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DOI 10.25789/YMJ.2024.86.28

UDC 616.921.5

M.B. Kutsyi, N.M. Kruglyakov, G.I. Bagzhanov, K.K. Gubarev, N.E. Altshuler, K.A. Popugaev

## POSITIVE CONTRIBUTION OF TIMELY DIAGNOSIS AND CORRECTION OF ADRENAL DYSFUNCTION REQUIRING EXTRACORPOREAL MEMBRANE OXYGENATION IN PATIENTS WITH SEVERE PNEUMONIA IN THE EARLY POSTPARTUM PERIOD

**Introduction.** The main diagnoses leading to the use of ECMO in pregnant women and the postpartum period are acute respiratory failure (62.7%). Adrenal dysfunction due to critical illness (CAD) often determines the severity of the patient's condition and the outcome of their illness.

**Aim.** Timely detection and adequate correction of CAD in women in labor using ECMO.

**Materials and methods.** A patient after delivery with community-acquired severe bilateral polysegmental pneumonia who required the use of ECMO. Results. Against the background of combined treatment with norepinephrine and hydrocortisone, early stabilization of hemodynamics and septic complications was achieved.

**Conclusions.** CAD is characterized by vascular insufficiency requiring the use of vasopressors. Timely and adequate correction of adrenal dysfunction during the development of a critical condition makes it possible to reduce the severity of the intensive care patient's condition and improve the outcome.

**Keywords:** critical illness, hydrocortisone, cortisol, extracorporeal membrane oxygenation, adrenal glands, adrenocorticotropic hormone, hypothyroidism, thyroxine.

Medical-biological University of Innovation and Continuing Education - Burnazyan Federal Medical Biophysical Center of Federal Medical Biological Agency: **KUTSYI Mikhail B.** – Ph.D., assistant of the Department, mkutsyy@gmail.com, <https://orcid.org/0000-0003-0096-905X>;

**KRUGLYAKOV Nikolay M.** – Chief of Anesthesia and Intensive Care Service, nik160@mail.ru, <https://orcid.org/0000-0001-5011-6288>; **BAGZHANOV German I.** – assistant of the Department, bag\_g1992@gmail.com, <http://orcid.org/0000-0003-3363-5195>; **GUBAREV Konstantin K.** – Ph.D., Head of the ECMO Center, head of the surgical department for coordination of human organs and tissues donation, the State Scientific Center of Burnazyan Federal Medical Biophysical Center of the Department, kkgubarev@gmail.com; <https://orcid.org/0000-0001-9006-163X>; **ALTSHULER Natavan E.** – Ph.D., Assistant of the Department, natavan.altshuler@gmail.com; **POPUGAEV Konstantin A.** – MD, Ph.D., professor, head of the Department of Anesthesiology, Resuscitation Intensive Care A.I. Burnazyan Federal Medical Biophysical Center FMBA, Deputy Director - Head of the Regional Vascular Centre of the Sklifosovskiy Research Institute for Emergency Medicine of Moscow Healthcare, stan.popugaev@yahoo.co, <https://orcid.org/0000-0003-1945-323X>

**Introduction.** Respiratory distress syndrome (RDS), associated with lung damage from the H1N1 influenza virus-RDS, can develop rapid and almost total lung damage [2]. Due to the long-term restoration of gas exchange in the lungs with H1N1 - RDS, the risk of the need for veno-venous extracorporeal membrane oxygenation (VV ECMO) increases. The combination of primary viral and secondary inflammatory lesions of the lungs causes the development of a combination of viral-bacterial sepsis with multiple organ dysfunction (MOD), one of the components of which may be adrenal dysfunction caused by critical illness (CAD) [11]. CAD determines the severity of the patient's condition and the outcome of their disease [4, 6]. Timely and adequate correction of CAD often improves the outcome of the disease in intensive care patients [5, 6, 7]. However,

the problem of adrenal dysfunction (AD) remains outside the scope of intensive care directions implemented by the treating team of the intensive care unit. The presented clinical observation illustrates for the first time the importance of timely detection and adequate correction of CAD in a postpartum woman with severe community-acquired pneumonia that required VV ECMO.

**Results and discussion.** Patient L., 37 years old, 28 weeks of pregnancy, on the 15th day of illness with a diagnosis of "Acute purulent right-sided otitis media" was hospitalized in the ENT department of the regional hospital. On the third day of hospitalization, during treatment, the severity of the condition worsened: cough with light sputum, shortness of breath, weakness. On examination, breathing is spontaneous, respiratory rate (RR) is 37 times per minute, O2

saturation in arterial blood is 60% with insufflation of humidified O<sub>2</sub> 10 l/min. According to laboratory data: acid-base balance of arterial blood: pH 7.39; partial pressure of carbon dioxide 30.7 mm. rt. Art.; partial pressure of O<sub>2</sub> 43 mm. rt. Art.; lactate 3.76 mmol/l; base excess -5 mm. rt. Art. Due to respiratory failure (RR>35 times per minute, respiratory index <90%, O<sub>2</sub> partial pressure <60 mmHg), the patient was transferred to artificial pulmonary ventilation (ALV). Hemodynamics after transfer to mechanical ventilation were unstable and were supported by norepinephrine 0.1 mcg/kg/min. Blood pressure (BP) 119/64 mmHg. Art. Chest X-ray shows signs of bilateral polysegmental pneumonia. Due to progressive intrauterine hypoxia of the fetus, an operation was performed: emergency laparotomy, cesarean section in the lower uterine segment. On the fourth day of hospitalization (19th day of illness), the patient's condition is extremely serious, sedation, mechanical ventilation is performed, meningeal symptoms and gross focal symptoms are not determined. Microbiological examination of sputum revealed *Acinetobacter baumannii*. swab from the oropharyngeal mucosa - the causative agent of the influenza virus - H1N1. Therapy provided: antibacterial, antiviral, sedative, proton pump blockers, diuretics, low molecular weight heparins, infusion therapy, Dostinex, immunoglobulin, paracetamol.

On the 5th day of hospitalization (20th day of illness), taking into account the progression of respiratory failure, the increase in hypoxemia with an increase in the O<sub>2</sub> fraction to 100% and positive end-expiratory pressure up to 12 cm H<sub>2</sub>O, it was decided to initiate veno-venous extracorporeal oxygenation (VV ECMO) with subsequent transfer on the same day by air ambulance to the ECMO center (State Scientific Center of the Russian Federation - FMBC named after A.I. Burnazyan of the Federal Medical and Biological Agency).

Admission to the ECMO center. At the time of admission to the ECMO center (C0), the patient's condition was extremely severe; on the Acute Physiology and Chronic Health Evaluation II scale, the condition corresponded to 20 points, and on the Sequential Organ Failure Assessment (SOFA) scale, 12 points. A CT scan of the head revealed subarachnoid hemorrhage. Sedation, analgesia and muscle relaxation during the observation period were carried out: Dexdor, queatiapine, pregabalin, morphine 1% 1 ml, Arduan 4 mg. Temperature 37.1° C. The results of computed tomogra-

phy of the chest, abdominal and pelvic organs show a bilateral infiltrative process in the lungs with subtotal damage to the parenchyma. According to laboratory data: hemoglobin 93 g/l, red blood cells  $3.16 \times 10^{12}/l$ , leukocytes  $12.2 \times 10^9/l$ , platelets  $208 \times 10^9/l$ , procalcitonin > 0.05. Ventilation: in Bi-Vent/APRV mode, with parameters: respiratory rate 19/min., positive end-expiratory pressure 12 cmH<sub>2</sub>O. Art., O<sub>2</sub> fraction 40%, tidal volume 350-400 ml, peak pressure - 27 cm H<sub>2</sub>O, O<sub>2</sub> saturation 99-100%. Parameters of VV ECMO: revolutions 2880 ml/min., volume 4.60 l/min., O<sub>2</sub> fraction 4 l/min. Hemodynamics were unstable; norepinephrine was infused at a dose of 0.27 mcg/kg/min. Blood pressure: 113/62 mmHg. ECG - sinus rhythm. Adrenal dysfunction (AD) was diagnosed. Based on clinical, laboratory and instrumental data, the condition was assessed as septic with the development of septic shock. The levels of cortisol and adrenocorticotrophic hormone (ACTH) in the blood plasma were: cortisol (1837 nmol/l) and ACTH (3 pg/dl). In accordance with existing recommendations for the treatment of patients with septic shock, on the day of admission to the ECMO center, hydrocortisone was added to therapy at an initial dose of 300 mg (100 mg IV bolus, then 50 mg every 6 hours) [7].

Thus, the severity of the patient's condition was due to H1N1-RDS, which required VV ECMO, MOD (cerebral, respiratory, cardiovascular, renal, intestinal, and endocrine). On the next day of ECMO treatment, the patient was removed from sedation, and consciousness was restored. The duration of VV ECMO was 11 days. During this period, when assessing the severity of the condition by C11 (the day of weaning from ECMO), the SOFA score decreased to 4 points. The level of leukocytosis decreased to  $11.2 \times 10^9/l$ , c-reactive protein to - 59 mg/l. Procalcitonin and lactate levels returned to normal by the third day of ECMO.

Hemodynamics also stabilized on the 3rd day of ECMO. Positive dynamics in the patient's condition made it possible to begin reducing respiratory support at C6 of the ECMO procedure, and to complete the ECMO procedure itself on the 11th day. On C1 ECMO, hydrocortisone was administered at a dose of 200 mg/day. 50 mg, IV, bolus, 4 times a day. Against this background, the need for norepinephrine decreased by the second day of observation with its complete abolition by the third day, when the dose of hydrocortisone was 100 mg/day. On the 4th day of ECMO, the dose of hydrocortisone was 50 mg/day; on the 5th day, due to stabili-

zation of hemodynamics, hydrocortisone was discontinued. At the same time, the level of sodium in the blood plasma was 152-144 mmol/l over the course of 4 days. During a dynamic assessment of cortisol levels, its concentration in plasma was at C1 - 1704 nmol/l, C3 - 641.00 nmol/l, C5 - 296 nmol/l, C7 - 347 nmol/l, C9 - 452 nmol/l and per day weaning from ECMO - 547 nmol/l. The ACTH level in the blood plasma was 2 ng/dL at C1, 1 ng/ml at C3, 10 ng/ml at C5, 28.1 ng/ml at C7, 29 ng/ml at C9, on the day of weaning from ECMO - 28.9 ng/ml. On the eighteenth day from the moment of admission to the ECMO center, the patient was transferred to the department with subsequent discharge.

The presented clinical observation illustrates for the first time the use of hydrocortisone when using ECMO in the early postpartum period. In pregnant women and women in labor, the problem of endocrine dysfunction becomes even more complicated. The course of the disease in the patient under discussion demonstrates that there is an urgent need to continue research into a deeper understanding of the pathophysiology of infection during pregnancy. Pregnancy is often not only an initially immunodeficient state that can lead to the development of infection, but also changes the response of the endocrine system in a woman's body, including the hypothalamus-pituitary-adrenal system. This analysis suggests that in pregnant women in the critical illness (CI) there is a rapid depletion of the synthesis of endogenous cortisol and an increase in receptor resistance to it, which can be considered as a manifestation of CAD [9]. During septic shock in pregnancy, an overactive immune response leads to hyperinflammation, causing vasodilation and hypotension. Under these conditions, the anti-inflammatory properties of hydrocortisone are an attractive therapeutic option for the treatment of sepsis-mediated hypotension in parturient women. Fluctuations in the level of ACTH and total cortisol during the development of CI characterize the phases of a critical condition: the acute phase is most often determined by an increase in the level of ACTH and, as a consequence, an increase in the level of cortisol. Subacute phase - characterized by persistently high levels of total cortisol with low levels of ACTH. In the acute phase of CI, a significant increase in cortisol levels in the first stages is caused by ACTH and is characterized by a stress reaction [10]. In the case of the development of POD syndrome, the CI enters the subacute (up to 14-21 days), and then

into the chronic phase (more than 14-21 days) [3, 12]. In the subacute and chronic phases of CI, cortisol levels are often higher than References values against the background of suppressed ACTH levels [10]. It is likely that overproduction of cortisol in this case, through negative feedback, suppresses the synthesis and secretion of ACTH. We observed this laboratory picture in the patient on the day of admission to the ECMO center. However, it should be remembered that a high level of cortisol is not always an indicator of the safety of the hypothalamus-pituitary-adrenal-target tissue system, since glucocorticoid resistance cannot be excluded [8, 1].

**Conclusion.** Thus, our observation showed that with a long history of the disease leading to the development of CI and the use of ECMO; unsTable hemodynamics requiring the use of vasopressors, it is necessary to consider the adrenal gland (without focusing on the levels of ACTH and cortisol) and carry out replacement therapy with hydrocortisone. Considering the properties of hydrocortisone, it is necessary to reduce the initially recommended treatment regimen (300 mg/day - the first day, then 200 mg/day the next day) after reducing and completely eliminating norepinephrine, and also adjusting the dose of hydrocortisone requires monitoring the level of sodium in the blood plasma. The duration of hydrocortisone administration after norepi-

nephine withdrawal depends on the target blood pressure and sodium levels. In particular, the patient needed three days to compensate for adrenal function.

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