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Research Article

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Adrenal Dysfunction Caused by Critical Illness and Its Correction by Controlling Body Temperature: Prospective Cohort Study

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BACKGROUND Critical condition (CC) is defined as any life-threatening condition that requires support of the functions of vital organs and systems to prevent imminent death. From the point of view of the course of CC and the survival of the patient, adequate functioning of the hypothalamic-pituitary-adrenal axis (HPA) is fundamentally important.

AIM OF STUDY To improve treatment outcomes for critically ill patients requiring temperature management through early diagnosis and timely correction of adrenal dysfunction.

MATERIAL AND METHODS Of the 59 patients, 45 (76.3%) patients were diagnosed with adrenal dysfunction upon body temperature management (BTM) caused by critical illness: group I with vascular failure (VF+); in 14 (23.7%) patients of group II adrenal disfunction wasn't revealed (VF-).

RESULTS In group I (VF+) there was a high SOFA score, the highest number of days from the moment of illness to admission to the intensive care unit and initiation of BTM, the presence of liver dysfunction, and a high level of C-reactive protein. Vascular failure in patients in group I developed earlier than other organ dysfunctions and sepsis. The high level of cortisol in the blood plasma in group II (VF-) was associated with the development of corticoresistance.

CONCLUSIONS 1. At body temperature management initiation, patients with adrenal dysfunction had a statistically significant high sofa score compared to patients without adrenal dysfunction (8 (5–9); 7 (6–8), respectively, p<0,05). 2. The number of days from the disease onset to admission to the icu and initiation of body temperature management was statistically significantly high in the group with adrenal dysfunction compared to the group without adrenal dysfunction (20 of 45 patients (44.4%); 4 of 14 (28.6%) respectively, p<0.05). 3. In the development of septic shock in patients with adrenal dysfunction, the criterion for the efficacy of the therapy was stabilization of the patient's condition: positive hemodynamic response to the introduction of hydrocortisone with reduced doses of noradrenaline and its subsequent cancellation. 4. Despite the fact that the rate of organ dysfunction, sepsis and septic shock were statistically significantly higher (p<0.05) in the group with adrenal dysfunction and the presence of vascular insufficiency, the performed treatment (hydrocortisone administration) allowed outcomes comparable to these in patients without adrenal dysfunction to be achieved (p>0.05).

Keywords: critical illness, hydrocortisone, body temperature management

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ACTH – adrenocorticotropic hormone
ALT – alanine aminotransferase
ALV – artificial lung ventilation
AST – aspartate aminotransferase
BTM – body temperature management
CCIAD – Critical Condition Induced Adrenal Dysfunction
ECMO – extracorporeal membrane oxygenation
HPA – hypothalamic-pituitary-adrenal axis
ICH – intracranial hypertension
MH – managed hypothermia
MN – managed normothermia
SBP – systolic blood pressure
VI – vascular insufficiency

INTRODUCTION

Critical condition (CC) is defined as any life-threatening condition that requires support of the functions of vital organs and systems to prevent imminent death [1, 2]. It can develop in a wide range of acute conditions, decompensation of chronic diseases and in complicated postoperative period in patients with extensive surgeries [1]. Artificial lung ventilation (ALV), renal replacement therapy and extracorporeal membrane oxygenation are intensive care methods that allow for the replacement and temporary replacement of partially impaired or completely lost functions of vital organs [3]. The only method of organ protection that has proven its effectiveness in the development of CC is body temperature management (BTM), which includes managed hypothermia (MH) and managed normothermia (MN) [4].

From the point of view of the course of CC and patient survival, adequate functioning of the hypothalamic-pituitary-adrenal (HPA) system is of fundamental importance [1, 2]. From the point of view of a resuscitator, among all possible endocrinopathies, the most important is adrenal dysfunction caused by CC (CCIAD). According to various authors, the frequency of adrenal dysfunction (AD) in the development of CC is 30–70% [5].

The aim of the study is to improve treatment outcomes in critically ill patients requiring temperature management through early diagnosis and timely correction of adrenal dysfunction.

MATERIAL AND METHODS

A prospective, single-center cohort study included 59 patients requiring BTM.

Inclusion criteria: patients over 18 years of age requiring BTM. Exclusion criteria: pregnancy, brain death, use of synthetic glucocorticoids, history of adrenal and thyroid diseases.

All patients received the full range of necessary intensive care in accordance with Russian and international recommendations [6]. Indications for sedation were intracranial hypertension (ICH), desynchronization with the ventilator, psychomotor agitation, muscle tremors against the background of the use of BTM. All patients underwent an echocardiogram.

The patients were divided into two groups: Group I (SI+) included patients with vascular insufficiency (VI) requiring norepinephrine at a dose of at least 0.2 μg/kg/min to stabilize blood pressure. Group II (VI-) included patients without vascular insufficiency; there was no need to administer vasopressor drugs, since systolic blood pressure (SBP) was more than 65 mmHg, or norepinephrine at a dose of less than 0.2 μg/kg/min was necessary to maintain this SBP level. Of the 59 patients, 45 (76.3%) were diagnosed with CCIAD during BTM — Group I (VI+); 14 (23.7%) patients did not have CCIAD — Group II (VI-). MN was understood as artificial maintenance of the patient's body temperature at 36.5–37°C. MH was understood as artificial maintenance of the patient's body temperature at a level of 35-35.5°C; MN and MH were combined under the concept of BTM. Managed normothermia was used when it was necessary to correct fever, for neuroprotection or correction of ICH, and managed hypothermia was used for neuroprotection or correction of ICH [4]. Body temperature was controlled by external cooling in the automatic control mode of the *BLANKETROL* II system (CSZ, USA). Monitoring of the central body temperature was carried out by inserting a 400 series esophageal probe. For MH, the target central temperature was 35°C, for MN it was 36°C. The duration was 48 hours, 7 days, depending on what

condition was the indication for BTM. Careful monitoring of the patient's condition was carried out, aimed at early detection of muscle tremors. When it occurred, a stepwise protocol for the correction of muscle tremors was initiated [4]. Determination of plasma cortisol and adrenocorticotropic hormone (ACTH) levels was performed on the day of admission (before induction), on the first day (maintenance phase), then every two days, on the 7th day the warming phase began and on the last day of observation (cessation of BTM). The time of blood sampling for determination of ACTH and total cortisol before BTM initiation depended on the time of BTM start. Subsequent assessment of hormone levels was performed from 6.00 to 8.00 from the central venous catheter. The values of the analyzed laboratory criteria for which intergroup differences did not reach the level of statistical significance (p >0.05) are available upon request from the correspondent. When CCIAD was detected (manifested by vascular insufficiency and the need for vasopressors at a dose of at least 0.2 mcg/kg/min), in addition to treatment with norepinephrine, intravenous hormone replacement therapy with hydrocortisone was prescribed to maintain SBP of 90 mm Hg and above or mean arterial pressure of 65 mm Hg and above. The initial dose of hydrocortisone on the first day was 300 mg (100 mg, intravenous bolus, then 50 mg 4 times a day, bolus), on the 2nd and subsequent days 200 mg, 4 times a day (6.00–12.00–18.00–24.00) [7]. The dose of hydrocortisone administered intravenously was reduced by 25–50 mg per day, starting at 00.00. The daily dose of hydrocortisone was reduced after complete withdrawal of the norepinephrine dose, followed by transfer of the patient, if necessary, to the tablet form of hydrocortisone.

The observation period of patients began from the moment of BTM and continued until its completion. Demographic characteristics are presented by descriptive statistics. Anamnesis was collected according to medical documentation. Hormone levels in blood plasma were studied on the day before BTM initiation, then on the 1st, 3rd, 5th day (C1, C3, C5) and on the day of BTM termination.

This study was approved by the Ethics Committee of the A.I. Burnazyan Federal Medical and Biological Center of the Federal Medical and Biological Agency of Russia (Protocol No. 9 dated 25.04.2016). Patients undergoing BTM were monitored in the intensive care units of the A.I. Burnazyan Federal Medical and Biological Center of the Federal Medical and Biological Agency of Russia.

Statistical data processing was performed in the *IBM SPSS Statistics program*. Descriptive statistics methods were used to evaluate the study groups (*Me* is the median, *Q*1 is the first quartile, and *Q*3 is the third quartile). The statistical significance of the data was determined by nonparametric criteria. The statistical significance of differences between two unrelated groups was estimated by the Mann–Whitney criterion (*U*). The critical level of significance when testing the null hypothesis was taken at p <0.05. Table 1 shows only those indicators that differed statistically significantly (p<0.05) or deserve special attention and careful interpretation.

SOFA score compared to patients without VI (median 7 points). Patients in the group without VI were hemodynamically stable and had no indications for hydrocortisone. The number of days from the onset of the disease to admission to the ICU and initiation of BTM was longer in the VI+ group compared to the VI- group. This is due to the predominance of patient transfers in the VI+ group from primary hospitalization clinics (Table 2). In the VI- group, most patients were initially hospitalized in our center with subsequent initiation of BTM. The number of neurocritical care patients with TBI, hemorrhagic stroke, malignant ischemic stroke, and circulatory arrest was statistically significantly greater in the VI- group.

RESULTS

At the time of initiation of BTM, patients in group I (VI+) had a statistically significantly higher *SOFA score* compared to patients in group II (VI-) (Table 2). The number of days from the onset of illness to admission to the intensive care unit and initiation of BTM was longer in group I compared to group II. This is due to the predominance of transfers of patients in group I (VI+) from primary hospitalization clinics (Table 1). In group II (VI-), most patients were initially hospitalized in our center with subsequent initiation of BTM.

The level of sodium (*Me* = 150 mmol/l) and chlorine (*Me* = 118 mmol/l) was statistically significantly higher in Group I at the research point immediately before the start of BTM (C0) and on the first day (C1) of BTM (t). Hypernatremia was caused by more frequent use of hypertonic solution in group I (VI+) (Table 2). As can be seen from the table, in

Table 1

Comparison of groups I (VI+) and II (VI-) according to clinical indicators and treatment methods

Parameters	Group I (VI+), *n*=45	Group II (VI-), *n*=14	*p*
Age, years	54 (40–63)	51 (35–67)	0.7
SOFA, *Me* (*Q*1–*Q*3)	8 (5–9)	7 (6–8)	0.004
Body mass index, kg/m^2, *Me* (*Q*1–*Q*3)	27.9 (25.2–31.4)	28.4 (25.9–29.6)	0.8
Concomitant pathology, n (%)			
Hypertension	23 (51.1)	6 (42.9)	0.01
Coronary artery bypass grafting	1 (2,2)	0	-
Hepatitis *C*	2 (4.4)	0	-
Type 2 diabetes mellitus	5 (11.1)	2 (14.2)	0.01
Parkinson's disease	2 (4.4)	1 (7.1)	0.03
Central body temperature immediately before BTM, *Me* (*Q*1–*Q*3)	37.9 (37.1–38.7)	37.7 (37.5–38.3)	0.2
Indications for normothermia, *n* = 16, *n* (%)			
Traumatic brain injury	2 (4.4)	1 (7.1)	0.01
Ischemic stroke	1 (2,2)	1 (7.1)	0,007
Aneurysmal subarachnoid hemorrhage	4 (8.9)		
Hemorrhagic stroke	5 (11.1)	2 (21.4)	0,001
Indications for hypothermia, *n* = 43, *n* (%)			
Malignant ischemic stroke	10 (22.2)	7 (50)	0.01
Hemorrhagic stroke	4 (8.9)	2 (7.1)	0.01
Hypoxic-ischemic brain injury after circulatory arrest	2 (4.4)	1 (7.1)	0,001
Traumatic brain injury	4 (8.9)	0	–
Venous stroke	8 (17.8)	0	–
Vasospasm and secondary ischemia after aneurysmal subarachnoid hemorrhage	3 (6.7)	0	–
Hemorrhagic impregnation of the ischemic focus in ischemic stroke	2 (4.4)	0	–
Managed normothermia, *n* (%)	12 (26.7)	4 (28.6)	0.01
Managed hypothermia, *n* (%)	33 (73.3)	10 (71.4)	0.01
Transfer from primary hospitalization clinic, *n* (%)	20 (44.4)	4 (35.7)	0.04
Days from the moment of illness to the initiation of BTM, *Me* (*Q*1–*Q*3)	2 (1–4)	1	0,001

Notes: VI — vascular insufficiency; BTM — body temperature management; SOFA — sequential organ failure assessment

Table 2

Comparison of groups I (VI+) and II (VI-) according to laboratory data in dynamics

Parameters	Group I (VI+), *n* =45	Group II (VI-), *n* = 14	*p*
Research point 1 (immediately before the start (C0) of BTM)			
Administration of 3% hypertonic sodium chloride solution	23 (51.1%)	3 (21.4%)	0,001
Sodium, mmol/l	150 (144–161)	143 (140–143)	0.01
Chlorine, mmol/l	118 (109–122)	106 (103–112)	0.03
Norepinephrine, mcg/kg/min	0.4 (0.11–0.51)	0.07 (0.02–0.1)	0.02
ALT, mmol/l	40 (19–79)	18 (12.7–27)	0.03
Total cortisol, nmol/l	466 (250–729)	748 (398–928)	0.04
Procalcitonin, ng/ml, *n* (%) <0.5 0.51–2 2.1–10 more than 10.1	 45 (100) 0 0 0	 14 (100) 0 0 0	-
Ejection fraction, %	61 (57.7–63)	59 (56–63)	0.3
Research point 2 (first day (C1) of BTM)			
Sodium, mmol/l	155 (145–164)	143 (141–150)	0.01
Chlorine, mmol/l	115 (107–125)	112 (104–118)	0.04
Norepinephrine, mcg/kg/min	0.38 (0.2–0.6)	0.1 (0.08–0.14)	0.03
ALT, mmol/l	57.5 (29.5–120)	14 (12–32)	0.003
Procalcitonin, ng/ml, *n* (%) <0.5 0.51–2 2.1–10 more than 10.1	 33 (73.3) 12 (26.7) 0 0	 5 (35.8) 9 (64.2) 0 0	 0.2 0.2
Ejection fraction, %	61 (58.7–62.3)	59 (55.5–63)	0.3
Research point 3 (C2 BTM)			
Norepinephrine, mcg/kg/min	0.2 (0.12–0.29)	0.05 (0.03–0.1)	0.03
ALT, mmol/l	35 (23.7–75)	17 (15–19)	0.03
Procalcitonin, ng/ml, *n* (%) <0.5 0.51–2 2.1–10 more than 10.1	 30 (66.7) 15 (33.3) 0 0	 5 (35.8) 9 (64.2) 0 0	 0.2 0.2
Ejection fraction, %	63 (56–65)	61 (54–67)	0.3
Research point 4 (C3 BTM)			
ALT, mmol/l	295 (58–614)	19 (18–28)	0.02
AST, mmol/l	119 (42–212)	17 (12.7–31.7)	0.002

Procalcitonin, ng/ml, *n* (%)			
<0.5	45 (100)	14 (100)	-
Research point 5 (C5 BTM)			
Norepinephrine, mcg/kg/min	0.15 (0.08–0.3)	0.05	0.03
Total cortisol, nmol/l	485 (329–880)	666 (653–1456)	0.03
Corticosteroid resistance index	1.1 (0.6–1.5)	0.7 (0.4–0.8)	0.01
Procalcitonin, ng/ml, *n* (%) <0.5 0.51–2	 28 (62.2) 17 (37.8)	 7 (35.8) 7 (64.2)	 0.2 0,1
Research point 6 (last day of BTM)			
Norepinephrine, mcg/kg/min	0.17 (0.08–0.32)	0.1 (0.04–0.12)	0.04
ALT, mmol/l	63 (28–275.5)	23 (13.5–36)	0.02
AST, mmol/l	51 (21.2–192)	17 (12.7–59)	0.034
C- reactive protein, mg/l	129 (74.5–207)	71 (28.3–91.5)	0.01
Total cortisol, nmol/l	392 (278–590)	565 (209.7–1082)	0.04
Procalcitonin, ng/ml, *n* (%) <0.5 0.51–2	 29 (64.4) 16 (35.6)	 7 (50) 7 (50)	 0.6 0.53
Ejection fraction, %	61 (53–64)	59 (55–64)	0.4

Notes: ALT — alanine aminotransferase; AST — aspartate aminotransferase; VI — vascular insufficiency; BTM — body temperature management

group I, liver dysfunction, manifested by increased levels of alanine aminotransferase (ALT) and aspartate aminotransferase (AST), occurred throughout the observation period, and its frequency was statistically significantly higher than in group II (VI-). The level of *C*-reactive protein on the last day of BTM was statistically significantly higher in group I (VI+).

The cortisol level was higher than the reference values in Group II (VI-) and statistically significantly differed from Group I. The high plasma cortisol level in Group II (VI-) was due to the onset of corticoresistance. Based on these results, it cannot be ruled out that the need for norepinephrine at a dose of less than 0.2 μg/kg/min should also be considered within the framework of AD. Further studies are needed. The median ejection fraction

Table 3

Time frame for the development of vascular insufficiency requiring the use of vasopressors at a dose of at least 0.02 mcg/kg/min and hydrocortisone

Days of development after the start of BTM	Group I (VI+), (*n* =45)
Initiation of BTM, C0, *n* (%)	14 (31.1)
C1, *n* (%)	9 (20)
C2, *n* (%)	21 (46.7)
C3, *n* (%)	1 (2,2)

Notes: VI — vascular insufficiency; BTM — body temperature management

according to Teicholz in Group I (VI+) did not differ from that in patients in Group II (VI-). Thus, the ejection fraction in Group I (VI+) was within the permissible standard values, which, therefore, was not the cause of arterial hypotension.

The results presented in Table 3 demonstrate the development of ND in the first three days against the background of BTM.

The results presented in Table 3 show that VI developed earlier than other organ dysfunctions and sepsis. It follows that sepsis is not the cause of VI and other organ dysfunctions developing early after the onset of BTM.

The development of adrenal dysfunction was statistically significantly observed in patients with complications such as lateral dislocation of brain structures, critical vasospasm and antiphospholipid syndrome (Table 4).

Although the incidence of organ dysfunction, sepsis and septic shock was statistically significantly higher in the VI+ group, mortality (Table 4) was comparable with such a group without VI -.

In group I (VI+), 5 out of 15 (33.3%) patients achieved stabilization of their condition and correction of septic complications, which was not the case in the group without VI- (Table 5).

In the development of septic shock in group I (VI+), the criterion for the effectiveness of the therapy was stabilization of the patient's condition, a positive hemodynamic response to the administration of hydrocortisone in the form of a reduction in the dose of norepinephrine followed by its cancellation (Table 2).

Table 4

Frequency of complications and timing of their development in the study groups during body temperature management

Types of complications	Group I (VI+), *n*=45	Group II (VI-), *n*=14	*p*
Lateral dislocation of brain structures more than 10 mm, *n* (%) Development time, days, *Me* (*Q*1–*Q*3)	7 (15.5) 0	2 (14.2) 1	0.01
Critical vasospasm (Lindegard index more than 6), *n* (%) Development time, days, *Me* (*Q*1–*Q*3)	4 (8.8) 0	1 (7.1) 1	0.02
Status epilepticus, *n* (%) Development time, days, *Me* (Q1–Q3)	2 (4.4) 0	1 (7.1) 0	0.01
Diabetes insipidus, *n* (%) Development time, days, *Me* (Q1–Q3)	3 (6.7) 2 (3)	0 -	-
Pulmonary embolism, *n* (%) Development time, days, *Me* (Q1–Q3)	1 (2,2) 1	1 (7.1) 3	0.01
Resistant hemodynamically significant bradycardiarrhythmia requiring pacemaker placement, *n* (%) Development time, days, *Me* (*Q*1–*Q*3)	2 (4.4) 2	0 -	-
Pneumonia, *n* (%) Development time, days, *Me* (*Q*1–*Q*3)	20 (44.4) 4 (3–6)	5 (35.7) 5 (3–6)	0.02
Antiphospholipid syndrome, *n* (%) Development time, days, *Me* (*Q*1–*Q*3)	2 (4.4) 1 (0)	0 -	-
Central nervous system infection, *n* (%) Development time, days, *Me* (*Q*1–*Q*3)	3 (6.7) 5 (6)	1 (7.1) 4	0.2
Sepsis, *n* (%) Development time, days, *Me* (*Q*1–*Q*3)	15 (33.3) 6 (5–7)	4 (7.1) 7	0,001
Intestinal dysfunction, *n* (%) Development time, days *Me* (*Q*1–*Q*3)	43 (95.5) 1 (2–3)	4 (28.6) 6 (8)	0,001
Renal dysfunction, *n* (%) Development time, days *Me* (*Q*1–*Q*3)	17 (37.8) 3 (2–5)	5 (35.7) 4 (7.5)	0.01
Liver dysfunction, *n* (%) Development time, days, *Me* (*Q*1–*Q*3)	10 (22.2) 3 (2–6)	3 (21.4) 4 (6)	0.04
Pancreatitis, *n* (%) Development time, days, *Me* (*Q*1–*Q*3)	1 (2.2%) 3	0 -	-
Overall mortality, *n* (%)	15 (33.3)	5 (35.7)	0.05

Notes: VI — vascular insufficiency; BTM — body temperature management

Table 5

Causes deaths in patients of the study groups who were in the critical condition during body temperature management

Parameters	Group I (VI+), *n* =45	Group II(VI-), *n* =14	*r*
Septic shock, *n* (%)	10 (22.2)	4 (28.6)	0,001
Intracranial hemorrhage, *n* (%)	4 (8.9)	1 (7.1)	0.02
Pulmonary embolism, *n* (%)	1 (2,2)	0	—

Notes: VI — vascular insufficiency; BTM — body temperature management

DISCUSSION

The consideration of AD in the context of a critical condition without sepsis and septic shock, requiring hormone replacement therapy with hydrocortisone, remains unresolved to date [8]. The administration of hydrocortisone in CCIAD, manifested by VI outside of septic shock, can be difficult due to a number of factors: the lack of diagnostic criteria for assessing CCIAD, which is also a dynamic process and can develop at any time during intensive care; CCIAD can be characterized not only by a decrease in cortisol production, but also by the development of resistance of target tissues to cortisol, which, in turn, is manifested by a high level of cortisol in the blood plasma, corticoresistance; the use of hypertonic sodium chloride solution to correct ICH in neurocritical care patients does not allow observing hyponatremia [9-11].

The results of our previous study showed that patients on extracorporeal membrane oxygenation (ECMO), who initially had clinical and laboratory signs of adrenal dysfunction (VI+, norepinephrine requirement of at least 0.2 μg/kg/min, hyponatremia), despite hydrocortisone therapy and sodium level compensation, showed higher mortality compared to patients with VI without hyponatremia [12]. The fundamental difference between patients with AD who underwent BTM and patients receiving ECMO is that in the first case there were no infectious complications or hyponatremia initially, but only organ dysfunction was observed. In this case, the key factor is the hemodynamic response to the administration of hydrocortisone, leading to a decrease in the dose of norepinephrine followed by its complete cancellation. This fact confirms that patients without sepsis and septic shock also have the right to develop CCIAD. Patients in CC and requiring the use of BTM due to the severity of their condition caused by damage to the central nervous system develop adrenal dysfunction, which is difficult or impossible to determine based on the clinical and laboratory picture. In some patients, VI without signs of organ dysfunction occurs on the first day of CC, which requires the administration of hydrocortisone. Then, these patients predictably develop various complications: organ dysfunction, sepsis, septic shock. But despite their development, in group I (VI+) we managed to stabilize the severity of the patients' condition and achieved outcomes comparable to those in patients without adrenal dysfunction - group II (VI-). Most likely, this is due

to the use of hydrocortisone, which was received by patients of group I (VI+) due to VI that developed early after the onset of BTM in the absence of sepsis. The analyzed groups differed fundamentally from each other in that patients of group I (VI+) received hydrocortisone, while patients of group II did not. In addition, patients of group I were statistically significantly more often given MH compared to group II, which does not exclude the fact of suppression of the HPA system not only due to hypoxia, ischemia of brain tissue, but also as a result of the use of MH.

CONCLUSION

In patients undergoing temperature management, the development of vascular insufficiency manifested by arterial hypotension against the background of normal or increased cardiac output should be interpreted as the presence of adrenal dysfunction after exclusion of sepsis. The observed hemodynamic response to the administration of hydrocortisone in the form of a decrease in the need for noradrenaline is key to assessing the effectiveness of hormone replacement therapy. Timely administration of an effective dose of hydrocortisone (300 mg/day) allows for regression of vascular insufficiency and other organ dysfunctions and improves disease outcomes in critically ill patients requiring temperature management. It should also be noted that based on these results, it cannot be ruled out that the need for norepinephrine at a dose of less than 0.2 mcg/kg/min should also be considered within the framework of adrenal dysfunction caused by a critical condition.

1. At the time of initiation of body temperature management, patients with adrenal dysfunction had a statistically significant higher *SOFA score* compared to patients without adrenal dysfunction (8 (5–9); 7 (6–8), respectively, p <0.05).

2. The number of days from the onset of illness to admission to the intensive care unit and initiation of body temperature management was statistically significantly longer in the group with adrenal dysfunction compared to the group without adrenal dysfunction (20 patients out of 45 (44.4%); 4 out of 14 (28.6%), respectively, p <0.05).

3. In the development of septic shock in patients with adrenal dysfunction, the criterion for the effectiveness of the therapy was stabilization of the patient's condition, a positive hemodynamic response to the administration of hydrocortisone against the background of a reduction in the dose of norepinephrine with its subsequent cancellation.

4. Despite the fact that the incidence of organ dysfunction, sepsis and septic shock were statistically significantly higher (p<0.05) in the group with adrenal dysfunction and vascular insufficiency, the treatment measures (administration of hydrocortisone) allowed us to achieve outcomes comparable to those in patients without adrenal dysfunction (p>0.05).

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