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HEMODYNAMIC PATTERNS DETERMINED BY NON-INVASIVE CW-DOPPLER ULTRASOUND CARDIAC MONITORING (USCOM) IN PRETERM NEONATES WITH RESPIRATORY DISTRESS SYNDROME DURING NON-INVASIVE RESPIRATORY SUPPORT

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Aim: To determine the hemodynamic patterns in preterm neonates with respiratory distress syndrome (RDS) using the USCOM-1A technology. ***Materials and Methods:*** The USCOM device is a bedside method of evaluating cardiac output (CO) based on continuous-wave Doppler ultrasound. Hemodynamic parameters were measured daily for 7 days in 32 preterm neonates 32 ± 1 weeks of gestation (1688 ± 111 g) with RDS requiring noninvasive respiratory support (NCPAP, NIPPV, HFNC) and no catecholamine support in comparison with 28 healthy term neonates (3100 ± 690 g). ***Results:*** At day 1, preterm neonates had lower SVI (18 ± 5 vs 28 ± 8 ml m^{-2}, $p = 0.043$) and higher SVRI (1585 ± 245 vs 1035 ± 358 dyn s cm^{-5} m^2, $p = 0.013$) with a tendency for lower cardiac index (2.6 ± 0.8 vs 4.0 ± 1.3 l min^{-1} m^{-2}, $p = 0.089$). Together with no difference in SMII, it indicates the presence of diastolic dysfunction with low preload. It is noted that all parameters had not changed by day 7 in preterm neonates, whereas term neonates demonstrated significantly increased SMII reflecting postnatal cardiovascular adaptation. Compared with preterm neonates with RDS requiring NCPAP/NIPPV, preterm neonates requiring HFNC had higher levels of FTc (330 ± 59 vs 388 ± 41 ms, $p = 0.045$), SVI (13 ± 3 vs 18 ± 4, ml/m^2, $p = 0.007$), SMII (0.41 ± 0.09 vs 0.57 ± 0.21, $p = 0.02$), and CI (2.2 ± 0.6 vs 4.5 ± 0.9 l/min/m^2, $p = 0.006$). ***Conclusions:*** Noninvasive respiratory support in preterm neonates with RDS may lead to diastolic dysfunction that is less prominent in neonates with HFNC.

Keywords: neonates; respiratory distress syndrome; heart-lung interactions; continuous positive airway pressure; noninvasive respiratory support; cardiac output; USCOM.

ГЕМОДИНАМИЧЕСКИЕ ПАТТЕРНЫ, ОПРЕДЕЛЯЕМЫЕ С ПОМОЩЬЮ НЕИНВАЗИВНОГО УЛЬТРАЗВУКОВОГО МОНИТОРА СЕРДЕЧНОГО ВЫБРОСА У НЕДОНОШЕННЫХ ДЕТЕЙ С СИНДРОМОМ ДЫХАТЕЛЬНЫХ РАССТРОЙСТВ ПРИ ПРОВЕДЕНИИ НЕИНВАЗИВНОЙ РЕСПИРАТОРНОЙ ТЕРАПИИ

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Цель исследования: оценить влияние неинвазивной респираторной терапии (НРТ) на показатели центральной гемодинамики (ЦГ), измеренные с помощью ультразвукового монитора сердечного выброса (USCOM) у недоношенных детей с синдромом дыхательных расстройств (СДР). ***Материалы и методы.*** Обследовано 32 ребенка 32 ± 1 неделя гестации с массой тела 1688 ± 111 г, у которых был диагностирован СДР, потребовавший проведения НРТ. Контрольную группу составили 28 здоровых доношенных детей с массой тела 3100 ± 690 г. Показатели ЦГ измерялись с помощью USCOM ежедневно в течение 7 первых дней жизни. ***Результаты.*** У недоношенных детей в 1-й день по сравнению с пациента-

ми контрольной группы наблюдались более низкий индекс сердечного выброса (SVI) (18 ± 5 и 28 ± 8 мл · м$^{-2}$, p = 0,043) и более высокий индекс системного сосудистого сопротивления (SVRI) (1585 ± 245 и 1035 ± 358 дин · с · см$^{-5}$ · м^2, p = 0,013), а также тенденция к снижению сердечного индекса (CI) (2,6 ± 0,8 и 4,0 ± 1,3 l/мин/м^2, p = 0,089). Принимая во внимание отсутствие различия показателей инотропного индекса (SMII), полученные данные позволяют думать о наличии у пациентов основной группы диастолической дисфункции и снижении преднагрузки, что может быть следствием НРТ. В течение первой недели жизни эти параметры не изменялись у недоношенных детей с СДР, в то время как у детей контрольной группы наблюдалось значительное повышение SMII, что расценено как отражение постнатальной адаптации здоровых доношенных детей. В сравнении с ними недоношенные дети имели значительно более низкие показатели SVI (18 ± 3 и 30 ± 5 мл · м$^{-2}$, p = 0,007), что свидетельствует о снижении инотропной функции. В сравнении с недоношенными детьми, потребовавшими проведения NCPAP или NIPPV, недоношенные с СДР, нуждавшиеся в HFNC, имели более высокий уровень коррегированного времени потока (FTc) (330 ± 59 и 388 ± 41 мс, p = 0,045), SVI (13 ± 3 и 18 ± 4, мл/м^2, p = 0,007), SMII (0,41 ± 0,09 и 0,57 ± 0,21, p = 0,02) и CI (2,2 ± 0,6 и 4,5 ± 0,9 л/мин/м^2, p = 0,006). ***Выводы.*** У недоношенных детей с СДР при НРТ наблюдаются гемодинамические изменения, обусловленные диастолической дисфункцией миокарда, которая в меньшей степени выражена при проведении НРТ с использованием HFNC.

Ключевые слова: новорожденные дети; синдром дыхательных расстройств; кардиореспираторные взаимоотношения; постоянное положительное давление в дыхательных путях; неинвазивная респираторная поддержка; сердечный выброс; ультразвуковой монитор сердечного выброса.

The ability to conduct noninvasive respiratory therapy in premature newborns with respiratory distress syndrome (RDS) has improved. To create positive end expiratory pressure (PEEP), high flow nasal canulae (HFNC), nasal continuous positive airway pressure (NCPAP), and noninvasive positive pressure ventilation (NIPPV) are utilized [1]. However, like any method of intensive therapy for premature infants in critical condition, the creation of a constant positive airway pressure (CPAP) can adversely affect immature organs and systems, including cardiopulmonary relationships that occur during inspiration and expiration. Because of this, the aim of the present study was to evaluate the indices of central hemodynamics in premature newborns with RDS during noninvasive respiratory therapy (NRT).

MATERIALS AND METHODS

Central hemodynamics (CH) measurement was noninvasively performed using an ultrasound cardiac output monitor (USCOM), which implemented a cardiac output estimation technique using continuous wave dopplerography. The principle of this method involves the measurement of blood flow velocity across the pulmonary or aortic valves, provided anatomical defects are absent. Using a preprogrammed algorithm based on statistically averaged data measured by echocardiography, a computer program based on the patient's height and weight calculates the valve diameter; thereafter, blood pressure data is entered and the program determines a number of indicators that enable assessment of preload level, contractility, and postload, thereby revealing certain hemodynamic patterns. The following indicators were studied: corrected flow time (FTc), stroke volume index (SVi), cardiac index (CI), Smith Madigan inotropic index (SMII), systemic vascular resistance index (SVRI), potentiokinetic ratio (PKR), and oxygen delivery (DO). Assessment of hemodynamic parameters using USCOM was conducted daily for the first seven days of life from 13.00 to 15.00 by the same researcher.

The study group included 32 premature infants with an average gestation period of 32 ± 1 week and a body weight of 1688 ± 111 g, who were diagnosed with RDS on the first day of life and required NRT in NCPAP mode (n = 9), NIPPV (n = 16), or HFNC (n = 7). RDS was diagnosed on the basis of clinical and X-ray data. None of the patients in this group received vasotonic or inotropic therapy. The control group consisted of 28 healthy full-term infants with an average body weight of 3100 ± 690 g with a typical neonatal physiological course.

Statistical analysis was performed using the Biostat program. Reliability of the differences was determined using the Student's t-test. Differences were considered statistically significant at $p < 0.05$.

RESULTS

Measurements of CH parameters in patients and control groups are presented in Tables 1 and 2. There were no significant changes in the index values studied in premature infants during the early neonatal period, whereas an increase in SMII by day 5 of life compared with day 1 (0.79 ± 0.21 and 0.68 ± 0.45, respectively, p = 0.043) and day 7 of life compared to day 2 (0.78 ± 0.15 and 0.68 ± 0.28, respectively, p = 0.045) was observed in full-term children

in the control group. SVRI also increased by day 4 compared to day 1 (1471 ± 354 and 1184 ± 368 dyne · s · cm^{-5} · m^2, respectively, $p = 0.009$) and by day 5 of life compared to day 1 (1439 ± 291 and 1184 ± 368 dyne · s · cm^{-5} · m^2, respectively, $p = 0.023$) in the control group.

When comparing patients of the study and the control groups in premature infants with RDS, lower SVi values (18 ± 5 and 28 ± 8 ml/m^2, $p = 0.043$) and higher SVRI values (1585 ± 245 and 1035 ± 358 dyne · s · cm^{-5} · m^2, $p = 0.013$) were observed on day 1 of life; there was also a tendency for CI to decrease (2.6 ± 0.8 and 4.0 ± 1.3 l min^{-1} · m^{-2}, $p = 0.089$) in the absence of differences in SMII values. On day 3 of life, the premature infants in the study group had lower SVi values compared to the control group (18 ± 3 and 30 ± 5 ml · m^{-2}, respectively, $p = 0.007$); they also had lower DO values (90.7 ± 33.7 and 127.5 ± 48.3 ml/min/m^2, respectively, $p = 0.045$).

A more detailed study of the hemodynamic effect of different NRT modes in premature infants was performed: we compared the above hemodynamic parameters according to the type of NRT used. Among premature infants, a subgroup of children who received respiratory support in the form of NCAP or NIPPV ($n = 25$) was identified, and this group was compared to a subgroup of children who received NRT with HFNC ($n = 7$; Table 3). When we compared the group of premature infants with RDS requiring NCPAP/NIPPV with the group of premature infants who received respiratory therapy with HFNC, we observed lower FTc values (330 ± 59 and 388 ± 41 ms, respectively, $p = 0.045$), SVi values (13 ± 3 and 18 ± 4 ml/m^2, respectively, $p = 0.007$), SMII values (0.41 ± 0.09 and 0.57 ± 0.21, respectively $p = 0.02$) and CI values (2.2 ± 0.6 and 4.5 ± 0.9 l/min/m^2, respectively, $p = 0.006$) with no differences in the SVRI levels.

DISCUSSION

Violations of cardiopulmonary relationships are inevitable while performing respiratory therapy, which requires timely diagnosis and rapid decisions regarding the necessity of correction. It is known that venous return is determined by the difference between systemic arterial pressure and right atrial pressure. Creation of CPAP is accompanied by a decrease in venous return and, as a consequence, a decrease in cardiac output [3]. This situation may be aggravated by hyperinflation of the lungs, accompanied by compression of the intrathoracic superior vena cava [4]. In addition, CPAP increases pulmonary vascular resistance, and this increase is proportional to mean airway pressure and the level of PEEP [5]. In addition, CPAP not only causes compression of the pulmonary vessels but also induces pulmonary vasoconstriction mediated through action

Table 1

Changes in hemodynamic indices in premature infants with RDS during the first seven days of life (mean ± standard deviation)

Таблица 1

Изменение показателей гемодинамики у недоношенных новорожденных с синдромом дыхательных расстройств в течение первых семи суток жизни (среднее значение ± стандартное отклонение)

Indices of USCOM	Days of life						
	1	2	3	4	5	6	7
FTc, ms	362 ± 70	354 ± 55	369 ± 48	399 ± 30	380 ± 26	355 ± 46	419 ± 61
SVI, ml/m^2	23 ± 9	20 ± 8	19 ± 3	19 ± 3	17 ± 3	16 ± 5	15 ± 3
SMII	0.68 ± 0.36	0.72 ± 0.55	0.59 ± 0.17	0.62 ± 0.27	0.43 ± 0.11	0.58 ± 0.24	0.43 ± 0.1
CI, l/min/m^2	3.1 ± 0.8	2.7 ± 0.3	2.8 ± 0.34	2.9 ± 0.6	2.9 ± 0.6	2.7 ± 0.9	2.6 ± 0.4
SVRI dyne · s · sm^{-5} · m^2	1453 ± 827	1498 ± 407	1382 ± 407	1382 ± 743	1620 ± 218	1600 ± 426	1522 ± 94
PKR	39 ± 23	37 ± 23	31 ± 9	48 ± 16	49 ± 19	51 ± 3	55 ± 2
DO_2, ml/min	90 ± 33	75 ± 20	83 ± 15	74 ± 16	58 ± 17	61 ± 23	68 ± 16

Table 2

Table 2. Changes in hemodynamic indices in healthy full-term newborns during the first seven days of life (mean ± standard deviation)

Таблица 2

Изменение показателей гемодинамики у здоровых доношенных новорожденных в течение первых семи суток жизни (среднее значение ± стандартное отклонение)

Indices of USCOM	Days of life						
	1	2	3	4	5	6	7
FTc, ms	362 ± 70	354 ± 55	369 ± 48	399 ± 30	380 ± 26	355 ± 46	419 ± 61
SVI, ml/m^2	23 ± 9	20 ± 8	19 ± 3	19 ± 3	17 ± 3	16 ± 5	15 ± 3
SMII	0.68 ± 0.45	0.68 ± 0.28	0.73 ± 0.28	0.72 ± 0.22	0.79 ± 0.21	0.81 ± 0.24	0.78 ± 0.15
CI, l/min/m^2	3.2 ± 0.1	3.2 ± 1.2	3.7 ± 0.7	3.0 ± 0.7	3.2 ± 0.3	2.9 ± 0.3	3.0 ± 0.3
SVRI dyne · s · sm^{-5} · m^2	1184 ± 368	1279 ± 324	1323 ± 362	1471 ± 354	1439 ± 291	1304 ± 206	1333 ± 125
PKR	37 ± 14	35 ± 13	34 ± 9	43 ± 9	38 ± 9	34 ± 3	39 ± 11
DO_2, ml/min	127 ± 48	118 ± 45	114 ± 38	105 ± 37	102 ± 24	111 ± 27	108 ± 24

Table 3

Indices of CH in premature infants with RDS, depending on the type of respiratory therapy used (mean ± standard deviation)

Таблица 3

Показатели центральной гемодинамики у недоношенных детей с синдромом дыхательных расстройств в зависимости от вида респираторной терапии (среднее значение ± стандартное отклонение)

Indices of USCOM	NCPAP/NIPPV $n = 25$	HFNC $n = 7$	p
FTc, ms	330 ± 59	388 ± 41	0.045
SVI, ml/m^2	13 ± 3	18 ± 4	0.007
SMII	0.41 ± 0.09	0.57 ± 0.21	0.02
CI, l/min/m^2	2.2 ± 0.6	4.5 ± 8.9	0.006
SVRI, dyne · s · cm^{-5} · m^2	1652 ± 734	1509 ± 537	0.252
PKR	60 ± 20	50 ± 22	0.179

on calcium channels, the rate of which is also proportional to the level of PEEP [8]. Increased pressure in the right atrium causes restriction of venous return and also leads to displacement of the interventricular septum into the cavity of the left ventricle, thereby reducing cardiac output [2]. In addition, CPAP affects transmural pressure in the left ventricle, which is defined as the difference between the pressure in the left ventricular cavity and pericardial pressure which increases with CPAP and results in a decrease in cardiac output [3].

The data obtained on the reduction of the SVi in NRT in premature infants with RDS may be due to a decrease in preload, contractility, and diastolic

function of the myocardium. However, taking into account the absence of a difference in the inotropic index (SMII, characterizing contractility of the myocardium), and the corrected flow time (FTc, which characterizes preload to a greater extent, the data obtained enable consideration of the presence in premature infants with RDS in performing the HPT of mainly diastolic dysfunction which can be a consequence of respiratory therapy with the creation of CPAP, which limits not so much the flow of blood to the heart as the diastolic relaxation of the myocardium.

During the dynamic observation of patients of both groups in the early neonatal period, we observed that the studied parameters did not change in premature infants with RDS, whereas there was a significant increase in the SMII and a decrease in the SVRI in the control group; we believe this reflects postnatal cardiovascular adaptation of healthy full-term children. To a certain degree, the observed dynamics may have also been caused by postnatal restructuring of blood circulation with the closure of fetal arteriovenous connections. Compared to the control group, the premature infants had significantly lower indices of SVi on day 3 of life which may indicate reduced inotropic function and cause a violation of systemic hemodynamics, including disorders of cerebral and mesenteric blood flow. This is confirmed by a lower DO in premature infants.

However, we observed that the degree of severity of hemodynamic changes during noninvasive respiratory support varies depending on the type of respiratory therapy used. The violations of cardiopulmonary relationships were observed to a greater extent in patients who required NCPAP or NIPPV. The indices of FTc and SMII, CI, and SVI were lower in infants requiring NCPAP or NIPPV than in those requiring HFNC. Although NRT through HFNC and NCPAP/NIPPV is designed to provide PEEP levels sufficient for treating RDS, it seems that the HFNC-generated CPAP does not cause serious violations of cardiopulmonary relationships.

It should be noted that in the present study we did not conduct a comparative study of hemodynamic parameters depending on the etiologic cause of RDS, nor did we investigate the level of airway pressure created during NRT. Another limitation of this study is the small number of patients in the group treated with HFNC-NRT. Further study of the hemodynamic patterns of different types of respiratory support is warranted; specifically, investigating the cause of respiratory disorders in premature infants, and also determining the influence of NRT on the indices of systemic blood flow (including cerebral and mesenteric blood flow) is required. These indices are initially compromised in premature infants but can be significantly impaired when performing respiratory, including noninvasive, therapy which can lead to hypoperfusion in the cerebral and splanchnic basins; consequently, cerebral ischemia, intraventricular hemorrhage, and necrotic enterocolitis may result. In this report, hemodynamics was studied using only USCOM, the effectiveness of which in detecting patterns of hemodynamic disorders in newborns has been demonstrated in a number of studies [6, 7]. However, taking into account a certain percentage of error in the dopplerographic study of hemodynamics in premature infants with RDS, it is advisable to conduct a comprehensive study including echocardiography methods.

CONCLUSIONS

Respiratory therapy in premature infants with RDS is associated with risk of hemodynamic disorders, which can subclinically act as risk factors for development of internal organ hypoperfusion because of low cardiac output. In premature infants with RDS, this is associated to a greater extent with the development of diastolic dysfunction of the myocardium, which brings into question the efficiency of bolus infusion load and inotropic therapy for its correction. At the same time, NRT as treatment with HFNC may be beneficial in terms of preventing cardiac output reduction.

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