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Risk factors of periventricular leukomalacia in singleton infants born from 23rd to 26th weeks of gestation – Retrospective study

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ABSTRACT

Introduction: Periventricular leukomalacia (PVL) is one of the most common hypoxic-ischemic pathologies among preterm newborns. The bracket most vulnerable to PVL are newborns born before 34 weeks' gestation, especially those with very low and extremely low birth weights. In a population of very low birth weight newborns, the frequency of periventricular white matter injury (PWMI) including PVL is 5–15%. The aim of our study was to verify the potential risk factors of the occurrence of PVL among infants born between 23 and 26 weeks' gestation. **Methods:** The retrospective study included a group of 115 unrelated infants born between 23 and 26 week's gestation, hospitalized in the Neonatal Intensive Care in the Department of Neonatology, Poznan University of Medical Sciences in 2010–2014, born in the clinic or transported to it after birth in the hospital of lower references. The diagnosis of PVL was based on transcranial ultrasound. **Results:** PVL was diagnosed in 17 (14.8%), including 5 (29.4%) infants born from 23 to 24 weeks' gestation and 12 (70.6%) born from 25 to 26 weeks gestation. Higher incidence of PVL was found among infants born outside tertiary hospital (OR 7.933 (2.206–35.19); $p = 0.0005$) and newborns diagnosed with III and IV intraventricular hemorrhage (IVH) (OR 3.273 (1.042–10.28); $p = 0.036$). **Conclusions:** Delivery in the third-level hospital as well as IVH prevention significantly reduces the risk of PVL. Well-developed prenatal care, fetus transport in utero and delivery in the third-level hospital seem to be crucial in the prevention of this pathology.

Introduction

One of the most common hypoxic-ischemic pathologies among preterm newborns is periventricular leukomalacia (PVL). The frequency of this pathology is inversely proportional to gestational age and birth weight. The most vulnerable bracket is newborns born before 34 weeks' gestation, especially with very low and extremely low birth weight. In a population of very low birth weight newborns

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the frequency of periventricular white matter injury (PWMI), including PVL is 5–15% [1].

PVL is a white matter injury (WMI) in the form of nerve tissue necrosis in the border zone of vascularization; this is dorsally and laterally to lateral ventricles. There are four stages of this pathology advancement, from increased periventricular echogenicity to the existence of large cavities, reaching deep into the white matter. WMI is a major cause of cerebral palsy, causing severe disability in motor and intellectual areas, as well as vision and hearing disorders [2–4].

The pathogenesis of PVL is complex. Among the risk factors are: chronic or subacute hypoxia, intrauterine infection, bradycardia, apnea, hypotension, and anemia. It often occurs in infants born to mothers with diabetes and pre-pregnancy obesity. PVL generally coexists with III and IV degree of intraventricular hemorrhage (IVH) and is located around post hemorrhagic changes [2, 5].

The aim of our study was to analyze of potential risk factors of PVL among newborns born between 23 and 26 weeks' gestation.

Material and methods

The study population

The study included infants born between 23 and 26 weeks' gestation, and hospitalized in Neonatal Intensive Care in the Department of Neonatology University of Medical Sciences in 2010–2014, born in the same clinic or transported to it after birth. The study included 115 unrelated newborns.

The study did not include infants born in a week of pregnancy other than 23–26 weeks, newborns from multiple pregnancies, pregnancies in which there was a death of one of the fetuses, infants with chromosomal aberrations and TORCH group intrauterine infections.

Periventricular leukomalacia – definition

The diagnosis of PVL was based on transcranial ultrasound, which was performed in accordance with local standards, based on the guidelines of Polish Neonatal Society – transcranial ultrasound was performed on 1st day of life, the 3rd, and the 7th day of life, and further research depending on the extent of changes found in previous studies. In newborns diagnosed with III and IV grade of IVH, ultrasound was performed at least once a week and after diagnosis of ventricle expansion; every 3 days [6]. Periventricular leukomalacia was defined according to de Vries criteria (Table I) [7].

Table I – Periventricular leukomalacia according to de Vries criteria

Grade	Cranial ultrasound findings	Number of patients $n = 17$(%)
I	Increased periventricular echogenicity persisting more than 7 days	3 (17.6%)
II	Increased periventricular echogenicity developing into small periventricular cysts	6 (35.3%)
III	Increased periventricular echogenicity developing into extensive periventricular, occipital and frontoparietal cysts	6 (35.3%)
IV	Increased periventricular echogenicity in deep white matter developing into extensive subcortical cysts	2 (11.8%)

Risk factors

The analysis included following potential risk factors of PVL:

1. Maternal: mother's age, maternal cigarette smoking during pregnancy, mother's hypertension, cervical incompetence, premature rupture of membranes (PROM), antenatal steroidotherapy (according to the recommendation of the Polish Society of Gynecology, used when mothers are at risk of preterm delivery between 24 and 34 weeks of pregnancy at a dose of 2 × 12 mg intramuscularly), the way of delivery (vaginal birth *vs.* cesarean section), delivery in (inborn) or outside (out born) third-level hospitals, placental abruption (partial or total).
2. Neonatal: gender, gestational age (GA; weeks), birth weight (BW; grams), intrauterine growth restriction (IUGR; defined as birth weight under 3rd percentile), birth asphyxia (defined as APGAR score less than 6 at 10 min and pH < 7.0 or blood base excess (BE) < −15 mmol/l in cord blood); intrauterine infection, kind of respiratory ventilation (invasive or non-invasive), hypotension therapy (defined as mean blood pressure below value corresponding to neonate's gestational age with pre-existing symptoms of hypotension such as blood circulation disorders, delayed capillary return, oliguria, metabolic acidosis) in the first 7 days of life (supply of crystalloid (bolus 10–15 ml/kg) and/or catecholamines), metabolic acidosis therapy with the use of $NaHCO_3$ in the first 7 days of life (when the blood pH <7.2 and/or BE <−10), occurrence and the final degree of IVH by Papille scale (Grade I – bleeding only in the germinal matrix; II – bleeding inside the ventricles; III – ventricles enlarged by the accumulated blood; IV – bleeding extends into the brain tissue around the ventricles) [8] and the presence of post-hemorrhagic hydrocephalus. Baseline characteristic of enrolled infants is shown in Table II.

Statistical analysis

Chi-square test without or with Yates correction was applied for comparisons of dichotomous variables, where appropriate. The odds ratio (OR) and 95% confidence intervals (95% CI) were calculated for statistically significant variables. Unconditional logistic regression analysis was used to adjust for the effect of confounders such as gender, GA, BW; intrauterine growth restriction (IUGR), birth asphyxia, intrauterine infection; respiratory ventilation, hypotension, acidosis, IVH, post-hemorrhagic hydrocephalus (PHH), maternal age, cigarettes, maternal hypertension, cervical incompetence, premature rupture of membranes (PROM), prenatal

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