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THE IMPACT OF REGIONAL ANALGESIA ON PAIN INTENSITY AND CORTISOLEMIA LEVELS IN WOUNDED PATIENTS WITH COMBAT TRAUMA OF THE EXTREMITIES

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Introduction. There is uncertainty of evidence regarding the effectiveness and safety of regional analgesic blocks during emergency care for wounded patients with combat trauma of the extremities at Role 2 medical treatment facilities and during interhospital transportation.

Objective. To optimize perioperative analgesia regimens for wounded patients with combat trauma of the extremities at Role 2 medical treatment facilities and during interhospital transportation based on a comparative assessment of the impact of regional or systemic analgesia on pain intensity and cortisolemia levels over time.

Materials and Methods. A prospective study included 100 patients with isolated combat trauma of one extremity. Patients were divided into two groups: Group 1 (n = 50) received systemic analgesia only, while Group 2 (n = 50) received ultrasound-guided regional anesthesia. Pain intensity was assessed over time using a Visual Analog Scale (VAS), additionally the level of cortisol in plasma was also measured. Study parameters were registered in four stages: 1st stage – at the time of admission to the Role 2 medical treatment facilities; 2nd stage – at the completion of surgical intervention; 3rd stage – at the beginning of interhospital transportation; 4th stage – at the completion of interhospital transportation.

Results. Between the 1st and 2nd stages, both groups demonstrated significant changes in VAS and Cortisol levels ($p < 0.05$, respectively). At the 2nd stage, a significant intergroup difference was observed for VAS 2 ($p < 0.05$), whereas Cortisol 2 levels did not differ significantly between groups ($p = 0.17$). Between the 2nd and 3rd stages, Group 1 showed significant changes in both VAS and Cortisol values ($p < 0.05$ respectively), while in Group 2 no significant change in VAS was observed ($p = 0.11$), despite a significant change in Cortisol levels ($p < 0.05$). At the 3rd stage, intergroup differences remained significant for VAS 3 ($p < 0.05$), with no significant difference in Cortisol 3 levels ($p = 0.41$). Between the 3rd and 4th stages, significant changes in VAS and Cortisol were observed only in Group 1 ($p > 0.05$ respectively), whereas no significant changes were detected in Group 2 ($p = 0.07$ and $p = 0.38$ respectively). At the 4th stage, significant intergroup differences were found for both VAS 4 and Cortisol 4 ($p < 0.05$ respectively).

Conclusions. The study results confirm that optimizing perioperative analgesia regimens at Role 2 medical treatment facilities and during interhospital transportation allows for minimizing systemic stress response manifestations, significantly improving treatment outcomes for wounded patients, and remains a priority task of modern military medicine.

Keywords: combat trauma, gunshot wound, gunshot injury, regional anesthesia, pain.

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ВПЛИВ РЕГІОНАРНОГО ЗНЕБОЛЕННЯ НА ІНТЕНСИВНІСТЬ БОЛЮ ТА РІВЕНЬ КОРТИЗОЛЕМІЇ У ПОРАНЕНИХ З БОЙОВОЮ ТРАВМОЮ КІНЦІВОК

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У статті представлено результати проспективного дослідження з визначення ефективності регіонарних аналгетичних блокад під час надання невідкладної допомоги пораненим із бойовою травмою кінцівок в умовах шпиталів Role 2 та під час міжгоспітального транспортування. До дослідження включено 100 поранених із бойовою травмою однієї кінцівки, яких розділено на дві групи: група 1 (n = 50) отримувала лише системну аналгезію, тоді як група 2 (n = 50) – регіонарну анестезію, що проводилася під ультразвуковим контролем. У динаміці фіксувалась інтенсивність болю та визначався рівень плазмового кортизолу. Результати дослідження підтверджують, що оптимізація схем періопераційного знеболювання в умовах шпиталів Role 2 та під час міжгоспітального транспортування дає можливість мінімізувати прояви системної стрес-відповіді, значно покращити результати лікування поранених та є пріоритетним завданням сучасної військової медицини.

Ключові слова: бойова травма, вогнепальне поранення, вогнепальна травма, регіонарне знеболення, біль.

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Стаття поширюється на умовах ліцензії

Introduction

The full-scale war on the territory of Ukraine has revealed a number of problematic issues regarding treatment and evacuation measures for the wounded with combat trauma of the extremities [1]. Many questions exist regarding the organization of emergency anesthesiological care and pain management for the wounded in Role 2 hospitals, as well as during subsequent interhospital transportation. It is known that the provision of emergency care is characterized by the probability of mass casualties arriving simultaneously, since sanitary losses are distributed unevenly both geographically and in terms of the time of their occurrence [2].

Effective pain management and continuous monitoring of analgesic efficacy across all stages of medical evacuation are critical to preventing the chronicity of pain in wounded patients [3]. According to Kuchyn YuL et al. (2023), studying the specifics of pain in the wounded requires in-depth research, as the subjective sensations and emotional experiences a person feels during a wound in combat conditions have their own unique characteristics [4]. Today, numerous publications indicate that determining the concentration of cortisol, as an integral "stress hormone" over time, is a criterion for assessing the adequacy of anesthesia and analgesia [5; 6]. Despite the extensive study of the effect of anesthesia on stress markers in elective surgery, data on the changes in cortisolemia in urgent patients remain limited, where the plasma cortisol level is mostly analyzed as an indicator of inflammation and a predictor of complications. In the study by Bisschop PH et al. (2011) involving 143 patients who were admitted urgently due to hip fracture, an increase in the level of cortisolemia was detected in patients with concomitant cognitive deficit [7]. At the same time, Mohammed HSE et al. (2022) evaluated plasma cortisol in 90 patients with acute pancreatitis, and it was established that high starting indicators of cortisolemia are a prognostic marker of mortality reduction [8]. The number of works dedicated to the changes of stress markers for evaluating anesthesia and analgesia regimens in combat trauma remains insignificant. In particular, Frank M et al. (2025) analyzed the changes of cortisolemia in 32 wounded patients with combat trauma of the extremities during elective repeated surgical debridement of gunshot wounds, noting more stable indicators under conditions of a combination of regional anesthesia with sedation [9].

The implementation of regional analgesic blocks as part of multimodal pain therapy during medical evacuation, effectively reduces the intensity of acute pain, significantly lowering the risk of pain chronification while ensuring better long-term treatment outcomes and improved quality of life for the wounded [10]. In the study by Laitselart P et al. (2025), it is noted that the earliest possible implementation of regional analgesia for the wounded with combat trauma provides stable analgesia without impairment of consciousness and significant fluctuations in vital function parameters [11]. In the publication by Carness JM et al. (2017), the effectiveness of regional analgesia was analyzed during the medical evacuation of 84 wounded patients with combat trauma of the lower extremities. A significant reduction in opioid use was recorded in patients who underwent regional analgesic blocks [12]. To minimize the risk of complications of regional blocks, the use of ultrasound guidance is recommended, which changes the principles and approaches of modern regional anesthesia. However, uncertainty exists regarding the effectiveness and safety of regional analgesic blocks during the provision of emergency care to the wounded with combat trauma. It is believed that regional blocks are technically more complex manipulations, and their performance requires special knowledge and experience from the anesthesiologist [13]. In the publication of Moshkivskyi VM et al. (2023), it is indicated that in 46 wounded patients with combat trauma of the upper extremity, during treatment at the Role 2 level, the share of regional methods of analgesia was only 8%. It is noted that the time required to perform infiltration of nerves and plexuses with a local anesthetic solution and the onset time of anesthesia are sometimes not expedient in the event of a mass influx of wounded.

The scarcity of data in the medical literature regarding the study of the effectiveness of regional analgesia, including through the determination of stress marker dynamics, in wounded patients with combat trauma of the extremities during the provision of emergency care and during interhospital transportation, determined the relevance of this study.

Objective. To optimize perioperative analgesia regimens for wounded patients with combat trauma of the extremities at Role 2 medical treatment facilities and during interhospital transportation based on a comparative assessment of the impact of regional or systemic analgesia on pain intensity and cortisolemia levels over time.

Materials and Methods

This study was prospective in design. The study was conducted in accordance with the principles of the World Medical Association Declaration of Helsinki. The study protocol was approved by the Bioethics Committee of Odesa National Medical University (Protocol No. 18 dated December 6, 2023). Written informed consent was obtained from all patients prior to their participation in the study.

The study included 100 wounded patients with combat trauma of the extremities who received emergency medical care during 2024–2025 at Role 2 medical treatment facilities (Kherson and Snihurivka, Mykolaiv region), followed by evacuation to higher levels of medical care (Mykolaiv and Odesa). Patients were allocated into two groups: the systemic analgesia group (Group 1, n = 50) and the regional analgesia group (Group 2, n = 50). All patients in the study groups were male. The study groups did not differ statistically in age (38.5 ± 9.4 years and 37.2 ± 9.3 years, respectively; p = 0.49), body mass index (BMI) (Me = 23.1 kg/m² (21.5; 26.6) and 24.1 kg/m² (22.1; 27.0), respectively; p = 0.36), or hemoglobin level (Me = 129.5 g/L (119; 137) and 133 g/L (122; 141), respectively; p = 0.22).

Pain intensity was evaluated over time using a visual analog scale (VAS, points), while the stress response marker level was evaluated by the concentration of cortisol in plasma (cortisol, nmol/l). Study parameters were recorded at four stages: 1) upon admission to the Role 2 medical treatment facilities; 2) after completion of surgery; 3) at the beginning of medical evacuation; 4) after completion of interhospital transportation.

Inclusion criteria were age over 18 years and the presence of a gunshot injury to an upper or lower extremity. Exclusion criteria were refusal to participate, critical patient condition, and a history of allergy to medications used in the study. Each group included 25 patients with combat trauma of upper extremity and 25 patients with combat trauma of lower extremity. In Group 1, surgical procedures were performed under intravenous anesthesia with either mechanical ventilation or preserved spontaneous breathing. In Group 2, combined anesthesia was administered (intravenous anesthesia and regional nerve blocks). A VF13-5 ultrasound transducer (4.1–12.1 MHz) connected to a SIEMENS ACUSON P500 ultrasound scanner (Germany) was used. A 0.5% bupivacaine solution was administered perineurally as the local anesthetic.

Regional analgesic blocks were performed immediately upon admission after assessment of injury severity and determination of the need for urgent surgical treatment using the Battlefield Advanced Trauma Life Support (BATLS) scale, which includes evaluation of three parameters: level of consciousness according to the Glasgow Coma Scale, systolic arterial blood pressure, and respiratory rate [15]. Each parameter was scored from 0 to 4 points. For the Glasgow Coma Scale, scores of 3, 4–5, 6–8, 9–12, and 13–15 corresponded to 0, 1, 2, 3, and 4 BATLS points, respectively. For systolic arterial blood pressure, values of 0, < 50, 50–75, 76–90, and > 90 mmHg corresponded to 0, 1, 2, 3, and 4 points, respectively. For respiratory rate, values of 0, < 5, 5–9, > 30, and 10–30 breaths per minute corresponded to 0, 1, 2, 3, and 4 points, respectively.

Based on the total score obtained, patient status was classified as follows: 0 points – deceased casualty; 1–3 points – moribund casualty; 4–10 points – casualty requiring immediate treatment; 11 points – casualty requiring immediate treatment, although a delay is possible; 12 points – delay of immediate treatment is acceptable. In cases where injury severity was assessed as 11–12 points according to the BATLS scale, regional analgesia was performed as the first intervention in the resuscitation area before any other medical procedures.

The algorithm and sequence of actions in the case of emergency regional anesthesia are shown in Figure 1.

To determine cortisol levels, venous blood samples were collected followed by serum separation using centrifugation. Cortisol concentration was measured by solid-phase enzyme-linked immunosorbent assay (ELISA) at the Educational and Research Laboratory of Molecular Pathology of Odesa National Medical University. Reference values ranged from 140 to 600 nmol/L.

Statistical analysis was performed using Statistica 12.6 software. Normality of data distribution was assessed using the Shapiro–Wilk test. Data with a normal distribution are presented as mean ± standard deviation (M ± σ) and were compared using Student's t-test. In cases where the null hypothesis of normal distribution was rejected, data are presented as median (Me) and the 25th and 75th percentiles (*Q25; Q75*), and comparisons were performed using

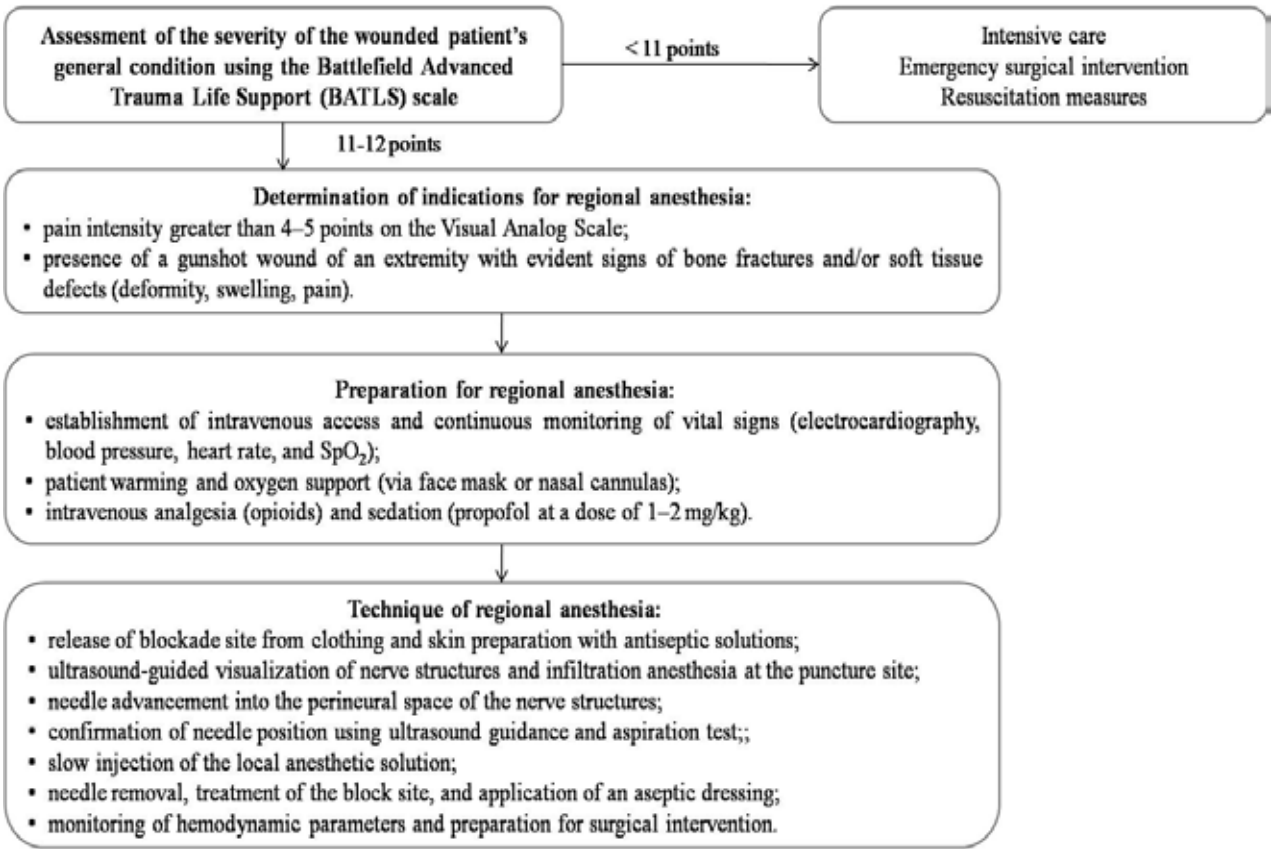

Fig. 1. Algorithm for conducting urgent regional anesthesia in wounded patients with combat trauma of the extremities

the Mann–Whitney U test. Changes over time were analyzed using the Wilcoxon signed-rank test. Statistical significance was considered at $p < 0.05$.

Research results and their discussion

At the time of admission to the Role 2 hospital, a high level of pain intensity was observed: 64 patients reported pain intensity of 7 to 9 points on the VAS, corresponding to severe pain. Plasma cortisol levels exceeding reference values were detected in 78 patients. No statistically significant difference was found between VAS 1 values in Group 1 and Group 2 (Me = 7 points (6; 8) and Me = 7 points (6; 7), respectively; p = 0.57). A comparative analysis of pain intensity scores over time in the study groups is presented in Table 1.

Similarly, no statistically significant difference was observed between Cortisol 1 values (Me = 941.6 nmol/L (667.5; 1281) and Me = 826.3 nmol/L (671.3; 1124), respectively; p = 0.77). A comparative analysis of plasma cortisol levels over time in patients of study groups is presented in Table 2.

Elevated cortisol levels in wounded patients were interpreted as a manifestation of a stress-induced physiological response to pain, a component of the systemic inflammatory response to gunshot injury, and an expression of psychoemotional stress. Between 1st and 2nd stages of the study, a reduction in pain intensity was observed in both Group 1 and Group 2, with a statistically significant difference between VAS 1 and VAS 2 values ($p < 0.05$). A decrease in plasma cortisol levels was also observed in both groups; however, in Group 1 this decrease was not statistically significant (p = 0.7), whereas in Group 2 the difference between Cortisol 1 and Cortisol 2 values was statistically significant ($p < 0.05$). Comparison of VAS 2 values between Group 1 and Group 2 revealed a statistically significant difference (Me = 3 points (3; 4) and Me = 1 point (1; 2), respectively; $p < 0.05$). In contrast, no statistically significant difference was found between Cortisol 2 values (Me = 874.6 nmol/L (608.8; 1363) and Me = 811.8 nmol/L (550.6; 1027), respectively; p = 0.17). Changes in pain intensity and plasma cortisol levels during the perioperative period demonstrate the overall effectiveness of analgesia. However, the statistically significant difference in VAS 2 values between the study groups indicates greater analgesic efficacy of regional anesthesia as part of combined anesthesia techniques.

Between 2nd and 3rd stages of the study, Group 1 demonstrated a further reduction in pain intensity, with a statistically significant difference between VAS 2 and VAS 3 ($p < 0.05$). In contrast, Group 2 maintained consistently low pain intensity levels, with no statistically significant difference between VAS 2 and VAS 3 (p = 0.11). The changes in pain intensity are presented in Table 1. Results confirm the high effectiveness of postoperative analgesia

Table 1

Comparative analysis of pain intensity scores over time in the study groups

Patients of study groups	VAS 1 (points) Me (Q25; Q75)	VAS 2 (points) Me (Q25; Q75)	VAS 3 (points) Me (Q25; Q75)	VAS 4 (points) Me (Q25; Q75)	p*
Group 1 (n = 50)	7 (6; 8)	3 (3; 4)	3 (2; 3)	5 (4; 6)	p1–2 < 0.05 p2–3 < 0.05 p3–4 < 0.05
Group 2 (n=50)	7 (6; 7)	1 (1; 2)	1 (1; 2)	1 (1; 2)	p1–2 < 0.05 p2–3 = 0.11 p3–4 = 0.07
p**	0.57	< 0.05	< 0.05	< 0.05	

Note: ***p**** – the Wilcoxon signed-rank test was used to assess the statistical significance of differences between values over time; $p_{1–2}$ – significance of differences between VAS 1 and VAS 2 values; $p_{2–3}$ – significance of differences between VAS 2 and VAS 3 values; $p_{3–4}$ – significance of differences between VAS 3 and VAS 4 values. ***p*** – the Mann–Whitney U test was used to determine the statistical significance of differences between groups.

Table 2

Comparative analysis of plasma cortisol levels over time in the study groups

Patients of study groups	Cortisol 1 (nmol/L) Me (Q_{25}; Q_{75})	Cortisol 2 (nmol/L) Me (Q_{25}; Q_{75})	Cortisol 3 (nmol/L) Me (Q_{25}; Q_{75})	Cortisol 4 (nmol/L) Me (Q_{25}; Q_{75})	p*
Group 1 (n = 50)	941.6 (667.5; 1281)	874.6 (608.8; 1363)	175.1 (153.9; 185.9)	738.9 (547.8; 1393)	$p_{1–2}$ = 0.7 $p_{2–3}$ < 0.05 $p_{3–4}$ < 0.05
Group 2 (n=50)	826.3 (671.3; 1124)	811.8 (550.6; 1027)	169.8 (98; 341.8)	177.3 (157.6; 185.4)	$p_{1–2}$ < 0.05 $p_{2–3}$ < 0.05 $p_{3–4}$ = 0.38
p**	0.57	0.17	0.41	< 0.05	

Note: ***p**** – the Wilcoxon signed-rank test was used to assess the statistical significance of differences between values over time; $p_{1–2}$ – significance of differences between Cortisol 1 and Cortisol 2 values; $p_{2–3}$ – significance of differences between Cortisol 2 and Cortisol 3 values; $p_{3–4}$ – significance of differences between Cortisol 3 and Cortisol 4 values. ***p**** – the Mann–Whitney U test was used to determine the statistical significance of differences between groups.

regimens based on multimodal analgesia principles. Additionally, a reduction in plasma cortisol levels was observed in both groups (within reference values in 59 patients), with statistically significant differences between Cortisol 2 and Cortisol 3 values in both groups ($p < 0.05$). The observed cortisol level changes are presented in Table 2. The results indicate the adequate effectiveness of the prescribed anti-inflammatory therapy which along with patient reports reflects the change from hazardous conditions of intense combat activity to relative calm within a medical facility. Comparison of VAS 3 values between Group 1 and Group 2 revealed a statistically significant difference (Me = 3 points (2; 3) and Me = 1 point (1; 2), respectively; $p < 0.05$), indicating greater effectiveness of postoperative analgesia regimens incorporating regional analgesic blocks. However, no statistically significant difference was found between Cortisol 3 values (Me = 175.1 nmol/L (153.9; 185.9) and Me = 169.9 nmol/L (98; 341.8), respectively; $p = 0.41$).

Between the 3rd and 4th stages of the study, patients in Group 1 demonstrated an increase in pain intensity (44 patients reported VAS scores from 4 to 9 points), with a statistically significant difference between VAS 3 and VAS 4 ($p < 0.05$). An increase in plasma cortisol levels was also observed in Group 1 (36 patients exceeded reference values), with a statistically significant difference between Cortisol 3 and Cortisol 4 ($p < 0.05$). Most Group 1 patients reported increased pain intensity during medical transportation, particularly during vehicle movement over damaged road surfaces. While the in-hospital analgesic regimen was sufficiently effective (also supported by plasma cortisol levels as markers of stress response), systemic analgesics were less effective during transportation. Even additional opioid administration did not substantially improve analgesia during movement. The increase in plasma cortisol levels beyond reference values in Group 1 indicates significantly reduced patient comfort during interhospital transportation, primarily due to increased pain intensity. In contrast, patients in Group 2 demonstrated stable pain intensity and plasma cortisol levels, with no statistically significant differences between VAS 3 and VAS 4 or between Cortisol 3 and Cortisol 4 ($p = 0.07$ and $p = 0.38$ respectively). Comparison of VAS 4 values between Group 1 and Group 2 revealed a statistically significant difference (Me = 5 points (4; 6) and Me = 1 point (1; 2), respectively; $p < 0.05$); Comparison of Cortisol 4 values between Group 1 and Group 2 revealed a statistically significant difference (Me = 738.9 nmol/L (547.8; 1393) and Me = 177.3 nmol/L (157.6; 185.4), respectively; $p < 0.05$). These findings demonstrate significantly greater analgesic effectiveness in patients receiving regional analgesic blocks. The stability of plasma cortisol levels in Group 2 reflects greater patient comfort during interhospital transportation, attributable to the use of regional analgesic blocks in perioperative care.

Conclusions

According to the results of the study, in wounded patients with combat trauma of the extremities during interhospital transportation, no statistically significant changes were detected in the parameters of pain intensity ($p = 0.07$) and cortisolemia level ($p = 0.38$) against the background of using regional analgesia, which indicates the stability of antinociceptive protection.

The stability of pain intensity and cortisol level parameters in patients receiving regional analgesia indicates a longer-lasting and more effective analgesic effect compared with systemic analgesia. In contrast, during interhospital transportation, patients receiving systemic analgesia demonstrated a progressive increase in pain intensity and cortisol levels ($p < 0.05$), reflecting a pronounced physiological stress response to pain.

The obtained results confirm the feasibility of regional analgesia as an effective component of multimodal pain management in patients with combat-related extremity injuries, allowing a significant reduction in the manifestations of the systemic stress response both in Role 2 medical treatment facilities and during subsequent stages of medical evacuation.

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