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Safety in application of neuromuscular electrical stimulation in critically ill patients: pilot study

Segurança na aplicação da eletroestimulação neuromuscular no doente crítico: estudo piloto

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RESUMO | INTRODUÇÃO: A Neuromuscular Electrical Stimulation (NMES) é um importante aliado do paciente crítico, favorecendo contrações ativas mesmo em estado que requer imobilidade. **OBJETIVO:** Verificar a segurança da aplicação da NMES em Unidades de Terapia Intensiva (UTIs) de um hospital público da cidade de Salvador. **MÉTODO:** Trata-se de estudo piloto, de intervenção. Os dados foram coletados no período de fevereiro a junho de 2018, com amostra por conveniência em uma população de pacientes críticos intubados e em uso de vasopressores. Foi aplicada uma única sessão de 45 minutos de NMES em ambos os quadríceps (músculo reto femoral e vasto lateral), sendo coletados os seguintes dados hemodinâmicos 5 minutos antes da aplicação e logo após a terapêutica: frequência cardíaca, pressão arterial sistólica, diastólica e média; e frequência respiratória. Estes dados foram avaliados seguindo recomendações de segurança já descritas previamente. Para análise estatística, as variáveis foram descritas através de médias e desvio-padrão, mediana e intervalo interquartílico e percentuais obtidos nas variáveis do estudo. A distribuição dos dados foi avaliada pelo teste Shapiro-Wilk, e os testes Mann Whitney e T de student foram utilizados. **RESULTADOS:** A amostra foi composta por 8 pacientes sendo 1 excluído. Destes, 85,7% era do sexo feminino, sendo o diagnóstico clínico de Sepse evoluindo para choque em 85,7%, média da idade de 61±9,5 anos e APACHE II de 29±5,5. Não foram evidenciadas diferenças estatísticas em relação aos dados hemodinâmicos coletados pré e pós eletroestimulação. Estes dados são semelhantes aos resultados encontrados por outros autores em populações sem uso de vasopressores. **CONCLUSÃO:** É possível sugerir que a aplicação da NMES no doente crítico em uso de vasopressores é uma técnica segura e viável desde que respeitando os limites estabelecidos e parâmetros corretos baseados em evidências.

PALAVRAS-CHAVE: Estimulação elétrica nervosa transcutânea. Metabolismo energético. Mobilização precoce. Unidades de terapia intensiva.

ABSTRACT | INTRODUCTION: Neuromuscular Electrical Stimulation (NMES) is an important ally of the critically ill patient, favoring active contractions even when in a state that requires immobility. **OBJECTIVE:** The objective of this study was to verify the safety of NMES application in Intensive Care Units (ICUs) of a public hospital in the city of Salvador. **MATERIAL AND METHODS:** This is a pilot, study of intervention. Data were collected from February to June 2018, having as population critically ill intubated patients using vasopressors. A single 45-minute NMES session was applied to both quadriceps (rectus femoris and vastus lateralis), and the following hemodynamic data were collected 5 minutes before application and soon after therapy: cardiac frequency, systolic, diastolic and medium blood pressure and respiratory frequency. Data were collected following security recommandations, described earlier. For statistical analysis, the variables were described by mean and standard deviation, median and interquartile interval and percentages obtained for the variables of the study. The distribution of data was evaluated by the Shapiro-Wilk test and Mann Whitney test and t test were used. **RESULTS:** The sample consisted of 8 patients, being 1 excluded. Of these, 85.7% were female, with a clinical diagnosis of Sepsis in 85.7%, mean age of 61±9.5 years and APACHE II of 29±5.5. No statistical differences were observed in relation to hemodynamic data collected before and after electrostimulation. These data are similar to those found by other authors in populations without vasopressors usage. **CONCLUSION:** It is possible to suggest that the application of NMES in critically ill patients using vasopressors is a safe and viable technique as long as respecting the established limits and correct evidence-based parameters.

KEYWORDS: Transcutaneous electric nerve stimulation. Energy metabolism. Early mobilizatio. Intensive care units.

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Introduction

The advance of medicine has provided numerous benefits in relation to the survival of critically ill patients. However, some of these patients experience negative effects from extended bed[1] rest periods. This situation is associated with immobility, which in turn has numerous adverse effects. Among them, generalized muscle weakness, which is caused not only by bed stasis, but also by sepsis, multiple organ failure, systemic inflammation, use of prolonged mechanical ventilation and medications such as neuromuscular blockers and corticoids[1,2].

Since the critically ill patient facing an acute situation is unable to perform any active mobilization, it is necessary to seek effective and safe alternatives to reduce this inertia and minimize the effects of immobility[3]. Given this fact, the Neuromuscular Electrical Stimulation (NMES) is an alternative for early prevention of muscle weakness acquired in the Intensive Care Unit (ICU) especially in critically ill patients requiring mechanical ventilation, sedation and vasoactive drugs[4,5].

The benefits of using this strategy have been previously described and proven by other researchers. Among them, these are highlighted: peripheral nerve regeneration, decreased muscle atrophy, change in muscle fiber conformation, and increased activity of oxidative enzymes[6,7]. Thus, these effects are achieved from a therapeutic electrical discharge in the local muscle fiber, which provides muscle contraction without changing the joint angle, generating an isometry. This type of muscle contraction results in the alteration of the individual's microcirculation, favoring mechanical obstruction of the muscular blood flow, causing accumulation of the metabolites produced during this contraction. In turn, this production results in muscle chemoreceptor excitation promoting a significant increase in sympathetic nerve activity leading to increased heart rate and increased vascular resistance that is associated with blood pressure[8].

Given the above data, regarding the benefits of NMES at the muscle level and its impact at the circulatory level, it is perceived the need to prove the safety of the technique application in critically ill patients, since this technique has results proven by previous studies impacting in outcomes related to reduction of mechanical ventilation time, early hospital discharge and prevention of the development of polyneuropathy in critically ill patients[4,5,7,10].

Therefore, from the observation of the positive effects of NMES, it is important to prove the safety of its application in critically ill patients. Thus, the objective of this study was to verify the safety of the applicability of neuromuscular electrostimulation and to determine if there are changes that substantially impact hemodynamics in critically ill patients admitted to ICUs of a public hospital in the city of Salvador.

This research was approved by the Research Ethics Committee of the Roberto Santos General Hospital, according to opinion n° 2,437410 and Certificate of Presentation for Ethical Consideration n°: 80977417.9.0000.5028. The anonymity and confidentiality of information was guaranteed to the research participants, and the family members were instructed to read and listen to the free and informed consent form that provided general information of the study and confirmed the voluntary participation of the patient in the research.

Inclusion criteria were established: having participation authorized by a family member or guardian, being aged between 18 and 75 years old; being on invasive mechanical ventilation, being on invasive blood pressure catheter, having an Acute Physiology and Chronic Health Evaluation (APACHE) II greater than or equal to 13; Richmond Agitation-Sedation Scale (RASS) ≤0; Positive End Expiratory Pressure (PEEP) ≤10 mmHg; Inspired fraction of oxygen≤60%; be at a limiting and stable dose for 1 hour before intervention of: Noradrenaline ≤ 0.2 µg / kg / min; Dobutamine ≤ 8 µg / kg / min; Inotropic ≤ 0.25 µg / kg / min[11,12].

Patients with pregnancy, brain death, pre-existing neuromuscular disease, lupus erythematosus, technical obstacles to implementing NMES such as bone fractures, end-stage malignancy, pacemaker, elevated cardiac enzymes (CK-MB > 16.0 U / L and Troponin I > 0.034 ng / mL), periodic hemodialysis, neuroprotective ventilation and intracranial pressure

measuring device, active hemorrhage, hemodynamic instability with Mean Arterial Pressure (MAP) outside the range of 65 to 110 mmHg, Systolic Blood Pressure (SBP) > 180 mmHg or < 90 mmHg, peripheral capillary oxygen saturation (SpO2) ≤90%; Respiratory Rate (RR)> 40 rpm, Heart Rate (HR)> 130 bpm 5, 11,13,14.

Hemodynamic measurements

Vital signs such as SBP, DBP, MAP, HR, RR were measured through a monitoring system available at the hospital. Patients had their vital signs evaluated throughout the procedure by safety criteria and these were recorded 5 minutes before and shortly after the protocol was applied.

Intervention Protocol

A single NMES intervention was performed using the Neurodyn III neuromuscular stimulator Ibramed® appliance for 45 minutes on both quadriceps, using 2 electrodes (5x5 cm) on each thigh. The electrodes were positioned according to the precepts of the electrotherapeutic application which is recommended the fixation of the negative pole in the motor point of the rectus femoris and the positive pole distally in the thigh prioritizing the myotendinous junction in order to optimize the propagation of the stimulus, using the technique known as "Myoenergetic", which places an electrode at the beginning of the muscular belly and another one from the same distal canal in the same muscle[4,5].

The parameters were used in the values already researched by other authors[4,5]: 50Hz frequency, 400μs pulse width, 6 seconds active time and 12 seconds rest time, the intensity was adjusted according to visible or palpable muscle contraction in the muscles mentioned.

Protocol Interruption Criteria: The intervention protocol would be interrupted if there were important events such as: 4% reduction in initial SpO2; 20% increase or decrease in MAP or leave the range between 65 and 110 mmHg, SBP > 180 mmHg; HR > 130 bpm and RR > 40 rpm13.14. In case it happened, the entire team would be deployed for patient safety and stability.

Statistical analysis

Continuous variables individually collected were grouped as mean, standard deviation, median and interquartile range, after which they were divided into moments before and after electrostimulation and compiled in a Microsoft Excel sheet. After that, the data were transferred to Bioestat 5.3 software, where the variables were expressed as mean and standard deviation, where the data distribution was normal, median and interquartile range for variables with asymmetric distribution and frequency measures for nominal variables.

To compare the results before and after NMES, the data distribution was initially evaluated using the Shapiro Wilk test and after this verification, T Student tests were used for variables with symmetrical distribution or Mann-Whitney for variables with asymmetric distribution, being defined the statistical significance through p value < 0.05.

Results

Eight patients were recruited for the study, but one was excluded for not having visible or palpable contraction. The largest distribution of patients was 85.7% of female, with clinical diagnosis (85.7%) as a whole due to Sepsis evolving to shock, mean age of 61 ± 9.5 years and APACHE of 29 ± 5, 5. According to data described in Table 1. All patients were using noradrenaline with safe criteria for mobilization.

Table 1. Population profile according to general characteristics. Salvador/BA, 2018

Variables	n=7	
Female (%)	6	85,7
Diagnostic		
Clinic (%)	6	85,7
Surgical (%)	1	14,3
Age, mean±SD		61 ± 9,5
APACHE II, mean±SD		29 ± 5,5

Legend: SD; Standard Deviation APACHE: Acute Physiology and Chronic Health Evaluation.

Table 2 shows the general description of the pre and post electrostimulation data. It is possible to observe through this distribution that the patients were in a threshold considered safe to perform the therapy, and there were no important changes to suspend the protocol.

Table 2. Individual distribution of variable data for each patient before and after electrostimulation. Salvador / BA, 2018

Patients	HR		SBP		DBP		MAP		RR	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
P1	105	106	116	135	59	72	78	93	18	24
P2	70	77	177	188	52	58	94	101	21	20
P3	77	79	120	118	60	60	80	79	18	18
P4	102	103	108	119	68	67	81	84	18	18
P5	96	98	125	122	74	72	91	89	17	17
P6	97	95	119	118	41	39	67	65	16	18
P7	105	95	107	96	62	60	77	72	30	31

Legend: HR: Heart Rate; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; MAP: Mean Arterial Pressure; RR: Respiratory Rate

Table 3 appoints values of mean, standard deviation, median and interquartile range, as well as the comparative tests used for each variable following the precepts of the Shapiro Wilk verification test. This table shows hemodynamic values with slight upward or downward variations, but without reaching statistical significance ($p > 0.05$).

Tabela 3. Comparison before and after hemodynamic variables - Salvador / BA, 2018

Variable	Pre		Post		P
	Mean±DP	Median (IQR)	Mean±DP	Median (IQR)	
HR		97(86,5-103,5)		95(87-100,5)	0,89*
DBP		60(55,5-65)		60(59-69,5)	0,84*
MAP		79(72-87)		84(68,5-92)	0,70*
SBP	124,6±24		119±28,8		0,81□
RR	19,7±4,8		20,9±5		0,67□

Legend: HR: Heart Rate; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; MAP: Mean Arterial Pressure; RF: Respiratory Rate; SD: Standard Deviation; IIQ: Interquartile Range; * Mann-Whitney test; □ T-student test

Discussion

According to the data collected in this study, NMES did not result in significant hemodynamic changes and there were no adjustments of vasoactive drugs in critically ill patients, making their use safe in this population. Thus, depending on the critical phase the patient is in - following the safety precepts of early mobilization - a program of muscle contraction activities can be initiated to minimize the damage caused by immobility[4-7,13,14].

Seeking an early interventionist strategy, Akar et al.[10] used NMES associated with active exercises in lung disease as early mobilization and identified a reduction in HR in this group, suggesting a reduction in cardiac work provided by NMES.

In contrast, Gerovasili et al.[5] found a significant increase in HR and SBP in critically ill patients, attributing these alterations to the activation of ergoreflexes and metaboreflex, generating an increase in sympathetic charge, which in turn results in changes in vascular resistance and cardiac work. However, in their study, a working relationship of 12 seconds of contraction to 6 seconds of relaxation was used, providing a shorter rest time with greater chance of muscle fatigue and alteration of microcirculation flow[8].

In another study, Segers et al.[3] sought to analyze hemodynamic changes and the quality of muscle contraction through NMES in patients with certain levels of edema and whether or not vasopressors were used. These authors did not find significant hemodynamic changes and suggested that the presence of edema, vasopressors and proinflammatory states, such as sepsis, may negatively impact muscle contraction.

Proinflammatory states may provide effects of hypermetabolism that triggers an increase in protein catabolism, resulting in cardiac and renal overload[15]. Nevertheless, in previous studies[5,16] there were reductions in inflammatory cytokine levels and increased release of progenitor endothelial cells - enhancing microcirculation and tissue regeneration - reaffirming the benefits of exercise through NMES. Even observing the advantages in the application, it is necessary to follow the safety criteria in the early mobilization of this critical population[11,12] so that the positive effects help in the recovery of the patients.

The results of this study are limited by the small number of the sample, but can be well tolerated as it is a case series that will serve as the basis for a larger study. However, a necessity of having more studies on the subject in the literature in order to influence early mobilization programs is noticed.

Conclusion

It was possible to show in this research that the application of neuromuscular electrostimulation in critically ill patients, provided that respecting the established limits and correct evidence-based parameters, is a safe and viable technique in the ICU, since no statistically significant differences were observed regarding the studied hemodynamic variables.

Author contributions

Pinto DS was responsible for writing, method design, data collection, and literature review. Duarte HB was responsible for critical content review, method design, data collection, organization and treatment, and literature review. Costta CA was responsible for the literature review, and data collection. Angels JLM was responsible for the critical review of the content, organization and treatment of the data and project supervision. Gaspar LC and Melo RL participated in the data collection and literature review. Menezes CS was responsible for the method design, literature review and critical review of the manuscript.

Competing interests

No financial, legal or political conflicts involving third parties (government, companies and private foundations, etc.) have been declared for any aspect of the work submitted (including but not limiting itself to grants and funding, advisory board membership, study design, preparation manuscript, statistical analysis, etc.).

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