AN EVALUATION OF THE PATHOPHYSIOLOGY, PREVENTION, AND REHABILITATION STRATEGIES FOR ICU-ACQUIRED WEAKNESS IN CRITICALLY ILL PATIENTS

ABSTRACT

Critically ill patients are often exposed to Intensive Care Unit-Acquired Weakness (ICUAW). The pathophysiology of this condition, the preventative measures, as well as the effective rehabilitation approaches are the core for improving patient functional status and the decrease of the healthcare system burden. ICUAW is a general term that is used to include a range of neuropathies of critical importance such as preparing polyneuropathy (CIP) and critical illness myopathy (CIM), most of which can coexist during the same patient. ICUAW mechanisms can be quite subtle and complex. Several mechanisms include factors like oxidative stress, inflammation, and endothelial dysfunction. The suggested mechanisms involved are microvascular dysfunction, inflammatory responses, mitochondrial dysfunction, and neural excitation-contraction coupling failure. Nonetheless, it is fairly evident from the current data that there may be a multifactorial interplay at the basis of this illness, but the full picture continues to be obscure. The preventive strategies are targeted mostly at reducing the risk factors involved in the development of ICUAW. Strategies like early mobilization, paying due attention to the sedation strategies, and using third-generation short-acting neuromuscular blockers that can be reversed. Furthermore, technology based on electrical muscle stimulation is one of the tools being used for secondary prevention. Rehabilitation has a vital role in recovering patients from

the ICUAW. The multidisciplinary approach is centered on rehabilitation development with physical therapy, occupational therapy, and respiratory therapy involvement as key elements of the overall care. Sustained exercise programs, respiratory therapy, and neuromuscular electrical stimulation are effective rehabilitation approaches in the treatment of these patients to restore muscle strength, function, and physical ability after their ICUAW. This review aims to reflect on the commonly encountered weakness in ICU patients to guide the relevant phyisicans on how to deal with them to improve the patient's condition, even if by a small fraction.

Keywords: ICU-acquired weakness, rehabilitation, preventive strategies, ICUAW, poor prognosis, unfavorable outcomes.

1. INTRODUCTION

Intensive care units (ICU)-acquired weakness (ICU-AW) also referred to as critical illness myopathy, skeletal muscle dysfunction, especially among patients in the ICU, which is often triggered by either sepsis, being bedridden, untreated, and or frequent hyperglycemia or use of glucocorticoids or neuromuscular blocking agents. (1)

This greatly affects the follow-up in the phase of disconnection from mechanical ventilation and prolongs the hospitalization.(2) The types of patients who often get the life-limited diagnosis have conditions ranging from incurable, limited mobility, and poor prognosis. This then results in a lack of quality of life. The mechanism and etiology are unclear where, also, moderate drugs and targeted treatment interventions are unavailable. Interestingly, the term ICU-AW has been redefined in modern medicine.(3)

As made evident by the high incidence and severity of ICU-acquired weakness (ICU-AW), critical care professionals need to grasp this knowledge regarding the physiological process, symptomatic manifestations, and the long-term implications of this condition.(4) Associated with many who have been admitted into intensive care units (ICUs) worldwide across the world reach up to 25% to 31%. (5)

These individual differences could result from various reasons including age, gender, genetic conditions, and the course of underlying diseases as well as the kind of therapy employed. The elderly patients in the ICU who have complicated surgical cases indicate a significant number of them to be prone to ICU caused by muscle and strength loss.(2)

ICU-AW is a term that encapsulates critical illness polyneuropathy (CIP) and critical illness myopathy (CIM). However, newer understandings point to CIPNM as a reflection of the true underlying pathology. Such an acknowledgment is evidence that there are several features involved in its development, involving molecular-level phenomena such as local immune activation, and microcirculation impairment among others. (6)

Symmetric limb strength is compromised mainly at the proximal shoulder and hip joints with the respiratory muscles requiring much effort in breathing and talking. To characterize ICU-AW from ventilator-associated diaphragmatic dysfunction (VIDD) is important as they have different anatomy, physiology, and ways of diagnosis.(7)

ICU-AW legacy is beyond the acute phase of illness also, having other death point implications for mortality and morbidity. For the patients, there is a possibility of some difficulties when they are weaning off mechanical ventilation, muscle weakness, reduced reflexes, and less development of the muscle tissue.(8)

The assessment and diagnosis of ICU-acquired weakness (ICU-AW) may become a serious matter as there are no established criteria to clinically evaluate it. While the MRC scale, which is a widely used measure of sedation depth, has some drawbacks it cannot be used to assess the depth of sedation in unconscious patients because they are not able to be sufficiently alert or cooperative.(9) It has been clear that for such uncooperative patients, the method of assessing muscle function has been a limiting factor in the diagnosis of ICU-AW. This realization has led to several new strategies in this area of research.(1)

The MRI is replaced by ultrasound imaging and the test of twitch force responds to the magnetic nerve stimulation while the MRC score takes center stage. The use of such non-invasive techniques targeted to evaluate muscle degeneration is highly useful to pick those patients, who may be uncooperative. (10)

In addition to the above, EMG differentiates CIP from CIM, the main differential amputation in ICU-AW. Although EMG is a powerful tool, that can provide a solid collection of data, because of its being long and costly, it is not widely utilized in a medical professional’s practice. Nonetheless, if it is used along with the MRC score, EMG improves the diagnosis and helps physicians for the recognition of the problem during a patient evaluation.(11)

However, any biopsy of nerve or muscle tissues can only be done whenever a definitive diagnosis is needed. Both options are anesthesia-demanding but come with associated risks and rare complications. As a consequence, it is rarely performed mainly in select cases where other and more accurate diagnostic modality procedures are not conclusive or when selective pathological assessments are warranted.(12)

2. THE PATHOPHYSIOLOGY OF SOME OF THE COMMON FACTORS ASSOCIATED WITH ICU-ACQUIRED WEAKNESS

Within the ICU, several parameters affect the patient and can become life-threatening for them. For this very reason, the ICU nursing staff and doctors must be highly vigilant about each patient and they know how to deal with all sorts of risk factors in the best possible way to minimize the damage.

2.1 HYPERGLYCEMIA AND ITS IMPACT ON ICU-AW

Hyperglycemia, characterized by elevated blood glucose levels, is prevalent among critically ill patients and contributes to the development of ICU-acquired respiratory muscle weakness.

Excessive glucose accumulation under stress leads to exaggerated inflammatory responses, immune system imbalances, and mitochondrial damage. (13)

Hyperglycemia-induced metabolic disorders, oxidative stress, and neurotrophic factor deficiencies can result in peripheral neuropathies and vascular injuries, particularly in patients with pre-existing diabetes or hyperglycemia. (14)

Intensified insulin therapy targeting tight glycemic control has shown promise in reducing mechanical ventilation duration and hospital stay in ICU patients. However, the intricate relationship between hyperglycemia and ICU-AW underscores the need for further research to elucidate underlying mechanisms and optimize management strategies.(15)

2.2 MULTISYSTEM ORGAN FAILURE (MOF)

Multiple organ failure (MOF) is a complex clinical syndrome which exhibits impaired functioning of at least two organs through interrelated steps, mostly after critical infections, resuscitation, major surgery, or delivery complications. (8)

MOS implies a relatively big chance that ICU AW (ICU-AW) is developed when patients' bodies undergo organ failure for a long time. Sepsis and septic shock particularly account for a few things that make the mortality rate of intensivists-awful (ICU-AW), and more than 70% of patients who pursue their treatment in the intensive care units (ICUs) face the criterion. (16)

Mitochondrial dysfunction, hydrogen-based production, and more free radical generation during this process cause muscle loss in patients with MOF. For instance, conditions such as acute pancreatitis, multiple contusions, and cardiac arrest with non-septicemia syndrome) that are not sepsis but are present in ICU admission have been shown to lead to MOF and ICU-AW incidence, bringing the multi-causal nature of the condition to light.(17)

2.3. IMMOBILITY

Like long-term non-movement in seriously ill patients, bed immobility also plays a prominent role in the formation of ICU-AW. The patients laid in the bed will have poorer stimulations of the organs and the body parts, resulting in a cascade of negative effects such as joint contractures, pulmonary infections, bed sores, deep vein thrombosis, constipation, and muscle atrophy. (18)

Disuse atrophy is caused by a diminution of muscle mass, volume, and fiber cross-section area which is accompanied by a shift in muscle fiber type from type I to type II. The degree of muscle atrophy increases in line with the lengthened period of immobilizations and with the patient's age. In addition, it was found that lean muscle mass decreases drastically during space missions which could be attributed to both lack of exercise and even being in a microgravity environment. (19)

Muscle mass can drop by 1 % per day of being on bed rest for healthy people, which means that it decreases by 3.65 % per 1 week. Muscle breakdown and oxidative stress become just that much more pronounced with mitochondrial dysfunction and increased reactive oxygen species. (20)

Prompt rehabilitation interventions based on resistance exercises starting while a patient is in ICU standoff with preventing AW and reduction of mechanical ventilation duration. It does so when helping the patient to restore muscle quantity.(19)

2.4 NEUROMUSCULAR BLOCKING AGENTS (NMBAS)

NMBAs are commonly used in the intensive care unit (ICU) for various indications, including emergency intubation, acute respiratory distress syndrome (ARDS), status asthmaticus, elevated intracranial or intra-abdominal pressure, and therapeutic hypothermia following cardiac arrest. (21)

They can be classified as depolarizing (e.g., succinylcholine) or non-depolarizing (e.g., atracurium) agents based on their mechanisms of action at the neuromuscular junction (NMJ).

While NMBAs play an essential role in managing critical conditions, concerns have been raised regarding their association with ICU-acquired weakness (ICU-AW). (22)

Despite their potential benefits in improving oxygenation and reducing mortality in ARDS, the clinical use of NMBAs has diminished due to reports linking them to neuromuscular dysfunction and muscle atrophy resembling denervation treatment. (23)

However, the evidence surrounding this association remains controversial. Some researchers argue that the observed effects may be influenced by confounding factors, necessitating further evaluation to establish appropriate guidelines for NMBA use in the ICU setting.(24)

3. PROPOSED REHABILITATION TECHNIQUES FOR ICU-ACQUIRED WEAKNESS IN ICU PATIENTS

The proper implementation of vigorous rehabilitation programs as a part of severely ill patients' critical illness management, especially in those who experience prolonged mechanical ventilation (PMV), has been advocated in several studies. These researches were directed at evaluating the effectiveness of PT in producing better functional outcomes and making them wean from mechanical ventilation.(25)

An initial single-arm prospective study on the cases of 150 patients with ICU-acquired weakness (ICUAW), of which 69% received PMV, came up with remarkable improvements in walking ability, muscle strength, as assessed with Medical Research Council (MRC) scores and handgrip strength), gait speed, and 6-minute walk distance following the target. (26)

Furthermore, two cohort studies, one prospective and another retrospective, evaluated the imposed effect of mobility and strength exercises incorporated in the rehabilitation interventions on the results of ICU survivors on PMV. Both researches considered high weaning rates (74 percent to 100 percent), which are equivalent to the 87 percent achieved with the current standard treatment. This result highlights the positive role of rehabilitation strategies in enabling the successful outcome of ventilation withdrawal patients.(27)(28)

Nevertheless, three RCTs were conducted by researchers to test the efficacy of rehabilitation interventions on outcomes like weaning from mechanical ventilation and home discharge. (29)Conspicuously, results were not uniform, with rehabilitation rates ranging from 22% to 75% in the intervention group. Nevertheless, the studies involved strengthening exercises for both the upper and lower limb muscles, walked training, and respiratory assistance throughout the rehabilitation.(30)

The comprehensive ventilator dependency management for prolonged acute patients in Long-Term Acute Care Hospitals (LTACHs) which is multi-component includes many aspects of the patient's care and they are: pain, agitation, delirium, and muscle weakness. Interdisciplinary techniques must be quite impactful throughout the diagnostics, prevention, and management of these issues.(31)It can be inferred that rehabilitation therapy can be equally effective at all stages of the recovery process. This reflects on the key importance of ongoing rehabilitation efforts during the entire course of care of critically ill patients even as they are being treated in LTACHs for continued management.(32)

Through a combination of physical rehabilitation and training, MRP would therefore be just what these patients who depended on PMV in LTACHs for functional improvement and weaning from the ventilator. Thus, it becomes apparent that the main aim of patient care requires not only an acute recovery but also a long-term approach.(28)

CONCLUSION

Management of patients requiring prolonged mechanical ventilation (PMV) in long-term acute care hospitals (LTACH) requires a multifaceted approach that addresses pain, agitation, delirium, and weakness. Implementation of a multidisciplinary rehabilitation program combining progressive physical therapy and exercise is promising for improving outcomes in these patients.

The feasibility and potential effectiveness of such programs suggest that they may contribute to successful ventilator weaning and improved discharge rates from LTACH. It is important that the benefits of rehabilitation extend beyond the acute phase of the disease and have a positive impact on the late recovery phase of disabled elderly intensive care patients.

By incorporating rehabilitation therapy into the continuum of care for critically ill patients, including those transitioning to LTACH, healthcare providers can optimize functional outcomes and improve the overall quality of life for these patients. Continued research and implementation of multidisciplinary rehabilitation strategies are essential to improve care and outcomes for patients requiring her PMV in LTACH and similar settings.

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