Precursors and metabolites of catecholamines in umbilical blood serum of full-term newborns and their after-birth adaptation

LYDIA SHEIBAK, VLADIMIR SHEIBAK, TATYANA SHERESHIK, ELENA KATKOVA, LYUDMILA GUTIKOVA

Abstract
The aim of the study was to investigate the indices of catecholamines exchange in umbilical blood serum of full-term neonates in some peculiar cases of delivery and to estimate the possibility of some pathological processes in early adaptation period. It has been shown that the content of dopamine degradation products decreases in umbilical blood serum of full-term newborns delivered by cesarian section and after induced labor. Amniotomy and induced labor with prostin lead to the increase of the content of dopamine precursor which level expresses synthesis of transmitter. The indices of catecholamines during the course of early adaptation period have been analyzed. The elevation of dopamine precursor concentration in umbilical cord blood serum of newborns may be associated with the development of icteritious, haemorragic syndromes and the syndrome of intrauterine infection. These features of dopamine metabolism should be taken into account when some therapeutic measures are performed in early adaptation period.

Key words: newborns, full-term, umbilical blood, catecholamines

Introduction
Transition of a child from the prenatal existence to the independent life and its adaptation to the new environment conditions is crucial to human health. At present, there is a distinct increase in the frequency of pathology of the fetus, resulting in adaptation failure in the neonatal period. Depending on several factors, inadequately low or too high functional activity of organs and systems can be observed among children in the early neonatal period. Poorly coordinated responses, increased function weakness and the adaptation disturbances in the form of cerebral circulatory disorders, respiratory distress syndrome, edema and hemorrhagic syndromes, hypoglycemia and hypokalemia, conjugation jaundice, hormone and energy deficiency states are revealed. On the basis of these pathological processes, encephalopathy, recurrent respiratory diseases, morpho-functional changes in cardiovascular system, anemia, allergies and other chronic diseases may develop. The identifications of early manifestations of pathological processes, their well-timed correction and prophylaxis may prevent complications or reduce their intensity. Crucial effect on the processes of adaptation has the sympathoadrenal system, the state of which can be reflected by levels of neurotransmitters and hormones (dopamine, norepinephrine and epinephrine) in biological fluids. Optimization of the adaptation processes is one of the most important reserves in reducing childhood morbidity and mortality rates.

The aim of the research was to study the catecholamine metabolism indices in the serum of umbilical cord blood in term infants under certain conditions of delivery, and the evaluation of the probable development of some pathological conditions in the early neonatal period [1, 2].

Materials and survey methods
143 full-term newborn babies were surveyed. Anthropometric indicators were as following: body weight – 3481.8 ± 40.1 g, body length – 52.5 ± 0.2 cm, head circumference – 35.4 ± 0.1 cm. Among the examined infants 25 (17.5%) children were born by cesarian section. Planned caesarean section was performed in 17 women. Surgical delivery under endotracheal anesthesia was performed in 92% cases. Amniotomy as a method of labor induction was used in 23 (16%) women, prostinom was used in 20 (14%) women, delivery stimulation with oxytocin in 20 (14%) parturient women.
The control group comprised 14 term infants, who were born naturally without any additional obstetric interventions, the early neonatal period of which proceeded without any peculiarities. Anthropometric indicators were as following: body weight – $3394.8 \pm 51.2$ g, body length – $52.1 \pm 0.4$ cm, head circumference – $34.9 \pm 0.2$ cm.

We have studied the peculiarities of the period of early neonatal adaptation in the research and control groups of infants and evaluated the content of precursors and metabolites of catecholamines in their umbilical cord blood serum. While analyzing the objective status of the newborn we considered the presence and severity of the border-line states in the early neonatal period, the manifestations of fetal contamination, jaundice, hemorrhagic and anemia syndromes, and the presence of birth underweight.

Intrauterine (fetal) contamination syndrome was observed in 45 (31.5%) term infants, local cutaneous hemorrhagic syndrome – in 34 (23.8%), icteric syndrome – in 21 (14.7%), anemia syndrome – in 11 (7.7%). 14 children were born low-weight in relation to gestational age. Average body weight of small-for-date infants was $2878.3 \pm 15.7$ g, body length – $50.4 \pm 0.3$ cm, head circumference – $34.1 \pm 0.2$ cm.

The measuring of tyrosine, 3,4-dihydroxyphenylalanin (DOPA), 3,4-dihydroxyphenylacetic acid (DOPAC) and homovanillic acid (HVA) concentrations was performed with Agilent 1100 chromatographic system, data receiving and processing – with Agilent ChemStation A10.01.

Statistical analysis of catecholamine exchange indicators was conducted with T-statistics and Student’s t-test.

**Results**

We found differences in the content of dopamine metabolites in umbilical cord blood serum of newborn babies born compared to control group. The level of tyrosine did not differ significantly from that of the infants of control group. DOPA concentration in the umbilical cord blood serum of infants born surgically averaged $59.8 \pm 7.2$ nmol/l, which did not differ from the indices of naturally born children. At the same time, a significantly lower content of dopamine degradation products – DOPAC and HVA was revealed (Table 1).

A typical clinical feature of the early neonatal period in infants delivered by cesarean section was a significant loss and later recovery of initial body weight. The physiological loss of body weight of mild degree was noted in 64% of cases. In 36% of the infants, the figure was $282.5 \pm 41.0$ g (6%, moderate degree). In the control group, physiological loss of body weight of a moderate degree was noted in 92% of children and averaged $142.1 \pm 11.0$ g. The umbilical remnant separation time did not differ in both groups. In 44% (11) babies born by cesarean section, fetal infection syndrome [3] and in 4 – disadaptation syndrome were observed.

We found a similar catecholamine metabolism indicators change in umbilical cord blood serum of newborns after amniotomy performed. A significant decrease of DOPAC and HVA concentrations was noted in the serum of umbilical cord blood (Table 1).

Isolated prostinom use for labor induction also affected precursors and metabolites of dopamine content in the neonates. We revealed a significant decrease of DOPAC indices, presence of increased DOPA level. HVA amount increased in the umbilical cord blood serum of these children. As a result, in response to increased production of dopamine precursors, the increased production of their metabolite (HVA) was observed.

Correction of labor in the parturient women with oxytocin influenced significantly the catecholamine metabolism rate in the infants. At almost the same content of tyrosine in the serum of umbilical cord blood, the newborns of the research and control groups demonstrated lower levels of DOPA, DOPAC and HVA. The lack of catecholamine response at birth was observed in this group of children.

**Table 1. Indicators of catecholamine metabolism in the blood serum of newborns born with some additional obstetric interventions**

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<tbody>
<tr>
<td>Cesarean section ($n = 25$)</td>
<td>$59.3 \pm 3.9$</td>
<td>$59.8 \pm 7.2$</td>
<td>$405.9 \pm 43.2^*$</td>
<td>$775.1 \pm 61.3^*$</td>
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<tr>
<td>Amniotomy ($n = 23$)</td>
<td>$59.3 \pm 4.3$</td>
<td>$108.4 \pm 39.9$</td>
<td>$407.4 \pm 38.2^*$</td>
<td>$613.4 \pm 55.3^*$</td>
</tr>
<tr>
<td>Prostinom labor induction ($n = 20$)</td>
<td>$60.9 \pm 3.2$</td>
<td>$318.2 \pm 59.0^*$</td>
<td>$342.2 \pm 34.0^*$</td>
<td>$1192.2 \pm 190.3$</td>
</tr>
<tr>
<td>Oxytocin labor stimulation ($n = 20$)</td>
<td>$60.5 \pm 4.9$</td>
<td>$45.1 \pm 5.7$</td>
<td>$356.8 \pm 34.7^*$</td>
<td>$582.7 \pm 68.3^*$</td>
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<tr>
<td>Control ($n = 14$)</td>
<td>$60.1 \pm 3.9$</td>
<td>$50.6 \pm 7.5$</td>
<td>$651.8 \pm 85.7$</td>
<td>$1346.2 \pm 80.9$</td>
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* reliability, when compared with the control group ($p < 0.01-0.001$)
When analyzing the features of the early neonatal period, and indicators of catecholamine exchange, we found an increase in the level dopamine precursor and decrease in the amount of its metabolites in the presence of local hemorrhagic syndrome (Table 2). A similar variation of dopamine metabolism was obtained in the group of children with jaundice syndrome.

Moreover, we discovered unidirectional changes in the synthesis and degradation of catecholamines in the jaundice syndrome and syndrome of fetal infection. In 16 infants we observed a combination of these syndromes (11%). We have found a significant increase in the concentration of DOPA and decrease of DOPAC and HVA in the serum of umbilical cord blood of the newborn children infected antenatally (fetal infection). Intraperinatal infection (congenital pneumonia) was observed in 8 infants. All indices of catecholamine metabolism tend to be reduced in these children (the level of tyrosine was 55.1 ± 8.1 nmol/ml, DOPA – 37.7 ± 8.1 nmol/l, DOPAC – 414.0 ± 66.0 nmol/l and HVA – 635.0 ± 138.6 nmol/l). The newborns with jaundice syndrome had weight loss by over 6% (28% vs. 7% in controls). Department of umbilical remnant, in the age aspect, did not differ significantly in the research and control groups.

DOPA concentration in the umbilical cord blood serum in the gestational age lower body weight infants averaged 45.6 ± 6.8 nmol/l compared with the control group (50.6 ± 7.5 nmol/l). Lower levels of the dopamine precursor followed decreased catecholamine content of the initial substrate – the tyrosine (55.6 ± 5.1 vs. 55.6 ± 5.1 nmol/l, p < 0.5). We found a decrease in dopamine degradation products in the serum of umbilical cord blood of the newborn infants with underweight at birth, DOPAC (553.2 ± 65.3 nmol/l vs. 651.8 ± 85.7 nmol/l, and HVA (882.0 ± 72.0 nmol/l vs. 1346.2 ± 80.9 nmol/l). At birth we observed deficiency of the precursors and the metabolites of dopamine.

**Discussion**

The initial substrate for the catecholamine formation is the amino acid tyrosine. Its hydroxylation results in DOPA, the first catecholamine precursor formation. It penetrates the blood-brain barrier easily, but has a relatively low biological activity. Later dopamine is formed from DOPA. The result of dopamine degradation is DOPAC and homovanillic (HVA) acids formation [4].

We observed a significant reduction in the amount of dopamine metabolites after during the operative delivery; it is probably because of the decrease in its synthesis and / or activity of the dopamine system. It can aggravate the course of early adaptive process. By natural delivery the amount of DOPAC and HVA is increasing, that indicates a high activity of the neuroendocrinal system, which helps the newborn to adapt better to the environment after birth [5, 6].

The changes of the catecholamine metabolism indices in the case of different obstetric interventions at delivery using, suggest their possible effect on the somatic status of a newborn after birth. The noted decrease of metabolites (DOPAC and HVA) and high precursors of dopamine content (DOPA) in umbilical cord blood serum of newborn infants, born with the use of amniotomy, may impair of the sympathoadrenal activity in newborns.

Isolated prostin use during the labor induction also contributed to the change in catecholamine metabolism performance of infants. However, intrapartum stress manifestations in this case are less marked. We releaved a significant decline in DOPAC level, whereas DOPA content was increased. Increased homovanillic acid formation indicated the active catecholamine utilization process. The catecholamine degradation products decrease in the presence of high their precursor level indicates the decreased synthesis of catecholamines.

The oxytocin labor correction in parturients shows significantly lower levels of DOPAC, DOPA and HVA. It is probably because of the decreased activity of enzymes that control these transformations, and the decreased dopamine release. These changes were observed in almost equal content of tyrosine in the umbilical cord blood serum of the newborns of the research and control groups.

**Table 2. Indicators of catecholamine metabolism in infants with some peculiarities of the current early adaptation period**

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<tr>
<td>Jaundice syndrome (n = 21)</td>
<td>58.9 ± 4.2</td>
<td>83.9 ± 4.3*</td>
<td>525.2 ± 41.1</td>
<td>897.3 ± 94.8*</td>
</tr>
<tr>
<td>Fetal infection (n = 45)</td>
<td>60.6 ± 2.6</td>
<td>92.3 ± 4.7*</td>
<td>505.3 ± 3.8</td>
<td>801.3 ± 63.9*</td>
</tr>
<tr>
<td>Hemorrhagic syndrome (n = 34)</td>
<td>59.9 ± 3.8</td>
<td>76.0 ± 5.4*</td>
<td>379.6 ± 3.4*</td>
<td>743.4 ± 83.4*</td>
</tr>
<tr>
<td>Control (n = 14)</td>
<td>60.1 ± 3.9</td>
<td>50.6 ± 7.5</td>
<td>651.8 ± 85.7</td>
<td>1346.2 ± 80.9</td>
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Probably, in this case a reduction of “catecholamine response” and a high probability of further depletion in the adaptation process occurs. According to the scientific literature, it is known that during the process of artificial enhancing of uterine contraction, a reduction in anti-stress stability of the fetus, and the suppression of its protective and adaptive capabilities take place. The oxytocin use in labor strengthening has less beneficial effects on the fetus and newborn, than prostaglandin containing preparations [7].

Conclusions

1) In the serum of umbilical cord blood of term newborn infants, dopamine metabolites concentration is reduced at delivery by cesarean section, amniotomy, oxytocin labor induction and prostinom labor stimulation. Significant decrease of dopamine degradation products indicates the prolongation of the stressful situation in a newborn baby after its birth.

2) Prostinom labor induction is less traumatic for the newborn child in obstetrics because of the rapid normalization of the dopamine degradation products.

3) Newborn children with disabilities in terms of catecholamine metabolism at birth are characterized by jaundice, hemorrhagic and fetal infection syndrome during the early neonatal adaptation.

References


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