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Unexpected inconsistency of cranial MRI and cranial US measurements: new normative values in the neonatal period

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Cranial ultrasonography (US) enables differentiation of normal from abnormal in a reasonable scanning time and without radiation. However, there is not enough data comparing measurements of cranial US and magnetic resonance imaging (MRI) for some intracranial structures in the neonatal period. We aimed to assess the reliability of cranial US compared with brain MRI. We also sought reference values of the pituitary gland and infundibulum, which is important in searching for growth retardation or abnormal growth in this population. Normative measurements of the width of the 4th, 3rd and lateral ventricles, length and width of the corpus callosum (CC), biventricular width (BVW), and biparietal diameter (BPD) were prospectively obtained from 95 healthy full-term neonates on both cranial US and brain MRI. Besides the well-known structures, the height of the pituitary gland, thickness of the infundibulum, height and width of the cerebellum were measured on MRI. Comparison of cranial US and brain MRI showed good correlation in the BPD, width of the splenium and genu of CC, anteroposterior length of CC, and width of the 3rd ventricle (κ=0.88-0.99). Correlation was poor in BVW, width of the corpus of CC, and width of the lateral ventricles (κ=0.28-0.56). New normative values of the height of pituitary gland and thickness of the stalk in the neonatal period are novel findings of this prospective study. In conclusion, cranial US and MRI measurements were not consistent in some brain structures. It is crucial to know the normative values, and to differentiate congenital and developmental brain anomalies in the neonatal period. The new reference values of the pituitary gland and infundibulum were also established in this period.

Key words: MAGNETIC RESONANCE IMAGING; INFANT, NEWBORN; PEDIATRICS; ULTRASONOGRAPHY

INTRODUCTION

Evaluation of the cerebral structure and size in the full-term neonatal brain has clinical importance. In this context, the primary non-invasive and safe method is cranial ultrasonography (US) for early diagnosis of brain injury. Although it is being used as a screening test in some medical centers (1-4), cranial US has some limitations, such as the quality of the images that depends on the skill and experience of the operator. Besides this, some areas of the brain are difficult to visualise by this technique (1-3,7-9). In the literature, most studies defined techniques for obtaining measurements, and give reference values for various cerebral structures (5-9).

It is usually believed that the measurements performed by cranial US are consistent with those obtained by magnetic resonance imaging (MRI), but very few studies have compared cranial US to MRI (8, 9). In the literature, significant differences between cranial US and MRI measurements were found for the ventricular index, depth of the posterior horn of the lateral ventricle, depth of the extracerebral space, and depth of the cortex along the cingulate gyrus (5, 10, 11). However, cranial US is still going to be the first diagnostic tool to evaluate neonatal brain. In this period, incon-

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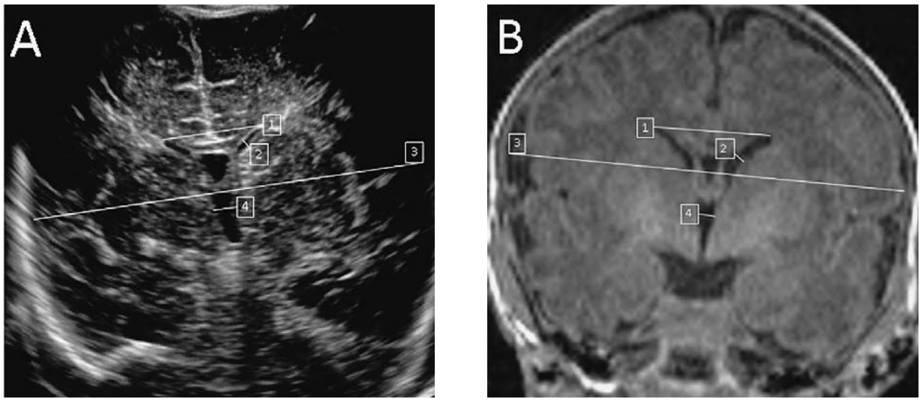

FIGURE 1. Measurement of the biventricular width (A, B-1), lateral ventricle (A, B-2), biparietal diameter (A, B-3), width of the 3rd ventricle (A, B-4) in the mid-coronal plane where the lateral and third ventricles were both seen on both coronal US (A) and MRI (B).

sistency with normative values, as well as variational or borderline morphological findings that draw attention during screening will play an important role in final decision or follow-up. Also, normal values of the pituitary gland and pituitary stalk are important in paediatric population when searching for growth retardation or abnormal growth.

In this study, we aimed to explore consistency of linear measurements of different cerebral structures on US and MRI in the neonatal period. We also obtained new normative values of some cerebral structures in neonates.

PATIENTS AND METHODS

This prospective study was approved by the Institutional Review Board (KA 15/47). Informed consent was obtained from parents. Between October 2014 and May 2016, healthy full-term neonates participated in this study. The indications for cranial US and brain MRI in the neonates were prolonged jaundice, minor trauma, and prolonged birth. The healthy neonates were first evaluated with US, at the age of one to fourteen days, then brain MRI was performed within two days. One hundred and six neonates were evaluated on both US and MRI. Exclusion criteria were the presence of any intracranial pathology (congenital anomaly, intracranial bleeding, ventricular irregularity, periventricular and subependymal echogenicity, ventriculomegaly, hydrocephalus, benign intracranial mass, etc.), and artifacts that reduced the quality of US and MRI images. According to the exclusion criteria, three neonates with periventricular and subependymal echogenicity, four neonates with reduced image quality, two neonates with mild ventriculomegaly, and two neonates with arachnoid cyst were excluded from the study. Finally, 95 healthy full-term neonates were included in this study. None of the subjects received sedation or contrast media. Perinatal clinical details were obtained from the hospital computerized database, and all neonates had normal physical and neurological examinations.

Ultrasonography

Ultrasonography scans were performed by using 4-9 MHz and 2.9-8 MHz transducers (Siemens Acuson Antares, Erlangen, Germany), through the anterior fontanel, and standard views were obtained in coronal and sagittal planes, and saved in the picture archiving and communication systems (PACS). The measurement of brain structures was performed by a neuroradiologist with 9 year of experience (G.C.).

Magnetic resonance imaging

Magnetic resonance imaging was performed by the standard protocol using a 1.5 T (Symphony vision, Siemens, Erlangen, Germany) machine. Measurements were obtained by G.C. too. The images were evaluated from the coronal fluid attenuated inversion recovery (FLAIR), sagittal T2-weighted, axial T1-weighted magnetization prepared rapid acquisition gradient echo (MPRAGE), axial T2-weighted, and diffusion-weighted sequences.

Linear measurements were obtained by using T1-weighted MPRAGE images (3D volume scans), which can be reconstructed in any plane and are more sensitive for accurate structural measures similar to US.

Both US and MRI measurements were obtained at the following sites:

- lateral ventricles (LV; width of the anterior horn of the right (R)/left (L) ventricles, and biventricular width (BVW), width of the 3rd ventricle, in the mid-coronal plane where the lateral and third ventricles were both seen (Figure 1);
- corpus callosum (CC), anteroposterior (AP) length and width of the genu, corpus, and splenium in mid-sagittal plane (Figure 2); and
- biparietal diameter (BPD in the mid-coronal plane, where the lateral and third ventricles were both seen (Figure 1).

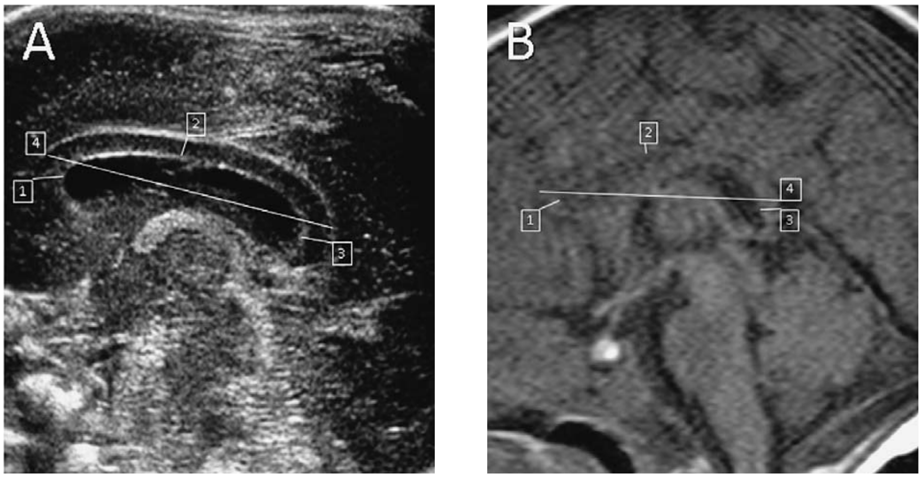

FIGURE 2. Measurement of the width of the genu (A, B-1), corpus (A, B-2) and splenium (A, B-3), and anteroposterior (AP) length (A, B-4) of the corpus callosum (CC) in the mid-sagittal plane on both coronal US (A) and MRI (B).

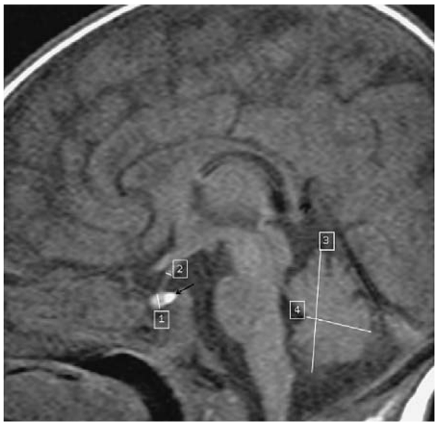

FIGURE 3. Measurement of the height of the pituitary gland (1), the expected high signal intensity of neurohypophysis (black arrow), AP thickness of the infundibulum (2), height (3) and AP width (4) of the cerebellum in the mid-sagittal plane on MRI.

Isolated MRI measurements were obtained at the following sites:

- pituitary gland (PG; height of the pituitary gland, expected high signal intensity of neurohypophysis, AP thickness of the infundibulum in mid-sagittal plane (Figure 3);
- cerebellum (height and width of the cerebellum in mid-sagittal plane (Figure 3); and
- fourth ventricle (FV; lateral and AP width of FV).

For each anatomical structure, at least three measurements were obtained, and the mean value was noted. Furthermore, the expected high signal intensity of neurohypophysis was evaluated on the sagittal T1-weighted plane.

Statistical analysis

Categorical variables (age and sex) were compared between the groups using the χ^2-test. Quantitative variables were tested for normal distribution with Kolmogorov Smirnov test. Descriptive statistics were expressed as mean ± standard deviation if variables were normally distributed, or median (minimum-maximum) if variables did not show normal distribution. Independent samples t-test was used for normally distributed items.

Kappa (κ) analysis was used to assess the agreement of measurements obtained on US *versus* MRI. In terms of agreement, the kappa value was interpreted as poor (<0.20), fair (0.21-0.40), moderate (0.41-0.60), good (0.61-0.80), or very good (0.81-1.00). Confidence intervals (95% CI) of the kappa values were used to find possible non-overlapping intervals.

All analyses were performed using IBM SPSS Statistics 23.0 software and the R 3.6.3 program. A p value <0.05 was considered statistically significant.

RESULTS

The mean gestational age of the neonates (65 females and 30 males) was 38 weeks. None had pathology on US and MRI. The mean time interval of US and MRI was four and 15 days, respectively. The mean value of the structures on US and MRI, and the agreement of measurements of US *versus* MRI are shown in Table 1.

The mean value of BPD, width of the splenium and the genu of the CC, AP length of CC, and width of the 3rd ventricle obtained on US were highly correlated with those obtained on MRI (κ=0.88-0.99). Although the mean values showed overlapping, the correlation was poor in the width of the corpus of CC, BVW, and width of both R/L lateral ventricles (κ=0.28-0.56).

The measurements of deeper structures such as the cerebellum, pituitary gland, infundibulum, and 4th ventricle

TABLE 1. Mean values of some intracranial structures on both US and MRI, and US *versus* MRI agreement

Intracranial structure	Mean (mm)	SD (±)	κ*	Confidence interval
BPD US MRI	 87.7 86.9	 4.9 4.4	0.96	0.941-0.985
CC AP US MRI	 50.3 51.4	 4.4 5.0	0.91	0.889-0.932
CC corpus US MRI	 50.3 43.55	 0.6 0.9	0.45	0.352-0.558
CC genu US MRI	29.2 29.1	0.3 0.4	0.97	0.961-0.993
CC splenium US MRI	 43.8 43.5	 0.6 0.8	0.94	0.890-0.989
R LV width US MRI	 1.78 1.53	 0.7 0.7	0.46	0.360-0.562
L LV width US MRI	1.85 1.60	0.7 0.7	0.46	0.359-0.564
Biventricular width US MRI	 24.6 22.2	 2.5 3.0	0.33	0.280-0.400
3. ventricle width US MRI	 2.3 2.3	 0.5 0.6	0.97	0.952-0.990

*kappa analysis; SD = standard deviation; US = ultrasonography; MRI = magnetic resonance imaging; BPD = biparietal diameter; CC = corpus callosum; AP = anteroposterior; R = right; L = left; LV = lateral ventricle

TABLE 2. Mean values of the cerebellum, pituitary gland, infundibulum and 4th ventricle on MRI

Intracranial structure	N (MRI)	Mean (mm)	SD (±, mm)
LT width of FV	95	7.92	0.09
AP width of FV	95	5	0.07
Height of PG	95	3.8	0.05
AP thickness of infundibulum	95	1.3	0.01
Height of cerebellum	95	47.4	9.3
Width of cerebellum	95	21.8	6.2

MRI = magnetic resonance imaging; SD = standard deviation; LT = lateral; AP = anteroposterior; FV = fourth ventricle; PG = pituitary gland

could not be applied on US to all patients due to movement artifacts and resolution problems. The measurements of these structures were performed on MRI solely. The mean values of MRI measurements for the cerebellum, pituitary gland, infundibulum, and 4th ventricle are shown in Table 2. In addition, in only one case (1.05%), we could not see the expected high signal intensity of neurohypophysis on T1 weighted image.

DISCUSSION

Comparison of cranial US and brain MRI showed good correlation in the BPD, width of the splenium and genu of the CC, AP length of CC, and width of the 3rd ventricle (κ=0.88-0.99). Similar to recent studies (7-9), we found that measurements performed on US and MRI had good correlation in most intracranial structures (width of the splenium and genu of CC, width of the 3rd ventricle, BPD, and AP length of CC), however, there was poor correlation in the width of the corpus of CC, BVW, and width of both R/L lateral ventricles (κ=0.28-0.56). Nevertheless, previous studies showed that the diagnostic ability of cranial US was comparable to that of brain MRI and suggested its clinical use in various diseases (6-13).

In the literature, low BPD values have been shown to be associated with regression in neurodevelopmental stages (14). Besides this, some congenital brain malformations manifest after the neonatal period, especially those that can create late onset cognitive effects and movement disorders (e.g., Arnold Chiari syndrome, Dandy Walker malformations, Joubert syndrome) (15). Hence, it is important to know normal values of the brain structures in different imaging modalities to distinguish the normal/variation from abnormal, especially considering brain malformations in the neonatal period.

In clinical practice, ventricular index (VI) is being used to diagnose ventriculomegaly (10). The mean value of VI is 9-11 mm in the literature (9, 11). Unfortunately, it is a very rough marker of ventriculomegaly, and varies greatly depending on the location and angle of the slice (16). As distinct from the literature, we measured BVW instead of VI. In our study, the mean value of BVW was 22.6±2.5 mm on US and 24.2±3 mm on MRI. Additionally, the mean BVW to BPD ratio was 0.25 on US and 0.27 on MRI. The mean BVW/BPD ratio obtained might be an appropriate ratio for hydrocephalus evaluation on US.

Furthermore, we evaluated the width of the fourth ventricle (lateral and AP), height of the pituitary gland, thickness of the infundibulum, height and width of the cerebellum on MRI solely. The mean values of the width of the fourth ventricle (lateral and AP), and height and width of the cerebellum are similar in the literature (7, 9). Those normal values of the posterior fossa structures are important in cases suspicious of movement disorders and developmental delay in the early years of life (17, 18).

Normal values of the pituitary gland and pituitary stalk are important in paediatric population when searching for growth retardation or abnormal growth. The incidence of neonatal hypopituitarism is 1/4,000-10,000 in this period. In neonates with suspected congenital hypopituitarism, brain and hypophysis MRI is highly recommended to exclude structural abnormalities. The severity of hypopituitarism will be proportional to the neuroimaging findings (19). Pituitary gland height, neurohypophysis brightness or ectopia, an undescended posterior lobe, and infundibulum morphology should be assessed with neuroimaging (20). This study presents the first quantitative analysis of the pituitary gland and infundibulum in the neonatal period. In our study, the mean height of the gland was 3.8 mm, and the mean AP thickness of the pituitary stalk was 1.3 mm. In the study by *Satogami et al.* (21), the mean AP thickness of the pituitary stalk was 2.3 mm, however, this study was based on adult population. In the literature, there are several studies of age-related changes in the height of the pituitary gland (19, 20). To our knowledge, the present study represents the largest population of the neonatal period.

The expected high signal intensity of neurohypophysis was evaluated on the sagittal T1 weighted plane. Only in one case, we could not see the expected high signal intensity of neurohypophysis on T1 weighted image, without ectopy. The high signal intensity reflects healthy storage of vasopressin, and distinguishes ectopic neurohypophysis, central diabetes insipidus, and rare infundibulum-neurohypophyseal system tumours such as Langerhans cell histiocytosis (22).

Our study had several limitations. First, our patient population reflected a certain region. Also, we could not correlate the cerebellum and 4th ventricle values on both cranial US and brain MRI because of insufficient resolution of the US in deep structures.

CONCLUSION

Contrary to what is known, comparison of the US and MRI measurements showed them to be inconsistent within some brain structures. Hence, the robust technique seems to be MRI with high tissue contrast. Briefly, knowing normal limitations will shed light on the early diagnosis of the underlying pathology, if any, as well as following the variational neurological developmental delay.

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SAŽETAK

Neočekivana nedosljednost mjerenja lubanje magnetskom rezonancijom i ultrazvukom: nove normativne vrijednosti u novorođenčadi

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Ultrazvuk (UZV) lubanje omogućava razlikovanje normalnog od nenormalnog u razumnom vremenu snimanja i bez zračenja. Međutim, nema dovoljno podataka o usporedbi mjerenja provedenih pomoću UZV-a glave i magnetskom rezonancom (MR) mozga za neke intrakranijske strukture u novorođenčadi. Cilj studije bio je procijeniti pouzdanost UZV glave u usporedbi s MR-om mozga. Također smo tražili referentne vrijednosti za hipofizu i infundibulum, što je važno kad se procjenjuje postoji li zaostajanje u rastu ili nenormalan rast u ovoj populaciji. Normativna mjerenja širine 4. i 3. lateralnog ventrikula, dužina i širina korpusa kalozuma (CC), biventrikulska širina (BVW) i biparijetalni promjer (BPD) prospektivno su bilježeni u 95-ero zdrave terminske novorođenčadi na UZV-u glave i MR-u mozga. Uz te poznate strukture, na MR-u smo također mjerili visinu hipofize, debljinu infundibuluma, visinu i širinu cerebeluma. Usporedba UZV-a lubanje i MR-a mozga pokazala je dobru korelaciju za BPD, širinu splenija i koljena CC-a, anteroposteriornu dužinu CC-a i širinu 3. ventrikula (κ=0,88-0,99). Korelacija je bila slaba za BVW, širinu korpusa CC-a i širinu lateralnih ventrikula (κ=0,28-0,56). Nove normativne vrijednosti za visinu hipofize i debljinu peteljke u novorođenačkoj dobi novi su nalazi ove prospektivne studije. U zaključku, mjerenja zabilježena pomoću UZV-a lubanje i MR-a nisu bila dosljedna u nekim moždanim strukturama. Bitno je znati normativne vrijednosti i diferencirati prirođene i razvojne anomalije mozga u novorođečadi. Također su utvrđene nove referentne vrijednosti za hipofizu i infundibulum u novorođenačkoj dobi.

Ključne riječi: MAGNETSKA REZONANCA; NOVOROĐENČE; PEDIJATRIJSKI ULTRAZVUK