EDITORIAL

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ABOUT THE ABSENCE OF THE NEED TO PRESCRIBE ANTIBACTERIAL THERAPY TO NEWBORNS FROM MOTHERS WITH CLINICAL CHORIOAMNIONITIS

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Background. The diagnosis of a woman in labor "chorioamnionitis" (CA) implies a high risk of infectious complications for the mother and fetus, which determines the need for additional examination of infants and the decision on the appointment of antibacterial therapy. The purpouse of this study was determine the need to administration antibiotic therapy to full-term newborns from mothers diagnosed with chorioamnionitis.

Materials and methods. 113 full-term newborns were examined, of which the main group consisted of children whose mothers were diagnosed with "chorioamnionitis" (n = 77), the comparison group – children born to healthy mothers (n = 36). All children performed clinical and laboratory monitoring, including a clinical analysis of capillary blood in the first 24 hours of life; determination of the level of C-reactive protein (CRP) in venous blood on the 3rd day of life. Bacteriological examination of newborns included sampling of material from the ear fold, buccal mucosa, umbilical cord blood, as well as the contents of the tracheobronchial tree (TBD) – during respiratory therapy with mechanical ventilation. Special research methods included studies of the proinflammatory cytokines (IL-1β, IL-6) in umbilical cord blood. Histological CA was diagnosed in the presence of morphological and functional signs of inflammation in the placenta.

Results. Newborns of the main group more often developed respiratory disorders requiring respiratory and oxygen therapy (p = 0,045). The production of IL-1β, IL-6 in umbilical cord blood in the examined newborns of the main group was higher than in the comparison group [Odds Ratio (OR) 8.4; 95% Confidence Interval (CI): 1.0–67.9; OR 7.4; 95% CI: 2.5–21.7 respectively]. The study of blood samples revealed leukocytosis (>34·10^9) 6.5% vs 0%, p > 0.05) and a shift in the leukocyte count to young forms of neutrophils (45.4% vs 16.7%, p < 0.05) in the peripheral blood of infants of the main group. Infants exposed to maternal clinical chorioamnionitis had increased level of CRP 10.3 times more frequent (95% CI: 2.8–37.1) than in newborns in the comparison group. With dynamic clinical and laboratory monitoring, 72 children of the main group (93.5%) had no data for the course of the infection, as a result of which they did not receive antibiotic therapy.

Conclusion: Administration antibiotic therapy to clinically healthy full-term newborns from mothers diagnosed with chorioamnionitis is unjustified. Infants of this group require clinical laboratory, dynamic observation with laboratory control, including a clinical blood test and determination of the CRP level, which is a preferred alternative to the appointment of antibiotic therapy.

Keywords: clinical chorioamnionitis; intra-amniotic infection; antibiotic therapy.

ОБ ОТСУТСТВИИ НЕОБХОДИМОСТИ НАЗНАЧЕНИЯ АНТИБАКТЕРИАЛЬНОЙ ТЕРАПИИ НОВОРОЖДЕННЫМ ОТ МАТЕРЕЙ С КЛИНИЧЕСКИМ ХОРИОАМНИОНИТОМ

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Введение. Диагноз роженицы «хориоамнионит» (ХА) предполагает высокий риск развития инфекционных осложнений для матери и плода, что определяет необходимость проведения дополнительного обследования младенцев и решения вопроса о назначении им антибактериальной терапии.

Материалы и методы. Обследовано 113 доношенных новорожденных, из них основную группу составили дети, матерям которых был диагностирован хориоамнионит (n = 77), группу сравнения — дети, рожденные от здоровых матерей (n = 36). Всем детям проводили клинико-лабораторный мониторинг, включая клинический анализ капиллярной крови в первые 24 ч жизни, определение уровня С-реактивного белка (СРБ) венозной крови на третьи сутки жизни, определение провоспалительных цитокинов (ИЛ-1β, ИЛ-6) в пуповинной крови. Бактериологическое исследование новорожденных включало забор материала с кожи заушной складки, отделяемого полости рта, пуповинной крови, а также содержимого трахеобронхиального дерева при проведении респираторной терапии — искусственной вентиляции легких. Воспалительные изменения экстраплацентарных оболочек, базальной пластинки и гладкого хориона, а также поражение пупочного канатика диагностировали при наличии лейкоцитарной инфильтрации.

Результаты. Новорожденные дети основной группы чаще имели клинические проявления дыхательных нарушений, требующие респираторной поддержки (p = 0,045). Продукция ИЛ-1β, ИЛ-6 в пуповинной крови у обследуемых новорожденных основной группы была выше, чем в группе сравнения [отношение шансов (ОШ) 8,4; 95 % доверительный интервал (ДИ): 1,0–67,9 и ОШ 7,4; 95 % ДИ: 2,5–21,7 соответственно]. При лабораторном исследовании были выявлены лейкоцитоз (>34·10^9/л, 6,5 % vs 0 %, p > 0,05) и сдвиг лейкоцитарной формулы до юных форм нейтрофилов (45,4 % vs 16,7 %, p < 0,05) в периферической крови новорожденных основной группы. Повышение уровня СРБ венозной крови у детей основной группы встречалось в 10,3 раза чаще (95 % ДИ 2,8–37,1), чем у новорожденных группы сравнения. При динамическом клинико-лабораторном мониторинге у 72 детей основной группы (93,5 %) отсутствовали данные о течении инфекционного процесса, вследствие чего они не получили антибактериальную терапию.

Заключение. Назначение антибактериальной терапии клинически здоровым доношенным новорожденным детям от матерей с диагнозом «хориоамнионит» можно считать неоправданным. Новорожденные данной группы нуждаются в клинико-лабораторном, динамическом наблюдении с лабораторным контролем, включающим клинический анализ крови и определение уровня СРБ, что является предпочтительной альтернативой назначению антибактериальной терапии.

Ключевые слова: клинический хориоамнионит; внутриамниотическая инфекция; антибактериальная терапия.

Chorioamnionitis (CA) or intra-amniotic infection is an acute antenatal inflammation of the chorion and/or amnion of the placenta, as well as the umbilical cord, with infection of the amniotic fluid (AF) that mainly arise due to an ascending polymicrobial (usually bacterial) infection and lead to the amniotic membrane with the possible fetal inflammatory response syndrome development and preterm delivery [4, 5, 7, 9, 11, 15, 35, 38].

The CA diagnosis suggests that the mother and the fetus are at increased risk of infectious complications, particularly, early neonatal sepsis (ENS). CA necessitates an additional examination of children and a decision on antibiotic therapy prescription.

The probability of sepsis in newborns from mothers with CA is proven to be inversely proportional to gestational age (GA) [10, 16, 29, 34, 36]. The literature reported that the incidence of ENS

in CA varies from 1%–4% [17] to 3%–20% [18]. The incidence of confirmed ENS with positive blood culture results in newborns with GA of 35 weeks or older from mothers with CA varies from 0.47% to 1.24% [3, 12, 28], whereas 5–10 times higher in children with extremely low body weight [25]. However, the widespread intrapartum use of antibiotic therapy in puerperas with clinical signs of CA and a long rupture to delivery interval (>18 h) led to a significantly decreased ENS.

CA is a determining risk factor for ENS development [1, 26, 28]. Concurrently, studies showed that ENS incidence remains low even in children who were exposed to CA [14, 37]. The clinical presentation of sepsis has no specific and pathognomonic signs and symptoms; therefore, CA in women is often accompanied by the routine administration of antibiotics to clinically healthy newborns. Unreasonably, frequent prescription of antibacterial drugs to newborns results in increased bacterial colonization of the child's body and antibiotic resistance. Currently, a consensus is unavailable on the need to prescribe antimicrobial drugs to clinically healthy full-term newborns from mothers with CA.

Earlier in 2012, the Center for Disease Control and Prevention and the American Academy of Pediatrics, together with the Committee on Fetus and Newborn (USA), recommended that all newborns from mothers with CA should undergo laboratory tests (complete blood count, bacteriological blood test) and antibiotic therapy for at least 48 h until negative research results are obtained [21, 32, 39]; however, in 2015, specialists of the National Institute of Child Health and Human Development (USA), the Society for Maternal-Fetal Medicine, the American College of Obstetricians and Gynecologists, and the American the Academy of Pediatrics did not recommend the routine prescription of antibiotic therapy based on case follow-up of healthy full-term and "late" premature infants from mothers with CA [23, 33, 34]. Modern international publications confirm these recommendations [13, 26, 27].

The follow-up was performed at the St. Petersburg Maternity Hospital No. 18 (currently City Perinatal Center No. 1). Laboratory studies, including microbiological tests, were performed in the laboratory of the North-West Center for Evidence-Based Medicine. Pathological and anatomical examination of the placentas was performed at the Department of Perinatal Pathology No. 4 of the St. Petersburg City Pathoanatomical Bureau. Therefore, 130 mother-child pairs were included in the study, including 113 full-term newborns and 17 premature babies (GA 22–36 weeks).

Inclusion criteria were neonates with GA of 37 weeks or more from mothers with clinically diagnosed CA.

Exclusion criteria were infants with GA of <37 weeks, meconium/blood aspiration syndrome, woman's body temperature of <37.8°C, congenital malformations, and genetic abnormalities.

Thus, the main group (I) consisted of 77 full-term newborns (GA of ≥37 weeks), whose mothers were clinically diagnosed with CA. All puerperas with clinical CA receive antibiotic therapy, despite the absence of clinical signs of infection. The comparison group (II) consisted of 36 newborns born to mothers without clinical CA (GA of ≥37 weeks) with the physiological course of the early neonatal period, who were discharged home on 3–5 days of life.

Children of the main group were monitored and treated in obstetric and physiological departments and the department of neonatal intensive care unit of St. Petersburg Maternity Hospital No. 18, as well as the children of the comparison group.

The criteria for clinical CA, which is necessary for the diagnosis, included the presence of the main (fever in the mother of ≥37.8°C) and one or more additional signs [15, 33]:

1) maternal tachycardia (heart rate [HR] of >100 per min);
2) fetal tachycardia (HR of >160 per min);
3) maternal leukocytosis (>15 × 10^9/L);
4) fetid discharge from the genital tract/fetid AF;
5) increased uterine tone, defined as palpatory tenderness in the absence of uterine contractions;
6) maternal C-reactive protein (CRP) of ≥5 mg/L.

Examination of newborns (physical examination, laboratory, and microbiological studies) was performed during the entire maternity hospital stay. Clinical materials of newborns for the study include a clinical analysis of the capillary blood taken from the heel region of newborns in the first 24 h of life; CRP of venous blood taken on the third day of life from newborns; the levels of proinflammatory cytokines (interleukin [IL]-1β and IL-6) in the umbilical cord blood; bacteriological examination of the skin behind the postural fold, discharge of the oral cavity, and umbilical cord blood, as well as the contents of the tracheobronchial tree of newborns during respiratory therapy (artificial lung ventilation).

In the presence of inflammatory changes in the clinical blood test (leukocytosis of >34 × 10^9/L, neutrophilia with a shift of the differential leukocyte count to the left), the clinical blood test was performed on the second day of life. With the clinical blood test normalization and absence of clinical infection manifestations, antibiotic therapy was not performed.

With an increased CRP level on the third day of life and the absence of clinical infection symptoms, the control of CRP in venous blood was performed on 4–5 days of life. Antibacterial therapy was not administered in children with satisfactory conditions and normal or decreased CRP levels.

Histological CA was diagnosed in the presence of leukocyte infiltration in the extraplacental membranes, basal lamina, and smooth chorion, as well as in an umbilical cord lesion.

Antibiotic therapy was performed in full-term newborn infants with congenital pneumonia according to the clinical recommendations of the Ministry of Health of the Russian Federation "Congenital pneumonia" [2], as well as in children with at least one clinical sign in combination with two or more laboratory signs of systemic inflammatory response syndrome during the first 72 hours of life [6]. The criteria for canceling antibiotic therapy included clinical condition improvement and laboratory parameter normalization by the third day of life. The transfer indication of children to the inpatient departments of children's city hospitals was a verified diagnosis of congenital pneumonia.

Semi-synthetic penicillin + broad-spectrum beta-lactamase inhibitor Sultasin® was the starting drug for antibiotic therapy in the neonatal intensive care unit of the maternity hospital.

Imminently, 89.6% of mothers in the main group ($n = 69$) received antibiotic prophylaxis on average 3.95 ± 5.21 h before delivery when diagnosed with CA by obstetrician-gynecologists. Of the mothers diagnosed with CA, 10.4% (8/77) started receiving antibiotic therapy only in the postpartum period.

Statistical data processing was performed using the statistical software packages International Business Machines Statistical Package for the Social Sciences v. 25. For a qualitative assessment of the trait frequency in the studied groups, Pearson's χ^2 was calculated. Differences were considered significant at $p < 0.05$.

Table 1 presents the comparative characteristics of newborns of both groups. Average GA and body weight and length at birth of the main group did not significantly differ from the comparison group, but with a lower Apgar score at the end of 1 and 5 minutes. By gender, girls predominated in the main group, whereas boys in the comparison group

Anamnestic information about the state of health of the mother, the course of pregnancy, and the nature of childbirth are important in assessing the newborn condition. Female patients of the main group more often have somatic (anemia and impaired fat metabolism), gynecological, and urogenital pathologies. However, statistical significance was achieved only for cervical ectopia in group I ($p = 0.002$). Vaginal diseases (vaginosis/vaginitis, including those associated with *Ureaplasma urealiticum*) were registered with equal frequency in both groups (55.8% vs. 55.5%). Mothers of group I more often had a history of preterm birth (2.6% vs. 0%), spontaneous miscarriages, ectopic pregnancies, and missed miscarriages compared with group II (16.9% vs. 1.1%). Mothers with clinically diagnosed CA were more often primiparous (84.4% vs. 69.4%). The incidence of pathology in the course of pregnancy, including the threat of termination at various terms during this pregnancy, and preeclampsia prevailed in group I. Diet-compensated gestational diabetes mellitus was detected more often in patients of the main group (23.4% vs. 16.7%). The differences between the groups according to the compared criteria for the pathology of pregnancy were statistically insignificant ($p > 0.05$). The intranatal factor analyses associated with the infectious process risk in newborns revealed that the prolonged rupture to delivery interval (>18 h) was the most frequent, with statistical significance between the compared groups ($p = 0.000$).

Table 1 / Таблица 1

Total characteristics of the examined newborns at birth ($M \pm SD$)
Общая характеристика обследованных новорожденных при рождении ($M \pm SD$)

Indicator / Показатель	Main group / Основная группа ($n = 77$)	Comparison group / Группа сравнения ($n = 36$)
Birth weight, g / Масса тела при рождении, г	3484.42 ± 460.54	3515 ± 437
Growth at birth, cm / Рост, см	52.23 ± 2.31	52.5 ± 2.4
Gestation period, weeks / Срок гестации, нед	39.76 ± 1.46	40.0 ± 1.2
Apgar score / Оценка по шкале Апгар, балл 1st minute / на 1-й минуте 5th minute / на 5-й минуте	 7.2 ± 0.63 8.2 ± 0.6	 8 ± 0.6 9 ± 0.5

The histological examination of the afterbirth ($n = 95$) revealed inflammatory changes of different localization and severity in 100% of cases of the main group and 96.7% of the comparison group. Leukocyte infiltration of the extraplacental membranes (membranitis) was registered in 75.4% of cases in the main group ($n = 49$) and 83.3% in the comparison group ($n = 25$). The basal plate (villous chorion) and smooth chorion (choriodeciduitis and deciduitis) were less frequently involved in the process, as 24.6% of cases ($n = 16$) in group I and 10% in group II ($n = 3$). Inflammatory lesions of the umbilical cord (funiculitis) were noted in 49.2% of cases ($n = 32$) of the studied afterbirth of the main group and 0% in the comparison group.

Differences in inflammatory signs in the maternal and fetal parts of the placenta between the compared groups were statistically insignificant ($p_{I–II} = 0.386$ and $p_{I–II} = 0.098$, respectively). However, the presence of funiculitis was statistically significantly associated with clinical CA ($p_{I–II} = 0.000$).

Clinical manifestations of respiratory disorders (RDs) developed in eight newborns of the main group, as well as congenital pneumonia in three and transient tachypnea in five pediatric patients. Respiratory pathology was diagnosed based on clinical and laboratory parameters and confirmed by X-ray examination of the lungs. The comparison group had no clinical manifestations of infectious processes. The analysis results revealed statistically significant differences in RDs based on the clinical CA in the mother ($p = 0.045$). All children with signs of RDs received respiratory and oxygen therapy. Two pediatric patients (2.6%) of the main group had hemodynamic disorders that require pharmacological correction with inotropic drugs. No statistically significant differences were determined between the compared groups in the incidence of hemodynamic disorders ($p = 0.330$).

Clinical CA was associated with increased proinflammatory cytokine synthesis. The study of the cytokine status, namely IL-1β (reference range 0–50 pg/ml) and IL-6 (reference range up to 50 pg/ml), revealed fluctuations in inflammatory cytokine levels in the umbilical cord blood in both groups. The mean value of IL-1β was 63.9 ± 294.29 pg/ml (min 0; max 2228) in group I ($n = 57$), whereas 10.833 ± 24.57 pg/ml (min 0; max 139) in group II ($n = 36$). The mean value of IL-6 was 344.3 ± 570.8 pg/ml (min 1; max 2874) in group I, whereas 35.5 ± 106.8 pg/ml (min 0; max 607) in group II. The levels of the studied IL-1β and IL-6 in the umbilical cord blood are presented in Figs. 1 and 2 and Table 2.

The production of IL-1β and IL-6 in the umbilical cord blood in the examined newborns of the main group was higher than in the comparison group (odds ratio [OR] 8.4; 95% confidence interval [CI]: 1.0–67.9; OR7.4; 95% CI: 2.5–21.7, respectively). Significant differences were revealed in the increased level of proinflammatory cytokines (IL-1β and IL-6) in the umbilical cord blood based on the clinical CA diagnosis ($p = 0.021$ and $p = 0.000$, respectively).

The blood test analysis revealed changes in the number of leukocytes and differential leukocyte count in the peripheral blood of newborns that are exposed to CA.

Leukocytosis (>34 × 10^9/L) in the peripheral blood of newborns in the first 24 h of life was detected in 5 (6.5%) newborns of the main group, whereas, in the comparison group, none exceeded 34 × 10^9/L. Leukopenia was not detected in any of the examined pediatric patients.

Neutrophilia with a shift of the leukocyte count to the left in the first 24 h of life was noted in 45.4% ($n = 35$) of cases in the study group and 16.7% ($n = 6$) in the comparison group ($p = 0.004$). The possibility of detecting a shift of the leukocyte count to the left

Table 2 / Таблица 2

Повышение показателей медиаторов воспаления пуповинной крови у обследуемых новорожденных
Increased indices of cord blood inflammation mediators in the examined newborns

Indicator / Показатель	Group I / I группа ($n = 57$)	Group II / II группа ($n = 36$)	$p_{I–II}$, value	Odds Ratio; 95% CI / Отношение шансов; 95 % ДИ
IL-1β pg/ml / ИЛ-1β, пг/мл (N 0–50pg/ml) (N 0–50 пг/мл)	11 (19.3%)	1 (2.8%)	<0.05	8.4; 1.0–67.9
IL-6 pg/ml / ИЛ-6, пг/мл (N 0–50 pg/ml) (N до 50 пг/мл)	31 (54.4%)	5 (13.9%)	<0.05	7.4; 2.5–21.7

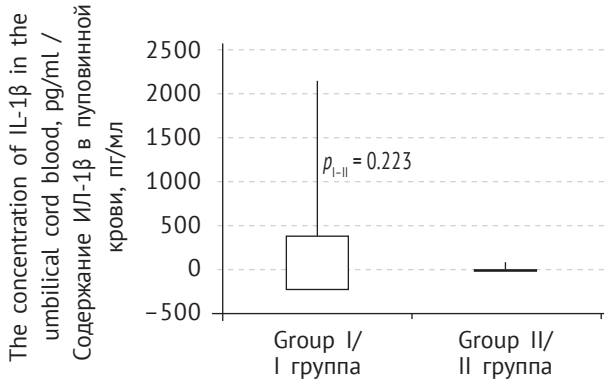

Fig. 1. The concentration of IL-1β in the umbilical cord blood in the examined newborns. Group I – children born to mothers with chorioamnionitis; group II – comparison group (healthy mother – child couple)

Рис. 1. Содержание ИЛ-1β в пуповинной крови у обследованных новорожденных. Группа I — дети, рожденные у матерей с хориоамнионитом; группа II — группа сравнения (здоровая пара мать – ребенок)

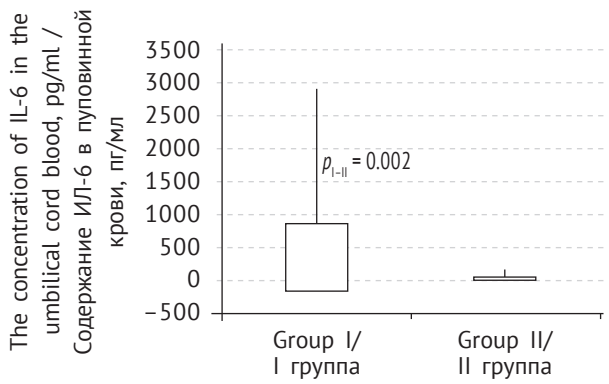

Fig. 2. The concentration of IL-6 in the umbilical cord blood in the examined newborns. Group I – children born to mothers with chorioamnionitis; group II – comparison group (healthy mother – child couple)

Рис. 2. Содержание ИЛ-6 в пуповинной крови у обследованных новорожденных. Группа I — дети, рожденные у матерей с хориоамнионитом; группа II — группа сравнения (здоровая пара мать – ребенок)

by 4.2 times (95% CI 1.557–11.154) in the clinical test of peripheral blood of newborns and an increase in the count of monocytes by 2.1 times (95% CI 0.756–6.164) was significantly increased in mothers with CA.

Children of the main group who had leukocytosis (>34 × 10^9/L) (n = 5) in a clinical blood test and/or neutrophilia (>61%) (n = 65) with a shift of the leukocyte count to the left, in the first 24 h of life, underwent a control clinical blood test on the second day of life. Concurrently, without clinical infectious process manifestations in the newborn, antibacterial therapy was not administered. The control analysis of the peripheral blood revealed that the leukocyte level returned to normal on the second day of life in 100% of cases (n = 5), the differential leukocyte count returned to normal in children by days 2.5 ± 1.0 of life in 88.6% of cases without the use of antimicrobial drugs.

The comparison group was not detected with leukocytosis in the blood tests in any child, whereas neutrophilia was noted in 31 (86.1%) cases and a shift in the leukocyte count to the left was revealed in six pediatric patients (16.7%). When monitoring the clinical blood test on the second day of life, all the studied parameters were within the age reference values.

The CRP indices (reference values 0–10 mg/l) [20] evaluation in the venous blood in full-term newborns revealed that the average value in group I (n = 64) was 13.6 ± 13.4 mg/l (min 0.4; max 66.69), whereas 4.47 ± 4.15 mg/l (min 0.3; max 15.6) in group II (n = 36). Therefore, significant differences were revealed in the increased CRP level in the venous blood of newborns on the third day of life based on the presence/absence of clinical CA of their mothers. Of the main group, 31 infants (48.4%), whereas 3 (8.3%) from the comparison group on the third day of life had an increased CRP level in the venous blood, of which the average value was 24.06 ± 12.47 mg/l (min 10.57; max 66.69) and 14.21 ± 1.73 mg/l (min 0.3; max 15.62), respectively, due to which all children were monitored for the studied indicator at the age of 72–120 h of life (OR10.3; 95% CI 2.8–37.1, p = 0.000). The average CRP value of the venous blood on the fifth day of life was 9.32 ± 4.08 mg/l in group I (n = 31) (min 3.76; max 20.76), whereas 4.4 ± 1.0 (min 3.44; max 5.45) in group II (n = 3).

Bacteriological examination of the postaural fold skin material, oral cavity discharge, and trachea contents in all compared groups showed a high frequency of isolated microorganisms. A higher frequency of positive inoculation results was revealed in the main group; however, the differences between the compared groups in the frequency of isolated microorganisms from the postaural fold skin and oral cavity discharge were statistically insignificant (p = 0.738, p = 0.158, respectively).

Positive inoculation results were predominantly represented by gram-positive (*Str. agalactiae* [group B streptococcus], *Enterococcus faecalis*, and to a lesser extent gram-negative flora [*E. coli*]). Representatives of the resident microflora, represented mainly by coagulase-negative staphylococci, primarily

Staphylococcus epidermidis, were isolated from all the studied loci. During the bacteriological examination of the umbilical cord blood in all studied cases, microorganisms were isolated from the enrichment medium.

Of 77 newborns in the main group, 3 (3.9%) received antibiotic therapy, the indication for which was diagnosed congenital pneumonia, which is following the approved clinical guidelines by the Ministry of Health of the Russian Federation [2]. Five full-term newborns of the main group were diagnosed with transient tachypnea of the newborn, of whom two received a course of antibiotic therapy due to clinical respiratory failure manifestations in combination with laboratory abnormalities (leukocytosis, neutrophilia with a shift of the leukocyte count to the left), which was regarded as a high risk of infectious processes. By the third day of life, antibiotic therapy was completed due to the absence of clinical infectious process symptoms and laboratory parameter normalization.

Thus, 72 (93.5%) children of the main group had no clinical manifestations of the infectious process, and antibiotic therapy was not performed, despite clinical blood test result deviations in the first 24 h of life and an increased CRP level on the third day of life. The case follow-up of these children was performed by a neonatologist. In the comparison group ($n = 36$), no child was prescribed antibiotic therapy due to the absence of anamnestic, clinical, and laboratory indications.

In group I, 74 (96.1%) children and 36 (100%) in group II were discharged home in satisfactory condition. Three children of the main group who are diagnosed with congenital pneumonia were transferred to children's city hospitals for further treatment.

The study results obtained indicate that in the presence of risk factors (CA) for the development of infectious complications in newborns, only three children (3.9%) had a pronounced clinical and laboratory infectious and inflammatory process, two more children (2.6%) had a high risk of an infectious process (clinical manifestations of RDs in combination with laboratory abnormalities, such as leukocytosis and neutrophilia with a shift of the leukocyte count to the left), which required the antibiotic therapy for 72 h with subsequent cancelation. In the remaining 72 cases (93.5%), no clinical manifestations of the infectious process were identified. These children underwent laboratory monitoring and were under the case follow-up of a neonatologist without the use of antibiotic therapy.

The predictive value of a hemogram in clinically healthy newborns from risk groups is low due to antibiotic prophylaxis in mothers in the intrapartum period [31]. The probability of sepsis increases only at low values of leukocytes and the absolute number of neutrophils [30]. Our study revealed inflammatory changes in the laboratory examination of children of group I in a clinical blood test in the first 24 h of life as in leukocytosis ($>34 \times 10^9$/L) in 6.5% of infants ($n = 5$), and neutrophilia in 84.4% of cases ($n = 65$), whereas, in group II, 86.1% ($n = 31$) of newborns had neutrophilia, and the level of leukocytes was within the age norm. Concurrently, none of the children in both groups had a leukocyte level of $<5.0 \times 10^9$/L. A controlled study of hemogram on the second day of life revealed that the indicators returned to normal in 100% of cases in group II, whereas 88.6% of cases in group I were without antimicrobial therapy. These indicators can be interpreted as a low risk of a septic process.

CRP is one of the standard indicators in diagnostics of neonatal sepsis. However, an increased CRP level should not always be interpreted as a marker of an infectious process [24]. Of the study group, 31 (48.4%) full-term infants and 3 (8.3%) of the comparison group were without high infectious risk and an increased level of CRP in the venous blood. The indicator returned to normal in 100% of cases in the comparison group and 90.3% in the main group without the use of antibiotic therapy. Considering that 93.5% of children of group I and 100% of children of group II had no clinical infection manifestations, an increased level of venous blood CRP in the examined newborns cannot be interpreted as an infectious process marker.

Increased indices of inflammatory mediators in the umbilical cord blood (IL-1β and IL-6) as markers of systemic fetal inflammatory response were revealed in both groups (IL-1β of 19.3% vs. 2.8%; IL-6 of 54.4% vs. 13.9%). However, the normalization of laboratory data in the absence of antimicrobial therapy interpreted the results obtained as a physiological (transient) neonatal syndrome of a systemic inflammatory response. N.P. Shabalov [8] distinguishes among the borderline transient conditions of newborns the physiological neonatal syndrome of the systemic inflammatory response, which develops as stressful and is appropriate for antigenic aggression, namely the transition from intrauterine to extrauterine life, where the primary colonization of "barriers" with saprophytic bacterial flora occurs upon external environment contact.

Given that puerperas with clinical signs of CA in the intrapartum period receive antibiotic prophylaxis, the probability of ENS and congenital pneumonia in a child decreases [19, 22]. C. Hershkovich-Shporen et al. [22] believe that the routine administration of antibiotic therapy to clinically healthy full-term

newborns from mothers with CA is unreasonable. Our study results revealed that 72 children (93.5%) did not need antibiotic therapy and were discharged home in satisfactory condition.

Based on our cases, the routine administration of antibiotic therapy to clinically healthy full-term newborns from mothers with CA was believed to be unjustified. Newborns of this group require clinical and laboratory case follow-up with laboratory control, including a clinical blood test and CRP level determination, which seems to be a preferable alternative to antibiotic therapy prescription.

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