EDITORIAL

Intensive Care Unit-acquired Weakness: A Frequent but Under-recognized Threat

Harsh Sapra

Indian Journal of Critical Care Medicine (2021): 10.5005/jp-journals-10071-23990

Advances in modern medicine have been quite successful in reducing intensive care unit (ICU) mortality but post-ICU morbidity and impaired quality of life continue to be major concerns. Neuromuscular weakness developed in the critical illness survivors is one of the leading causes of incomplete functional recovery and persistent disability. In this issue of the journal, Baby et al. have published a prospective analysis of incidence, clinical course, and outcome of ICU-acquired neuromuscular weakness.[1]

ICU-acquired weakness (ICUAW) is a syndrome of generalized weakness defined as, "clinically detected weakness in critically ill patients in whom there is no plausible etiology other than critical illness."[2] It is usually present beyond the first week of ICU stay with a reported incidence of >25%, which increases significantly in patients with sepsis (>60%).[3]

ICUAW is classified into critical illness polyneuropathy (CIP), critical illness myopathy (CIM), and critical illness neuromyopathy (CINM). The pathophysiological pathway is incompletely understood but may involve micro- or macrocirculatory impairment; bioenergetics failure; sodium channel inactivation; neurotoxins, like lipopolysaccharide and interleukins; hyperglycemia-induced oxidative stress; muscular atrophy; and mitochondrial or contractile protein dysfunction. The diagnosis can be made based on clinical features, neurophysiological testing, or nerve and muscle biopsy. It is characterized by generalized, symmetrical weakness including respiratory muscles and sparing cranial nerves, developing after critical illness onset with medical research council grade <4 in all testable muscle groups and distal sensory loss in CIP. Muscle wasting is usually variable and difficult to assess in the presence of edema. Neurophysiological testing includes nerve conduction studies determining nerve conduction velocities, compound motor action potentials (CMAP), sensory nerve action potentials (SNAP), and electromyography (EMG). CIP is characterized by reduced CMAP and SNAP with normal or near normal nerve conduction velocities. CIM is characterized by short duration, low-amplitude motor unit potentials on EMG, reduced CMAP on direct muscle stimulation, and muscle biopsy showing atrophy with thick filament loss or necrosis. Muscle biopsy further classifies CIM into three subtypes: cachectic myopathy, thick filament myopathy, and necrotizing myopathy. CIM patients have a better prognosis in terms of recovery than CIP. CINM will demonstrate overlapping features of both CIP and CIM. Baum et al. identified four different clusters of electrophysiological impairments, which can be useful for further categorization of severity and prognostication.[4] The differential diagnosis may include conditions like Guillain–Barre syndrome, Myasthenia gravis, spinal cord injury, metabolic neuropathies, and toxic neuropathies. These can be ruled out based on the timing of onset of weakness in relation to critical illness and presence or absence of cranial nerves or extraocular muscles involvement.

Neuroanaesthesia and Neurocritical Care, Medanta: The Medicity, Gurugram, Haryana, India

Corresponding Author: Harsh Sapra, Neuroanaesthesia and Neurocritical Care, Medanta: The Medicity, Gurugram, Haryana, India, e-mail: harshsapra@hotmail.com

How to cite this article: Sapra H. Intensive Care Unit-acquired Weakness: A Frequent but Under-recognized Threat. Indian J Crit Care Med 2021;25(9):969–971.

Source of support: Nil

Conflict of interest: None

Recently, qualitative assessment of muscles with ultrasonography (USG) has been successfully used for the early detection of ICUAW. Other several techniques, such as computed tomography, magnetic resonance imaging, dual-energy X-ray absorptiometry, and neutron activation analysis, have also been used with more accuracy but these are time consuming, expensive, and associated with radiation exposure. Bioimpedance spectroscopy is another useful technique but its accuracy is limited by skin temperature, edema, or body position.[5] Respiratory muscle strength can also be assessed for early detection of ICUAW. Maximum inspiratory pressure can be used as a surrogate parameter for early diagnosis of ICUAW.[6] USG-guided evaluation of diaphragmatic excursion and diaphragmatic thickening fraction can be used to predict weaning outcomes.[7]

ICUAW has several non-modifiable risks factors, like age, female gender, and severity of illness [Acute Physiology And Chronic Health Evaluation (APACHE) II score >15], and modifiable risk factors, like dyselectrolytemia, hyperglycemia, hyperosmolarity, mechanical ventilation (MV), parental nutrition, drugs like neuromuscular blockers (NMBs), amikacin, steroids, and vasopressors. Initial studies have shown a higher risk of ICUAW with older age; however, a recent meta-analysis did not find any significant association between age and ICUAW.[8,9] In this study, the mean age of patients developing ICUAW was 62.64 ± 14.4 years. Less muscle mass in females explains the higher susceptibility to develop ICUAW compared to males. Recent studies have shown a higher incidence of ICUAW with longer exposure to MV due to induced diaphragmatic weakness,[3] but it is difficult to determine if prolonged MV leads to ICUAW or ICUAW increases the duration of MV. In this study, the mean duration of MV for patients developing ICAW was 9.27 ± 5.28 days compared to 3.87 ± 3.65 days in non-ICUAW patients. The association between corticosteroids and ICUAW is uncertain,[9,10] but their anti-inflammatory effect can exert some protective effect if hyperglycemia occurring secondary with their use is avoided with intensive insulin therapy.[11] NMBs promote

ICUAW by aggravating the muscle weakness especially when administered for >48 hours or coadministered with steroids.[12] Routine use of such drugs should be avoided, especially when coadministered, and their indications, dosage, and duration should be regularly reviewed.

The short-term consequences include prolonged MV, extubation failure, re-intubation, prolonged ICU stay, and increased cost. Long-term consequences include late death and reduced physical quality of life even 5 years after ICU discharge. In this study, the number of ICU days for patients with ICUAW was more than double and MV duration was three times higher than those who did not develop ICUAW. ICU mortality was also significantly higher in patients with ICUAW. In a study by Hermans et al., ICU and hospital mortality were not different but 1-year mortality was increased by 13% in patients with ICUAW.[13] The likelihood of 1-year mortality was even higher with persisting weakness or increased severity of weakness after ICU discharge.

Till date, no intervention has been proven to improve the outcome in ICUAW. Various preventive measures minimizing the risk factors have been used to reduce the prevalence of ICUAW. Hermans et al. in the secondary analysis of randomized controlled trials (RCTs) found that intensive insulin therapy (target blood glucose 4.5–6.0 mmol/L) reduces the incidence of ICUAW, duration of MV and ICU stay, and 180-day mortality.[14] However, this was associated with a significant increase in life-threatening hypoglycemia. The current practice supports more liberal blood sugar control (target blood glucose 6.0–10.0 mmol/L) in critically ill patients. An RCT showed the positive effect of neuromuscular stimulation applied to limb muscles in improving walking distance and muscle strength in mechanically ventilated patients.[15] Electrical muscle stimulation may also promote skeletal muscle growth and improve skeletal muscle microcirculation thus exerting a positive effect on tissue healing and prevention of bedsores. Limiting bed rest or inactivity with early mobilization and active or passive exercises can improve muscle function and reduce complications, like muscle shortening, contracture, and deformities. Schweickert et al. assessed the efficacy of early physical and occupational therapy along with daily interruption of sedation in mechanically ventilated patients.[16] This strategy resulted in better functional status at hospital discharge and more ventilator-free days in the ICU. Therapeutic exercises should begin as soon as patients are hemodynamically stable; however, safety during mobilization should be assured to avoid falls, hemodynamic disturbances, desaturation, or accidental removal of medical lines.

ICUAW continues to be an important healthcare concern in critically ill patients. It is associated with increased mortality and functional dependency in ICU survivors. Though exact prevalence is not known due to different diagnostic criteria, timing of assessment, and heterogeneous patient population, the incidence does not seem to be reducing with time. In the absence of any effective therapy, timely implemented preventive measured and early diagnosis should be the aim to improve the functional outcome in patients with ICUAW. Prolonged use of NMB with deep sedation should be avoided. Corticosteroids can be used especially in the treatment of refractory shock with adequate glycemic control. Early and aggressive measures to treat sepsis and maintain electrolyte balance and early institution of enteral nutrition along with a frequent review of medications can help in reducing the incidence of ICUAW. Manual muscle testing should be done at regular intervals in all cooperative patients to determine muscle strength. For unconscious or uncooperative patients, USG-guided qualitative muscle and diaphragmatic assessment is an inexpensive, bedside, and promising technique for early detection of muscle mass loss and ICUAW. Early institution of physical therapy in ICU is safe and feasible and should be started as soon as the patient is hemodynamically stable.

In this study, Baby et al. have evaluated various patient factors and critical illness severity and correlated them with outcome parameters, including ICU days, MV days, and mortality. The higher age and APACHE score on ICU admission were associated with significantly higher ICU days, MV days, and mortality. More research work is required to establish therapeutic targets in the pathological pathway and to explore rehabilitation strategies starting within the ICU.

References

1. Baby S, George C, Osahan NM. Intensive Care Unit-acquired Neuromuscular Weakness: A Prospective Study on Incidences, Clinical Course, and Outcomes. Indian J Crit Care Med 2021;25(9):1006–1012.
2. Stevens RD, Marshall SA, Cornblath DR, Hoke A, Needham DM, de Jonghe B, et al. A framework for diagnosing and classifying intensive care unit-acquired weakness. Crit Care Med 2009;37(10 Suppl.):S299–S308. DOI: 10.1097/CCM.0b013e3181b6ef67.
3. Fan E, Cheek F, Chlan L, Gosselink R, Hart N, Herridge MS, et al. An official American Thoracic Society Clinical Practice guideline: the diagnosis of intensive care unit-acquired weakness in adults. Am J Respir Crit Care Med 2014;190(12):1437–1446. DOI: 10.1164/rccm.201411-2011ST.
4. Baum P, Bercker S, Villmann T, Classen J, Hermann W. Critical-illness-Myopathie und -Neuropathie (CRIMYN). Elektroneurographische Klassifikation [Critical illness myopathy and neuropathy (CRIMYN). Electroneurographic classification]. Nervenarzt 2011;82(4):468–474. DOI: 10.1007/s00115-010-3094-5.
5. Joskova V, Patkova A, Havel E, Najpaverova S, Uramova D, Kovarik M, et al. Critical evaluation of muscle mass loss as a prognostic marker of morbidity in critically ill patients and methods for its determination. J Rehabil Med 2018;50(8):696–704. DOI: 10.2340/16501977-2368.
6. Tzanis G, Vasileiadis I, Zervakis D, Karatzanos E, Dimopoulos S, Pitsolis T, et al. Maximum inspiratory pressure, a surrogate parameter for the assessment of ICU-acquired weakness. BMC Anesthesiol 2011;11:14. DOI: 10.1186/1471-2253-11-14.
7. Qian Z, Yang M, Li L, Chen Y. Ultrasound assessment of diaphragmatic dysfunction as a predictor of weaning outcome from mechanical ventilation: a systematic review and meta-analysis. BMJ Open 2018;8(9):e021189. DOI: 10.1136/bmjopen-2017-021189.
8. Chlan LL, Tracy MF, Guttormson J, Savik K. Peripheral muscle strength and correlates of muscle weakness in patients receiving mechanical ventilation. Am J Crit Care 2015;24(6):e91–e98. DOI: 10.4037/ajcc2015277.
9. Yang T, Li Z, Jiang L, Wang Y, Xi X. Risk factors for intensive care unit-acquired weakness: a systematic review and meta-analysis. Acta Neurol Scand 2018;138(2):104–114. DOI: 10.1111/ane.12964.
10. Yang T, Li Z, Jiang L, Xi X. Corticosteroid use and intensive care unit-acquired weakness: a systematic review and meta-analysis. Crit Care 2018;22(1):187. DOI: 10.1186/s13054-018-2111-0.
11. Hermans G, Wilmer A, Meersseman W, Milants I, Wouters PJ, Bobbaers H, et al. Impact of intensive insulin therapy on neuromuscular complications and ventilator dependency in the medical intensive care unit. Am J Respir Crit Care Med 2007;175(5):480–489. DOI: 10.1164/rccm.200605-665OC.
12. Bourenne J, Hraiech S, Roch A, Gainnier M, Papazian L, Forel JM. Sedation and neuromuscular blocking agents in acute respiratory distress syndrome. Ann Transl Med 2017;5(14):291. DOI: 10.21037/atm.2017.07.19.
13. Hermans G, Van Mechelen H, Clerckx B, Vanhullebusch T, Mesotten D, Wilmer A, et al. Acute outcomes and 1-year mortality of intensive care unit-acquired weakness. A cohort study and propensity-matched

analysis. Am J Respir Crit Care Med 2014;190(4):410–420. DOI: 10.1164/rccm.201312-2257OC.
14. Hermans G, De Jonghe B, Bruyninckx F, Van den Berghe G. Interventions for preventing critical illness polyneuropathy and critical illness myopathy. Cochrane Database Syst Rev 2009;(1):CD006832. DOI: 10.1002/14651858.CD006832.pub2.
15. Kho ME, Truong AD, Zanni JM, Ciesla ND, Brower RG, Palmer JB, et al. Neuromuscular electrical stimulation in mechanically ventilated patients: a randomized, sham-controlled pilot trial with blinded outcome assessment. J Crit Care 2015;30(1):32–39. DOI: 10.1016/j.jcrc.2014.09.014.
16. Schweickert WD, Pohlman MC, Pohlman AS, Nigos C, Pawlik AJ, Esbrook CL, et al. Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial. Lancet 2009;373(9678):1874–1882. DOI: 10.1016/S0140-6736(09)60658-9.