Journal of Neonatal Biology

OPEN ACCESS Freely available online

Research Article

# The Importance of Monitoring Cerebral Blood Flow in Preterm Neonates

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## ABSTRACT

**Objectives**: Aim of this paper is to establish prognostic significance and reliability of Doppler ultrasound measurement of cerebral blood flow in preterm neonates with intracranial hemorrhage.

**Methods:** A prospective study based on the Doppler ultrasonography by measuring the resistance index (RI) through an anterior cerebral artery, in 50 premature neonates with diagnosed intracranial hemorrhage. The obtained results are grouped on the values of resistance index, RI into three groups and were analyzed using arithmetic mean, standard deviation, testing the significance of the average difference, T-test.

**Results**: There were significant differences $p<0.05$, between the RI values of RI1 and RI2 lower than 0.61 during the first and during the second examination. Statistical analysis values RI1 and RI2 lower than 0.85 and higher than 0.61, shows that there were differences between value RI1 and RI2 in premature newborns with intracranial hemorrhage, $p<0.05$. There were significant differences between values RI1 and RI2 higher than 0.85, $p<0.05$. There were significant differences between RI values lower than 0.61 in the first, and in the second ultrasound examination $p<0.05$. We found significant difference between the two groups of values RI1 and RI2 in patients with PDA, $p<0.05$.

**Conclusion**: With increasing gestational age RI is decreasing. With increasing body weight RI is decreasing. With closing PDA, RI is decreasing. Doppler neurosonography is the method of choice, which is now used in the measurement of neonatal cerebral circulation, or for non-invasive testing neonatal brain perfusion.

**Keywords:** Ultrasound; Cerebral blood flow; Resistance index; Preterm neonates

## INTRODUCTION

Ultrasound has become a useful instrument in everyday work with neonatal patients because it is safe, cheap bed-side diagnostic method. The benefit of ultrasound increases over time, because thanks to it, the diagnosis of hemorrhage, tumor, and vascular pathologies improve. This especially makes it much easier to work with premature born neonates, who are the most vulnerable part of the population, and demanding as patients during other diagnostic procedures as MRI [1].

Brain pathology is an important cause of morbidity and mortality in the premature born neonates. Neurosonography is used for screening, diagnosis and monitoring of brain disorders such as germinal matrix hemorrhage, periventricular leukomalacia and hydrocephalus [2]. The purpose of this article is to present the potential applications of three-dimensional ultrasonography, with Doppler Effect in monitoring cerebral blood flow in preterm neonates. Today, are in use appliances with continuous, pulsed and color Doppler Effect, as well as 3D and 4D Doppler. The Doppler effect of the wave propagation of variation of the frequency of the emitted and reflected waves, during the relative movement of the receptor relative to the transmitter speed from which the ultrasonic wave, emitted from the probe, is rejected, is proportional to the change of wavelength and frequency of reflected waves received in probe. The movement of erythrocyte from which the ultrasonic wave, emitted from probe is rejected, is proportional to the change of wavelength and frequency of reflected waves received at the probe. When the probe is approaching the erythrocyte wavelength is reduced, and vice versa, which in addition determines the speed and flow of blood. When the sound of the highest tonality, it is achieved parallel ultrasonic beam and the vessel.

Cerebral artery newborns have a narrow inner diameter. Red

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**Received:** December 17, 2019, **Accepted:** September 27, 2020, **Published:** October 04, 2020

**Citation:** Gojkovic T, Zdravkovic V (2020) The Importance of Monitoring Cerebral Blood Flow in Preterm Neonates. J Neonatal Biol. 9:285. doi:10.35248/2167-0897.20.9.285.

blood cells are the fastest moving in the middle of the vessel. This is a parabolic profile of blood. The arterial resistivity index, also called as Resistance index, abbreviated as RI developed by Leandre Pourcelot, is a measure of pulsatile blood flow that reflects the resistance to blood flow caused by microvascular bed distal to the site of measurement. Pourcelot flow resistance index, RI, is calculated by formula RI=S-D/S. S is maximal systolic speed; D is the final end-diastolic velocity. This index is sensitive to small changes in the speed at the end of diastole and the determination of the resistance in blood vessels where is no flow in diastole RI=1. Defect of this numerical table is varying in proportion to changes in the driving speeds blood, if the systolic and diastolic frequencies change in the same rhythm. Nowadays appliances themselves calculate these parameters after localization cursor over the pericallosal artery, distal portion of the anterior cerebral artery, (ACA). During routine work is usually estimated RI, which is indication of resistance in the blood vessels and which is not dependent upon the angle of insonation (Figure 1). It is known that RI decreases with gestational age after the first 48 hours of life, which is associated with the closure of ductus arteriosus. With persistence of ductus flow during diastole is very low or even null. This results in high values of RI to 1. When the ductus close diastolic component is higher and is lower RI. The reason for the low diastolic flow rate of the ductus open in the reduced volume of blood in cerebral blood flow, and not the elevated vascular resistance or elevated intracranial pressure. RI drop can be observed due to the increase in $PaCO_2$ vasodilatory effect of $CO_2$ in pneumothorax, birth asphyxia, neonatal convulsions, is suctioned off the upper respiratory tract. Elevated RI is found in intraventricular hemorrhage, post-hemorrhagic hydrocephalus, brain death, and hyperviscosity syndrome. Cerebral perfusion is significantly elevated in purulent meningitis. RI in children with hypoxic-ischemic encephalopathy (HIE) is substantially reduced. Maintaining low values of RI at these children, according to many authors is bad prognostic sign. At the speed of neonatal cerebral blood flow and myocardial contractility influence in conditions asphyxia, leads to redistribution of blood to vital organs, brain, heart, adrenal. After that, there is an increased blood flow to the brain and other vital organs, which is made possible chemical, neurogenic, and other factors. Neonate with intrauterine growth restriction RI values are low, and high value of D. This process of autoregulation of cerebral takes place regardless of the changes of the blood pressure and is reversible. When the value of the cerebral perfusion pressure falls below 6.7 kPa, autoregulation stops due to ischemia and leads to the accumulation of acidic metabolites in the brain and lowering the tone of blood vessels. Then cerebral blood perfusion depends on systemic blood pressure when the value of the cerebral perfusion pressure falls below 3.3 kPa generated cell death. In the first phase of a compensatory increase in cerebral blood flow may cause intraventricular hemorrhage, mostly in most vulnerable region, germinal matrix in premature infants. If the level of increase in cerebral blood perfusion higher this damage will be greater and accordingly the degree of hemorrhage weight. Intraventricular hemorrhage occurs in the ventricular zone in 90% of cases, and in the choroid plexus in 10% of cases. It is more common in term newborns. Germinal matrix hemorrhage (GMH), usually occurs in the first week of life, especially in the first 72 hours post-natal, very rare, and after two weeks. If the bleeding is expanding in the chamber, but no volume change that. Sized chamber, it is hemorrhage of a second stage. If it happens that ventricle is dilated, it is the third stage, if hemorrhage is expanding into the brain parenchyma, it is fourth degree [3].

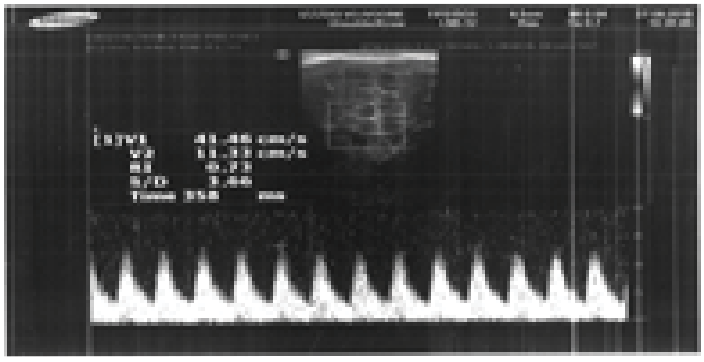

**Figure 1:** Resistance index, Normal Doppler wave.

## MATERIALS AND METHODS

### A statement regarding informed consent (or waiver)

"By signing this consent, I acknowledge that I have received oral and written notifications of ultrasound examinations of the brain of a child and have read and understood the information received. I had enough time to consider my child's participation and I had the opportunity to ask questions and I received satisfactory answers to all questions. I understand that my participation is voluntary and that I am free to terminate my participation in the study at any time without giving any reason, and that this will in no way affect the future treatment of my child. I understand that only medical professionals and clinical staff at the pediatric clinic can have access to my child's medical record to ensure that this study is conducted correctly and that the data is properly recorded. All personal information will be considered strictly confidential. Database are analyzed and will only be used for scientific purposes. I will get one signed and dated copy of this notice. I agree that my child is participating in this clinical trial."

The use of data obtained by ultrasound examination of the infant brain, only for scientific purposes is approved by Ethics Committee of Institute for Child and Youth Health Care of Vojvodina.

A prospective study of results based on the Doppler ultrasonography by measuring the resistance index (RI) through an anterior cerebral artery, in 50 infants of gestational age between 26 and 36 weeks, and diagnosed with intracranial hemorrhage, independent of the degree of localization of hemorrhage. Neurosonographic checks are performed within the first 72 hours, and the first seven days of life in preterm infants. Doppler ultrasonography was performed during the same ultrasound examination every premature newborn from whom it was established intracranial hemorrhage. Big fontanelle is used as an acoustic window. Doppler ultrasonography is accompanied by cerebral blood flow through the anterior cerebral artery in the first 72 hours at the latest by the age of seven days of life, and from the age of two weeks, seven days after the first ultrasound examination. Ultrasonic curve reflected the frequency proportional to the speed of red blood cells in the blood vessel. Following parameters were measured: peak systolic, end-diastolic pressure and resistance index RI. Depending on the value RI results were grouped in three groups: I group RI values that are lower than 0.61, II group RI values are between 0.61 and 0.85, a group III with the values of R above 0.85. The resulting data were analyzed using univariate statistical methods: arithmetic mean, standard deviation, testing the significance of the average difference, T-test. The values

of resistance index RI1 representing the measured resistance value of the index in the first neurosonographic views, and RI2 are values of resistance index measured in the second neurosonographic view.

## RESULTS

The results are shown in (Tables 1-3). There were significant differences p<0.05, between the RI values of RI1 and RI2 lower than 0.61 during the first and during the second examination. Statistical analysis values RI1 and RI2 lower than 0.85 and higher than 0.61, shows that there were differences between value RI1 and RI2 in premature newborns with intracranial hemorrhage, p<0.05. There were significant differences between values RI1 and RI2 higher than 0.85, p<0.05. There were significant differences between RI values lower than 0.61 in the first, and in the second ultrasound examination p<0.05. We found significant difference between the two groups of values RI1 and RI2 in patients with PDA, p<0.05 (Table 4).

## DISCUSSION

The most common value RI is between 0.61 and 0.85 which is the world and domestic literature interpreted as a physiological value. Domestic author, Obradovic refers mean value RI of 0699. The literature also recorded approximates the mean RI in their studies, which move in the physiologic range [1,2]. Meerman and associates in the sixth hour of life are values RI 0.70 ± 0.12. In the twelfth hour of life RI amounted to 0.63 ± 0.06, in the twenty-fourth hour of life 0.64 ± 0.10, in the age of 48h RI amounted to 0.66 ± 0.07.

They showed that the biggest changes in the neonatal cerebral circulation occurring during the first days of life and that they are proportional to body weight and gestational age and postnatal age. RI values below 0.61 were obtained in five preterm infants with hemorrhage (10%) at the first treatment in the second review the RI value lower than 0.61 were measured at four (8%) premature infants with intracranial hemorrhage. The mean RI1 for this group of patients is 0.60. RI values were lower than 0.61 in two children with hemorrhage of fourth degree. One child has a value of 0.61 or RI is placed in the second group of the RI values between 0.61 and 0.85, three patients had hemorrhage of the first degree. In one of them was diagnosed with PVL, one was low gestational age, 27 weeks, birth weight 1070g, the third was from a twin pregnancy and had heart defect of significant effect on cerebral blood flow. After second measurement RI is in this patient moved

**Table 1:** Gender structure, birth weight, stage and localization of ICH.

| Variables | 26-28 GW | 29-32 GW | 33-36 GW | Male | Female | Singletons | Twins | Multiple Pregnancies | - | - |
|---|---|---|---|---|---|---|---|---|---|---|
| Patients | 14 (28%) | 13 (26%) | 23 (46%) | - | - | - | - | - | - | - |
| Weight | < 1000 g | < 1000 g 1500 g | > 1500 g | - | - | - | - | - | - | - |
| Patients % | 6 (12%) | 24 (48%) | 20 (40%) | 27 (54%) | 23 (46%) | 37 (74%) | 12 (40%) | - | - | - |
| Stage (Localization) | I | II | III | IV | PVL | Bilat. | Left | Right | PVL, Unilat. | Bil. PVL, Bil. ICH |
| Patients (%) | 40 (64%) | 6 (11%) | 4 (8%) | 6 (11%) | 3 (6%) | 26 (52%) | 11 (22%) | 10 (20%) | 2 (4%) | 1 (2%) |

**Table 2:** Grade of ICH, AS.

| Variables | Grade I | Grade II | Grade III | Grade IV |
|---|---|---|---|---|
| Singletons | 28 (56%) | 5 (10%) | 4 (8%) | - |
| Twins | 1 (2%) | 10 (20%) | - | 1 (2%) |
| Multiple p. | 1 (2%) | - | - | - |
| - | AS | AS <4 | 4<AS<7 | AS >7 |
| - | 1st minute | 13 (26%) | 26 (52%) | 11 (22%) |
| - | 5th minute | 1 (2%) | 25 (50%) | 24 (48%) |

**Table 3:** PDA, FOA, VSD.

| Variables | PDA | FOA | FOA, PDA | VSD | VSD, PDA |
|---|---|---|---|---|---|
| % | 13 (41%) | 10 (31%) | 5 (6%) | 3 (9%) | 1 (3%) |

**Table 4:** RI1, RI2, p, Mean RI.

| RI1, RI2 | RI1, RI2<0.61 | 0.61<RI1, RI2<0.85 | RI1, RI2>0.085 | |
|---|---|---|---|---|
| Patients | 5 (10%) | 41 (82 %) | 4 (8 %) | - |
| Patients | 4 (8%) | 46 (92%) | - | - |
| *P-value* | *P* < 0.05 | *P* < 0.05 | *P* < 0.05 | - |
| **RI1,RI2** | **Hemorrhage Grade I** | **Hemorrhage Grade II** | **Hemorrhage Grade III** | **Hemorrhage Grade IV** |
| *P-value* | *P* > 0.05 | *P* < 0.05 | *P* > 0.05 | P < 0.05 |
| Mean RI | 0.061<RI1<0.85 | | 0.061<RI2<0.085 | |
| Patients | -0.7195 | | -0.7417 | |
| % | 41 (82%) | | 46 (92%) | |

to a second group of higher RI values 0.61 but lower than 0.85, which represents a physiological value. Premature born newborn in the first ultrasonography had RI value of 0.61. In the second measurement it was 0.60 which is classified as a first group with the values of RI below 0.61, which is a bad prognostic sign. If prematurely born infant had diagnosed hemorrhage of third degree in the first ultra-sonographic examination, to be carried out next review was ascertained hemorrhage fourth degree which is forced into hydrocephalus [3].

This patient with associated heart defects had FOA and was born as the first newborn from twin pregnancy. Patient with the measured value RI below 0.61 was an infant gestational age of 24 gestational weeks, birth weight 680g. It is known that children of low birth weight and low gestational age correlated with low RI and with increasing body weight and gestational age get more value RI. Many authors have confirmed that the reduction in RI occurs in children with ischemic changes. Many followed the subcortical echogenicity, later cysts and atrophy in term newborns, such as Saliba, Levene and Stevenson, but noted that even in premature infants with periventricular leukomalacia occurs low index of resistance and reducing vascular resistance. That is what we concluded in our sample. A patient with PVL and hemorrhage of the first degree, which is the first neurosonographic review had RI physiological values is at the second measurement had values RI 0.58 which is a bad prognostic sign for further psychomotor development of a child. Respondents who had a low value RI 0.58 in the second review and the first 0.73 the subjects in whom the diagnosis of PVL. The fourth patient with values RI lower than 0.61 during the second review had value RI 0.58. At the initial RI amounted to 0.6. This is a child of 28 gestation weeks, birth weight 960g, AS in 1st minute was 2, and after 5 minutes was 4. This is also in accordance with findings from the world literature and indicates the reliability of this method in monitoring neurological sequels.

Values RI over 0.85 are not represented in the second measurement but only at the first examination, which means that in four patients who had at first check RI high (above 0.85) during the second examination had physiological RI. The mean RI1 is 0.92. These patients are low gestational age (27,28GW), with diagnosed heart defects PDA, FOA, which significantly increases the value of RI. These subjects in the second ultrasonography have physiological value RI by closing fetal circulation (PDA, FOA). RI2 mean value for this group of patients has reached 0718. RI1 mean of the first group of subjects with PDA amounted to 0.7638, RI2 and the mean value in the second group of subjects was 0, 7485. PDA in these patients was found to affect the RI values for the first group of subjects, but after its closure, there was a significant drop in the value of RI in the second group subjects. RI values in both groups are above 0.61. In the first group, one patient has a value of 0.86 and the value RI is 0.84 in the second measurement after the closure of the PDA. Two patients have RI 0.9 and 0.96 during the first ultrasound examination, but their value later normalize closing PDA. Bada and the authors found that by measuring the velocity of blood flow and its fluctuations by using Doppler can predict intraventricular hemorrhage. These changes in cerebral blood flow reduced muscle relaxants and thus exercised the prevention of intraventricular hemorrhage or worsening of pre-existing hemorrhage. These patients, during the second ultrasound examination, had physiological value RI. This is also in accordance with national and world literature, that with the closure of the PDA, FOA comes to lowering the value RI. Lipman and Martin in his work showed that the significant effect of persistent ductus arteriosus on cerebral hemodynamics and that he is responsible for the low diastolic pixel which explains the high RI. At healthy newborn neonates in addition to the closure of the ductus to fall RI leads and increase $PCO_2$, it is known that carbon dioxide is a powerful vasodilator and causes neonatal brain hyper perfusion. Archer et al are found in low RI values asphyxic infants and attributed to a reduced or absent in the reaction troughs cerebrovascular $PaCO_2$. Van Belle et al found that the abnormal speed fluctuations of cerebral blood flow in the anterior cerebral artery, prior to the commencement of intraventricular hemorrhage also found that fluctuations of cerebral blood flow in the artery of the extension preceding the hemorrhage [4-11].

## CONCLUSION

Doppler neurosonography is the method of choice, which is now used in the measurement of neonatal cerebral circulation, or for non-invasive testing neonatal brain perfusion. In this way it can in premature infants, measuring the resistance in the relevant cerebral blood vessels, predict the occurrence, progression or regression of hemorrhage. Resistance index (RI) can be used as a useful factor in the clinical management of premature newborns with intracranial hemorrhage. With increase in gestational age RI falls. With increase in body weight RI is decreasing. With closing PDA value of resistance index is decreasing.

## DISCLOSURE

There is no conflict of interests.

## ACKNOWLEDGMENTS

No disclosures or acknowledgments.

## REFERENCES

1. Kurian J, Sotardi S, Liszewski MC, Gomes WA, Hoffman T, Taragin BH. Three-dimensional ultrasound of the neonatal brain: technical approach and spectrum of disease. Pediatr Radiol 2017;47:613-627.
2. Vasiljevic B, Gojnic M, Maglajlic-Djukic S, Antonovic, O. Normal values of cerebral blood flow velocities in neonates. Serbian Archives of All Medicine. 2010;1381:86-191.
3. Veyrac C, Couture A, Saguintaah M, Band C. Brain ultrasonography in the preterm infant. Pediatr Radiol. 2006;36:626-35.
4. Mainous RO, Looney S. A pilot study of changes in cerebral blood flow velocity, resistance, and vital signs following a painful stimulus in the premature infant. Neonatal Care. 2007;7:88-104.
5. Shea OTM, Kuban KCK, Allred EN, Paneth N. Neonatal cranial ultrasound lesions and deleopmental delays at 2 years of age among extremilyloe gestational age children. Pediatrics. 2008;122:662-69.
6. Leijser LM, De Vries L, Cowan FM. Using cerebral ultrasound effectively in the newborn infant. Early Hum Dev. 2006:82:827-35.
7. Riccabona M, Resch B, Eder HG, Ebner F. Clinical value of amplitude-coded colour Doppler sonography. Child Nerv Syst. 2002;18:12.
8. Noori S, McCoy M. Changes in cardiac function and cerebral blood flow in relation to peri/intraventricular hemorrhage in extremely preterm infants. J Pediatr. 2014;164:264-270.
9. Forster DE, Koumoundouros E. Cerebral blood flow velocities and cerebrovascular resistance in normal-term neonates in the first 72 hours. J Paediatr Child Health. 2017;54.
10. Schwaberger B, Pichler G, Binder-Heschl C, Baik N, Avian A,

Urlesberger B. Transitional changes in cerebral blood volume at birth. Neonatology. 2015;108:253-8.

11. Vutskits L. Cerebral blood flow in the neonate. Paediatr Anaesth. 2015;24.