Numerical Values of the Angle between the Brainstem and Cerebellar Vermis in Normal Fetuses and in Fetuses with Posterior Fossa Abnormalities in the Second Trimester of Pregnancy

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Abstract
The aim of the study was to evaluate numerical values of the angle between the brainstem and the cerebellar vermis in normal fetuses and in fetuses with posterior fossa abnormalities on ultrasound examination in the second trimester of pregnancy. In order to assess the angle between the brainstem and fetal cerebellar vermis in the median sagittal plane of scanning, we used the results of the study of 292 fetuses at time of gestation from 18 to 28 weeks, which formed the control group. In all patients pregnancy resulted in term deliveries of normal healthy children. Main group consisted of 32 patients, whose fetuses were prenatally diagnosed with posterior fossa abnormalities in the period from 18 to 28 weeks of gestation: 7 fetuses with persistent Blake’s pouch cyst (BPC), 12 fetuses with cerebellar vermis hypoplasia (CVH), and 13 fetuses with Dandy-Walker malformation (DWM). The study found that the numerical values of the angle between the brainstem and the cerebellar vermis in normal fetuses in the period from 18 to 20 weeks of pregnancy were 9.25 ± 3.42 degrees, from 20 to 24 weeks - 7.74 ± 2.53 degrees, and from 24 to 27 weeks - 7.79 ± 2.43 degrees. In cases of BPC, the numerical values of the angle between the brainstem and the cerebellar vermis did not exceed 28 degrees, in case of CVH - no more than 40 degrees, and in case of DWM the angle was always greater than 45 degrees. Thus, the evaluation of numerical values of the angle between the brainstem and the cerebellar vermis allows to perform differential diagnosis between main posterior fossa abnormalities.

Keywords: fetus, brain, brainstem, cerebellar vermis, Dandy-Walker malformation, Blake’s pouch cyst, prenatal diagnosis.

INTRODUCTION
Screening evaluation of fetal brain in the second trimester of pregnancy includes an evaluation of posterior fossa structures: hemispheres and the cerebellar vermis, as well as the cisterna magna [11]. For screening ultrasonography of the fetal brain, the International Society for Ultrasound Diagnostics in Obstetrics and Gynecology (ISUOG) recommended the use of the series of axial sections of the fetal head [7]. When assessing the posterior cranial fossa, a third axial plane of scanning is used, passing through the posterior cranial fossa and the cerebellum. In this plane, one needs to carry out an evaluation of the cerebellum, including evaluation of hemispheres and vermis as well as cisterna magna. When an abnormal structure of the posterior cranial fossa is identified, correct prenatal diagnosis is important, as various anomalies have different prognosis and an appropriate survey and observation algorithm [13].

There are various classifications of malformations of the posterior fossa structures. In our opinion, the most appropriate classification of malformations of the posterior fossa structures includes their division into two large groups [18]:
1) with the presence of cyst in the region of posterior cranial fossa;
2) without cystic formation in the region of posterior cranial fossa.

Anomalies with the development of cyst in the region of the posterior cranial fossa include Dandy-Walker malformation (DWM), persistent Blake’s pouch cyst (BPC), and enlargement of the cisterna magna. In addition to these anomalies, visualization of the cyst in the region of the posterior cranial fossa is possible in the presence of an arachnoid cyst. Cerebellar vermis hypoplasia (CVH) belongs to the group of anomalies without cyst in the region of the posterior cranial fossa.

Detection of the cyst in the region of the posterior fossa requires the doctor of prenatal diagnosis to perform differential diagnosis between all of the above-noted pathologies. And while the differential diagnosis of an isolated increase of arachnoid cyst and cisterna magna in size is quite simple, since the cerebellum is not changed in case of these anomalies, the remaining anomalies require more detailed evaluation. Scanning only in axial planes is not enough for this purpose, since it is necessary to obtain a median sagittal plane for a more detailed evaluation of the cerebellar vermis, brainstem, ventricle IV and cisterna magna. It is not always possible to obtain this plane by means of conventional scanning, so it is advisable to use volumetric reconstruction regimes (3D) in order to obtain an image of the median sagittal plane regardless of the position of the fetal head [8; 14; 16]. This plane is necessary primarily to assess the size of the cerebellar vermis, which is crucially important for ensuring objective differential diagnosis [20].
DWM is characterized by complete or partial agenesis of the cerebellar vermis. By the way in case of this anomaly the vermis is hypoplastic, it also decreases in sizes, and in case of the BPC, the size of the vermis is within the normal range [12].

In addition to the estimation of the size of the cerebellar vermis during the differential diagnosis, it is necessary to evaluate interposition of three structures: occipital tubercle - tentorium - torcular Herophili [12], since anomalous location of the tentorium is typical for DWM. On the one hand, evaluation [2]. However, on the other hand, visualization of the confluence of sinuses (torcular Herophili) is not always possible on ultrasonography due to the acoustic shadow from the skull bones [5].

Several years ago it was suggested to measure the angle between the brainstem and the cerebellar vermis in order to measure differential anomalies in the development of posterior fossa structures. In cases of DWM, the angle always exceeded 45 degrees, and in case of BPC the angle was always less than 30 degrees [3].

Until recently, scientists have used to distinguish Dandy-Walker variant. In case of this pathology, in contrast to DWM, there is part of the vermis, i.e. partial agenesis is observed [18]. But herewith the question arises of what is the difference between CVH, when the size of the cerebellar vermis decreases and the angle between it and the brainstem is not more than 40 degrees, and Dandy-Walker variant, when the cerebellar vermis is also reduced and the angle between the vermis and the brainstem is less than 40 degrees. Up to date, there has been no clear idea of what Dandy-Walker variant consists of. In some publications, one can read about CVH, other authors use term “partial agenesis”, but agenesis and hypoplasia are not synonymous. Thus, clear criteria for the formulation of the diagnosis are necessary. The question regarding the terms to be used was raised long ago. Back in 2006 Guibaud and des Portes [6] published an article stating that it was necessary to adhere to clear criteria describing each case. Agenesis means the complete or partial absence of an anatomical structure. Complete agenesis of cerebellar vermis means that it is completely absent, and in case of partial agenesis only part of vermis is absent. Hypoplasia is the reduction of the organ in size with preservation of anatomical structure. When the vermis is hypoplastic, all its lobules are present, but its dimensions are less than the normative values. Thus, only visualization of all lobules of the cerebellum (in case of suspicion of its decrease in size) suggests a conclusion about hypoplasia. However, ultrasonography may contribute to evaluation of all lobules of the cerebellum from 28 weeks of pregnancy [17].

Although a number of authors continue to single out the Dandy-Walker variant as a separate nosological form [1], an increasing number of specialists in prenatal diagnostics attribute this pathology to the group of CVH [4; 15]. Diagnosis of an isolated CVH form continues to cause certain difficulties. Both specialists in ultrasound diagnostics and radiologists using magnetic resonance imaging in some cases have established a mismatch in prenatal diagnosis of an isolated CVH and results of postpartum diagnosis [5; 9]. In some cases, diagnosis of an isolated CVH was not confirmed after the birth of a child, i.e. there was a false positive diagnosis of this pathology. Therefore, measuring the angle between the cerebellar vermis and the brainstem is an extremely important criterion for differential diagnosis of vermis hypoplasia both in case of its normal development, and in case of DWM, since in case of CVH the angle is always less than 45 degrees [19]. It should also be taken into account that in case of an isolated hypoplasia the size of the vermis is reduced, but all its parts are present [10].

Therefore, the aim of this study was to explore the numerical values of the angle between the brainstem and the cerebellar vermis in normal fetuses and in fetuses with posterior fossa abnormalities on ultrasound examination in the second trimester of pregnancy.

**METHODS**

The results of the survey of 292 pregnant women with end-to-end echographic observation in the period from 18 to 28 weeks were used to assess the angle between brainstem and cerebellar vermis of the fetus. These fetuses formed a control group. In all patients, pregnancy resulted in term deliveries and the birth of normal healthy children. The mean age of the examined patients was 28 years. Criteria for selecting patients were the following:

1) known date of the last menstruation in case of 26-30-day cycle;
2) uncomplicated course of pregnancy;
3) monocarpic pregnancy without signs of any pathology in fetus;
4) withdrawal from oral contraceptives within 3 months before the conception cycle;
5) term birth and normal fetus with birth weight within normative values (more than 10th and less than 90th percentile by weight and body length depending on the gestational age).

Main group consisted of 32 patients, whose fetuses were prenatally diagnosed with posterior fossa abnormalities in the period from 18 to 28 weeks of gestation: 7 fetuses with persistent Blake’s pouch cyst (BPC), 12 fetuses with cerebellar vermis hypoplasia (CVH), and 13 fetuses with Dandy-Walker malformation (DWM). Among posterior fossa abnormalities, BPC was diagnosed in 7 cases, CVH - in 12 cases, and DWM - in 13 cases. Age of patients varied from 16 to 39 years and averaged to 28.4 years.

Measurements of the size of the angle between the brainstem and the cerebellar vermis were made retrospectively after taking brain images of fetuses on the ultrasound device Voluson E8 (GE) by using a convection abdominal volume scan sensor. Analysis of volumetric reconstructions was carried out on a personal computer by using the special software 4D View (GE). In order to estimate the angle between the brainstem and the cerebellar vermis, VCI Omni View regimen of volume reconstructions was formed on a personal computer by using the special software 4D View (GE). Analysis of volumetric reconstructions was carried out on a personal computer by using the special software 4D View (GE). In order to estimate the angle between the brainstem and the cerebellar vermis, VCI Omni View regimen of volume reconstruction was used. This allowed to obtain an average sagittal section of 1-2 mm thickness depending on the gestational age. After this, we measured the angle between the brainstem and the cerebellar vermis.
RESULTS
In course of our studies, in 292 normal fetuses in the period from 18 to 28 weeks of gestation, we were able to obtain an image of sufficient quality for measuring the angle between the brainstem and the cerebellar vermis in 280 (95.9%) observations, which indicates a high reproducibility of the method. Therefore, the final analysis included the results of the 280 fetuses survey.

Our analysis showed that the numerical values of the angle between the brainstem and the cerebellar vermis in the period from 18 to 28 weeks of gestation averaged to $8.22 \pm 2.89$ degrees ($M \pm \delta$). In this case, numerical values of the angle between the brainstem and the cerebellar vermis varied in our studies from 3.7 to 18.2 degrees.

We have also analyzed the numerical values of the angle between the brainstem and the cerebellar vermis depending on the gestational age. For this purpose, the results obtained were subdivided into 3 groups: 18/0-20/6, 21/0-23/6 and 24/0-27/6 weeks (table 1).

<table>
<thead>
<tr>
<th>Pregnancy, weeks/days</th>
<th>Angle between the brainstem and the cerebellar vermis, degrees</th>
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<tbody>
<tr>
<td></td>
<td>5th</td>
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<tr>
<td>18/0-20/6</td>
<td>3.70</td>
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<tr>
<td>21/0-23/6</td>
<td>3.74</td>
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<tr>
<td>24/0-27/6</td>
<td>3.72</td>
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The obtained data showed that the numerical values of the angle between the brainstem and the cerebellar vermis gradually insignificantly decreased between 18 and 28 weeks of gestation, averaging 9.25 degrees in 18/0-20/6 weeks and 7.79 degrees in 24/0-27/6 weeks.

Thus, the numerical values of the angle between the brainstem and the cerebellar vermis during normal development of the fetus in the second trimester of pregnancy in our studies did not exceed 19°.

When assessing the angle of fetuses with posterior fossa abnormalities, numerical values were significantly higher. In course of the study, the results of prenatal echography of 7 fetuses with BPC were analyzed. When scanning the head in the axial plane, all fetuses showed an increase in the size of the cisterna magna over the 95th percentile of normative values. In the median sagittal plane all fetuses had normal sizes of craniocaudal and anteroposterior size of the cerebellar vermis. The dimensions of the angle between the brainstem and the cerebellar vermis in fetuses with BPC ranged from 10.9 to 28 degrees.

CVH was diagnosed in 12 fetuses. In assessing the structures of the posterior fossa in the third axial plane of scanning passing through the posterior cranial fossa, an increase in the depth of the cisterna magna was detected in 8 fetuses (67.33%), in 4 fetuses (33%) the numerical values of the depth of the cisterna magna did not exceed the numerical values of the 95-th percentile. Based on this fact, it can be concluded that in case of CVH depth of the cisterna magna can be either normal or increased. When assessing the sizes of the cerebellar vermis in the median sagittal plane of scanning, it was found that only anteroposterior size was reduced in 4 (33.3%) of 12 fetuses, while craniocaudal size was within the normal range. In 8 (66.6%) of fetuses there was a decrease in the craniocaudal and anteroposterior size of the cerebellar vermis. During the study of the numerical values of the angle between the brainstem and vermis, it was found that they ranged from 14.9 to 40 degrees.

Analysis of the results obtained after the examination of 13 fetuses with DWM showed the presence of an increase in the depth of cisterna magna in all cases. Three fetuses showed complete agenesis of the cerebellar vermis, while partial agenesis of the cerebellar vermis was observed in 10 cases. When scanning in the median sagittal plane, a decrease in both sizes of the cerebellar vermis was found in the vast majority of cases. Only in one fetus the craniocaudal size was within the normal range, and the anteroposterior size was reduced. At the same time, the sizes of the angle between the brainstem and the cerebellar vermis ranged from 47.4 to 116 degrees.

DISCUSSION
The obtained results showed that numerical values of the angle between the brainstem and the cerebellar vermis in normal fetuses in the period from 18 to 28 weeks of pregnancy in our population did not have significant differences from results obtained by the other researchers. In our population, numerical values of the angle between the brainstem and the cerebellar vermis averaged to $8.22 \pm 2.89$ degrees ($M \pm \delta$), and in the studies of Italian researchers in the period from 19 to 28 weeks of the pregnancy - 9.1 ± 3.5 degrees [19]. The numerical values of the angle between the brainstem and the cerebellar vermis varied in our studies from 3.7 to 18.2 degrees, and in the studies of the Italian specialists - from 4 to 17 degrees [19]. Hence, in case of normal fetal development in the second trimester of pregnancy the numerical values of the angle between the brainstem and the cerebellar vermis are less than 20 degrees.

In fetuses with BPC, the numerical values of the angle between the brainstem and the cerebellar vermis varied in our studies between 10.9 and 28 degrees. The obtained data were not significantly different from the results of other researchers. According to these data, all fetuses with BPC had the angle between the brainstem and the cerebellar vermis less than 30 degrees [3].

When studying the numerical values of the angle between the brainstem and vermis in fetuses with CVH, it was revealed that they ranged from 14.9 to 40 degrees, which also did not differ significantly from the results of the other researchers [13]. In cases of DWM, numerical values of the angle between the brainstem and the cerebellar vermis in all the fetuses examined by us exceeded 45 degrees, which also agrees with the results of the previous studies [3].
CONCLUSION

Thus, up to date, final prenatal diagnosis in the presence of malformations of the posterior fossa structures has been possible only when using median sagittal plane of scanning, in which it is necessary to measure the dimensions of the cerebellar vermis as well as the angle between the brainstem and the cerebellar vermis. Prenatal diagnostic criteria for DWM are the following: reduction in the size of the cerebellar vermis and an increase in the numerical values of the angle between the brainstem and the cerebellar vermis do not exceed 45 degrees; for CVH - reduction of the cerebellar vermis in size, however, the numerical values of the angle between the brainstem and the cerebellar vermis do not exceed 40 degrees; BPC is characterized by normal size of the cerebellar vermis, and the angle between the brainstem and the cerebellar vermis does not exceed 30 degrees.

REFERENCES