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SERUM CORTISOL CONTENTS IN NEWBORNS WITH DISTURBANCE RENAL FUNCTION DUE TO ASPHYXIA

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The objective. *To study the dynamics of the cortisol level during the neonatal period in infants with violation kidney function after asphyxia.*
Materials and methods. *100 full-term infants with a gestational age 38–41 weeks and signs of kidney damage were examined: 50 children who had severe asphyxia and 50 children with moderate asphyxia. The comparison group consisted of 20 children without birth asphyxia. The cortisol level in serum was determined on 1–2, 7–8 and 25–30 days of life by ELISA.*
Results. *Newborns with signs of kidney damage due to moderate asphyxia are characterized by significant increase in serum cortisol concentration at 1–2 days of life ($p<0.001$). Reduction to physiological levels observed only in the late neonatal period. Children with renal damage after severe asphyxia have the highest content of serum cortisol in the first two days of life — 505.28±36.96 nmol/l. At the end of the neonatal period we observed suppression of cortisol production. The cortisol level in children with impaired renal function negatively correlated with low blood pH and base deficiency (BE). The high content of sodium in the serum in infants with impaired renal function caused by asphyxia in the first two days of life is an adaptive response due to elevated cortisol level.*
Conclusion. *Investigation found that disturbance renal function after neonatal asphyxia accompanied with increase synthesis of cortisol in the early neonatal period. Depletion synthesis of cortisol in case of severe asphyxia at the end of the neonatal period may contribute disadaptation infants, predispose to metabolic disorders.*
Keywords: *newborn, asphyxia, cortisol, kidney, sodium.*

Introduction

Physiological birth is a strong stress factor for the newborn. They are accompanied by the release of a number of hormones that ensure the preservation of homeostasis [3].

An imbalance of stress hormones due to their excessive secretion or, conversely, lack is typical to newborns suffered from asphyxia. These changes can disrupt the regulation of metabolic processes, inhibit energy production, reduce protein synthesis, provoke activation free radical oxidation, etc. [10].

In neonates with asphyxia may occur transient renal dysfunction (ischemic nephropathy, hypoxic nephropathy, shock kidney, transitory renal failure) or acute renal failure [8]. The frequency of kidney damage lies between 47 to 70% in case of asphyxia in newborn [7, 9].

One of the hormones that provide a response to stressful influences is cortisol. It regulates the processes of filtration and reabsorption in the kidneys, has a diuretic action, and takes part in the water and sodium excretion [3]. Cortisol content in the serum depends from the severity of perinatal asphyxia and hypoxic injury of CNS [1]. The level of cortisol is increased more significantly in case of acute asphyxia than chronic [6]. After intrauterine hypoxia in neonates are observed such deviation of adaptation as disturbance of

Table 1

Cortisol content in blood serum during the neonatal period (M±m and confidence interval (CI)), nmol/l

	Newborns with disturbance of kidney function after severe asphyxia, n=50	Newborns with disturbance of kidney function after moderate asphyxia, n=50	Comparison group, n=20
1-2nd days of life	505.28±36.96 CI 430.98–579.57 p, p_1	374.4±11.36 CI 351.58–397.22 p	207.65±20.23 CI 165.32–249.98
7-8th days of life	34.119±27.76 CI 285.41–396.97 p, p_2	285.16±9.11 CI 266.86–303.46 p, p_2	145.59±12.05 CI 120.38–170.80 p_2
25-30th days of life	100.74±7.53 CI 85.59–115.88 p, p_1, p_2, p_3	165.42±10.53 CI 144.25–186.58 p_2, p_3	144.55±10.78 CI 121.99–167.10 p_2

Notes: p – reliability relative to comparison group; p_1 – reliability relative to newborns with moderate asphyxia; p_2 – reliability relative to 1-2nd days of life; p_3 – reliability relative to 7-8th days of life.

Table 2

Correlation between serum cortisol and blood gases at 1–2 days of life in infants with severe asphyxia and renal dysfunction

	pH	pO_2	pCO_2	BE
Spearman's correlation coefficient	-0.508 p<0.05	-0.240	0.195	-0.314 p<0.05

sleep and wakefulness rhythms, desynchronization parameters of hemodynamics, respiratory rate, body temperature and cortisol secretion [5]. But information about cortisol level in infants with impaired renal function after asphyxia is missed, that's why our study is actual and important.

The objective. To study the cortisol level during the neonatal period in infants with violation kidney function after asphyxia.

Materials and methods

100 full-term infants with a gestational age 38–41 weeks and signs of kidney damage were examined: 50 children who had severe asphyxia and 50 children with moderate asphyxia. The comparison group consisted of 20 children without birth asphyxia.

Renal dysfunction was diagnosed if creatinine level increased over 89 mcmol/l, blood urea more than 8 mmol/l, urine output less than 1 ml/kg per 1 hour. The diagnosis of moderate and severe asphyxia confirmed according to the «Protocol of resuscitation and post-reanimation newborn care» (Order of Ministry of Health of Ukraine dated 08.06.2007 № 312). The serum cortisol levels were determined at 1–2, 7–8 and 25–30 days of life by ELISA using a kit of reagents «ELISA cortisol» produced by «Imunoteh» (Russia).

Statistical data processing performed using the program Statistica 6.1 (StatSoft, USA). Our results were non-normally distributed, and therefore non-parametric testing was used such as Wilcoxon's test. Correlations were calculated nonparametrically by Spearman's method. P values < 0.05 were considered significant.

Results and discussion

In healthy infants after birth were significant increases of cortisol level in the blood (called «cortisol surge») caused by increase of its secretion from suprarenal glands and reduce speed converting cortisol to cortisone. Cortisol content was significantly decreased at the end of the early neonatal period and subsequently was stable (Table 1).

Stimulation of the adrenal glands of the fetus and the mother is required to run the child birth and causes a significant increase in activity of cortisol in infants. Child's adaptation to extrauterine life was accompanied by decreasing cortisol levels in serum [3].

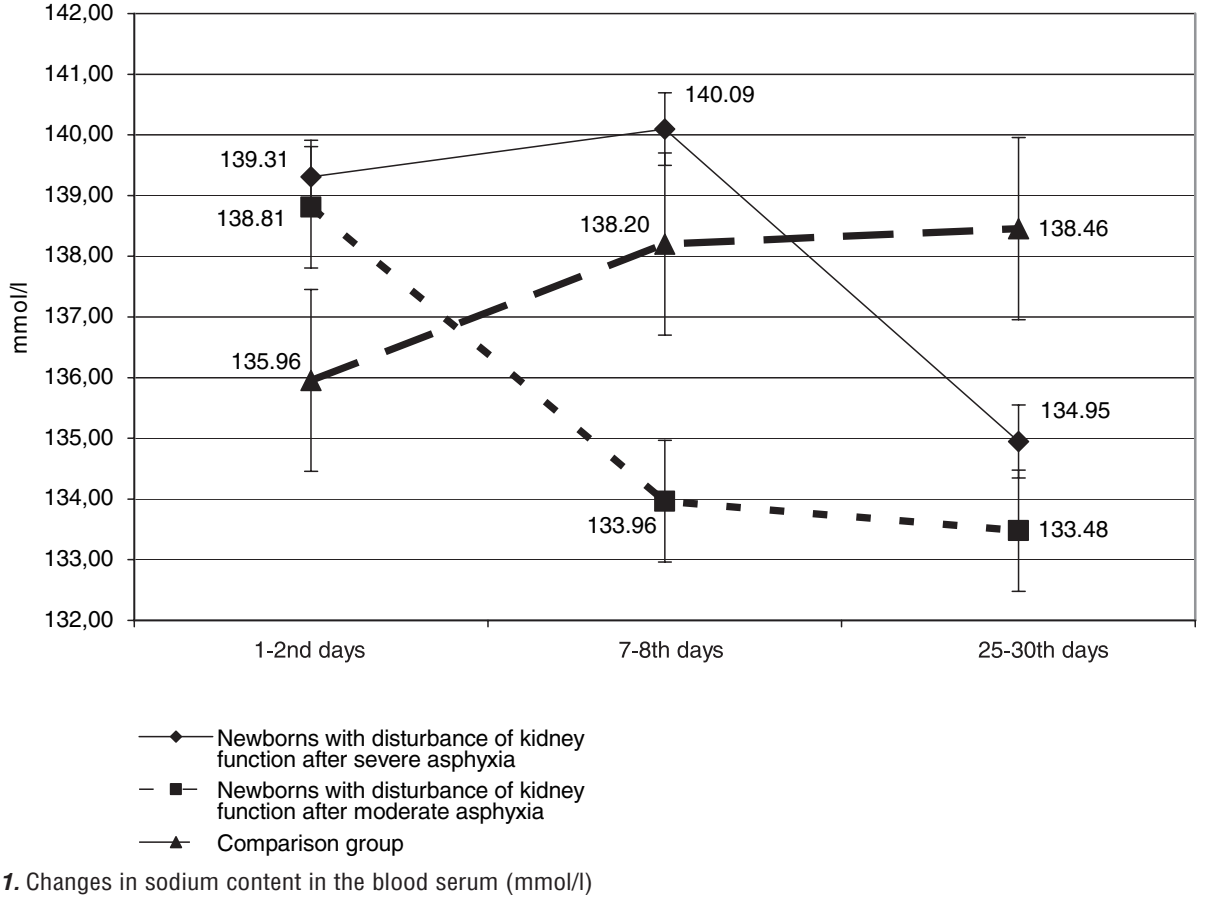

Fig. 1. Changes in sodium content in the blood serum (mmol/l)

Table 3

Spearman's correlation coefficient for cortisol and sodium in serum during the neonatal period in infants with impaired renal function due to asphyxia

	Newborns with disturbance of kidney function after severe asphyxia, n=50	Newborns with disturbance of kidney function after moderate asphyxia, n=50	Comparison group, n=20
1-2nd days of life	0.569 p<0.05	0.448 p<0.05	0.083
7-8th days of life	0.521 p<0.05	0.269	0.107
25-30th days of life	0.173	0.382	0.250

Infants who had symptoms of kidney damage due to moderate asphyxia characterized by significant increase in serum cortisol concentration at 1–2 days of life ($p<0.001$). At the end of 1st week of life hormone content exceeded nearly 2 times the level in the comparison group. Reduction to physiological levels observed only in the late neonatal period.

In children with renal damage after severe asphyxia noted the high value of serum cortisol levels in the first two days of life — 505.28±36.96 nmol/l. To 7–8th days content significantly decreased ($p<0.05$), but still higher than the rates in other groups of children. Late neonatal period observed inhibition of cortisol production.

Other researchers found a significant increase cortisol level in the blood of children with severe hypoxic injury of CNS during the first three days and a significant decrease in the 6–10 times to 5–7 days with subsequent inhibition of its products [1]. In our study, reducing the concentration of cortisol after severe asphyxia was more gradual, only at the end of the 1st month of life revealed its significant deficit.

One of the diagnostic criteria to detect the severity of asphyxia is the pH of blood from the umbilical artery [4]. It is shown that in case of asphyxia at birth there is an inverse correlation between the level of cortisol and cord blood pH ($r = - 0.96$). That is why, low pH, reflecting severe asphyxia at birth is associated with a higher content of cortisol in umbilical cord blood [6].

In newborns with severe asphyxia and renal dysfunction which were on artificial lungs ventilation, we performed the calculation of Spearman's correlation coefficient for serum cortisol and baselines blood gases at 1–2 days of life. Results are shown in Table 2.

The presence of significant negative relationship between cortisol levels and pH, and BE parameters is found.

Thus, lowering the pH and alkaline deficit caused by asphyxia and reflect its severity are inversely correlated with the content of cortisol in serum. That is why, the severity of asphyxia significantly affect the level of serum cortisol levels after birth.

Cortisol isn't only a stress hormone. It has a mineralocorticoid activity. Therefore, it can influence on fluid balance and sodium level in newborns. High cortisol level causes sodium retention in the organism, leading to hydration and causes swelling [2], which can be dangerous in infants with impaired renal function. Therefore, we investigated the sodium content in the blood serum in newborns with disturbance of kidney function after asphyxia.

Impaired renal function is accompanied by significant increase sodium in the blood serum at 1–2 days of life, regardless of the severity of asphyxia. At the end of the early neonatal period in case of nephropathy due to severe asphyxia sodium level remained high, while toddlers with moderate asphyxia had subnormal sodium values. Completion of 1st month of life in all infants with impaired renal function is characterized by a tendency to sodium decrease.

More often renal impairment after asphyxia has pre-renal etiology and caused by hypovolemia [8]. That's why increased sodium can be considered as adaptive-compensatory response aimed at restoring blood volume and normalization of hemodynamics.

To decide about the relationship between cortisol and sodium level in the blood serum we made correlation analysis.

Weak positive correlation was peculiar for healthy infants that indicated little effect of cortisol on sodium exchange in physiological conditions. Late neonatal period was some strengthening of correlation.

Newborn babies with impaired renal function, regardless of the severity of asphyxia at 1–2 days after birth had a statistically positive correlation between cortisol and serum sodium. So, in case of asphyxia cortisol level is increased. This hormone can play role as a regulator of water and electrolyte balance, as evidenced by the correlation coefficient $p<0.05$. Significant influence of cortisol on sodium exchange in infants with impaired kidney function after severe asphyxia persists during the early neonatal period. Correlation between cortisol and sodium content in serum is significantly weakened at the end of the first month of life.

Glucocorticoid hormones, such as cortisol, are necessary to ensure the stability of newborn metabolism [10]. Asphyxia causes significant tension of adaptation processes (increase glucose needs of the brain, increase the load on the cardio — vascular system, kidneys, changes of electrolyte and acid-base balance, etc.) which are regulated predominantly by cortisol. Deplet-

ion of cortisol synthesizing function in severe asphyxia during the neonatal period may lead to dysadaptation of infants, predispose to metabolic disorders and inadequate response to stress. Thus, cortisol level in children with impaired renal function during the neonatal period depends on the severity of asphyxia. Depletion of hypothalamic-pituitary-adrenal system in the event of severe asphyxia disrupts stress-induced response and adaptation newborn to extrauterine life.

Conclusion

1. Disturbance of renal function after neonatal asphyxia accompanied with increase synthesis of cortisol in the early neonatal period.

2. Depletion synthesis of cortisol in case of severe asphyxia at the end of the neonatal period may contribute disadaptation infants, predispose to metabolic disorders.

3. The cortisol level in children with impaired renal function negatively correlated with low blood pH and base deficiency (BE).

4. The high content of sodium in the serum in infants with impaired renal function caused by asphyxia in the first two days of life is an adaptive response due to elevated cortisol level.

Prospects for further research

Perspective area of future research is to study the concentration of cortisol in premature infants with impaired renal function due to asphyxia and study the influence of cortisol on the exchange of other trace elements (potassium, calcium).

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