Fetal cerebral circulation assessment by Doppler ultrasound in normal and pathological pregnancies

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Summary

During normal pregnancies (n = 40) the cerebral index (Rc = S - D/S) (with S = systolic and D-telediastolic amplitudes) is always higher than the placental index (Rp), and the cerebro/placental ratio (Rc/Rp) greater than 1.

Of 29 pregnant women with hypertension (including two twins), 17 delivered normally (Rc, Rp and CPR normal), 14 delivered an hypotrophic fetus, in 12 out of these 14 pregnancies one of the two indices (Rc or Rp) was abnormal and the cerebro/placental ratio, CPR, was always less or equal to 1. CPR sensitivity was 86% the specificity 100%.

In 11 pregnancies with idiopathic fetal-growth retardation, the CPR was less or equal to 1 in eight cases (73% of the cases), and greater than 1 in three cases (three false-negative results).

Doppler; Umbilical artery; Placental index; Cerebral artery; Cerebral index; Cerebro/placental ratio

Introduction

Most of the fetal vessels can be explored by ultrasound. Till now the main haemodynamic parameters have been provided by a Doppler spectrum of the umbilical arteries. The amplitude of the end-diastolic frequency in comparison to the maximum systolic one is directly related to the placental resistances.

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Different authors have proposed indices in order to assess the vascular placental resistances especially during pregnancies with hypertension. In these pregnancies the increase in placental resistance is generally associated with an intra-uterine fetal-growth retardation [1-8]. However, the sensitivity of the placental resistance index method for the detection of intra-uterine growth retardation (IUGR) is no more than 65-70% [8,9]. This result could probably be improved on by doing Doppler investigations more frequently during the last trimester, or as soon as maternal pathology or IUGR are suspected. In addition, the placental function may be disturbed, leading to fetal hypoxia and an IUGR even if no placental vascular lesion (infarctus fibrosis) exists (in such a case, the placental index, Rp, could remain within the normal range). Moreover, it is possible that a deterioration in placental function will provoke a redistribution of the blood flow in the main fetal areas (cerebral area?).

For this reason we investigated various circulations, and in particular that of the brain, in order to detect and evaluate in those areas the vascular adaptation that results from the deterioration of the placental exchange.

The aim of this work was to study simultaneously the placental (Rp) and the cerebral (Rc) vascular resistances and to compare their evolution by using the cerebro/placental ratio (CPR = Rc/Rp) on normal and pathological pregnancies. This could probably make the Doppler method more accurate for the detection of the IUGR.

Material and method

Ultrasound device

The device we used was a prototype duplex system built up by our laboratory. It includes a 2.9 MHz B-mode linear scanner, and a 2.9 MHz pulsed Doppler scanner with a 100 Hz filter (Fig. 1) [1]. The Doppler beam was generated by 48 of the 300 transducers of the array and steered in a preselected direction by electronic deflection. The audio signal was then displayed on a real-time spectral analyser (DMS Spectradop). The maximum depth of exploration was 15 cm, the Doppler sample size along the beam was adjustable and ranged between 2 and 16 mm. The -6 dB beam-width was 2 to 3 mm.

Umbilical artery assessment (placental index Rp)

Several indices measured on the umbilical artery Doppler spectrum have been proposed: the A = S/D ratio [7], with S the maximum systolic amplitude and D the maximum end-diastolic amplitude; the resistance index R = (S - D/S) [10]; and the pulsatility index PI = (S - D/M) [5], where M is the mean frequency. Note that the two first indices are mathematically simply related, R = (A - I/A), and both try to evaluate the diastolic flow amplitude in comparison with the systolic one.

For our study we used the placental resistance index, Rp = (S - D)/S. This index is generally accepted to be an indication of the vascular resistance in the distal area from the point of measurement [1,2,10,11]. During normal pregnancies, the end-diastolic amplitude increases and the Rp decreases. In pathological pregnancies, with hypertension, the decreased diastolic flow (increased Rp) is in most of the cases associated with an intra-uterine growth retardation.
Cerebral artery assessment

The intracerebral artery examination requires a duplex echo-pulsed Doppler system with a real-time Doppler frequency analyser. In order to identify the Doppler waveform of the main cerebral vessels among all the different Doppler spectra which can be recorded inside the brain area, we have to locate the vessel of interest by echography.

The principal well-known cerebral structures (ventricles, thalamus, ...) are easily visualized by echography and are used to locate the arteries and to guide the Doppler investigation. In our study we recorded on all fetuses the anterior cerebral arteries (Fig. 1).

Examination. The pregnant patient was in dorsal-supine position. The cerebral structures (thalamus, ventricles ...) were visualized on a biparietal incidence, the Willis circle was generally clearly visualized, and the probe moved until we detected on an upper scan level on the midcerebral line the pulsation of the anterior cerebral arteries. The Doppler sample volume was then placed at this level and the Doppler sound recorded (Fig. 1).

Cerebral index (Rc). In order to quantify the cerebral vascular resistances we used a cerebral resistance index, \( Rc = (S - D/S) \), with \( S \) = systolic and \( D \) = diastolic amplitude, both measured on the anterior cerebral artery spectrum. This index has already been used for cerebral resistance assessment on adults with cerebral atheromatous disease [10] and on newborn infants [11] with intracranial hypertension or underassisted ventilation. This index clearly exhibits changes in the cerebral vasomotricity.

Cerebro placental ratio (CPR)

The evolution of these indices concerns two different vascular phenomena which in the case of pregnancy may or may not be associated with hypertension. Abnormal values of Rp (higher than the normal range) lead to suspicion of vascular lesion

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Fig. 1. Anterior cerebral artery Doppler recording. (a) Echography with the Doppler sample location; (b) Doppler spectrum.
which increases the placental resistances and probably disturbs the placental function. On the other hand, the Rc seems to be related to the cerebral vascular adaptation due to a deterioration of the placental exchanges (blood oxygenation). In this case one can expect an increase in the cerebral blood flow and a decrease in the cerebral resistance index, Rc. Then abnormal values of Rc will be below the normal range of this parameter.

The evolution of the cerebral circulation was compared to those of the umbilical arteries by using a cerebro/placental ratio (CPR) defined as follows: CPR = Rc/Rp. (Rc, cerebral index, Rp, placental index).

**Results**

*The population*

The population consists of three groups:

*Normal pregnancies* (n = 40) of 27.4 ± 4 year old women with no particular pathology, normal clinical data, and an echographic fetal biometry above the 10th percentile; deliveries and neonatal period were uncomplicated.

*High-risk pregnancies with hypertension* (diastolic blood pressure > 9 mmHg) (n = 29) of 27 ± 4.2 year old women without proteinuria. Fifteen of them developed normally and delivered normal fetuses. Twelve of them showed an intra-uterine fetal growth retardation diagnosed by echography (biparietal and/or an abdominal diameter less than the 10th percentile during the pregnancy) and delivered 12 hypotrophic fetuses (fetal weight < 10th percentile). Two pregnancies were twins; each of them delivered one normal and one hypotrophic fetus.

No other pathology than hypertension was present in these pregnancies. No morphological abnormalities were diagnosed on the fetus.

*Pregnancies with idiopathic fetal growth retardation* (n = 11) of 26 ± 5 years olds, without any pathology. The IUGR was diagnosed by echo-graphy (fetal biometry < 10th percentile) and confirmed at delivery (fetal weight < 10th percentile).

*Doppler measurements performed*

- 1 to 4 Doppler examinations (2.5 ± 1.7) were done for each pregnancy between 15 and 40 weeks of gestation.
- 3 or 4 Doppler recordings were made during each examination.
- 5 measurements were done on each Doppler trace.

The variation from one operator to another and from one measurement to another during the same session was less than 10%.

*Doppler indices (Rc, Rp and CPR) during normal pregnancies*

Umbilical and cerebral artery waveforms were recorded between the 15th and 40th postmenstrual weeks (Fig. 2). Until the 20th week we generally do not observe any diastolic flow on the cerebral Doppler spectrum (Rc = 1), whereas the diastolic flow is present on the umbilical artery traces (Rp < 1). In fact, the diastolic component probably exists but is too small at this stage in the pregnancy, and the Doppler filters mask the low frequencies due to this flow.
Fig. 2. Evolution of the umbilical and cerebral Doppler waveform during normal pregnancies.

After the 20th week, the cerebral diastolic flow increases progressively until the delivery, but remains at all times smaller than the umbilical flow. The cerebral index ($R_c$) decreases with the advancement of the pregnancy, but this evolution appears to be later than for the placental index ($R_p$) and is more marked (Fig. 3a and b). At the end of the pregnancy the normal range of both $R_c$ and $R_p$ overlaps partially (Fig. 6).

During a normal pregnancy the cerebro/placental ratio CPR = $R_c/R_p$ is greater than 1 (cerebral resistance higher than placental resistance during the pregnancy) and shows a slight increase at the end of the pregnancy (Fig. 3c).

Doppler indices ($R_c$, $R_p$ and CPR) during pregnancies with hypertension ($n = 29$) (Fig. 4)

Out of the 29 pregnant women with hypertension 15 delivered normal fetuses with normal echo biometry, normal values of $R_c$ and $R_p$, and a CPR greater than 1 ($R_c > R_p$) (Fig. 4).

Fourteen pregnant women delivered an hypotrophic fetus: (Fig. 4a, b and c).
- The placental index was abnormal (increased) in 50% of the cases (7/14), whereas the cerebral index was abnormal in four out of these seven cases.
- The cerebral index was abnormal (decreased) in 50% of the cases (7/14), whereas the placental index was abnormal in four out of these cases.
- These indices were both abnormal in only 28% of the cases (4/14).
Fig. 3. (a) Cerebral index, Rc; (b) placental index, Rp; and (c) cerebro/placental ratio, CPR, during normal pregnancies (n = 40; 100 measurements).
The cerebroplacental index, \( \text{CPR} = \frac{R_c}{R_p} \), was abnormal (CPR < 1) in 86% of the cases (12/14).

Note that in each of the two twin pregnancies a normal fetus (Rp, Rc and CPR normal) and an hypotrophic fetus (Fig. 4c) were delivered.

In one of these two pregnancies the weight of the hypotrophic fetus was under the 5th percentile; Rc and Rp were abnormal and the CPR also (less than 1). In the second twin pregnancy the weight of the hypotrophic fetus was at the 10th percentile; the Rp had a normal value, the Rc was pathological (decreased) and the CPR was abnormal (less than 1).

**Idiopathic fetal growth retardation \((n = 11)\) (Fig. 5)**

- The placental index was significantly elevated in 45% of the cases (5/11). The cerebral index was abnormal (decreased) in three of these cases.
- The cerebral index was abnormal (decreased) in 36% of the pregnancies (4/11). The placental index was abnormal for three of these cases.
- The cerebral and placental indices were both pathological in 27% of the cases (3/11).

The cerebro/placental ratio was abnormal (CPR < 1) in 72% of the cases (8/11).

**Discussion**

(a) For this study we used the normal diagram of Rp we proposed in 1983 [1]. The validity of that diagram has been confirmed by a recent study in our depart-
ment [9] concerning 60 normal and 82 pathological pregnancies (with hypertension). The values of Rp concerning the present study have been tested with this diagram.

(b) The normal range of the cerebral index is much more extended than for the placental index at the same gestational age (Fig. 3a). Therefore this parameter is probably less sensitive than the Rp index. However, the combination of both Rc and Rp recorded at the same time allows the definition of a new parameter, the

![Diagram](image)

**Fig. 4.** (a) Cerebral index, Rc; (b) placental index, Rp; and (c) cerebro/placental ratio, CPR, on pregnancies with hypertension. ○ Normal fetus (n = 17); ■, hypotrophic fetus (n = 14).
cerebro/placental ratio (CPR = Rc/Rp) which is more sensitive than any of these two indices taken alone. Results obtained from normal pregnancies show clearly that the cerebral vascular resistances were higher than the placental resistances (Rc > Rp; CPR > 1) all along the pregnancy (Figs. 3 and 6).

(c) Comments concerning the 29 pregnancies with hypertension.

For the 17 normal fetuses, all the haemodynamic parameters were in their normal range, the cerebral index was superior to the placental index and therefore the CPR was greater than one.

If we consider the 14 hypotrophic fetuses, one can note that the placental index was significantly elevated in seven cases and that the cerebral index was noticeably decreased in seven cases. However, these pathological values of Rc and Rp did not occur always simultaneously in the same pregnancies. In four cases Rc and Rp were normal, and in two cases they were at the limit of the normal range.

This observation points out the importance of comparing the haemodynamic parameters of the umbilical and the cerebral circulation for the same fetus. The cerebro/placental ratio (CPR = Rc/Rp) is considered to be abnormal when it is less or equal to 1, even if either Rc or Rp or both have normal values. In Fig. 6 we summarize the different situations encountered. For normal pregnancies Rc is always superior to Rp (CPR > 1 arrow up in Fig. 6). For pathological pregnancies with hypotrophy (CPR < 1) the arrow is down in the diagram whenever either Rc or Rp or both are pathological. Finally, when we consider the 14 hypotrophic fetuses, we note that the CPR was pathological (CPR < 1) in 12 cases. 86% of the hypotrophies were diagnosed, of which two were false negative and none false positive (Fig. 4).

In the 29 pregnancies the sensitivity was 86% and the specificity 100%.

(d) Comments on the idiopatic IUGR. In this population the use of the cerebroplacental ratio increased also the accuracy of the Doppler method. However, in only eight cases of the 11 pregnancies (73% of the cases) the haemodynamic
parameters and CPR were modified. We observed three false-negative results corresponding in 27% of the cases (Fig. 5).

This result may be explained by the fact that in these pregnancies the placental vascular pathology is not the major cause of IUGR. However, this method could allow the detection of IUGR, including vascular abnormalities with modification of the cerebral perfusion in a population in which the diagnosis of IUGR had already been made by echography.

Fig. 5. (a) Cerebral index Rc; (b) placental index, Rp; and (c) cerebro/placental ratio, CPR, on pregnancies with idiopathic IUGR (n = 11).
(e) General remarks. In our population we noted that when the Rp was only slightly elevated, the CPR index clearly showed a pathological (CPR < 1) or normal value (CPR > 1).

![Graph](image)

**Fig. 5. (continued).**

**Fig. 6.** Different values of Rc and Rp leading to an abnormal CPR associated with a IUGR. ▲, cerebral index; ■, placental index Rp; — — —, normal pregnancy; ———, hypotrophy.
Another advantage of the CPR index is that this parameter does not depend on the heart rate. It is well-known that an elevation of the fetal heart rate increases the end-diastolic velocity and therefore decreases the resistance index \((R_c \text{ or } R_p)\). On the other hand, the diminution of the heart rate increases the value of the index. This effect of the heart rate is partially eliminated by the use of the CPR. Both indices, \(R_c\) and \(R_p\), are measured on the same fetus and the ratio is supposed to be non-heart-rate dependent.

All throughout the pregnancy the cerebral and umbilical circulation showed the same development. The increase in the diastolic flow, since the beginning of the pregnancy in the umbilical arteries and later on (after 25 weeks) in the cerebral arteries, may be related to the decrease in the vascular resistance in the corresponding areas because of the growth of the placenta and the brain.

In the cases of pregnancies with hypertension, the increase in the placental index \((R_p)\) is generally due to vascular diseases which probably disturb the maternal-to-fetus blood exchange and in particular the fetal blood oxygenation. The decrease in the cerebral resistance index \((R_c)\) at the same time could be considered as a vasomotor reaction (vasodilatation) coming from the brain area. The marked decrease of the brain resistance would increase the cerebral flow in order to fight against a relative hypoxia [10,12].

This kind of adaptation has already been observed in the cerebral arteries of neonates and in adult carotic arteries after inhalation of air and CO\(_2\) [6]. On the other hand, in neonates under assisted ventilation we noted an increase in the cerebral resistance (decrease of the diastolic flow) when the CO\(_2\) pressure decreases.

Moreover, the placental function may be disturbed without any evident placental disease or any haemodynamic signs in the waveform of the umbilical arteries. In this case the placental index will remain quite normal; however, the cerebral index (and even better the CPR) could take abnormal values \((\text{CPR} < 1)\). A CPR \((R_c/R_p)\) of less than 1 means that the cerebral resistances are less important than those in the placental area.

A study of both the umbilical and cerebral flows may significantly increase the sensitivity of the Doppler method for detecting fetal growth retardation and provide a better understanding of the fetal vascular regulation.

References