

THE MAIN SEQUELAE OF PRETERM BIRTH: FOCUS ON NEURODEVELOPMENTAL DISORDERS

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ABSTRACT

Preterm birth is a traumatic event that interrupts the physiological processes that allow the development of the Nervous System and the body systems, resulting in a multi-organ dysfunction, of an entity in inverse proportion to the gestational age, which causes respiratory, cardiovascular, metabolic, infectious endocrine problems. and neurological. In particular, at a neurological level, in the most serious cases, for macroscopic lesions of the Central Nervous System, there is the risk of incurring in evolutionary Disabilities (Infantile Cerebral Palsy etc.); but in the absence of severe damage, since the birth occurs at a critical moment of the cerebral development in which the cortex is being organized, it is possible to establish minor deficits, arising from alterations in neural connectivity.

Keywords: preterm birth, periventricular leukomalacia, Neonatal Intensive Care Unit.

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Background

The main indicator of physical and neurological maturation in newborns, main criterion for their classification, is the gestational age (duration of pregnancy), calculated from the first day of the last menstrual period and considered as normal if 40 weeks.

Based on gestational age, children born between 37 weeks and 41 weeks + 6 days are identified as term infants and those born before the 37th week are preterm.

The latter are distinguished in:

• Late Preterm or Near Term (LPT): 34 sett - 36 sec + 6g;

• Moderate Preterm (MPT): 32 wk - 33sett + 6g;

• Very Preterm (VPT) 28 wk - 31 + 6g;

• Extremely Preterm (EPT): 22 wk - 27sett + 6g;

Moreover, based on weight, newborns may be classified into:

• Low birtweight (LBW): <2000 gr;

• Very low birtweight (VLBW): <1500 gr;

• Extremely low birtweight (ELBW): <1000 gr.

In general, survival appears directly proportional to weight and gestational age, while the morbidity rate is inversely related to these parameters⁽¹⁻⁵⁾.

Based on parameters such as weight, length and head circumference, there is a further distinction:

- AGA (Adapted for gestational age) if the weight is between the 10th and 90th percentile for the gestational age;
- SGA (small for gestational age) if the weight is less than the 10th percentile for management age;
- LGA (large for gestational age) if the weight is above the 90th percentile for management age.

Causes of preterm birth

In 50% of cases the preterm birth is determined by the early spontaneous onset of labor, in 30% it is caused by premature rupture of the membranes, while in 20% it is due to iatrogenic induction of labor for maternal, obstetric-gynecological or fetal indications⁽¹⁻⁵⁾.

Regarding the maternal problems, the main ones are: pre-eclampsia and eclampsia, infections (from group B Streptococcus, persistent bacillary diseases, etc.), chronic pathologies (eg heart disease and kidney disease), drug or drug abuse, trauma. The possible causes of obstetric-gynecological nature are: detachment of placenta, uterine malformations, cervical incontinence. Finally, among the fetal indications, there are: fetal distress, pathological alterations of the cardiotocographic tracing, erythroblastosis, multiple pregnancy and important malformations. There are also numerous other factors, including psychological stress or exogenous toxic substances such as smoking, cocaine and opioids, which have potent vasoconstrictive action that can cause a decrease in uteroplacental flow and consequent restriction of fetal growth and preterm birth⁽¹⁻⁵⁾.

Brain damage

The set of events that led to premature birth may themselves be a causal factor of brain damage. Moreover, the immaturity of the nervous system associated with that of all the other organs, mainly the cardio-vascular and respiratory system, expose the brain to a greater risk of damage, or make it more vulnerable to hypoxic-ischemic and inflammatory insults. The risk is also increased by being exposed to the extra-uterine environment, and therefore to non-physiological stimulations, to

invasive stimuli and to atypical relational and attachment modalities⁽¹⁻⁵⁾.

The subplate neurons, still predominant in LTP, are particularly vulnerable to hypoxic-ischemic insults which would compromise the development of cortical organization and thalamo-cortical connectivity. In addition, LPTs are also at risk of white matter damage due to various mechanisms such as: the development of oligodendrocytes, cytokines, the damage caused by free radicals and the lack of antioxidant enzymes that regulate oxidative stress⁽¹⁻⁵⁾. The pathologies to which the premature brain is most exposed are the cystic periventricular leukomalacia (c-PVL), the hemorrhage of the germinative and intraventricular matrix (GMH-IHV) and the cerebellar hemorrhage⁽¹⁻⁵⁾.

Periventricular Leukomalacia

Periventricular leukomalacia is a white matter disease (the most vulnerable structure of the developing brain) adjacent to the ventricular cavities, which is softened following hypoxic-ischemic or infectious insult. The extent of the damage may vary from small areas of gliosis and necrosis to widespread involvement. The incidence in VLBW is about 2-4%⁽¹⁻⁵⁾.

In VLBW the main neurological disorder is the intraventricular hemorrhage. Hemorrhage of the germinative and intraventricular matrix (GMH-IHV) is the most frequent form of intracranial hemorrhage; the risk is inversely proportional to the gestational age and affects 10-30% of the VLBW. It is located in the germinal matrix of the lateral ventricles, which in the last quarter of gestation is particularly fragile due to the presence of vessels richly sprayed with thin walls. The bleeding can stop near the germination matrix or spread inside the lateral ventricles, the III ventricle and the IV ventricle and in the communicating subarachnoid spaces. It typically occurs within the first 3-4 days of life and the most serious complications are the parenchymal venous infarct and the posthemorrhagic hydrocephalus. Cerebellar hemorrhage originates from germination matrix bleeds and involves about 10-25% of the VLBW and 12% of the ELBW. In most cases it affects the cerebellar hemispheres, while the worm is less involved. The involvement of the worm increases the risk of distant unfavorable neurological outcomes such as cognitive, behavioral and language deficits⁽⁶⁻⁴⁰⁾ (Figures 1).

The preterm birth sequelae

Preterm birth is therefore a traumatic event that occurs at a critical period for the development of the CNS, exposing the child, still immature, to atypical, invasive and painful environmental stimulation. The clinical signs found at birth or during the first month of life can potentially evolve into an established disease, in minor brain dysfunctions or in “transient disorders” of development⁽⁶⁻⁴⁰⁾. In the most severe cases, for macroscopic lesions of the CNS (periventricular leukomalacia, intraventricular hemorrhage, hypoxic-ischemic encephalopathy, hydrocephalus) there is the risk of incurring developmental disabilities, such as Infantile Cerebral

Conversely, in the absence of severe damage, alterations in neural connectivity, related to anomalies in the organization phase of the cerebral cortex, can lead to various cognitive, linguistic, behavioral and relational deficits⁽⁶¹⁻⁷⁰⁾.

The phase of organization of the cerebral cortex corresponds to the period in which the premature babies remain in the Neonatal Intensive Care Unit, therefore, besides the impact on the central nervous system integrity of the numerous morbid conditions to which the preterm infant is exposed, a fundamental role in Determinism of minimal neurological damage is also played by the unfavorable environment of intensive care⁽⁶³⁻⁶⁹⁾. The spectrum of mild neurobehavioral disabilities to which prematurely born children can meet (including alterations in language, attention, socio-emotional development, executive functions and development of coordination) is large and complex, but in all cases determines significant effects on the quality of life of the child⁽⁶¹⁻⁷⁰⁾.

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In the most severe cases, for macroscopic lesions of the CNS (periventricular leukomalacia, intraventricular hemorrhage, hypoxic-ischemic encephalopathy, hydrocephalus) there is the risk of incurring developmental disabilities, such as Infantile Cerebral Palsy, blindness, deafness, etc.

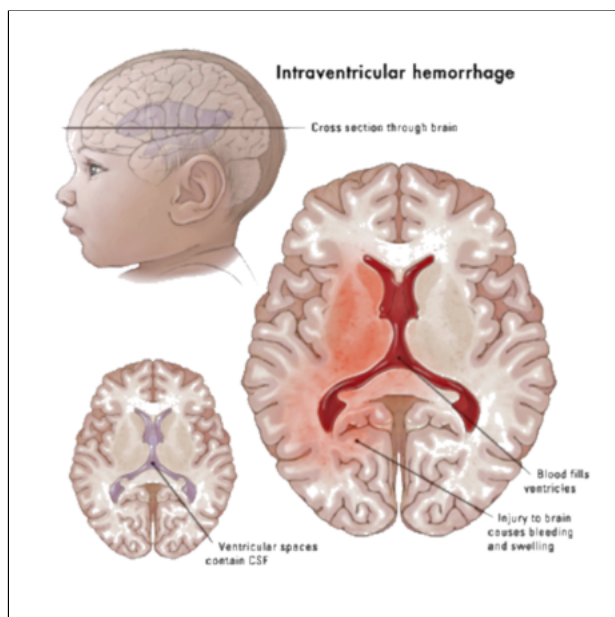


Figure 1: shows the typical aspect of intraventricular hemorrhage in preterm children.

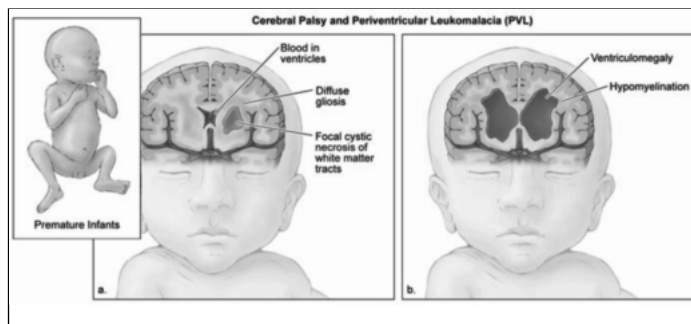


Figure 2: shows the effect of periventricular leukomalacia (PVL) on preterm child brain.

Palsy, blindness, deafness, etc. The risk of severe neurodevelopmental deficit or mortality is inversely proportional to the gestational age: 98% to 22 weeks, 84% to 23 weeks, 57% to 24 weeks. and 38% at 25 wk.⁽⁴¹⁻⁶⁰⁾ (Figures 2).

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On the other hand, in the absence of severe damage, alterations in neural connectivity, related to anomalies in the organization phase of the cerebral cortex, can lead to various cognitive, linguistic, behavioral and relational deficits⁽⁴⁰⁻⁴⁸⁾.

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minimal neurological damage is also played by the unfavorable environment of intensive care⁽⁵⁰⁻⁵⁶⁾. The spectrum of mild neurobehavioral disabilities to which prematurely born children can meet is large and complex, but in all cases determines significant effects on the quality of life of the child and may include speech disorders, attention deficit, learning disorders, socio-emotional development impairment, executive functions and development of coordination, borderline intellectual functioning, mental retardation and many other neurological troubles⁽⁵⁰⁻⁵⁶⁾.

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