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# IMPROVING DIAGNOSIS OF THE PROLONGED JAUNDICE IN FULL-TERM BREAST-FED INFANTS

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The article presents clinical and anamnestic characteristics and features of the pro- and anti-inflammatory cytokines balance in infants with prolonged jaundice (PJ) at breastfeeding.
Factors of prolonged jaundice in newborns on the part of mothers (risk of abortion, somatic pathology, impaired lactation) and infants (morphofunctional immaturity of the newborn, diseases during the neonatality) were identified. Distribution of infants in groups was based primarily on the of total bilirubin indices, and secondly, jaundice was divided into jaundice due to breastfeeding and jaundice from mother's milk. Pro-inflammatory cytokines indices growth and epidermal growth factor (EGF) in all infants with prolonged jaundice were determined. A correlation between IL-1β, EGF and total bilirubin in blood serum of infants with breast milk PJ was established. The prolonged course of jaundice from breast milk can be explained by the increased content of EGF in blood serum. In infants with PJ due to breastfeeding, inadequate lactation is accompanied by the increased hepatic circulation and the increased serum bilirubin concentration.

**Key words:** prolonged jaundice, cytokines, epidermal growth factor, breastfeeding .

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At present, the tendency of increasing neonatal jaundice incidence in newborns is observed [1, 4, 5]. Neonatal jaundice manifests itself in the first week of life in 25-50% of full-term and in 70-90% of preterm infants. Physiological jaundice prevails (60-70%), and among neonatal jaundice prolonged hyperbilirubinemia occurs most frequently, having the tendency of a longer, protracted course (more than 1 month.) [2, 3, 7].

Protracted (prolonged) jaundice is diagnosed after 14 days of life in the infected and after 21 days of life in the preterm infant. In infants with prolonged jaundice (PJ), an increase in indirect bilirubin, a moderate increase in direct bilirubin and hepatic enzymes in the blood indicates involvement of hepatocytes into the pathological process.

Newborn infants PJ at the present stage, are considered as multifactorial status. A large number of research works are devoted to the studying the immune response in newborn infants [2, 4, 6, 9, 10] and it is established that in newborns with PJ the proinflammatory cytokines indices grow. Therefore, the studying the balance of pro- and anti-inflammatory cytokines in PJ is an urgent task. It is known that EGF in a newborn infant is vital for adaptation after birth: it is responsible for growth, proliferation and formation of the digestive tract [2, 6, 7]. It is believed that the EGF affects intestinal absorption processes in the neonatal period. Therefore, elevated EGF indices can explain the mechanism of increasing absorption of bilirubin in the intestine and unconjugated hyperbilirubinemia in the breast milk jaundice [9].

Some clinical studies have demonstrated a direct correlation between unconjugated bilirubin and the serum-blood EGF in breast-fed children and the EGF levels in the breast milk of their mothers [6]. Recently, Xiao et al. studied the EGF indices in blood serum of newborns with a late onset of breast milk jaundice and in the breast milk of their mothers [9]. After ablactation, the total bilirubin and EGF in the blood serum of infants reduced significantly within 72 hours after ablactation.

Although the exact mechanisms of the EGF hyperbilirubinemic action are not completely known, inhibition of stomach mobility, increased absorption and activation of bilirubin transport [1, 8, 9] were suggested as possible mechanisms.

Studying serum cytokines in infants with prolonged jaundice may have a diagnostic and prognostic value.

**The purpose** of the work was to improve the diagnosis of prolonged jaundice in infants during the first 3 months of life based on the blood serum cytokines and epidermal growth factor (EGF) study.

**Materials and methods.** The study was carried out at the clinical base of the Department of Pediatrics No.5 of the O.O. Bogomolets National Medical University. The total of 57 infants at the age of 4 weeks - 3 months (average age 7.18±2.4 days of life) with protracted jaundice were examined at the Infant Department No.1 of the CCH No. 3 in Kyiv during 2015-2017. The incidence of prolonged jaundice has remained the same for three years.

Group I (main) included 57 infants (30 (52.6%) boys and 27 (47.4%) girls) who were breastfed since birth. In terms of total bilirubin, group I was divided into IA subgroup, which included 37 infants

with mild to moderate hyperbilirubinemia (up to 205 μmol/l) and IB subgroup including 20 infants with severe hyperbilirubinemia (more than 205 μmol/l).

The main criteria for inclusion into the study were the presence of indirect hyperbilirubinemia in the infant, which originated from the early neonatal period, the age of patients up to 3 months of life inclusive, vaccination against hepatitis B in the first 24 hours of life, absence of newborns hemolytic disease, hypothyroidism and organic pathology of the liver and bile ducts.

Criteria for exclusion from the study were: a clear infectious process, congenital malformations, presence of physiological jaundice, established causes of jaundice, and in all the newborns, the hemolytic, parenchymatous and mechanical nature of the jaundice was excluded during the examination.

The second group (control) consisted of 20 practically healthy children of the same age without hyperbilirubinemia manifestations. The control group of infants was selected by means of the "case-control" method. The main and the control groups did not significantly differ by mother's age, gestation period, the infant's body weight at birth ($p < 0.05$).

Clinical and anamnestic data were analyzed based on the course of pregnancy and medical documentation. The examination plan included a clinical examination and the results of biochemical blood tests (direct and indirect bilirubin level, activity of transaminases: alanine aminotransferase (ALAT) and aspartate aminotransferase (ASAT), alkaline phosphatase (AP), C-reactive protein, ultrasound examination of the liver, gall bladder, bile ducts, neurosonography (NSG). The medical and biological risk factors and their influence on formation of a protracted variant of the hyperbilirubinemia course were determined purposefully based on a specially developed PRO (patient report outcome).

Dynamics of the total bilirubin and its fractions indices, features of the protracted hyperbilirubinemia course have been analyzed.

The study of cytokines was performed using reagent kits produced by the ELISAKit (Finland) catalogue No. TNF 021, Human and KAC2211 by means of the enzyme-linked immunosorbent assay. The EGF content was studied by means of the enzyme immunoassay method using Human EGF (Invitrogen, США) kits.

Statistical processing was carried out using licensed statistical programs Biostat and Statistica 6.1. For all the parameters studied, in each group of infants, depending on the distribution, the following values were calculated: in the normal distribution - the mean value, the mean value error, standard deviation; in a nonnormal distribution - the 95% confidence interval.

The reliability of the differences between the infants groups for quantitative indices having normal distribution, parametric methods were used (Student's criterion). The significance level critical value was taken as 5%. To test the correlation between the variables, the coefficient of the Spirman rank correlation was used. The difference between the compared indices was considered reliable at $p < 0.05$.

**Results of the study and their discussion.** All the examined children were full-term and were breastfed. The health status of mothers was analyzed and it was revealed that compared to the control group, the vast majority of infants with PJ (91.2%) were born from mothers with a variety of extragenital pathologies (diffuse diseases of the thyroid gland, diabetes mellitus, chronic diseases of the digestive system, kidneys, chronic infections exacerbation, anemia) and obstetric pathology, to treat which the women received long courses of therapy during pregnancy ($p < 0.05$). In mothers of the PJ infants, concomitant pathology was found more frequently than in the control group during the given pregnancy: acute respiratory infections (40.3%), exacerbation of chronic diseases (chronic tonsillitis, chronic pyelonephritis, chronic gastritis) occurred in 31.6% of women ($p < 0.05$).

In the history of the PJ infants' mothers, the following diseases were more frequently observed: obsessive obstetric history - the risk of miscarriage (22.8%), genital candidiasis, urogenital infections (19.3%), dyshormonal and gynecological diseases (15.8%), infertility, late gestosis ($p < 0.05$).

The intranatal period was analized and its complicated course was detected in mostinfants: the umbilical cord encirclement was observed in 13.5% of infants in the IA group, 45% in the IB group and 10% in the control group, premature rupture of the fetal membranes - 10.8%, 35% and 5%, respectively, births by caesarean section - in 6.8%, 13.5% and 5% respectively, green amniotic fluid and the weakness of labor – in one third of group IB infants. Moderate or severe asphyxiation in childbirth was observed in 3 children of the IB group. Symptoms of morpho-functional immaturity were observed in 26.3% of the cases - intrauterine development was delayed in 16.2% of full-term infants in the IA group, 45% of infants in group IA and 5% in the control group ($p < 0.05$).

Among the examined infants, children from the first pregnancy predominated - 61.4%. In group I, in 70.2% of infants, body weight at birth was 2500 g - 3500 g; over 3500 g - the rest 29.9% of infants; in the control group - 64% and 35% respectively, $p > 0.05$. The main and the control groups did not differ

reliably by mother's age, gestation period, body weight of the newborns at birth (p <0.05). The score of 4-6 points by the Apgar scale at the first minute of life in group IA was 21% versus 10 % in group IB; in the control group - 5%, p <0.05. At the 5th minute of life, all infants' rating by the Apgar scale was 7-10 points. Phototherapy was performed to 24.5% of infants in the maternity hospital.

When admitted to hospital, the general status of infants with prolonged jaundice was considered satisfactory. Ochrodermia was defined by the modified Cramer scale and the total serum bilirubin level and its fractions were determined. The analysis of the jaundice dissemination showed that it was more frequently observed in zone 2 - on the face, neck, back, chest and abdomen up to the level of the umbilicus (in group IA - 67.6%, in group IB - 65%), less often in zone 3 - on the face, neck, chest, back, abdomen, on the arms up to the elbow bend and on the legs up to the knees (in group IA - 27.1%, in group IB - 25%).

The in-depth analysis of examined PJ infants' feeding permitted to identify two subgroups of children. In the first subgroup (27 infants) jaundice was manifested on the 4th-5th day of life, the physiological lost of weight exceeded 10%, there was anxiety, the slow formation of lactation, weakened suckling, finish watering of an infant, reduced feeding frequency, weight loss; during the first month of life, these infants only gained weight from 200 to 400 g, while during the control feeding it was found that the single feeding volume was reduced. It all may indicate a delay in the formation of lactation and the mother's hypogalactia. This permits to suggest the breastfeeding jaundice development.

In another subgroup (30 infants) jaundice was manifested on the 2nd-3d day with a peak of hyperbilirubinemia on the 5th-7th and (or) on the 14th day. These infants had a good appetite and physiological loss of body weight. This type of jaundice was considered as jaundice from mother's milk.

The hypoxic injuries of the central nervous system in the form of increased echogenicity of the periventricular zone (47.4%) and functional disorders of the gastrointestinal tract (31.6%) were detected while analyzing the concomitant pathology in infants with PJ.

Studies on the dynamics of the total bilirubin and its fractions level revealed these indices growth in all patients of the main group. Indices of the total bilirubin, its fractions and transaminases by groups are presented in table 1.

Table 1

**Indices of total bilirubin, its fractions and transaminases in the examined children**

| Index M±m | 1A group (n=38) | 1B group (n=20) | Main group (п=57) | Healthy infants (п=20) |
|---|---|---|---|---|
| Total bilirubin | 139.3± 22.6* | 241.6±26.18* | 175.1±47.6* | 11.6±1.4 |
| Indirect bilirubin | 123.18±20.4* | 212.94 ±25.36* | 154.6± 43* | 8.66±1.83 |
| Direct bilirubin | 16.42± 5.89* | 29.52±5.87* | 21.02 ± 7.96* | 2.84±3.76 |
| ALT | 40.75±10.71 | 44.84±10.82 | 42.19±10.96 | 28.41±6.56 |
| AST | 39.71 ±13.82 | 36.73±11.83 | 38.66±12.66 | 27.65±6.23 |

Notes: * Difference with healthy infants indices is reliable (p <0.05).

The mean total bilirubin values in the examined infants were -175.1 ± 47.6 μmol/l; in the reference group, the total serum bilirubin index was significantly lower - 11.6 ± 1.4 μmol/l (p <0.05). In the IA and IB groups, the mean indirect bilirubin values were 123.18 ± 20.4 μmol/l and 212.94 ± 25.36 μmol/l respectively, mean values of direct bilirubin were 16.42 ±

5.89 and 29.52 ± 5.87 mg/l. In the case of 10 examined infants (17.5%) - 13.5% in the IA and 25% in the IB group - the direct bilirubin values exceeded 15% of the indirect bilirubin fraction. In all infants with PJ during the stay in the hospital, the bilirubin indices tended to decrease.

In infants with PJ in the main group, the mean serum transaminases (ALAT and ASAT) were 42.19 ± 10.96 μmol/l and 38.66 ± 12.66 μmol/l. While analyzing the individual parameters, it was found that the mean ALT and AST levels in the groups amounted 40.75 ± 10.71 μmol/l and 39.71 ± 13.82 μmol/l in the IA group and 44.84 ± 10.82 and 36, 73 ± 11.83 μmol/l in the IB group.

Growth in the level of ALAT and ASAT above the norm (0-40U/l) was found in 39.6% and 36.6% of cases, i.e. increased activity of transaminases was observed in almost every third child of the IA and IB groups compared to the control group.

Ultrasound examination of the abdominal cavity was performed for all patients in the main and the control groups. In all infants of the main group, changes manifested as an increase in the anterior-posterior size of the liver and the increased parenchyma echogenicity were observed, which may indicate the toxic effect of hyperbilirubinemia on the liver parenchyma.

In the IA and IB groups, motor-tonic bile duct disorders were detected in 32% and 67% of infants, respectively, mainly hypotonic type of gallbladder motility was observed 21.6% and 55% of infants.

In the study of cytokine status, it was found that infants with prolonged jaundice had differences from practically healthy children (table 2).

In the group of infants with PJ, changes in the immunological regulation were observed as an increase in the proinflammatory cytokines IL-1β and IL-6 indices compared to healthy ones, indicating the activation of the immunological regulation compensatory mechanisms.

An analysis of the blood serum cytokines content in infants, depending on the duration of jaundice, was carried out.

Table 2

**Cytokines indices in infants with PJ as a result of breastfeeding (n = 27)**

| Index | Duration of jaundice | | | | | Healthy infants |
|---|---|---|---|---|---|---|
| | Basal level | 3-4 weeks | 5-6 weeks | 7-9 weeks | Mean index | |
| IL-1β pg/ml | 14.41± 5.23* | 12.72± 2.47 | 11.9 ± 4.47 | 10.97±4,83 | 13.3±3.81 | 10.27±4.12 |
| IL-6 pg/ml | *15.28±1.34* | *13.2 ±1.21* | *13.09± 2.47* | 12.56±2,12 | 13.5±2.72 | 12.46±0.57 |
| IL-10 pg/ml | 3.62±0.34 | *3.09± 2.47* | 2.83±0.67 | 2.18±1.57 | 2.93±1.73 | 3.18±0.67 |
| EGF ng/ml | 334.6±49.7 * | 323.9 ±39.7 * | 255.8±39.7* | 184.11±16.43 | 287.6±32.7 | 164.11±11.53 |

In the analysis of individual parameters, it was found that in children with PJ as a result of breastfeeding, basal levels of IL-1β and IL-6 cytokines were the highest - 14.41 ± 5.23 pg/ml in 74.1% of infants and 15.28 ± 1, 34 pg/ml in 62.9% of infants, respectively. But already for 3-4 weeks, in almost half of the infants, these indices were normalized and for 5-7 weeks of jaundice duration, only in one-third of children the cytokines values remained elevated - 11,9 ± 2,47 pg/ml and 13,09 ± 2,47 pg/ml. At 7-9 weeks, in almost all the infants, the indices were within the normal range. The EDF index was also at its highest level, when children were admitted to the hospital: the baseline level was 334.6 ± 49.7 ng/ml in 66.6% of infants, with a trend to reduce within 7-9 weeks. In infants with PJ due to breast milk, the basal of cytokine levels were not significantly increased (table 3).

Table 3

**Cytokines indices in infants with PJ due to breast milk (n = 30)**

| Index | Duration of jaundice | | | | | Healthy infants |
|---|---|---|---|---|---|---|
| | Basal level | 3-4 weeks | 5-6 weeks | 7-9 weeks | Mean index | |
| IL-1β, pg/ml | 11.4± 3.23 | 14.92± 2.47* | 13.9 ± 2.47 | 12.97±2.56 | 12.5±2.81 | 10.27±4.12 |
| IL-6, pg/ml | *12.28±1.34* | *14.2 ±1.21* * | 13.09± 2.47 | 12.56± 2.12 | 13.03±2.83 | 12.46±0.57 |
| IL-10, pg/ml | 3.79±0.34 | *2.91± 2.48* | 2.89±0.69 | 2.18±1.69 | 2.94±1.76 | 3.18±0.67 |
| EGF ng/ml | 383.9±41.7* | 594.6±49.7* | 355.8±39.7 | 224.11±14.57 | 397.1±42.7 | 164.11±11.53 |

The maximum values for IL-1β and IL-6 cytokines were observed at 3-4 weeks of jaundice - 14.92 ± 2.47 pg/ml in 70.5% and 14.2 ± 1.21 pg/ml in 53.3 % of patients. The EDF index also had its maximum level during this period - 594.6 ± 49.7 ng/ml in 70% of infants. At 5-6 weeks of jaundice, high levels were observed in almost 75% of patients, and at 7-9 weeks in half of the infants these rates remained elevated.

The analysis of mean values of IL-1β and IL-6 cytokines in patients with prolonged course of jaundice and healthy infants showed an increase of these parameters -12.72 ± 2.47 pg/ml and 13.26 ± 2.51 pg/ml versus 10, 27 ± 4.12 pg/ml and 12.46 ± 0.57 pg/ml. The analysis of the content of IL-1β and IL-6 cytokines in infants with PJ, depending on the duration of jaundice, has shown that in patients with PJ for more than 1 month, these indices were higher compared to the infants with PJ less than 1 month.

A correlation analysis was carried out to assess the interrelations between pro-inflammatory cytokines IL-1β, EEG indices and total bilirubin in serum of infants with PJ due to breast milk. At 3-4 weeks of the course of prolonged jaundice, the levels of IL-1β and EGF increased simultaneously with the level of total bilirubin, which is confirmed by a positive correlation ($r = 0.33$, $r = 0.29$, $p = 0.044$, respectively). While for 5-6 weeks the decrease in the level of TB against the background of increased indices of IL-1β and EGF is indicated that it reflects a negative correlation ($r = -0.21$, $r = -0.16$, $p = 0.041$, respectively).

Indices of anti-inflammatory cytokine IL-10 in the blood of infants were within the reference values, not significantly differing between groups.

The EDF serum index in the main group amounted 343.9± 42.5 ng/ml and in the control group it was 164.11 ± 11.53 ng/ml, the difference between the groups was statistically reliable according to Student's criterion ($p < 0.05$).

In the analysis of individual EDF parameters in children with PJ, it was found that the highest EDF levels (513.82 ± 4.18 ng / ml) were observed in 8 children (40%) in the IB group (with the total bilirubin value over 205 μmol/l) and the jaundice duration for over 1 month, which may indicate an adaptation disorder.

Thus, it can be noted that infants with prolonged jaundice, particularly with a longer-term hyperbilirubinemia (more than 5 weeks), require a more in-depth examination in the form of the cytokine profile determination in order to predict the conjugative jaundice course and to prevent damage to liver cells by bilirubin metabolism products.

In general, our studies are consistent with the results of other authors [5, 8]. Thus, the cytolytic syndrome with an enzymes activity 1.5-fold growth was found in almost every third child with prolonged course of jaundice, which may be the result of hypoxic damage to hepatocyte membranes. In the control group of patients, only 5% of infants demonstrated changes in the form of cytolysis signs. Other changes in the hepatobiliary system have not been registered. The activity of aminotransferases, according to literature, is increased due to the liver cells structure disorders, especially hepatocytes, which in PJ infants may be due to the toxic effect of bilirubin on hepatocytes or to the influence of pathological factors in the perinatal period [1, 3, 4, 5, 8].

Violation of the cytokine profile compared with healthy children is observed in our study and studies by other authors. The immune response in newborns was studied and it was found that in newborns with prolonged course of jaundice an increase in indicators of pro-inflammatory cytokines and epidermal growth factor occurs [2, 4, 6, 9, 10].

## Conclusion

In mothers, prolonged jaundice of newborns is caused by a risk of abortion, diffuse changes in thyroid gland, taking medications during pregnancy, late gestosis, complicated labor, which is associated with the risk of developing prolonged jaundice.

In children, the risk factor causing PJ is the concomitant pathology: morphofunctional immaturity of the newborn (intrauterine growth retardation, chronic intrauterine fetal hypoxia) and diseases in the period of neonatality: hypoxic injuries of the central nervous system, functional disorders of the gastrointestinal tract, disorders of the colostral stage formation in the mother.

It is advisable to distinguish between jaundice due to breastfeeding and jaundice from mother's milk. In the first case, insufficient formation of lactation is accompanied by an increase in enterohepatic circulation and, as a result, an increase in the serum bilirubin concentration. In the second case, the protracted course of jaundice may be due to high levels of EDF in blood serum.

In newborns with PJ, serum transaminases (ALT and AST) indices are growing in almost every third child, all of them showing liver ultrasound abnormalities indicating the involvement of the liver parenchyma into the pathological process.

Indices of pro-inflammatory cytokines and their dynamics are an additional diagnostic criterion of PJ in infants at breastfeeding.

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**Реферати**

**УДОСКОНАЛЕННЯ ДІАГНОСТИКИ ПРОЛОГНІГОВАНОЇ ЖОВТЯНИЦІ У ДОНОШЕНИХ ДІТЕЙ НА ГРУДНОМУ ВИГОДОВУВАННІ**

**Єсипова С.І.**

В статті представлено клініко-анамнестичні характеристики та особливості балансу про- і протизапальних цитокінів у дітей раннього віку з пролонгованою жовтяницею (ПЖ) на грудному вигодовуванні. Виявлено чинники пролонгованої жовтяниці новонароджених з боку матерів (ризик переривання вагітності, соматична патологія, порушення становлення лактації ) та дітей (морфофункціональна незрілість новонародженого, захворювання в періоді новонародженості). Розподіл дітей з ПЖ проводили за показниками загального білірубіну, з іншого боку, виділяли жовтяницю внаслідок грудного вигодовування та жовтяницю від грудного молока. Встановлено підвищення показників прозапальних цитокінів та епідермального фактору роста (ЕФР) у всіх дітей з ПЖ. Виявлено кореляційний зв'язок між показниками IL-1β, ЕФР та загального білірубіна у сироватки крові у дітей з ПЖ грудного молока. Затяжний перебіг жовтяниці від грудного молока може пояснюватися підвищеним вмістом ЕФР в сироватці крові. У дітей з ПЖ внаслідок грудного вигодовування недостатнє становлення лактації супроводжується підвищенням ентерогепатичної циркуляції і підвищенням концентрації сироваткового білірубіну.

**Ключові слова**: пролонгована жовтяниця, цитокіни, епідермальний фактор роста, діти раннього віку, грудне вигодовування.

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**УСОВЕРШЕНСТВОВАНИЕ ДИАГНОСТИКИ ПРОЛОНГИРОВАННОЙ ЖЕЛТУХИ У ДОНОШЕННЫХ ДЕТЕЙ НА ГРУДНОМ ВСКАРМЛИВАНИИ**

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В статье представлены клинико-анамнестические характеристики и особенности баланса про- и противовоспалительных цитокинов у детей раннего возраста с пролонгированной желтухой (ПЖ) на грудном вскармливании. Выявлены факторы пролонгированного течения желтухи новорожденных со стороны матерей (риск прерывания беременности, соматическая патология, нарушения становления лактации) и детей (морфофункциональная незрелость новорожденного, заболевания в период новорожденности). Распределение детей проводили по показателям общего билирубина, с другой стороны, выделяли желтуху вследствие грудного вскармливания и желтуху от грудного молока. Установлено повышение показателей провоспалительных цитокинов и эпидермального фактора роста (ЭФР) у всех детей с ПЖ. Выявлена корреляционная связь между показателями IL-1β, ЭФР и общего билирубина в сыворотке крови у детей с ПЖ грудного молока. Затяжное течение желтухи от грудного молока может объясняться повышенным содержанием ЭФР в сыворотке крови. У детей с ПЖ вследствие грудного вскармливания недостаточное становления лактации сопровождается повышением печеночной циркуляции и повышением концентрации сывороточного билирубина.

**Ключевые слова:** пролонгированная желтуха, цитокины, эпидермальный фактор роста, дети раннего возраста, грудное вскармливание

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# ВЗАЄМОЗВ'ЯЗОК СТАНУ ЗДОРОВ'Я І ПСИХОФІЗІОЛОГІЧНИХ ХАРАКТЕРИСТИК ВІЙСЬКОВОСЛУЖБОВЦІВ

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Стаття присвячена виявленню психофізіологічних передумов трансформації стану професійного здоров'я військовослужбовців і розробці алгоритму оцінки цього стану. За допомогою програмно-апаратного комплексу для проведення психофізіологічних досліджень, було проведено психофізіологічні дослідження 96 льотчиків та штурманів, які приймали участь в бойових діях. Реєструвались: критична частота світлових миготінь, час простої та складної зорово-моторної реакції, функціональна рухливість нервових процесів, час простої та складної слухо-моторної реакції, реакція на рухомий об'єкт та інші психофізіологічні показники. За допомогою факторного аналізу були виявлені три приховані фактори, що пояснюють 35,1% дисперсії аналізованих характеристик. Виділені фактори, що описують фундаментальні стани організму людини: ступінь втоми, активації і витривалості. Виявлення та кількісна оцінка цих характеристик дозволяє пояснити погіршення яких психофізіологічних якостей організму є передумовою розвитку негативних відхилень в стані здоров'я військовослужбовців та використати ці оцінки для завбачення та своєчасного попередження про потенційну можливість майбутніх негативних змін його здоров'я. Виділено фундаментальні психофізіологічні фактори, що описують функціональний стан військовослужбовців, які приймали участь в бойових діях, показано, що факторні значення факторів «бадьорості-втоми», «активації» і «витривалості-слабкості» достовірно відрізняються у військовослужбовців з задовільним станом здоров'я та тих в кого є негативні зрушення цього параметру та розроблено розв'язувальні правила, що дозволяють з точністю до 70% оцінити стан здоров'я військовослужбовців за комплексом психофізіологічних показників.

**Ключові слова:** здоров'я, психофізіологічний стан, психофізіологічні якості, льотчики, учасники бойових дій.

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Стан здоров'я будь-якої людини не є константою. Він постійно змінюється в ту або іншу сторону і ці зміни часто залежать від умов професійного середовища, рівня напруженості пережитих ситуацій на роботі, функціональних резервів і стресостійкості її організму [2]. В процесі трансформацій зовнішніх і внутрішніх факторів трудового середовища відбувається синхронна