ISSN: 1607-8322, e-ISSN: 2220-5799 Anaesthesia, Pain & Intensive Care
Vol 28(4); August 2024 DOI: 10.35975/apic.v28i4.2405

ORIGINAL RESEARCH INTENSIVE CARE

The effect of early neuromuscular electrical stimulation in intensive care unit-acquired weakness

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ABSTRACT

Background & objective: Intensive Care Unit-Acquired Weakness (ICU-AW) is a weakness found in critically ill patients, and this weakness can persist even after discharge from the Intensive Care Unit (ICU). Various rehabilitation medicine procedures have been shown to be effective in prevention as well as managing the established weakness in this cohort of the patients. We analyzed the effect of Neuromuscular Electrical Stimulation (NMES) therapy on the global muscle strength, quadriceps femoris muscle, and creatine kinase examination in patients known to have ICU-AW.

Methodology: The type of study used a pre-experimental one-group pre-posttest, and the study population consisted of 23 patients who experienced ICU-AW. Patients were given NMES therapy at the beginning of treatment in the ICU and then evaluated using the Medical Research Council Scale for Muscle Strength (MRC-SS), Manual Muscle Test (MMT), and creatine kinase levels.

Results: NMES therapy provides significant results on increasing muscle strength on the fifth day with MRC-SS 42.78 (24-60) and MMT 3.57 (2-5) ($P < 0.001$), as well as a significant decrease in creatine kinase levels given therapy at the beginning of ICU admission.

Conclusion: NMES therapy increases global muscle strength and quadriceps femoris muscle and decreases creatine kinase levels.

Abbreviations: ICU-AW - Intensive Care Unit-Acquired Weakness, NMES - Neuromuscular Electrical Stimulation, ICU - Intensive care unit, MRC-SS - Medical Research Council Scale for Muscle Strength, MMT - Manual Muscle Testing, CK-MM - Creatine kinase muscle specific

Key Words: Neuromuscular electrical stimulation; Intensive Care Unit-Acquired Weakness, Creatine kinase

Citation: Yustiawan A, Semedi BP, Arfianti L, Maulydia, Edwar PPM, Airlangga PS, Santoso KH, Andriana M. The effect of early neuromuscular electrical stimulation in intensive care unit-acquired weakness. Anaesth. pain intensive care 2024;28(4):706−711; **DOI:** 10.35975/apic.v28i4.2405

Received: March 04, 2024; **Reviewed:** April 29, 2024; **Accepted:** May 10, 2024

1. INTRODUCTION

The incidence of Intensive Care Unit-Acquired Weakness (ICU-AW) has adverse short-term and long-term consequences. The global prevalence of ICU-AW is estimated to be 25% - 85% in the ICU and approximately 36% after recovery.[1] ICU-AW is defined as frailty found in critically ill patients, which is the sole cause of the condition, and this frailty may persist until post-treatment from the ICU.[2] Patients who experience ICU-AW will impact length of stay, duration of mechanical ventilation, and mortality in the ICU and hospital. Some ICU-AW patients fully recover, but others may experience long-term weakness.[3] Prolonged weakness will lead to functional limitations and decreased quality of life. ICU-AW is associated with the severity of illness, duration of mechanical ventilation, sepsis, multiple organ failure, hyperglycemia, long-term immobilization, and length of ICU stay.[4,5]

Neuromuscular Electric Stimulation (NMES) is a form of physiotherapy that can be given to patients in the ICU, even early during critical illness. NMES devices provide a contraction effect on muscles that leads to functional recovery.[6] Several previous studies have shown that NMES positively impacts ICU-AW patients, which can effectively increase muscle strength and reduce ICU hospitalization.[7] NMES can be performed on patients who are uncooperative during physiotherapy due to sedation or decreased muscle strength and patients who perform exercises in passive, assisted, and active modes. NMES can be applied regardless of patient effort and produces muscle contractions in response to low-voltage electrical impulses generated externally through electrodes placed on the skin over the muscle bundle to be stimulated.[7,8]

Several biomarkers associated with musculoskeletal disorders include creatine kinase (CK). CK is primarily found in skeletal muscle and heart and small amounts in the brain and other tissues. Increased creatine kinase results are associated with damage, disorders, or other neuromuscular diseases. CK is divided into three isoenzymes, namely creatine kinase myocardial band (CK-MB), creatine kinase brain-specific (CK-BB), and muscle-specific creatine kinase (CK-MM). CK-MM type is most commonly found in the musculoskeletal system. CK-MM is essential in skeletal muscle damage and is a biomarker used to diagnose, assess, and monitor musculoskeletal disorders or diseases. It is also included in disease prognosis and treatment.[9]

Based on the differences in the results of NMES therapy in ICU-AW patients, this study aimed to determine the effect of the initial administration of NMES therapy on changes in creatinine kinase values, global muscle strength, and quadriceps femoris in ICU-AW patients.

2. METHODOLOGY

This study was approved by the ethics committee of Dr. Soetomo Hospital Surabaya. A total of 23 patients were enrolled in this study after obtaining written consent from each of them, and fulfilled the inclusion criteria; from April to December 2023. The inclusion criteria were treatment in the ICU for more than 48 h, age 18-60 y, and patients on ventilators for more than 24 h. Patients with neuromuscular disease, stroke, brain injury, spinal cord injury, body mass index more than 35 kg/m^2, peripheral vascular disease, motor paralysis before admission to the ICU, bone fractures in the extremities, leg edema, wounds in the electrode installation area, cognitive impairment, deep sedation, stiffness or spasticity of upper and lower limbs, and utilizing pacemaker devices were excluded.

The study hypothesized an increase in the global muscle strength and quadriceps femoris, and decrease in the creatine kinase level in patients with ICU-AW who receive NMES therapy. This study used pre-experimental with a one-group pretest-posttest design and sampling technique using consecutive sampling. Eligible patients underwent an initial examination by measuring Medical Research Council Scale for Muscle Strength (MRC-SS), and Manual Muscle Testing (MMT) and blood collection before being given NMES therapy; then, all patients were given NMES therapy every day until the fifth day. Patients were coded and recorded on the first, third, and fifth days.

The NMES device is an EMS EV-906 type, using rectangular symmetrical biphasic pulses. NMES is administered supine, and electrodes are placed on the right and left quadriceps femoris muscles. Besides that, the patient continues to undergo routine medical rehabilitation therapy. NMES therapy is given for five consecutive days. At the beginning of the session, a warm-up for 5 min is given for 30 min; after that, a recovery session for 5 min every day. The NMES setting

dose is given a frequency of 50 Hz, an amplitude of 350 microseconds, a contraction time of 10 sec, a time-out of 10 sec, and an intensity of 0-80 mA. The intensity is increased until the patient feels the sensation of muscle

contraction and feels comfortable according to the patient's tolerance, asked every 5 min. In addition, muscle contraction can be confirmed by observing and palpating the muscles that are being stimulated. During NMES administration, hemodynamic monitors such as blood pressure, heart rate, temperature, and oxygen saturation are monitored. The medical intensivist and rehabilitation physician record all data on the sheet provided and analyzed.

Table 1: ICU-AW patient demographic characteristics data

Characteristics	Total sample (n = 23)	Normality test (P-value)
Age (y)	50 (23-60)	0.010
Body Mass Index (kg/m$^{2)}$	24.4 ± 3.051	0.099
Ventilator duration (days)	3 (1-8)	< 0.001
Sedation duration (days)	1 (1-4)	< 0.001
Gender		
Male	9 (39.1%)	
Female	14 (60.9%)	

Shapiro-Wilk normality test; Data presented as median (min-max) or mean ± SD or n (%)

Statistical analysis

The collected data were recorded and tabulated. We used SPSS 26.0 software (SPSS Inc., Chicago, IL, USA). All demographic characteristics data (age, gender, etc.) were summarized using descriptive statistics. All the data measurements are presented as mean ± standard deviation or median (interquartile range). The data normality test used the Shapiro-Wilk test. Analysis of differences in muscle strength data on the first, third, and fifth days after NMES administration used Friedman and Wilcoxon sign rank tests. $P < 0.05$ indicates significant results. Analysis of creatine kinase levels using Mann-Whitney test.

3. RESULTS

A total of 23 patients were included in this study, aged 23-60 y, males 9 (39%) and females 14 (61%). Body mass index was 24.4 ± 3.051 kg/m^2, duration of ventilator use was 3 (1-8) days, and duration of sedation was 1 (1-4) days (Table 1).

The bivariate analysis results using the Friedman test measuring three times (day one, three, and five) showed a significant increase in global muscle strength and quadriceps femoris p-value < 0.001. Furthermore, to determine the relationship of measurements compared between the first, third, and fifth days with the Wilcoxon test, there was no decrease in the results of global muscle strength or quadriceps femoris (Table 2).

The relationship between the duration of mechanical ventilation use with global muscle strength and quadriceps femoris on the fifth day after NMES administration in patients experiencing ICU-AW with the Spearman test showed significant where patients who were given NMES therapy had more increased muscle strength and faster weaning to extubation (Table 3).

The CK-MM examination using the Mann-Whitney test obtained significant differences in CK-MM levels before and after NMES therapy with a value of $P < 0.05$, which can be seen in Table 4.

4. DISCUSSION

ICU-AW adversely affects short- and long-term outcomes; therefore, it is essential to understand its etiology and identify patients at the most significant risk of neuromuscular weakness.[5] Some effects of deep sedation are associated with a longer duration of mechanical ventilation, weaning time, and length of stay in the ICU, as well as increased mortality.[10] In addition to sedating medications, ICU-AW occurs in the presence

Table 2: MRC-SS and MMT measurements

Variables	N = 23			p-friedman	P-value		
	D1	D3	D5		D1 vs D 3	D1 vs D5	D3 vs D5
Global muscle (MRC-SS) Median (min-max)	34.4 (24-48)	40.17 (24-48)	42.78 (24-60)	< 0.001	0.002	< 0.001	0.025
Quadriceps Femoris (MMT) Median (min-max)	2.87 (2-4)	3.35 (2-4)	3.57 (2-5)	< 0.001	0.002	< 0.001	0.025

Friedman test day one, three, and five, significance level P < 0.05; Wilcoxon test all measurements significance level P < 0.05

Table 3: Duration of mechanical ventilation

Variables	Duration of mechanical ventilation	r
Global muscle D5	P < 0.001*	-0.709
Quadriceps femoris muscle	P < 0,001*	-0.709

Spearman test significant P < 0.05 with correlation coefficient (r) negative correlation direction

Table 4: CK-MM levels before and after NMES therapy

Variable	Mean ± SD) Median (min-max)	P-value
CK-MM pre NMES	113.74 (63.96 – 646.30)	0.026
CK-MM post NMES	111.48 ± 126.43	

Mann-Whitney test P < 0.05

of critical illnesses that induce metabolic responses.[11] Muscles are essential in the adaptive processing of amino acids, from increased proteolysis to gluconeogenesis and acute phase protein production by the liver. Peripheral resistance to anabolic signaling further exacerbates hyperglycemia and alters substrate availability in muscle.[12] The driving forces of this hypermetabolic response include sympathetic nervous system stimulation, inflammation, immobilization, and anterior pituitary hormone release. Malnutrition due to poor digestive and metabolic function can contribute to muscle shrinkage and the accompanying weakness in the acute stage of critical illness. Nutritional status is linked to weakness; starvation in a healthy person leads to loss of muscle mass, strength, and function.[13,14]

The production of various types of cytokines leads to degeneration of nerve conduction, microvascular hyperpermeability due to microvascular degeneration, and the production of neurotoxic agents.[15] In addition, muscle damage is directly affected by metabolic diseases, inflammatory changes, and loss of energy. In ICU-AW patients, skeletal muscles and the diaphragm can be affected.[16] Physiological differences in body composition, muscle strength, and energy metabolism may contribute to ICU-AW. In addition, it was found that the insulin sensitivity index was most impaired in critically ill women. More Sex-specific analysis adds evidence that critically ill women are more affected by decreased insulin sensitivity and, thus, more prone to reduced muscle mass.[17]

The Medical Research Council (MRC) is one of the most recognized and used instruments worldwide to assess peripheral muscle strength, the gold standard for diagnosing ICU-AW. This scale assesses the voluntary muscle strength of 6 muscle groups (shoulder abductors, elbow flexors, wrist extensors, hip flexors, knee extensors, and ankle dorsiflexors) on each side. MRC-SS muscle strength is assessed on 12 muscle groups. Summarized scores below 48 out of 60 indicate ICU-AW or significant weakness, and MRC-SS scores below 36 out of 48 show severe weakness.[18,19]

NMES is suggested as an intervention in critically ill patients who are admitted to the intensive care unit because the patient is in a state of decreased consciousness and is uncooperative.[20] NMES is a technique where tiny electrical impulses are applied to skeletal muscles to cause contraction when muscle contraction is difficult or impossible using the patient's efforts.[21] NMES can induce anabolic stimulus in critically ill patients. Hence, the use of NMES also needs to be combined with standard therapy in the ICU to get good results in reducing the length of hospitalization and increasing muscle strength.[22]

Systematic assessment of ICU-AW in the ICU using MRC-SS should be integrated daily into decision-making for extubation to identify high-risk patients and implement appropriate strategies in providing ventilatory support after extubation.[23,24]

Damage in musculoskeletal tissues can lead to increased levels of CK-MM in blood circulation. One of the biomarkers of muscle tissue damage can be found in CK-MM, which can be used as a marker for disease determination and prognosis. Increased serum CK-MM activity has been reported in critically ill patients with acquired myopathy, with a more pronounced increase in the necrotizing type of myopathy. However, serum creatine kinase's timeframe, sensitivity, and specificity still need to be well known.[25] This condition should be diagnosed by muscle biopsy, but CK-MM can be a good and more accessible alternative. CK-MM is generally considered an indicator of muscle damage and inflammatory response.[26]

5. LIMITATION

This study has heterogeneity in patient selection, which may affect the results of data analysis. Intervention modalities were not compared with comprehensive rehabilitation measures.

6. CONCLUSION

Neuromuscular electrical stimulation therapy increases global muscle strength and quadriceps femoris muscle and decreases creatine kinase levels in the ICU patients on ventilatory support.

7. Ethical considerations

This study was approved by the ethics committee of Dr. Soetomo Surabaya Hospital (0800/KEPK/X/2023). Written consent was obtained from all patients and/or families before being included in this study.

8. Availability of data

The datasets generated and analyzed during this study are available from the authors.

9. Conflict of interests

This study used only hospital resources; no external or industry funding was involved.

10. Acknowledgments

The authors would like to thank the manager of Dr. Soetomo Surabaya Hospital and the head of the ICU for their valuable contribution to data recording.

11. Authors' contributions

All authors contributed to data analysis, article preparation, and paper revision and have collectively assumed responsibility for all aspects of this work.

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