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CORTISOL AND LABORATORY INDICATORS OF SYSTEMIC INFLAMMATION IN CASE OF BACTERIAL PURULENT MENINGITIS AND VIRAL ENCEPHALITIS IN CHILDREN

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Pediatric bacterial purulent meningitis (BPM) and viral encephalitis (VE) are significant medical and social problems due to their course severity, high frequency of death cases, and formation of neurologic deficiency at the disease outcome. Activation of hormonal regulation and severity syndrome of systemic inflammatory response are important factors to evaluate the character of BPM and VE course. **Objective.** To study the level of cortisol and laboratory indicators of systemic inflammation in children with various variants of BPM and VE course depending on the period of the disease (acute period, reconvalescence) to specify their role in the pathogenesis of acute neuroinfections. **Object and methods.** There were investigated hematological indicators, the level of cortisol, C-reactive protein in blood serum of 60 children, 39 of them had BPM and 21 ones – VE. The comparison group included 14 children aged from 1 to 14 years old who were undergoing rehabilitation care due to neurologic problems at the Federal State-Financed Institution Pediatric Research and Clinical Center for Infectious Diseases under the Federal Medical Biological Agency. **Results.** The patients were divided into some subgroups according to the severity of their condition at the moment of hospitalization, i.e. urgent condition or critical condition requiring organ replacement therapy. The maximum increase of cortisol level and laboratory markers of systemic inflammation during the acute period was revealed in case of BPM in comparison with VE with a subsequent normalization to the stage of reconvalescence. The level of cortisol during the acute period of BPM was reliably higher in the subgroup with urgent conditions, whereas in case of VE – in the subgroup with critical conditions. There were no significant differences in the laboratory indicators of systemic inflammation response among the subgroups. There was established a correlation interrelation of cortisol level and the content of granulocytes and blood lymphocytes. **Conclusion.** There were identified characteristic features of cortisol content in children with bacterial and viral neuroinfections depending on the course of the disease.

Keywords: bacterial purulent meningitis; viral encephalitis; children; cortisol; systemic inflammation; laboratory indicators.

КОРТИЗОЛ И ЛАБОРАТОРНЫЕ ПОКАЗАТЕЛИ СИСТЕМНОГО ВОСПАЛЕНИЯ ПРИ БАКТЕРИАЛЬНЫХ ГНОЙНЫХ МЕНИНГИТАХ И ВИРУСНЫХ ЭНЦЕФАЛИТАХ У ДЕТЕЙ

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Бактериальные гнойные менингиты (БГМ) и вирусные энцефалиты (ВЭ) у детей представляют значимую медико-социальную проблему в связи с тяжестью течения, высоким процентом летальных исходов, формированием неврологического дефицита в исходе заболевания. В определении характера течения БГМ и ВЭ имеет значение активация гормональной регуляции и тяжесть синдрома системного воспалительного ответа (ССВО). **Цель работы.** Изучить динамику уровня кортизола и лабораторных показателей системного воспаления у детей с различными вариантами течения БГМ и ВЭ в зависимости от периода заболевания (острый, период реконвалесценции) для уточнения их роли в патогенезе острых нейроинфекций. **Материалы и методы.** Проведено исследование гематологических показателей, уровня кортизола, С-реактивного белка в сыворотке крови 60 детей, среди которых 39 переносили БГМ, 21 — ВЭ. Группу сравнения составили 14 детей в возрасте от 1 года до 14 лет, находившихся на

реабилитации в «Детском научно-клиническом центре инфекционных болезней» Федерального медико-биологического агентства в связи с неврологическими проблемами. **Результаты.** По тяжести состояния на момент поступления в стационар пациенты были разделены на подгруппы с неотложным, либо критическим состоянием, требующим дополнительных реанимационных пособий. В остром периоде максимальные уровни кортизола и лабораторных маркеров системного воспаления обнаружены при БГМ по сравнению с ВЭ с последующей нормализацией к стадии реконвалесценции. Содержание кортизола было достоверно выше в подгруппе пациентов с неотложным состоянием в остром периоде БГМ, тогда как при ВЭ — в подгруппе с критическим состоянием. Достоверных различий в лабораторных показателях ССВО между подгруппами не выявлено. Установлена корреляционная взаимосвязь уровня кортизола с содержанием гранулоцитов и лимфоцитов крови. **Заключение.** Установлены характерные особенности содержания кортизола у детей с бактериальными и вирусными нейроинфекциями в зависимости от тяжести течения заболевания.

Ключевые слова: бактериальный гнойный менингит; вирусный энцефалит; дети; кортизол; системное воспаление; лабораторные показатели.

INTRODUCTION

Bacterial purulent meningitis (BPM) and viral encephalitis (VE) in children represent a significant medical and social problem due to the severity of the course, a high rate of lethal outcomes, and the development of neurologic impairment in the residual period [4]. The study of various aspects of the pathogenesis of acute neuroinfections, including the assessment of hormonal regulation disorders, the intensity of inflammatory and immune responses, and their relationship is of both scientific and practical interest. In response to pathogen permeation, the hypothalamus–pituitary–adrenal cortex axis is activated with an increase in the synthesis of adrenal cortex hormones, the most active of which is cortisol [14]. Cortisol has a pronounced anti-inflammatory effect and can reduce capillary permeability, inhibit cell division processes and protein biosynthesis, stabilize lysosomal membranes, affect immune responses, in particular cytokine synthesis, influence the functional activity of immunocompetent cells, and participate directly in the pathogenesis of an infection [6, 7, 13].

In addition to hormonal regulation, systemic inflammation is important in determining the nature of the course of BPM and VE. In assessing VE, laboratory parameters are considered in addition to clinical signs (such as temperature, respiratory rate, and heart rate). Leukocytosis (i.e., over 12×10^6 cells/l), leukopenia (below 4×10^6 cells/l), or a left deviation of the leucogram with an increase in the number of stab forms over 10% help diagnose systemic inflammatory response syndrome (SIRS) [11]. Moreover, determining the concentration of C-reactive protein (CRP) is important, as its level increases over the first 24 h of the disease with a maximum level in bacterial infection than in viral infection [2].

Literature data interpret ambiguously changes in cortisol level in the blood serum of patients with neuroinfections, which is possibly due to various functions and mechanisms of action of cortisol on different body systems, including the immune system [1, 3, 7]. Data on the relationship between the level of endogenous cortisol and the severity of neuroinfections as well as the laboratory markers of SIRS are limited and contradictory. Cortisol and CRP levels are the highest in pediatric patients with meningococcal meningitis and are relatively low in patients with fulminant meningococcal septicemia and septic shock [15]. Woensel et al. [15] reported that a low cortisol concentration in the blood serum in combination with high concentrations of adrenocorticotrophic hormone indicates an extremely severe course of meningococcal infection in pediatric patients with a high risk of unfavorable outcome. Another study revealed that the majority of patients with sepsis and septic shock have increased serum cortisol levels [12]. In patients with sepsis, variability in free cortisol levels at different disease stages was noted, while a significant increase in the total cortisol levels was not detected [9]. A few studies have noted a relationship between cortisol levels and changes in the clinical blood test. A significant relationship was established between the levels of leukocytes, platelets, and serum cortisol in a random sample of patients with various pathologies, including infectious, only at examinations 2 and 3 [8]. Moreover, a certain cortisol level is required to maintain an elevated level of white blood cells.

Thus, despite the well-known role of cortisol in the regulation of inflammation and immunity, the variability and ambiguity of literature data on the involvement of cortisol in the pathogenesis of neuroinfections and the relationship between the level of endogenous cortisol and the severity of systemic inflammation reactions determine the relevance and novelty of studying the adaptive capabilities of the human body to adjust therapy and improve disease outcomes.

The work aimed to investigate the dynamics of cortisol levels and laboratory indicators of systemic inflammation in pediatric patients with different BPM and VE courses depending on the disease period (acute or convalescence) to clarify their role in the pathogenesis of acute neuroinfections.

MATERIALS AND METHODS

A comparative study of the levels of cortisol and laboratory markers of systemic inflammation in 60 pediatric patients aged 2 months to 17 years, hospitalized at the Pediatric Research and Clinical Center for Infectious Diseases of the Russian Federal Medical-Biological Agency, Saint Petersburg (PRCCID) in the period from 2010 to 2017, was performed. Of these patients, 39 had BPM and 21 patients had VE. In the acute period (days 1–3 from the disease onset) and at the early convalescence stage (days 7–14 from the disease onset), the dynamics of hematological parameters, cortisol content, and CRP level in the blood serum were assessed. According to the severity of the condition upon hospital admission, the patients were distributed into subgroups with an emergency or critical condition requiring additional resuscitation activities.

The comparison group consisted of 14 pediatric patients aged 1–14 years who were undergoing rehabilitation due to neurological conditions at the PRCCID. The etiology of BPM and VE was established using microbiological methods, polymerase chain reaction, and enzyme immunoassay. In the BPM group, meningococcal etiology was established in 21, hemophilic etiology was detected in 11, pneumococcal etiology was found in three, and unclear etiology was noted in four patients. In the VE group, one patient had herpetic encephalitis, one had chickenpox, one had tick-borne encephalitis, one had disease caused by the Epstein-Barr virus, and two patients had a mixed etiology of the disease (herpes + Epstein–Barr virus, Epstein–Barr virus + cytomegalovirus). In other pediatric patients, the etiology was not established.

The study of the blood serum cortisol level was performed by enzyme-linked immunosorbent assay on an Infiniti analyzer (Tecan, Austria) with the use of reagents by Vector-Best (Russia). The clinical analysis of the blood was performed on an automatic hematological analyzer Sysmex XP-300 (Japan); the leucogram count was performed in a blood smear using an Axio Lab. A1 microscope (Germany). Biochemical studies were performed on automatic analyzers Cobas c 50 (Roche, France) and Taurus (Instrumentation Laboratory, Italy). Values of hematological and biochemical parameters were compared with generally accepted age norms.

Statistical data processing was performed using the statistical analysis package Microsoft Office Excel 2007 and GraphPad Prism 5.0 (GraphPad Software Inc., La Jolla, CA). The mean value (M), median (Me), and interquartile range [Q_{25}–Q_{75}] of each sample were evaluated. The significance of the differences between the groups was established using Student's t-test and Mann–Whitney U-test. A correlation analysis was performed using Spearman's nonparametric rank correlation to establish a relationship between the cortisol level and severity of laboratory indicators of systemic inflammation.

RESULTS AND DISCUSSION

The cortisol level in the comparison group was within a narrow range and averaged 414.8 ± 39.2 nmol/L, which is generally comparable with literature data. Hematological and biochemical parameters in pediatric patients of this group were within the generally accepted age norms. With BPM and VE, the results of the analysis of the blood serum level of cortisol varied significantly depending on the nosological form and disease period. In the acute period of BPM, the average cortisol level was approximately five times higher than that of the comparison group, decreasing by the convalescence stage. With VE, the cortisol level exceeded the indices of the comparison group by an average of 2.5 times, with the same values in the convalescence stage (Table 1).

Standard laboratory parameters of SIRS (i.e., leukocyte count, stab forms, CRP level) also revealed maximum deviations from the age reference range in patients with acute BPM, while maintaining a minor leukocytosis and an increase in CRP in the convalescence stage. In the acute period of VE, only insignificant leukocytosis was found without an increase in stab forms and CRP concentration (Table 1).

According to the severity of the condition at the time of hospital admission, patients with BPM and VE were distributed into subgroups with an emergency condition (BPM subgroup 1 and VE subgroup 3, respectively) or critical condition (BPM subgroup 2 and VE subgroup 4, respectively). Subgroups 2 and 4 included patients with an extremely critical condition caused by the development of septic shock or cerebral edema, manifested by severely depressed consciousness and convulsive status. All patients of these subgroups received intensive therapy, including resuscitation support (such as artificial lung ventilation, extracorporeal detoxification, hemo- and plasma transfusion) due to the development of organ/multiple organ failure. The subgroups with an emergency condition included pediatric patients whose condition upon admission was assessed as severe due to pronounced manifestations of intracranial hypertension and SIRS, with clinical and laboratory signs of sepsis, but without signs of organ failure. In this group, no resuscitation was required to stabilize the condition of the patients. BPM subgroup 2 included 19 (49%) patients, and BPM subgroup 1 consisted of 20 (51%) patients. In the VE group, the condition of 14 (67%) patients was regarded as critical and that of seven patients (33%) as emergency.

Table 1 / Таблица 1

Blood indicators in the dynamics of bacterial purulent meningitis and viral encephalitis in children
Лабораторные показатели крови в динамике бактериального гнойного менингита и вирусного энцефалита у детей

Nosological form, period / Нозологическая форма, период (*n*)	Statistical indicators / Статистические показатели	Laboratory indicators / Значения лабораторных показателей			
		cortisol, nmol/l / кортизол, нмоль/л	leucocytes, $\times 10^9$/l / лейкоциты, $\times 10^9$/л	band neutrophils, % / палочкоядерные нейтрофиллы, %	C-reactive protein, mg/l / С-реактивный белок, мг/л
Bacterial purulent meningitis, acute period / Бактериальный гнойный менингит, острый период (*n* = 39)	*M* ± *m* *Me* Q_{25}–Q_{75}	2150.3 ± 191.2*§# 2628.5 1196.0–3137.0	19.5 ± 2.0§# 16.3 8.5–24.9	16.4 ± 1.7§# 14.0 10.0–20.0	192.8 ± 15.2§# 178.0 121.4–266.0
Bacterial purulent meningitis, recovery period / Бактериальный гнойный менингит, период реконвалесценции (*n* = 27)	*M* ± *m* *Me* Q_{25}–Q_{75}	703.4 ± 116.6 514.3 395.5–638.7	9.7 ± 0.6 8.6 7.2–12.2	3.6 ± 0.5 3.0 2.0–5.0	12.6 ± 3.4# 6.2 2.5–16.8
Viral encephalitis, acute period / Вирусный энцефалит, острый период (*n* = 21)	*M* ± *m* *Me* Q_{25}–Q_{75}	931.6 ± 225.8 539.3 182.3–1447.0	12.3 ± 1.1 10.5 9.1–15.5	3.1 ± 0.5 2.5 2.0–5.0	6.2 ± 1.4 4.0 2.5–8.1
Viral encephalitis, recovery period / Вирусный энцефалит, период реконвалесценции (*n* = 13)	*M* ± *m* *Me* Q_{25}–Q_{75}	1007.0 ± 230.5* 811.0 316.7–1433.0	8.2 ± 0.9 7.2 5.5–9.7	3.4 ± 0.6 2.5 3.0–4.0	3.3 ± 0.7 3.0 1.7–5.0
The comparison group / Группа сравнения	*M* ± *m* *Me* Q_{25}–Q_{75}	414.8 ± 39.2 406.5 315.0–517.0	–	–	–

* Difference from the comparison group; § difference between the values of recovery period and acute period in each nosological form; # difference between the values of BPM and VE in the same period. Confidence level $p < 0.05$.*

* Отличия от группы сравнения; § отличия значений острого периода от реконвалесценции в каждой нозологической форме; # отличия значений при БГМ и ВЭ в одном периоде. Уровень достоверности $p < 0.05$.

Data analysis revealed significant differences in the cortisol level in BPM and VE subgroups (Tables 2, 3). In the acute period (Table 2), a significant increase in the cortisol level was found in BPM subgroup 1 as compared with that in BPM subgroup 2. In the convalescence stage, the cortisol levels reached those of the comparison group in both subgroups. No significant differences were found in hematological parameters, CRP, and albumin concentrations in the subgroups; however, at the convalescence stage, the average cortisol and CRP levels in the subgroup with a critical condition were insignificantly higher (773.0 versus 652.4 nmol/L, and 7.2 versus 17.8 mg/L for cortisol and CRP, respectively).

Compared to patients with BPM, pediatric patients with critical VE condition has significantly higher level of cortisol than those with an emergency VE condition and their values exceeded those of the comparison group in the acute period (Table 3). At the convalescence stage, the cortisol level in patients with critical illness remained high, which is significantly different from the comparison group and subgroup with an emergency condition. Among the laboratory criteria for systemic inflammation in the acute period, moderate leukocytosis was revealed without an increase in the count of stab leukocytes and CRP level. No significant differences were observed in hematological parameters between the subgroups.

Thus, the most significant increase in the cortisol level was detected in the acute period of BPM, which was associated with the maximum increase in laboratory markers of systemic inflammation, in particular, leukocytosis and stab leukocyte count. Probably, the activation of the hypothalamic–pituitary–adrenal axis, caused by the penetration of bacteria leads to an increase in cortisol synthesis, which contributes to the manifestation of compensatory inflammatory and immune reactions at an early disease stage. In the course

Table 2 / Таблица 2

Blood indicators in children with different course of bacterial purulent meningitis
Лабораторные показатели крови у детей с разным характером течения бактериального гнойного менингита

No. Subgroups – Status / Номер подгруппы больных — состояние (*n*)	Statistical indicators / Статистические показатели	Cortisol, nmol/l / Кортизол, нмоль/л	Leucocytes, $\times 10^9$/l / Лейкоциты, $\times 10^9$/л	Band neutrophils, % / Палочкоядерные нейтрофиллы, %	C-reactive protein, mg/l / С-реактивный белок, мг/л
Acute period / Острый период					
1 – Urgent / Неотложное (n = 20)	$M \pm m$ Me Q_{25}–Q_{75}	2640.0 ± 211.2*§# 2877.0 2516.0–3214.0	20.4 ± 2.9§ 17.8 9.0–25.3	15.1 ± 1.7§ 15.5 10.0–20.0	205.8 ± 18.0§ 192.0 143.2–258.0
2 – Critical / Критическое (n = 19)	$M \pm m$ Me Q_{25}–Q_{75}	1750.0 ± 281.4*§ 1859.0 534.2–2696.0	18.7 ± 2.9§ 16.3 8.9–24.9	17.8 ± 2.9§ 13.0 10.0–25.0	178.4 ± 25.4§ 162.0 90.9–282.3
Recovery period / Период реконвалесценции					
1 – Urgent / Неотложное (n = 15)	$M \pm m$ Me Q_{25}–Q_{75}	652.4 ± 160.0 522.6 395.5–638.7	9.0 ± 1.0 7.7 6.8–11.5	3.4 ± 0.7 3.0 2.0–5.0	7.2 ± 1.5 6.3 4.3–9.5
2 – Critical / Критическое (n = 12)	$M \pm m$ Me Q_{25}–Q_{75}	773.0 ± 174.9 506.0 420.4–564.3	10.6 ± 0.8 10.8 9.5–12.2	3.8 ± 0.6 3.0 3.0–5.0	17.8 ± 7.5 5.2 2.5–38.8
The comparison group / Группа сравнения (n = 14)	$M \pm m$ Me Q_{25}–Q_{75}	414.8 ± 39.2 406.5 315.0–517.0	–	–	–

* Difference from the comparison group; § differences between subgroups in different periods of the disease; # differences between subgroups in the same period of the disease. Confidence level $p < 0.05$.
* Отличия от группы сравнения; § отличия внутри подгруппы в разные периоды заболевания; # отличия между подгруппами в одном периоде заболевания. Уровень достоверности $p < 0,05$.

Table 3 / Таблица 3

Blood indicators in children with different course of bacterial purulent meningitis
Лабораторные показатели крови у детей с разным характером течения вирусного энцефалита

No. Subgroups – Status / Номер подгруппы больных — состояние (*n*)	Statistical indicators / Статистические показатели	Cortisol, nmol/l / Кортизол, нмоль/л	Leucocytes, $\times 10^9$/l / Лейкоциты, $\times 10^9$/л	Band neutrophils, % / Палочкоядерные нейтрофиллы, %	C-reactive protein, mg/l / С-реактивный белок, мг/л
Acute period / Острый период					
3 – Urgent / Неотложное (n = 7)	$M \pm m$ Me Q_{25}–Q_{75}	463.6 ± 160.4 423.6 269.0–591.8	11.9 ± 3.2 10.5 10.0–10.5	3.2 ± 1.1 3.0 2.0–5.0	6.3 ± 2.3 4.8 3.4–8.1
4 – Critical / Критическое (n = 14)	$M \pm m$ Me Q_{25}–Q_{75}	1251.3 ± 327.2*# 558.8 199.5–2585	12.5 ± 1.4 10.6 9.1–15.5	3.1 ± 0.6 2.5 2.0–5.0	6.2 ± 1.8 4.0 2.5–8.5
Recovery period / Период реконвалесценции					
3 – Urgent / Неотложное (n = 4)	$M \pm m$ Me Q_{25}–Q_{75}	433.2 ± 321.3 174.5 32.0–316.7	7.5 ± 2.1 5.5 5.2–11.7	2.7 ± 0.7 2.0 2.0–4.0	2.1 ± 0.8 2.3 1.7–2.9
4 – Critical / Критическое (n = 9)	$M \pm m$ Me Q_{25}–Q_{75}	1263.2 ± 267.3*# 1394.0 589.8–1440.0	8.4 ± 1.2 7.3 6.6–9.7	3.7 ± 0.8 3.0 2.0–6.0	5.2 ± 1.5 4.9 2.2–7.2
The comparison group / Группа сравнения (n = 14)	$M \pm m$ Me Q_{25}–Q_{75}	414.8 ± 39.2 406.5 315.0–517.0	–	–	–

* Differences from the comparison group; # differences between subgroups in the same period of the disease. Confidence level $p < 0.05$.
* Отличия от группы сравнения; # отличия между подгруппами в одном периоде заболевания. Уровень достоверности $p < 0,05$.

of the study, a higher cortisol level was registered in the group with emergency condition, which may indicate the effective functioning of this hormonal axis. In pediatric patients with critical illness, low cortisol levels may indicate an impairment of the regulatory mechanisms and depletion of the adrenal cortex functions and can be one of the factors that aggravate the course of BPM. Our data are in part consistent with the indication of a lower cortisol level in patients with severe sepsis [5, 15].

With VE, in contrast to BPM, the cortisol level in the acute period was higher in patients with a critical condition than in patients with an emergency condition. This finding was probably due to the differences in the etiopathogenesis of BPM and VE. In particular, in case of VE, cytotoxic cerebral edema and cerebral injury play a decisive role in the disease severity, compared with the greater significance of systemic inflammation in patients with BPM.

Correlation analysis for the BPM group as a whole did not establish a relationship between the cortisol level and laboratory criteria of SIRS, as well as hematological and biochemical (CRP) indicators. With acute VE, a relationship was noted between the cortisol level and absolute lymphocyte count ($r = 0.51$), and in the convalescence stage, a direct relationship was found with the absolute granulocyte count ($r = 0.75$).

Analysis of the correlations in the subgroups with critical and emergency conditions revealed the relationship between cortisol level and some hematological parameters, in both acute and convalescence stages. In acute BPM, a mild direct relationship between the cortisol level and absolute granulocyte count ($r = 0.38$) was established in the subgroup with a critical condition, while in the stage of convalescence, an inverse relationship was noted ($r = –0.33$). In the subgroup with an emergency condition, an inverse relationship between the cortisol level and granulocytes was noted ($r = –0.31$) in the acute period, and in the convalescence stage, a direct relationship was observed ($r = 0.28$). At the same time, no significant differences were observed in the absolute granulocyte count in these subgroups either in the acute period ($15.4 \pm 2.9 \times 10^6$ and $18.9 \pm 3.1 \times 10^6$ cells/l) or in the convalescence period ($6.7 \pm 0.8 \times 10^6$ and $5.1 \pm 1.1 \times 10^6$ cells/l for subgroups with critical and emergency conditions, respectively).

In the acute period of VE subgroup 4, a direct correlation between cortisol and absolute count of not only granulocytes ($r = 0.66$) but also lymphocytes ($r = 0.89$) was revealed. At the convalescence stage in this subgroup, the direct relationship of cortisol with the granulocyte count ($r = 0.75$) remained, but there was an inverse relationship with the lymphocyte count ($r = –0.31$). In VE subgroup 3, an inverse correlation relationship with the granulocyte count was observed ($r = –0.60$), and no relationship with the lymphocyte pool was found in the acute period. At the convalescence period in this subgroup, a direct relationship between cortisol level and granulocyte count was noted ($r = 0.87$), and an inverse relationship was found with the pool of lymphocytes ($r = –0.50$). In VE subgroups 3 and 4, as well as in BPM subgroups, no significant differences were found in the absolute counts of granulocytes and lymphocytes at different disease stages. In the acute period, the granulocyte counts were $7.8 \pm 1.3 \times 10^6$ and $10.5 \pm 2.3 \times 10^6$ cells/l and the lymphocyte counts were $1.9 \pm 0.5 \times 10^6$ and $1.4 \pm 0.2 \times 10^6$ cells/l in the subgroup with critical and emergency conditions, respectively. At the convalescence stage, the granulocyte counts were $3.5 \pm 0.6 \times 10^6$ and $4.2 \pm 2.0 \times 10^6$ cells/l and the lymphocyte counts were $3.4 \pm 0.7 \times 10^6$ and $2.5 \pm 0.1 \times 10^6$ cells/l in subgroups with critical and emergency conditions, respectively.

Correlation analysis of data indicate the involvement of cortisol in the pathogenesis of viral and bacterial neuroinfections of varying severity in pediatric patients by affecting the blood cells involved in the formation of innate and adaptive immune responses. The data obtained are consistent with literature data, indicating the role of cortisol in attracting marginal (located in the parietal pool) leukocytes into the bloodstream [10].

CONCLUSION

The results of this study established the role of cortisol in the pathogenesis of neuroinfections and the regulation of compensatory reactions in BPM and VE in pediatric patients. A dynamic study of the levels of cortisol and laboratory markers of systemic inflammation established the characteristic aspects of the content of cortisol in pediatric patients with bacterial and viral neuroinfections, depending on the severity of the disease course and disease period (i.e., acute and early convalescence). In the acute period, the maximum increase in the levels of cortisol and laboratory markers of systemic inflammation was found in patients with BPM compared with VE with subsequent normalization to the convalescence stage in the groups as a whole. In the subgroups with critical and emergency conditions upon hospital admission for BPM and VE, significant differences were found in the cortisol levels. At the same time, in the acute period, the BPM subgroup with an emergency condition had higher cortisol level than the subgroup with a critical condition; in VE, the cortisol level was higher in the subgroup with a critical condition. A correlation was established between the cortisol level and absolute granulocyte count in BPM, and the level of granulocytes and lymphocytes in VE

may indicate the participation of cortisol in the pathogenesis of acute neuroinfections in pediatric patients by influencing innate and adaptive immune responses.

The work revealed significant differences in the cortisol level in patients with BPM and VE, which was especially associated with their pathogenesis. In both viral and bacterial neuroinfections, a difference in the cortisol level was established depending on the disease severity. The data obtained are novel and, with additional clinical and laboratory studies, can be used to adjust therapy and predict the disease outcome, which makes the continuation of research in this field relevant and promising.

The authors declare no conflict of interest.

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