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TRANSFONTANEAL BRAIN ULTRASOUND: A POWERFUL ASSESSMENT TOOL FOR CRITICALLY ILL NEONATES

TRANSFONTANEALNI ULTRAZVUK MOZGA: MOĆAN ALAT ZA PROCJENU KRITIČNO BOLESNE NOVOROĐENČADI

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ABSTRACT

The ultrasound in medicine today is already tested and proven method, with relatively long tradition and training period. It has been versed and still tested in various branches of medicine, and among the first experiences, it was in neonates around the 1970s. Today, monitoring and supervision critically ill neonates, particularly premature infants, placed in incubator, is almost impossible without ultrasound. By this method, we are able examine and evaluate critically ill neonates at the patient's bedside, with minimum manipulating, without sedation, without anesthesia or contrast agents.

Transfontaneal neonatal brain ultrasound provides diagnosis and assessment trend of brain changes through repeated examinations, without harmful radiation to child, which is important because in some conditions, serial examination is necessary to detect the full spectrum of lesional change. This review aims to highlight the importance of transfontanel brain ultrasound in neonates, and to provide a tool for structured neonatal brain ultrasound scanning, reporting and quality assessment.

Key words: ultrasound, brain, neonate, assessment.

SAŽETAK

Ultrazvuk u medicini danas je već testirana i dokazana metoda, sa relativno dugom tradicijom i periodom obuke. Proučen je i dodatno testiran u raznim granama medicine, a među prvim iskustvima bila je njegova primjena kod novorođenčadi oko 1970-ih. Danas je praćenje i nadzor teško bolesne novorođenčadi, posebno prijevremeno rođene djece, smještenih u inkubatoru, gotovo nemoguć bez ultrazvuka. Ovom metodom možemo pregledati i procijeniti kritično bolesnu novorođenčad pored pacijentovog kreveta, uz minimalne manipulacije, bez sedacije, bez anestezije ili kontrastnih sredstava.

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Transfontanealni ultrazvuk mozga novorođenčadi omogućava dijagnostiku i procjenu trenda promjena mozga kroz ponovljene preglede, bez štetnog zračenja za dijete, što je važno jer je u nekim stanjima neophodna serija pregleda da bi se otkrio cijeli spektar lezijskih promjena. Ovaj pregled ima za cilj da naglasi značaj transfontanealnog ultrazvuka mozga u novorođenčadi, te da predoči strukturirani pristup metodologiji samog pregleda, načinu izvještavanja i opcijama procjene kvaliteta.

Ključne riječi: ultrazvuk, mozak, novorođenče, procjena.

INTRODUCTION

Transfontaneal brain ultrasound (TBUS) is still a first-line modality for neuro-imaging studies of the neonatal brain. The examination is radiation free and can be performed immediately after birth, providing a quick orientation with real-time overview of the neonatal brain (Siegel, 2011). arly identification of neonates with brain injury, which are therefore at risk of impaired neurological development, can benefit every single child. This allows for a personalized approach while creating and initiating appropriate early interventions aimed at improving neurological outcomes. Ultrasound is less expensive and less complicated method of examination in comparison to other imaging methods, for example, magnetic resonance imaging (MRI), which involving more professionals with takes more time, requires transportation and longer sedation, and often neonatal anesthesia (Ibrahim et al., 2018). Brain ultrasound is indicated for all neonates at risk or suspicion of brain injury, that can be antenatal, perinatal and postnatal according to time of onset. Antenatal and perinatal causes of neonatal brain injury include twin-related problems, obstetric intervention, infections, prolonged resuscitation, prematurity, low birth weight, microcephaly and macrocephaly, suspected genetic syndrome etc. Postnatal causes of neonatal brain injury include all neonatal diseases and disorders such as seizures, apnea, encephalopathy, sepsis, meningitis, unexplained clinical deterioration, unexplained decrease in hemoglobin level, symptomatic hypoglycemia, congenital metabolism errors, abnormal movements and muscle tone, congenital heart disease, need for surgery, etc (Guillot et al., 2020). Brain ultrasound enables the detection of brain injuries associated with perinatal hypoxic-ischemic insult. Cerebral edema and impaired perfusion are often noticed at early stage, but for tipicall findings of hyperechogenicity basal ganglia and thalamus, to develop a need for about 2-3 days. For cortical and subcortical changes may take 5-7 days, before lesions become evident. In addition, before therapeutic hypothermia, it is necessary to make a brain ultrasound, to exclude congenital malformations and intracranial hemorrhage (Fabre et al., 2018).

In addition to highlighting the importance of transfontanel brain ultrasound in neonates, this review aims to provide a tool for structured neonatal ultrasound brain scanning, reporting and quality assessment.

Optimizing scan settings

Ultrasound device have many adaptable settings, which configuration can dramatically affect image quality. In addition to technical skills and knowledge of handling ultrasound machine, neonatal brain ultrasound professionals need to know neonatal brain normal and abnormal developmental neuroanatomy and pathology, including the time course of brain injury Patient safety should always come first. Prior to the ultrasound examination, it must be ensured that neonates have stable vital signs. The transducer should be sized according to the fontanelle, the pressure on the baby's head should be minimal and the gel should be warmed. The examination is usually performed with a frequency of 7.5-11 MHz (Dudink et al., 2020).

Safety ultrasound

Neonatal brain ultrasound is considered non-invasive. However, acoustic waves can cause thermal and mechanical effects in the tissue. Studies on the harmfulness of ultrasound to the developing brain, especially in neonates born before 28 weeks of gestation, are still limited. Clinicians must constantly compare the risk of benefit. In the absence of sufficient safety data, the standard ALARA principle should be applied. Transducers should be thoroughly cleaned after use, and overall use, maintenance and servicing must be in accordance with standards (Anonymous, 2020).

Reporting and writing neonatal brain ultrasound findings

Writing and presenting ultrasound findings should be clear, concise, in timely manner, with careful interpretation. Abbreviations should be avoided. Reporting should include both normal and abnormal findings. Specific diagnoses, differential diagnoses, should be noted, considering that ultrasound is still a partially subjective method. The size of the lesions should be detailed using appropriate anatomical terminology with, if possible, gradation of the lesions. Measurements and deviations from the normal size should be documented with reference values. In some cases, it may be useful to compare findings with previous ones to present the evolution of lesions, with the recommendation of the dynamics of further controls. Additional recorded images should be made whenever necessary, including video sequences. It should also be mentioned the possible limitations that affected the quality of the examination (neonates health status, technical problems, etc.) (Maller an Cohen, 2019).

Timing of neonatal brain ultrasound examinatio

It should make effort to introduce at least one mandatory brain ultrasound screening for each neonate. In some cases, a single examination may be sufficient to rule out suspected abnormality. On the other hand, in children at risk, and especially in critically ill neonates, a series of ultrasound brain examinations is needed to reveal the full spectrum of a changes in the brain lesions. Multiple examinations, if required, are usually scheduled on days 1, 3, 7, 14, 28, at 6 weeks and at the age corresponding to the corrected full-birth equivalent. Whenever a clinical condition dictates, an extra examination should be performed.

The first examination after birth is usually used to rule out antenatal brain injury and congenital malformation. Examination during the first week of life aims to detect intraventricular hemorrhage into the germinal matrix. At least 50% of the affected neonates, germinal matrix hemorrhage can be detected in first day of life, and about 90% of the lesions are identified in the first three days postnatal age (Reubsaet et al., 2017). Neonatal brain ultrasound performed between 2 to 6 weeks, identifies posthemorrhagic ventriculomegaly, and late forms of intraventricular hemorrhage. Cystic periventricular leukomalacia can become evident within 14 days after injury, although occasionally small cysts may develop up to 6 weeks after birth. Therefore, careful and detailed examination of brain structures after the first two weeks of life, is crucial to detecting all cases of cerebral white matter injury. Special focus is on neonatal brain ultrasound at the time which corresponds to the time of achieving full gestation. Scanning at term-equivalent age is very important because it can confirmed and identify permanent consequences of brain lesions. The value of this late neonatal brain ultrasound scan for predicting the outcome of extremely preterm neonates, is compared with the predictive value of conventional MRI (Boran et al., 2018).

Specificities of neonatal morbidity

It is believed that changes in the perinatal period not only determine the short-term postnatal outcome and early neonatal conditions and diseases, but their negative impact can be expected from childhood to adulthood. Immediate neonatal problems that can affect neonates range from physiological adaptation difficulties to life-threatening illnesses. Studies report that about 9% of neonates require intensive treatment in the neonatal intensive care unit – NICU (Freeman and Hwang, 2022). With the development and ongoing progress of neonatal intensive care, there has been a marked decrease in perinatal mortality. Still it is considered that about 70% of infant deaths in the early neonatal period and 75% of morbidity are directly caused by preterm delivery. More worrying that the increased frequency of the respiratory, metabolic and neurological disorders, in premature infants can be lifetime and permanent (Maller and Cohen, 2019). Most studies analyzing neonatal morbidity and mortality have highlighted perinatal asphyxia and hypoxic ischemic encephalopathy as major causes in term neonates, and respiratory distress syndrome and intracranial hemorrhage in preterm infants. Hypoxic-ischemic encephalopathy (HIE) is the major acute manifestation of perinatal asphyxia and is associated with significant neonatal morbidity and mortality. Predictors of neurological dysfunction and poor outcome in neonates are most commonly low Apgar score, quality of resuscitation, and quality of intensive neonatal care. Intracranial hemorrhage is more common in preterm infants. With increasing gestation, reported a fall in mortality and incidence of morbidity, except for periventricular leukomalacia whose risk actually increases (Epelman et al., 2010).

Consequences of prematurity

Early and late preterm infants outcome is the greatest challenge of modern medical practiceIt is a medically proven fact that the grounds of death (60 percent) in neonates occurs due to being undervveight, especially the premature ones. The efforts are to avoid premature birth

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and give the best care to the ones that have been born already by finding ali the components that are causing it (Maller and Cohen, 20119). Very encouraging results have been achieved associated, planned and organized multidisciplinary activities of health professionals from different fields who take care of vulnerable pregnancy and vulnerable neonates. Thanks to modern medical technology it has become easier to deal with prenatal care and undervveight babies but the most important factor to truly succeed in the hereafter is the human factor, nurses and doctors and possibly the mother of a child who with their knovvledge, experience, dedication and conscience will continue to use medical technology for the benefit of healthy child (Hand et al., 2020).

Despite progress, there is no significant reduction in preterm birth. All we have to do is look for other ways to prevent possible neonatal morbidity and mortality. In addition to improving the ways of neuroprotection of the sensitive structures of the immature brain, there is also a need to improve the other side, such as technological, pharmacological and other treatments, which would continue to sustain physiological processes, growth and development. Improved neonatal intensive care represents the greatest pledge for the future, for the proper growth and development of children (Hwang et al., 2022).

Critically ill neonates in Neonatal intensive care unit (NICU)

The most common cause for admission in the NICU are signs of respiratory, circulatory and neurological dysfunctions. These three aspects of endangerment of life of the newborn are interconnected and intertwined. Different diseases and pathological conditions usually trigger one aspect of life threatening, and the other two aspects of life threatening are joined very quickly. Therefore, life-threatening conditions have a very similar clinical presentation, regardless of the etiological reason and underlying disease. However, clinical assessment of respiratory and circulatory dysfunction is quite reliable from earlier, with additional and readily available diagnostic tools. Quality assessment of neonatal neurological dysfunction has long been neglected, which with the use of brain ultrasound in neonates in recent decades, has been significantly altered and improved (Freeman and Hwang, 2022).

Neonatal transfontaneal brain ultrasound

Ultrasound examination of the brain is an imaging examination of brain structures. It provides an overview of normal brain structures, anomalies of brain development, inflammatory brain processes, brain tumors, various types of brain hemorrhage, and hypoxic-ischemic brain changes. It is performed by ultrasonic waves that, when passing through a large fontanelle, repel different brain structures. The large fontanelle represents an "acoustic window", a space through which ultrasonic waves can penetrate brain structures.

Frequencies ranging from 5Mhz to 7.5 MHz are used for the search of the children's brain. Higher frequency allows better detail resolution (Dudink et al., 2020).

The examination is usually performed via a large fontanelle. The child lies on his back, his head fixed with pillows or lying in the examiner's hand. The contact agent (aquagel) improves the passage of ultrasonic waves. It is applied to the skin above a large fontanelle. The probe is placed in the middle of a large fountain, and by tilting and moving the probe at

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certain angles and directions, the corresponding sections are obtained. Because different pathological conditions and some physiological changes may give a similar finding at initial examination, for the correct and complete interpretation of the examination, in addition to good technique, the frequency and timing of the examination and the experience and knowledge of the diagnostician are particularly important (Anonymous 2020). Indications for brain ultrasound examination in neonates include:

- Prematurity (especially gestational age less than 35 weeks)
- Neurological disorder in neonates, convulsions
- Neuro-risk factors in the perinatal period (asphyxia, intrauterine growth retardation, respiratory distress syndrome, apnea, perinatal infection, neonates from mothers with gestational diabetes, hemorrhagic diathesis, traumatic birth, etc.)
- Age-appropriate head circumference (macrocephaly or microcephaly)
- Facial asymmetry and other irregularities
- Neonates with a neural tube cleft (meningomyelocele)
- Central nervous system infections
- Head injuries
- Symptoms and signs of elevated intracranial pressure in infants
- Conditions after neurosurgical intracranial surgery in infants, etc.

Neonatal brain injury

The location of the infant's brain injury depends on the gestational age, which is explained by changes in the central nervous system's blood supply during maturation. In infants younger than 35 gestational weeks, lesions are located in the deeper parts of the brain (periventricular area), and in infants over 35 weeks of age, they are usually located in and below the cortex (Hwang et al., 2022). The most common cause of neonatal brain damage is intracranial hemorrhage and hypoxic-ischemic injuries (injuries resulting from inadequate oxygen supply). Neurological development depends on the time of the damage, the location and the extent of the damage (Hirtz and Ment, 2016).

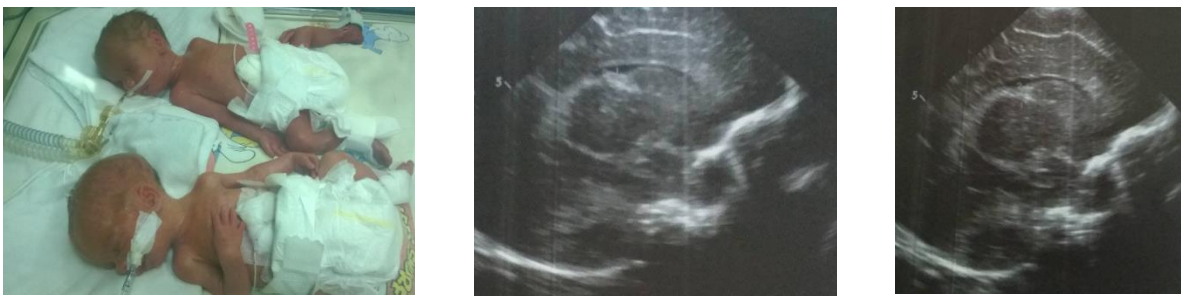

Figure 1. Premature twins in NICU with transfontaneal brain ultrasound exam

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Neonatal intracranial hemorrhage

Intracranial hemorrhage is common in the neonatal age. The frequency and type depends on gestational age; neonates less mature have higher incidence of bleeding, which can range from 2% to 30%, and even more according to some data sources (Hirtz and Ment, 2016). Intracranial hemorrhages are divided into extracerebral and intracerebral hemorrhages. Extracerebral hemorrhages are haemorrhages above the brain itself and depending on the brain sheaths can be epidural, subdural and subarachnoid. Epidural bleeding is usually associated with a fracture of the skull. It is accompanied by progressive worsening of neurological symptoms and usually, unfortunately, has a fatal outcome. Subdural hemorrhage is rare today and is primarily caused by trauma at birth, particularly in conditions that require surgical completion of delivery. It usually occurs in term newborns. Depending on the localization and intensity, the symptoms can be minimal or asymptomatic, to severe clinical forms, even with fatal outcome. Subaarachnoid hemorrhage has the best prognosis. More often in premature infants. The cause is usually hypoxia, less often trauma. It is manifested by various symptoms that can be very mild but may also have a severe, progressive course with a fatal outcome (Parodi et al., 2015).

Intracerebral hemorrhage is bleeding into brain tissue. Periventricular and intraventricular hemorrhages are distinguished, depending on the involvement of the ventricles. It is primarily a pathology of preterm infants, although they are also increasingly found in term infants. They are usually caused by hypoxia or trauma. The ideal diagnostic method is ultrasound, which can detect these changes with an accuracy of 95% compared to a CT scan, and the ultrasound scan correlates well with the MR brain scan (Ibrahim et al., 2018). We distinguish four stages of intracranial hemorrhage. First degree hemorrhage is localized to the so-called germinal matrix, the most common place where bleeding occurs (Reubsaet et al., 2017). In the second stage, the bleeding penetrates into the brain chambers but does not spread them. Grades I and II are also referred as uncomplicated bleeding. Third-degree hemorrhage occurs if the blood penetrates deeper into the brain ventricles, causing their expansion. The fourth stage is is caused by the penetration of blood from the ventricle into the brain tissue. Grades III and IV are complicated bleeding, manifested by substantial structural changes in the brain tissue and disturbances in the neurological development of children. The major factors affecting the prognosis are the extent of bleeding and possible complications (Leijser et al., 2018).

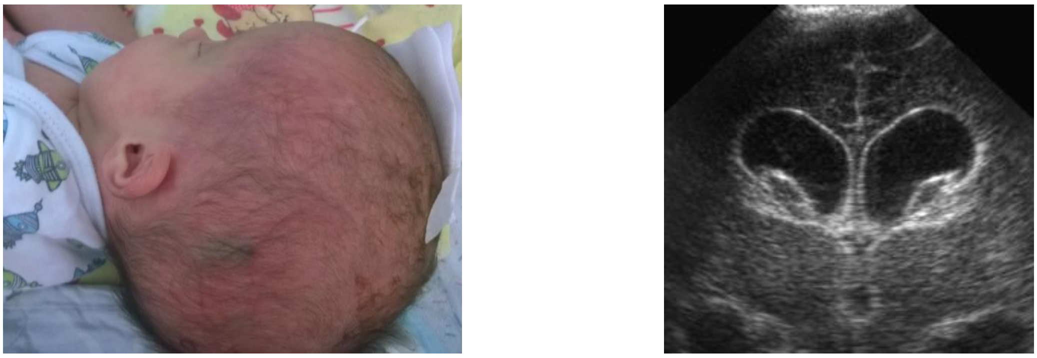

Figure 2. Term neonate in NICU with posthemorrhagic hydrocephalus and his brain ultrasound exam

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It is necessary to monitor children with cerebral hemorrhage during development in order to assess the severity of their neurological impairment and subsequent mental (cognitive) development. Grade I and II hemorrhages less frequently cause motor and cognitive sequelae, although up to 30% of children with these bleeding levels show some neurodevelopmental disorder, according to some authors (Hirtz and Ment, 2016). In children with grade III hemorrhage, cerebral palsy or some form of neuromotor deviation can develop in a high percentage. In stage IV bleeding, the mortality rate is high (81%) or if the child survives there is severe neurological impairment in the form of significant motor impairment, often accompanied by cognitive impairment (Kurian et al., 2017).

Hypoxic-ischemic encephalopathy (HIE)

Hypoxic-ischemic encephalopathy (HIE) is a non-progressive encephalopathy resulting from a lack of oxygen in the blood (hypoxemia) and/or a disturbance of oxygen supply to the brain (ischemia). The incidence of hypoxic-ischemic encephalopathy is not exactly known, but it is more common in preterm infants. HIE may result in permanent impairment, cerebral palsy, mental retardation and epilepsy. Usually, HIE is associated with cerebral hemorrhage, suggesting that both types of brain damage are actually two episodes during the same, underlying infant disease. (Epelman et al., 2010).

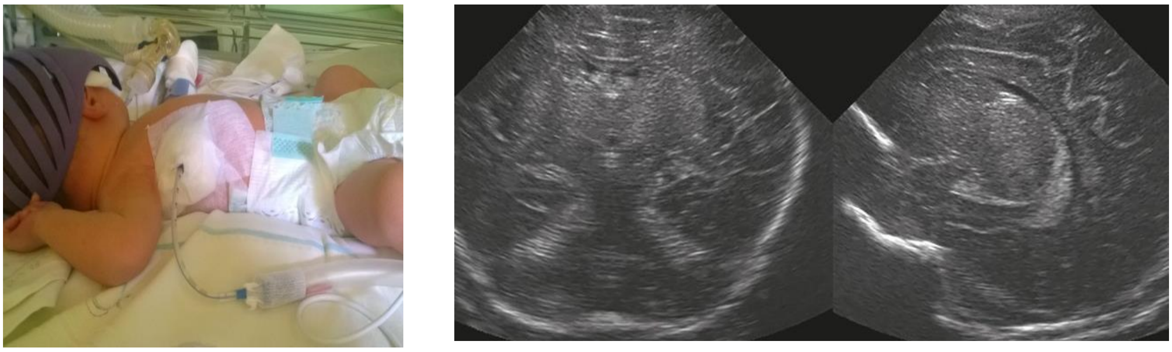

Figure 3. Term neonate in NICU with hipoxic ischemic encephalopathy and his brain ultrasound exam

HIE is divided into three stages: mild, moderate and severe. From subtypes HIE should emphasize the focal, multifocal injuries and periventricular leukomalacia. The most common cause of focal or multiple focal brain damage are thromboembolic events associated with placental infarction, infection, trauma, thrombus formation, clotting disorders, etc. In 50% of infants with focal ischemic lesions, the middle cerebral artery is affected (Epelman et al., 2010). Venous thromboses are less common. Focal and multiple lesions can occur at different stages of brain development and lead to cell death with loss of brain tissue and cavity formation. The clinical manifestation is dominated by focal seizures, cerebral palsy with hemiparesis, while generalized damage results in spastic tetraparesis. Periventricular leukomalacia is hypoxic-ischemic damage, which typically occurs in preterm infants with low gestational age, precisely because of the specific degree of development of their brain.

Due to cell death, cavities are formed, located near the brain chambers, and are usually accompanied by enlargement of the brain chambers (ventriculomegaly). The cerebral motor

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pathways responsible for the motor cycle pass through exactly the part of the brain where periventricular leukomalacia occurs most frequently. Periventricular leukomalacia almost always results with cerebral palsy (Neuberger et al. 2018).

CONCLUSION

Critically ill neonates, especially with postnatal complications, brain ultrasound required to be done during the hospital stay. In preterm neonates, usually be the reason for a minimum of one screening examination prior to discharge from the hospital. At the same time it is very likely that term neonates, without major complications usually remain through ultrasound unviewed. For technical reasons, brain ultrasound is reserved for children with some risk or neurological problem. In the future, a brain ultrasound should be a routine examination such as a hip ultrasound, or hearing screening. This would allow detection of some congenital brain malformations, developing hydrocephalus, clinically intractable bleeding in the brain, screening of infants at increased risk for neuromotor development, subsequent behavioral or learning disorders. Preventive brain ultrasound would screen newborns in whom vaccination should be delayed, genetic testing performed, or included in physical habilitation, or some medical treatment. Thus, the consequences of some conditions could be reduced and better psychomotor development results of at-risk children could be achieved. Therefore, the high efficiency of neonatal brain ultrasound in detecting the presence of brain damage, and analyzing its evolution by regular repeated examinations and monitoring, may well guide further clinical decisions and prognoses.

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