

INTERLEUKIN-18 AS A MARKER OF ACUTE KIDNEY INJURY IN ASPHYXIA OF NEONATES

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Asphyxia remains a common problem in the neonatal nursery and is a significant cause of morbidity and death in the term and preterm neonate. The incidence of asphyxia is estimated to be between 1 and 10 per 1000 live births and is influenced by the local availability of medical resources. Asphyxia can lead to multi-organ dysfunction and a redistribution of cardiac output to maintain cerebral, cardiac, and adrenal perfusion while potentially compromising renal, gastrointestinal, and skin perfusion.

Acute kidney injury (AKI) is a common consequence of perinatal asphyxia, occurring in up to 56% of infants. A major difficulty in diagnosing this condition is the lack of a consensus definition of neonatal AKI, largely because of a dearth of specific measurable variables and biochemical markers. As markers of AKI may be used such substances as: NGAL (Neutrophil Gelatinase- Associated Lipocalin), KIM-1 (Kidney Injury Molecule 1), Cystatin C, NHE3 (Sodium-Hydrogen Exchanger, isoform 3), Interleukin-18 etc.

Interleukin-18 (IL-18, also known as interferon-gamma inducing factor) is a [protein](#) which in humans is encoded by the IL-18 [gene](#). IL-18 is a [cytokine](#) that belongs to the [IL-1](#) super family and is produced by [macrophages](#) and other cells. Also IL-18 is synthesized by the proximal renal tubular epithelium under the influence of ischemic or nephrotoxic factors. Determine its level in urine allows at an early stage to determine the presence of renal tissue damage.

This work will be given to the investigation of potential biomarker that may aid the clinician in the diagnosis of renal injury in this population.

The main aim of the work is to demonstrate the importance of IL-18 as a marker of kidney injury/damage as a result of asphyxia in newborns.

The study involved 100 full-term newborns with disturbance kidney function. Among them 50 children had severe asphyxia and 50 had moderate asphyxia. Comparison group included 20 healthy newborns. The actual material used for the tests were urine samples from the neonates, that's why laboratory method was non-invasive. The level of IL-18 in urine was determined on 1–2, 7–8 and 25–30 days of life by ELISA.

In neonates with impaired kidney function due to asphyxia the contents of IL-18 in urine during the neonatal period exceeded the concentration of healthy children. At 1–2 days of life the content of IL-18 in the urine was almost 4,5 times higher (14.56 ± 0.83 pg/ml, $p < 0.05$) in the case of moderate asphyxia and 9 times higher (30.55 ± 2.62 pg/ml, $p < 0.05$) in the case of severe asphyxia. Thus, urine IL-18 may be an early predictor of renal dysfunction in infants who are exposed to asphyxia. High content of IL-18 in the urine of children with severe asphyxia indicates significant damage to the epithelium of the proximal renal tubules.

Further dynamics of IL-18 in the urine was similar in both groups of children with asphyxia. Cytokine content declined by one-third to the end of the first week of life (9.75 ± 0.19 pg/ml and 21.65 ± 2.38 pg/ml in newborns with moderate and severe asphyxia respectively), but remained statistically higher than the comparison group. Thus the difference between the groups of neonates with asphyxia was still present, indicating the dependence of renal tubular injury from the severity of asphyxia.

In the late neonatal period cytokine levels were equal in the examined groups of children with asphyxia and more than 3.5 times higher ($p < 0.05$) than the content in the comparison group. So, after asphyxia tubular dysfunction persists long enough, requiring a prolonged monitoring the renal function in this category of infants.

Conclusion. Level of IL-18 in the urine in the first 24–48 hours of life is an early diagnostic sign of kidney damage in newborns with asphyxia. After asphyxia tubular dysfunction persists long enough. This is evidenced by the high content of IL-18 in the urine during whole neonatal period.

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