Medicina Intensiva 46 (2022) 277–287

medicina intensiva

http://www.medintensiva.org/en/

SCIENTIFIC LETTER

Chronic critical illness, how to manage it?☆

Enfermedad crítica crónica ¿cómo abordarla?

To the Editor,

Advances in intensive medicine have increased the survival rate of a growing number of patients with chronic critical illness. However, new situations have come up too: post-intensive care syndrome, persistent critical illness, and a population of chronic critically ill patients (CIP) who require intensive care for long periods of time. The latter situation is a condition recently described that challenges the treatments available today and leaves frail patients with little capacity to breath or move adequately.[1,2] The common denominator is that they have single organ failure that prevents proper weaning from mechanical ventilation. For a unit like ours, the incidence rate sits at around 6.7% of all patients admitted. The medical literature reports an overall rate between 5% and 8%, 19% in trauma patients, and 40% in septic patients.

These patients are characterized by:[3,4]

- Stays at the intensive care unit (ICU) >15 days.
- Dependency of mechanical ventilation (>4 weeks).[1]
- Advanced age.
- Evidence of persistent organ dysfunction.
- Survival to early aggression, but often recovered not well enough to be discharged from the hospital and sent back home.

This entity is defined by the Persistent Inflammation, Immunosuppression, and Catabolism Syndrome'' (PICS)[5,6] (Table 1),[3] and is characterized by a depressed adaptative immunity, low—but persistent—level of inflammation, diffuse apoptosis, loss of lean mass, and poor scarring-pressure ulcers.

The overall in-hospital mortality rate of these patients is 31%. This mortality rate is 16%, and 30% in trauma and septic patients, respectively, at the 6-month follow-up. However, this rate can go up to 75% at the 3-year follow-up.

In the management of the PICS complete recovery is almost impossible because from the standpoint of catabolism, the syndrome drains all the energy from the body ultimate reserves. Also, because the immune system panics in response to the aggression and to the different therapies used: the bone marrow releases a large number of immature cells that have mixed effects on the patient causing greater swelling and leaving the organism unprotected with the same efficacy compared to mature cells. From the pathophysiological standpoint, we should consider that emergency myelopoiesis emerges in response to an acute aggression at the expense of less lymphopoiesis and erythropoiesis, which enhances anemia, and lymphopenia. Also, it conditions the expansion—via signal transducer and activation of transcription 3 (STAT3) associated with the cyclooxygenase 2 (COX2) promoter—of a heterogeneous population of immature myeloid cells (IMC) with immunosuppressant properties (IP).[6] Fig. 1 shows the complex scheme of therapeutic approach both of immunosuppression and catabolism.[7]

From the clinical standpoint, these patients are often ventilator-dependent, and show cerebral dysfunction (delirium), neuromuscular weakness, endocrinopathy (loss of pulsatile secretion of the anterior pituitary, hypogonadism), malnutrition, anasarca, decubitus ulcers, and discomfort (pain, thirst, dyspnea, anxiety, and poor verbal communication due to tracheostomy).

Chronic critical illness is a devastating condition whose mortality rate exceeds that of malignant diseases. In the United States alone, the healthcare costs derived from the management of CIP are over US$200 billion (nearly €18 000 million) and counting.[8]

We should bear in mind that, on many occasions, to safeguard patients and prevent the collapse of the healthcare personnel at the different hospital floors, ICU discharges

Table 1 Diagnostic criteria of the Persistent Inflammation, Immunosuppression, and Catabolism Syndrome.

	Clinical-analytical determinants
Persistent Inflammation	Stay at the ICU setting >14 days CRP >50 μg/dL
Immunosuppression	Total lymphocyte count <0.80 × 10^9/L
Catabolism	Weight loss > 10% during hospitalization or BMI <18 CHI < 80% Albumin levels <3.0 g/L Prealbumin levels <10 mg/dL RbP <10 μg/dL

BMI, body mass index; CHI, creatinine/height index; CRP, C-reactive protein; ICU, intensive care unit; RbP, retinol binding protein.

☆ Please cite this article as: García-de-Lorenzo A, Añón JM, Asensio MJ, Burgueño P. Enfermedad crítica crónica ¿cómo abordarla? Med Intensiva. 2022;46:277–279.

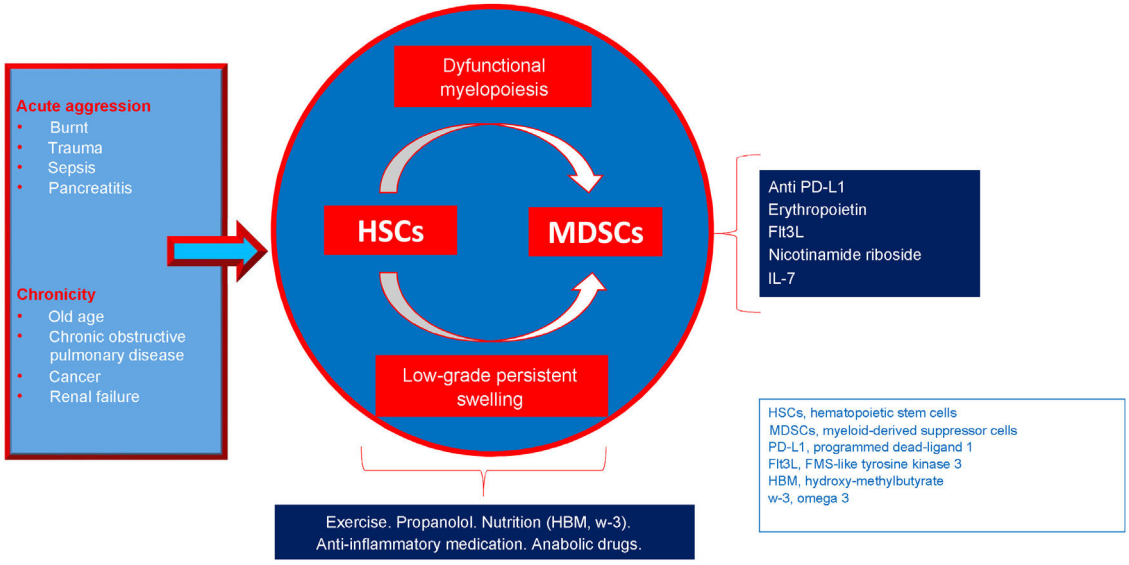

Figure 1 Therapeutic approach for the management of chronic critical illness.

are often delayed. This translates into longer ICU stays for clinically stable patients from LOC I, and LOC II groups (Levels of Critical Care. ESCIM-Level of Care. 2011). Also, they need constant care from the nursing team (routine postural changes, complex healing procedures, repeated lab tests, strict control of hydric balance, aspiration of secretions, etc.) that often exceed the capabilities of a conventional hospital ward. Although these patients are often physiologically stable, they are still exposed to complications associated with their primary diagnosis, as well as to subsequent organ failures due to the interrelations among sepsis, immune function, and nutritional status. This means that they need to be transferred to a different more friendly environment with a more suitable doctor/nurse ratio (lower actually) where all nutritional, rehabilitation, and psychological needs are duly met; we should mention that these units—necessarily cross-sectional—should be led by specialists in intensive medicine.

All these aspects have sparked interest in specific units for less severe critically ill patients as a bridging therapy between the level of care provided at the ICU setting and at a conventional hospital floor, which, in turn, is an opportunity to create more modern, efficient, and human structures.[9] They should be transferred to chronic units in centers specialized in the management of these patients (long-term acute care) including the possibility of continuous monitorization: ECG, SpO_2, and non-invasive arterial blood pressure monitoring. Nurse control through telemetry and alarms, mechanical ventilators, BiPAP ventilation, and different ventilation accessories and consumables facilitate the weaning process from the ventilator. Rehabilitation equipment for chronic patients, electrostimulation, bicycles, spirometers, physical therapists—including respiratory physical therapists—rehabilitators, psychologists, and nutritionists, added to a friendly setting for the proper physical and mental rehabilitation increase the patient's autonomy, humanization, palliative care, and the social, and familial perspective.[10]

References

1. Nelson JE, Cox CC, Hope AA, Carson SS. Chronic critical illness. Am J Respir Crit Care Med. 2010;182:446–54.
2. Khan JM, Le T, Angus DC, Cox CE, Hough CL, White DB, et al. The epidemiology of chronic critical illness in the United States. Crit Care Med. 2015;43:282–7.
3. Mira JC, Cuscieri J, Ozrazgat-Baslati T, Wang Z, Ghita GL, Loftus TJ, et al. The epidemiology of chronic critical illness after severe trauma injury in two level-one trauma centres. Crit Care Med. 2017;45:1989–96.
4. Stortz JA, Murphy TJ, Raymond SL, Mira JC, Ungaro R, Dirain ML, et al. Evidence for persistent immune suppression in patients who develop chronic critical illness after sepsis. Shock. 2018;49:249–58.
5. Mira JC, Brakenridge SC, Moldawer LL, Moore FA. Persistent Inflammation, Immunosupression and Catabolims Syndrome (PICS). Crit Care Clin. 2017;33:245–58.
6. Rosenthal MD, Moore FA. Persistent inflammation, immunosuppression, and catabolism: evolution of multiple organ dysfuntion. Surg Infect. 2016;17:167–72.
7. Efron PA, Moore FA, Brakenridge SC. Persistent Inflammation, Immunosuppression and Catabolism after severe injury or infection. In: Vincent JL, editor. Annual Update in Intensive Care and Emergency Medicine 2018. Switzerland: Springer; 2018. p. 25–35.
8. Marchioni A, Fantini R, Antenora F, Clini E, Fabbri L. Chronic critical illness. The price of survival. Eur J Clin Invest. 2015;45:1341–9.
9. Hickman RL, Douglas SL. Impact of chronic critical illness on the psychological outcomes of family members. AACN Adv Crit Care. 2010;21:90–1.
10. Martin MC, García deLorenzo A. Sobrevivir a las unidades de cuidados intensivos mirando a través de los ojos de la familia. Med Intensiva. 2017;41:451–3.

García-de-Lorenzo A. [a,b,*], Añón J.M. [a,c], Asensio M.J. [a], Burgueño P. [d]

[a] *Servicio de Medicina Intensiva, Hospital Universitario La Paz, IdiPAZ, Madrid, Spain*
[b] *Facultad de Medicina, Universidad Autónoma de Madrid, Madrid, Spain*
[c] *CIBER de Enfermedades Respiratorias, ISCIII, Madrid, Spain*
[d] *Servicio de Medicina Intensiva, Hospital 12 de Octubre, Madrid, Spain*

* Corresponding author.
E-mail address: agdl@telefonica.net
(A. García-de-Lorenzo).

2173-5727/

Methadone as a rescue drug for difficult-to-sedate critically ill patients suffering from ARDS related to SARS-CoV-2 infection☆

Metadona como fármaco de rescate para el control de la sedoanalgesia difícil en pacientes con SDRA asociado a infección por SARS-CoV-2

To the Editor,

The prolonged administration of sedatives and opiates (SED-OPI)—especially in patients ventilated due to SARS-CoV-2-related ARDS—in whom elevated requirements for these drugs have been reported[1]—is often associated with phenomena of tolerance and dependency. Deprivation syndrome can occur when reducing the dose blocking or delaying the process of weaning from mechanical ventilation (MV).[2,3]

The concept of «difficult sedation» (DS) includes these problems and different management strategies have been proposed such as sequential sedation with SED-OPI rotation or the administration of alpha2-agonists and/or antipsychotics.[4,5] These strategies rarely contemplate the administration of methadone, possibly because, unlike it happens in the pediatric population, this drug is not very much used in adult critically ill patients.[6,7] Methadone is a long semi-life opiate available in solution for its enteral administration with high bioavailability that has the capacity of blocking the NMDA receptors whose activation is highly involved in the development of tolerance, and hyperalgesia.[8,9]

The objective of this retrospective, observational, and cohort study is to describe the experience gained with the use of methadone to control DS in ventilated patients due to COVID-19-related ARDS in whom the use of common drugs has failed and admitted between March 2020 and May 2020. Approval from the hospital clinical research ethics committee was obtained to review the patients' health records and analyze those patients who received methadone for, at least, 48 h to control DS. DS was considered as the impossibility to reduce the dose of SED-OPI to start weaning from MV or RASS scores > 1 despite high doses of SED-OPI[4] and/or the presence of uncontrolled pain with the usual opiates.

Information from demographic and clinical data, duration, and cumulative dose of SED-OPI at the beginning of treatment and 5 days before and 5 days after starting treatment was obtained (Table 1). The dose of opiates is expressed in mg of IV morphine being the equianalgesic dose ratio as follows: 100 μg of fentanyl = 100 μg of remifentanil = 10 mg of IV morphine. Registries from the nurse records of the RASS scales, the numeric visual scale or ESCID, and the side effects due to methadone were analyzed. Methadone was administered as an enteral solution at 1% and prepared by the hospital pharmacy unit. The decision to use methadone was made by the treating physician and once the routine therapeutic strategy had failed.

Qualitative variables were analyzed using the X^2 test or Fisher's exact test. Quantitative variables were analyzed using the Mann–Whitney U test.

During the study period, a total of 92 patients required MV due to SARS-CoV-2-related ARDS. Fourteen patients received, at least, 1 dose of methadone, 13 of whom met the study criteria. Methadone was started after 46 ± 16 days on MV, and the administration of SED-OPI with a range from 21 to 66 days. The early daily dose was 45 ± 23 mg distributed in 2–3 doses; then it was adjusted between 0.1 mg/kg and 0.4 mg/kg every 8 or 12 h depending on each patient's response.

Methadone was started in 9 patients due to the impossibility of reducing the dose of SED-OPI to start the process of weaning from MV or due to the presence of RASS scores > 1 despite high doses of SED-OPI. In addition to propofol, 6 patients were on alpha2-agonists, 4 were infused with midazolam, and 5 with cisatracurium. In 4 patients, treatment was indicated due to uncontrolled pain following tolerance to high doses of opiates and despite multimodal analgesia.

In 11 out of 13 patients (85%) the quality of sedoanalgesia improved and values of −2 and 0 were obtained in the RASS score, and pain went under control with a numerical visual scale < 4. Also, the dose of drugs used was reduced to adapt to MV (Fig. 1) with progression towards weaning from the ventilator. After 5 days of treatment, conventional opiates were withdrawn in 11 patients and the dose was reduced by 64% in 2 patients. In 5 out of 9 patients the dose of propofol was reduced in 68% ± 26% while in 3 out of 4 patients the dose of midazolam was reduced in 51% ± 31%. Also, cisatracurium was withdrawn in 3 patients while in the remaining 2—although still needed—it stopped progression

☆ Please cite this article as: Fernández-Tobar R, Chamorro-Jambrina C, Pérez-Torres M, Castiñeiras-Amor B, Alcántara-Carmona S, Romera-Ortega MA. Metadona como fármaco de rescate para el control de la sedoanalgesia difícil en pacientes con SDRA asociado a infección por SARS-CoV-2. Med Intensiva. 2022;46:279–281.