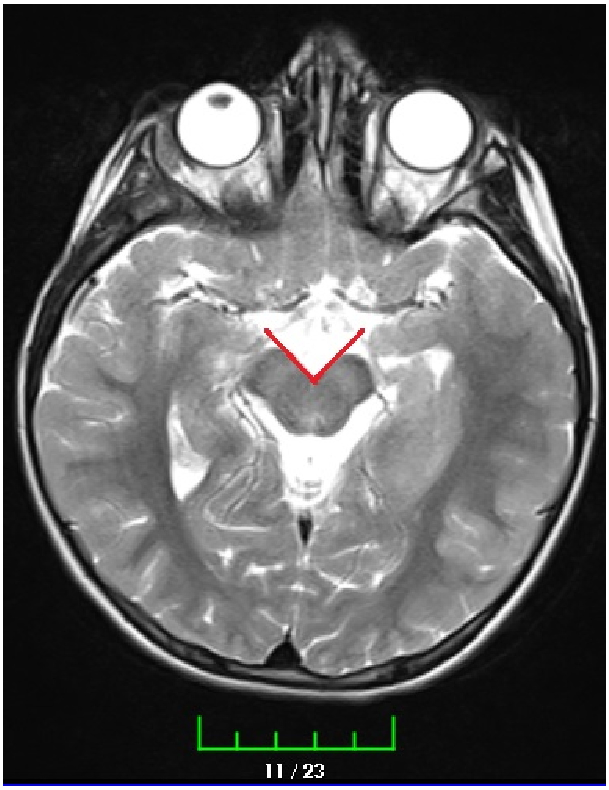

Figure 2. Shows interpedinculer angle measurement

Table 1. The interpeduncularangle (IPA) measurementsbetween 5 groups.

Variable	Groups	n	Mean rank
IPA	Control	49	88.80
	Epilepsy	35	126.83
	Headache	82	96.01
	Syncope	19	130.84
	Sinusitis	21	103.43
	Total	206	

Table 2. Thecomparison of IPA values yielded statistically significant differences between headache-epilepsy, headache-syncope, epilepsy-control, andsyncope-controlgroups.

	n	Mean rank	Total rank	Mann-Whitney U	Asymptotoic p-value(two-tailed)
Headache	82	54.17	4442.00	1039.000	0.018
Epilepsy	35	70.31	2461.00		
Total	117				
Headache	82	47.90	3928.00	525.000	0.027
Syncope	19	64.37	1223.00		
Total	101				
Epilepsy	35	51.63	1807.00	538.000	0.004
Control	49	35.98	1763.00		
Total	84				
Control	49	30.17	1478.50	253.500	0.004
Syncope	19	45.66	867.50		
Total	68				

Table 3. The pontomesencephalic angle (PMA) measurements between 5 groups.

Group	n	(Mean ±S td	Standard Error
Headache	82	67.83± 10.022	1.107
Epilepsy	35	72.00± 9.068	1.533
Control	49	63.00± 6.107	.872
Syncope	19	70.26± 7.943	1.822
Sinusitis	21	64.71± 7.383	1.611
Total	206	67.30± 9.095	.634

Results

The average age in this series was 11.05 ± 3.78 (range, 5 to 17) years. Our population consisted of 101 females (49 %) and 105 males (51 %). Three age groups comprised as follows: 5-9 years (n = 74, 35.9 %), 10-14 (n = 81, 39.3 %), and ≥ 15 (n = 51, 24.8 %).

There was no difference between groups in terms of sex distribution ([AB53?]2 = 4,413; p = 0.353). On the other hand, there was a statistically significant difference between 5 groups as for the distribution of age groups ([AB53?]2 = 33, 191; p < 0.001).

The average values for IPA and PMA in our series were 62.40 ± 9.21 (range, 43 to 88) and 67.30 ± 9.10 (range, 44 to 96), respectively.

We observed that there was a remarkable difference between 5 groups in terms of IPA ([AB53?]2 = 13.656; p = 0.008). Table 1 demonstrates the mean rank values of IPA in 5 groups and Table 2 demonstrates the comparative analysis between groups for IPA values.

Post hoc Tamhane test demonstrated that there were significant differences between groups with respect to PMA values (F = 6.755; p < 0.001). Table 3 displays the average values for PMA measurements in 5 groups under investigation.

Multiple comparisons carried out between 5 groups in terms of PMAs demonstrated that there were remarkable differences between headache-control, epilepsy-control, control-syncope groups and epilepsy-sinusitis (Table 4).

Considering the consistency of the measurements made by each researcher, no significant difference was observed for both researchers (p > 0.05). While the consistency between the measurements made by the general researcher himself was 88% and 91% for researcher 1, the consistency was determined as 90% and 92% for researcher 2. It was determined that all measurements were highly consistent for the two researchers and there was no significant difference in both measurements of the researchers (p > 0.05). Considering the consistency of the measurements between researchers; It was observed that the reliability of intraclass correlation coefficient values between investigator 1 and investigator 2 measurements varied between 0.844 and 0.889. These values were found in the confidence interval. There was no statistically significant difference between the measurements of the researchers (p > 0.005).

Discussion

The differential diagnosis of headaches is important because a misdiagnosis may lead to dire consequences for the patient. The main findings in this study were that both IPA and PMA display significant differences between various pediatric patients suffering from headache. Especially in patients with non-specific headache, these quantitative metric measures may provide useful data in the differential diagnosis. We think that the associations between IPA, PMA and headache types must be taken into account during diagnostic work-up. In other words, IPA and PMA may serve as quick and reproducible markers in the diagnosis of headache types in the pediatric population. Not only the choice but also the appropriate interpretation of

Table 4. Multiple comparisons between groups for pontomesencephalic angle (PMA) demonstrated remarkable differences between headache-control, epilepsy-control, epilepsy-sinusitis and control-syncope groups.

Groups	Groups	MeanDifference (I-J)	Std. Error	Sig.	95% ConfidenceInterval	
					LowerBound	UpperBound
Headache	Control	4.829*	1.409	.008	.82	8.84
Epilepsy	Control	9.000*	1.764	.000	3.86	14.14
Epilepsy	Sinusitis	7.286*	2.224	.019	.77	13.80
Syncope	Control	-7.263*	2.020	.013	-13.43	-1.10

* Themeandifference is significant at the 0.05 level.

the imaging modality is critical to set the diagnosis and initiate the treatment without delay.

Previous publications suggest that headaches can be accompanied by structural alterations in the brain. These data remind us of the importance of discrimination between headache subtypes and evaluate the MRI images with respect to important hallmarks [9].

Rather than by any tests or imaging modalities, headaches, which occur often in children, are diagnosed on a clinical basis. These clinical entities constitute diagnostic and therapeutic challenges for both the radiologist and the clinician. Current guidelines suggest thatin children with repeated headaches and those with a normal neurologic examination, the obtainment of a neuroimaging study on a routine basis is not indicated [5]. Nevertheless, in order to exclude an intracranial pathology, as well as for parental reassurance, cerebral CT scans or MRI studies are frequently used in clinical practice. In many cases, no noteworthy relationship could be established between the abnormality detected in neuroimaging and age and sex of children, type of the headache, headache starting age, duration, frequency, location, and intensity. With respect to these results, the use of stricter guidelines for the rational utility of neuroimaging is required in pediatric headache patients. The current practice principles recommend the use of neuroimaging in those children who show abnormal results of neurologic examination or in cases when other physical findings suggest the existence of a disease in the central nervous system [5].

Due to a number of clinical and practical considerations, the primary investigation mostly used to confirm the diagnosis and exclude other entities, is the contrast-enhanced MR imaging of the head [3]. In a recent publication, MRI findings demonstrated typical features of the intracranial hypotensive syndrome (IHS). It was also maintained in the publication that in order to clinically diagnose the subjective findings of IHS, the quantitative indicators including mamillopontine distance and PMA were useful [7].

Practicality is the biggest advantage of the IPA, in addition to its high sensitivity and specificity. While most reported measures rely on the sagittal plane, the evaluation of the IPA on a standard T2-weighted axial image implies that it is smoothly incorporated into a routine search pattern [3]. Moreover, considering that the anatomic landmarks used to make the measurements of IPA and PMA are well-known, no further reference lines are necessitated for the measurement. Apparently, its characteristic of being simple contributes to its high ability of being reproduced.

It must be remembered that all abnormalities may not be necessarily related to the presented complaint [1]. These data are also supported by another publication, where it is maintained that roughly 20% of pediatric headache patients who underwent brain imaging showed benign abnormalities, which did not cause any difference in the headache management [10].

In the future, it will be important to better define those patients likely to have an intracranial pathology and candidates who are more likely to benefit from early imaging studies.

This study has several strengths. To the best of our knowledge, this is the first study focusing on the significance of IPA and PMA in pediatric headache patients. Besides, the separate analysis of different categories allowed the performance of multiple comparisons. The selection of controls randomly from the same population as the cases was considered to be the best method [11].

Conclusion

In conclusion, development of better MRI technology accompanied with exploration of useful quantitative metric measures can be helpful in understanding the headache pathophysiology and may provide establishment of more effective strategies in the differential diagnosis of pediatric headaches. More attention and effort should be paid to the MRI demonstration of possible causes and co-existent pathologies.

Limitation

Our preliminary findings in our study need to be confirmed and validated by more multicenter trials on larger series. This study has some weaknesses such as retrospective design, relatively small sample size and limited data from single center experience, and possible effects of genetic and ethnic factors.

References

1. Maytal J, Bienkowski RS, Patel M, Eviatar L.The value of brain imaging in children with headaches. Pediatrics 1995;96:413-416
2. Yılmaz Ü, Çeleğen M, Yılmaz TS, Gürçınar M, Ünalp A. Childhood headaches and brain magnetic resonance imaging findings. Eur J PaediatrNeurol2014;18:163-170
3. Wang DJ, Pandey SK, Lee DH, Sharma M () Theinterpeduncular angle: a practical and objective marker for the detection and diagnosis of intracranial hypotension on brain MRI. AJNR Am J Neuroradiol.2019;40:1299-1303

4. Aslan K, Gunbey HP, Tomak L, Ozmen Z, Incesu L Magnetic Resonance Imaging of Intracranial Hypotension: Diagnostic Value of Combined Qualitative Signs and Quantitative Metrics. J Comput Assist Tomogr2018;42:92-99
5. Martens D, Oster I, Gottschlling S, Papanagiotou P, Ziegler K, Eymann R, et al.Cerebral MRI and EEG studies in the initial management of pediatric headaches. Swiss Med Wkly2012;142:w13625
6. Lewis DW, Ashwal S, Dahl G, Dorbad D, Hirtz D, Prensky A, etal.Practice parameter: evaluation of children and adolescents with recurrent headaches: report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. Neurology 2002;59:490-498
7. Tian W, Zhang J, Chen J, Liu Y, Chen X, Wang N.A quantitative study of intracranial hypotensive syndrome by magnetic resonance. ClinNeurolNeurosurg2016;141:71-76
8. Headache Classification Committee of the International Headache Society (IHS) The International Classification of Headache Disorders, 3rd edition. Cephalalgia2018;38:1-211
9. Honningsvåg LM, Håberg AK, Hagen K, Kvistad KA, Stovner LJ, LindeM.White matter hyperintensities and headache: A population-based imaging study (HUNT MRI). Cephalalgia2018;38:1927-1939
10. Schwedt TJ, Guo Y, RothnerAD."Benign" imaging abnormalities in children and adolescents with headache. Headache 2006;46:387–398
11. Nishioka SA, Gyorkos TW, Joseph L, Collet JP.Selection of subjects for hospital-based epidemiologic studies based on outward manifestations of disease. Clin Invest Med 2001;24: 299–303