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Use of microcurrent in muscle regeneration: integrative review

Abstract

Introduction: Muscle injuries are commonly found and controlled by endogenous muscle mechanisms. However, when this system fails, other interventions are necessary to accelerate the regeneration process and ensure the maintenance of functional capacity, including the application of microcurrent (MIC). Therefore, there is little evidence on the effects of MIC on muscle regeneration. Within this context, MIC therapy may be an alternative for the treatment of muscle-related injuries.

Objective: To synthesize the available scientific evidence on the effects and parameters of MIC used in the muscle regeneration process . Methodology: This is an integrative literature review study , where the search was conducted from January to October 2022, through the Scientific Electronic Library Online (Scielo), Latin American and Caribbean Literature (LILACS), and US National Library of Medicine National Institutes of Health (PubMed) databases , using the following keywords: microcurrent, muscle injury, muscle regeneration. The articles were selected based on the analysis of their titles, followed by their abstracts.

Results: After applying the eligibility criteria, 166 articles were found , of which 7 studies were selected for data extraction. The studies showed that application intensities of 10 to 50 µA , 50 to 100 µA , and 100 to 500 µA were more effective than therapies with higher intensities, above 1000 µA , and in a shorter time of 15 to 60 minutes.

Conclusion: The application of microcurrent proved effective in the muscle regeneration process, when applied at low intensities , between 10 and 50 µA and in a shorter time, for 60 minutes . However, further studies are needed to elucidate which ideal parameters and durations should be applied to better synthesize this statement.

Keywords: regeneration, electrical stimulation therapy, musculoskeletal system

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Introduction

The human body is composed of various organs, cells, tissues, and systems that, working together and in harmony, ensure its proper functioning, ensuring life and health. Among these structures, we have muscle tissue, which, coordinated by a system, is responsible for joining joint and bone structures and generating forces that enable movement. Therefore, it is a broad system that encompasses the entire body and performs multiple functions. Therefore, it is prone to various types of injuries, whether from traumatic episodes, overuse, sports injuries, or surgical procedures.[1-4]

Skeletal muscle, due to its intrinsic properties, has an enormous capacity to regenerate after an injury, but for this to occur in a coordinated manner and achieve a good result, several factors need to be triggered.

After an injury, several cells are attracted to the affected area.[5] In other words, an inflammatory response is initially activated, causing an increase in blood circulation and membrane permeability, where inflammatory cells are carried and diffused to the damaged site. Therefore, the muscle regeneration process involves a cascade of cellular actions and can be divided into an inflammatory phase, a satellite cell proliferation or differentiation phase, and a maturation phase.[6–9]

In the inflammatory phase, the first response is triggered by neutrophils, macrophages, and leukocytes, which initiate the initial phase of tissue repair. The early attraction of these cells, especially neutrophils, to the injured muscle is fundamental and indispensable, as they influence the activation of the main cells responsible for muscle tissue regeneration: satellite cells.[8,9,10-14]

Satellite cells are myogenic stem cells present on the surfaces of muscle fibers, just below the basal lamina, in a resting state.[7,14-16] When they receive information that there is muscle injury or degeneration, they are activated, leaving their quiescent state and proliferating, initiating the proliferation phase. In this phase, satellite cells co-express myogenic transcription factors such as PAX7 and MYOD, an important marker and regulator of myogenic impairment. Subsequently, these cells migrate to the affected area where they fuse with the damaged fibers, giving rise to myoblasts. After this junction, the cells differentiate into myocytes, which then fuse to give rise to the myotube and the maturation phase where the myofiber is formed and differentiated by centrally located nuclei.[1,9,13,17]

At the same time as the process of differentiation and proliferation of satellite cells occurs, daughter cells are formed and return to quiescence so that there is self-renewal of the same and thus a population of reserve cells is created in order to protect the regenerative capacity of the muscle.[9,14,18]

However, some factors can interfere in this process, directly impacting physiological muscle regeneration, such as aging, serious injuries and immobilization, which can cause failure in the activation and differentiation of essential cells during this process, thus generating impaired regeneration or a delay in it.[9,19]

If this complex physiological process fails or is delayed, other interventions become necessary to prevent this delay from being so

detrimental to the individual's recovery that it may result in future functional limitations and reduced quality of life. According to some studies, one such intervention is the application of microcurrent to the affected area.[20]

Microcurrent (MIC) or microcurrent neuromuscular electrical stimulation (MENS) is a low-intensity and subsensory electrical current , that is, it is below human sensations, and therefore does not cause pain or discomfort and does not induce muscle contraction, therefore, it has no adverse effects . It is used as one of the treatment resources employed in physiotherapy where the currents applied to the tissue are in the form of microamperes, that is, they are currents with extremely low intensity (<1mA), which differs from other electrotherapy current modalities.[21-24]

The application of microcurrent is quite effective in processes such as pain relief, tissue repair of skin lesions, such as ulcers, wounds, bedsores and burns, repair of ligament and tendon injuries and, currently, studies are being carried out on its effects on muscle regeneration.[25-30]

Studies show that the use of microcurrent in muscle regeneration is effective, as it can influence the activation of cellular processes, including proteins and satellite cells that are crucial in muscle tissue repair, making post-injury recovery faster and with satisfactory results.[21,23,31]

However, the effects and correct dosage that are effective in muscle regeneration are still unclear, and there is little evidence in the literature to support this thesis. However, it is necessary to further understand the effects of MIC on muscle tissue stimulation and regeneration, as well as to establish the ideal MIC parameters to define the best application protocols.[23,32,33]

Therefore, the study aims to identify, analyze and discuss current studies found, through database searches, on how microcurrent acts in the muscle regeneration process and what its effects are during this process.

Methodology

Integrative literature review study. This research method involves a broad approach to existing studies in the literature on a given subject, with the aim of facilitating thematic understanding and aiding in the clinical applicability of results. Thus, according to Whitemore and Knafl,[34] this review model consisted of five stages: 1) Elaboration and identification of the problem and guiding question; 2) Literature search stage using inclusion and exclusion criteria; 3) Analysis of data obtained through the literature search; 4) Presentation of the results found; 5) Integration and synthesis of the findings to form the review and synthesize the knowledge.[34-36]

Scientific Electronic Library Online (Scielo), Latin American and Caribbean Literature (Lilacs) and US National Library of Medicine databases . Institutes of Health (PubMed).

For the research and obtaining of the studies, the Health Sciences Descriptors (DeCS) were used, whose keywords used were: regeneration, satellite cells, muscle cells, fractures, orthopedic surgery, microcurrent/microcurrent neuromuscular electrical stimulation (MENS), ruptures, wounds, injuries, burns, immobilizations and atrophies in English and Portuguese, associated with Boolean operators (OR and AND). Studies published between 2014 and 2022 were considered.

To select the studies that would be used in this review, the following eligibility criteria were applied:

Inclusion criteria: Articles with randomized controlled clinical trial designs, uncontrolled studies, and review articles were selected. All included studies were applied to human and animal models;

Exclusion criteria: articles that were not available in full, duplicates, studies where the theme and abstract were not in line with the theme addressed in this review and studies that investigated the use of microcurrent in healing and tissue repair, but did not focus on muscle tissue regeneration, were excluded.

Results

After critical analysis of the data obtained, a total of 166 articles were found, of which only seven were included in this review because they met the inclusion criteria and were analyzed. The others were excluded because they did not specifically address the chosen topic, as shown in Figure 1 below.

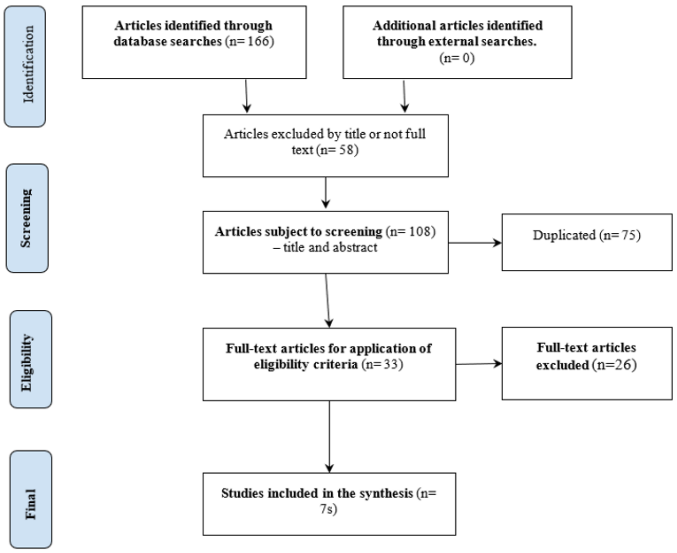

Figure 1 Steps followed during the integrative literature review.

Of the seven articles included, all were randomized controlled trials, with only one having other characteristics of a parallel, double-blind design. All were conducted abroad, and only one in Brazil. It was observed that most of the studies found (n=6) used animal models such as rabbits, mice, and rats, or cell cultures, and only one involved adult human males. The objectives of both studies were to investigate the influence of microcurrent on different types of muscle injuries, determining its effects at the tissue and cellular levels. Table 1 below presents the characteristics and design of the studies, with their respective target audiences.

Table 2 shows the main outcomes, methodology and instruments used in the studies obtained.

To evaluate the effects that the use of microcurrent can cause on muscle tissue at cellular levels, several parameters were tested, using different intensities.

Kwon, Suk and Kwon,[37] used alternating current with an intensity of 26 μA and a frequency of 8 Hz for 60 minutes for 2 weeks, in the gastrocnemius muscle region of New Zealand white rabbits after plaster immobilization, associated with injection of polydeoxyribonucleotide (PDRN) and the result obtained was that the microcurrent associated with PDRN was significantly more effective in muscle atrophy of the gastrocnemius muscle than both applied separately.

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Table 1 Study design and characteristics of the studied population

Author/ year	Type/characteristics	Location/space	Population characteristics	Objective of the study
Kwon et a.[37]	Randomized controlled trial	Daegu Federal University College of Medicine	Zealand and White rabbits	To evaluate how PDRN and MENS acted in a rabbit model with atrophied calf muscle immobilized by plaster.
Bravo et al.[38]	Randomized controlled trial	Londrina, Brazil	L929 fibroblast cells	To analyze the effects of microcurrent application at different intensities in the culture of L929 fibroblast cells.
Ohno et al.[31]	Randomized controlled trial	Japan	Mouse myoblast C2C12 cell culture plates	Investigate the effects of MENS on muscle protein content
Fujiya et al.[23]	Randomized controlled trial.	Toyohashi University SOZO	7-week-old male mice	Investigate the effect of MENS on the regenerative process of injured muscle
Park.[39]	Randomized controlled trial.	Catholic University of Daegu .	New Zealand White Rabbits	To investigate the regenerative effect of MENS on gastrocnemius atrophy induced by immobilization in rabbits.
Zickri.[22]	Randomized controlled trial.	Cairo University Faculty of Medicine, Egypt	Male albino rats	To investigate the relationship between MIC and local stem cells in the regeneration of muscle injury induced in albino rats.
Naclerio et al.[40]	Randomized controlled trial/ Parallel/Double blind	University of Helsinki, USA	Men between 18 and 45 years old	To compare the effects of resistance training in combination with MIC or sham training on body composition and muscle architecture.

Caption: PDRN, polydeoxyribonucleotide; MENS, microcurrent electrical neuromuscular stimulation; MIC, microcurrent; USA, united states of america

Table 2 Methods, instruments used and main outcomes.

Author/year	Procedures	Variables studied	Microcurrent parameters	Main outcomes
Kwon; Suk; Kwon.[37]	Saline injection PDRN injection Microcurrent application PDRN + MIC Injection	Right calf circumference; right tibial nerve CMAP amplitude; medial and lateral GCM thickness	Single square pulse alternating current of 26 μA , frequency of 8 Hz for 60 minutes/2 weeks	PDRN + MIC effective in the treatment of atrophy
Bravo et al.[38]	Application of MIC in L929 cells grown in six-well plates	Application of MIC in the cell well with an electrode attached to the paper cone (M1) and directly in the well (M2)	G60: intensity of 60 μA; G100: intensity of 100 μA ; G500: intensity of 500 μA and G900: intensity of 900 μA, both at a frequency of 600 Hz for 3 min.	There were no significant differences in any of the MIC intensities; Fibroblastic cells were dispersed and exhibited typical elongation.
Ohno et al.[31]	Application of MIC in C2C12 cells grown in six-well plates	Effect of MENS on protein content in C2C12 myotubes (experiment 1) and its effect on intracellular signals in C2C12 myotubes (experiment 2)	Intensity 10 or 20 μA, duration: 0-120 min. (experiment 1) Intensity of 10 μA for 60 min. (experiment 2), both with a frequency of 0.3 Hz, pulse width of 250 ms.	MENS had a stimulating effect on the muscle protein content of myotubes
Fujiya et al.[23]	Cardiotoxin injection + MENS treatment	Muscle weight, muscle protein content, mean fiber cross-sectional areas, relative percentage of fibers with central nuclei, and number of muscle satellite cells	Intensity of 10 μA, frequency of 0.3 Hz and pulse width of 250 ms for 60 min.	There was no significant effect on body weight, TA with many regenerating fibers, increased cross-sectional area, and the percentage of fibers with central nuclei.
Park[39]	Application of MIC after plaster removal	Calf circumference; anterior tibial nerve CMAP; GCM thickness	Single-phase regular pulse alternating current with an intensity of 25 μA (group 2) and 5,000 μA (group 3), for 60 min. and sham MIC for 2 weeks.	Group 2 showed significant atrophic and cross-sectional area changes Lower intensities are more effective than high intensities

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Table 2 Continued....

Zickri.[22]	Application of MIC in rats subjected to soleus muscle injury	Histological, immunohistochemical and morphometric studies for analysis of cells and fiber area	Intensity of 100 µA, frequency of 10 Hz for 20 min. (group M) Group S did not suffer any injury and group I did not undergo any treatment	Few atypical fibers and partial loss of striations were evidenced in groups M
Naclerio et al.[40]	Familiarization, assessment, body composition, muscle architecture, performance, DOMS measurement, dietary monitoring, training protocol and intervention	Body composition, muscle architecture, performance and DOMS + MIC Pre and post intervention	Complex pulsed wave, with a frequency of 1.0309 kHz, intensity between 50 and 400 µA , in a 2:1 ratio with 2 cycles for 45 min (3h total)	There were no significant differences in body composition and performance; Significant reduction in DOMS, increased pennation angle and improved muscle architecture

Caption: PDRN, polydeoxyribonucleotide; MENS, microcurrent electrical neuromuscular stimulation; MIC, microcurrent; CMAP, compound muscle action potential; GCM, Gastrocnemius; microampere; DOMS, delayed onset muscle soreness; TA, tibialis anterior

Bravo et al.[38] used an intensity of 60 µA, 100 µA , 500 µA and 900 µA, both with a frequency of 600 Hz, which were applied to cultured cell plates once a day, for 3 days and the main outcome obtained was that despite there being no significant differences between the current intensities, it was possible to conclude that in just two microcurrent applications it was possible to observe an increase in cell proliferation and in the modulation of the inflammatory response, thus aiding muscle regeneration.

Ohno et al.[31] in turn, performed two experiments with different intensities and times, the first being an intensity of 10 µA or 20 µA , lasting from 0 to 120 minutes, while in experiment 2 the intensity applied was 10 µA for 60 minutes, both with a frequency of 0.3 Hz and a pulse width of 250 milliseconds , in a mouse myoblast C2C12 cell culture system. In this study, the main outcome obtained was that the microcurrent stimulated an increase in muscle protein content.

Already Fujiya et al.[23] applied an intensity of 10 µA, with a frequency of 0.3 Hz and a pulse width of 250 ms for 60 minutes, in the region of the tibialis anterior of the left hind limb of male mice forty-eight hours after induction of muscle injury through an injection of cardiotoxin , and the results obtained were an increase in protein content, dry muscle weight and cross-sectional area, in addition to an increase in the number of satellite cells positive for Pax 7.

Park, Kwon and Moon[39] used a monophasic regular pulse alternating current with an intensity of 25 µA (group 2) and 5,000 µA (group 3) for 60 minutes during 2 weeks, applied to the gastrocnemius muscle of rabbits after plaster removal and the result obtained was that the application of low intensity microcurrent can be more effective than a high intensity.

Zickri[22] applied an intensity of 100 µA, with a frequency of 10 Hz for 20 minutes, in the gastrocnemius and soleus muscle region of male albino rats, which were subjected to muscle injury and after analyzing the findings, they concluded that the application of microcurrent can be quite effective in the regeneration of a skeletal muscle injury.

Finally, Naclerio etal.[40] used in their study a complex pulsed wave, with a frequency of 1.0309 kHz, intensity between 50 and 400 µA, in a 2:1 ratio with 2 cycles for 45 min (3 h total), which was self-administered after a resistance training program in men with 2 years of experience for this type of training for 8 weeks. The training sessions were performed 3 times a week and the microcurrent was applied pre- and post - intervention. Thus the results obtained were that although there were no significant differences in body composition and performance, there was a change in muscle architecture, with an increase in the pennation angle of the studied muscles and delayed-onset muscle soreness (DOMS).

As mentioned previously, intensity can directly impact the effect of microcurrent. Therefore, Graph 1 analyzes the time variables as a function of intensity, where, for each intensity, the application occurred at different times. That is, at intensities from 10 to 50 µA , six studies (n=6) used applications lasting 60 minutes (n=4); from 0 to 120 minutes (n=1); and for 45 minutes (n=1). At intensities between 50 and 100 µA, the microcurrent was applied for 20 minutes (n=1); for 45 minutes (n=1), and for 3 minutes (n=1). At intensities between 100 and 500 µA, the application time was 60 minutes (n=1); 20 minutes (n=1); 45 minutes (n=1) and 3 minutes (n=1), while with an intensity of 500 to 1000 the time used was 3 minutes and, above 1000 the application lasted 60 minutes.

Discussion

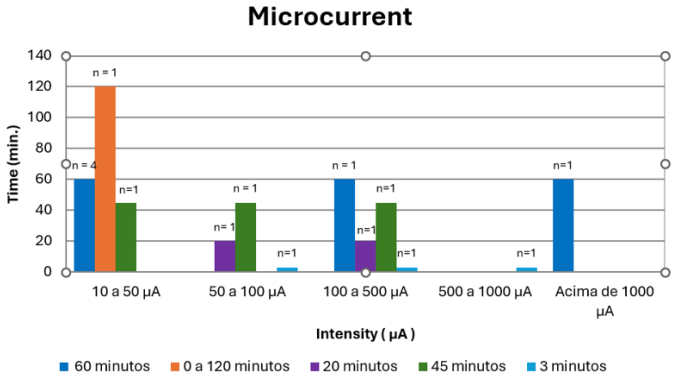
The evidence found in the literature on the role of microcurrent in the muscle regeneration process and its effects during this process, which the present study aimed to analyze, suggested that the application of microcurrent can assist and significantly influence the muscle regeneration process after an injury.

Kwon, Suk and Kwon (2022), in their study, used the application of microcurrent associated with the injection of polydeoxyribonucleotide , which is a drug created by a mixture of deoxyribonucleotides with a chain of approximately 50 to 2,000 base pairs, where, according to Kwon and Moon;[41] Ruy et al.[42] and Yoon et al.[43] it can assist in the process of tendon regeneration and tendinopathy, due to its anti-inflammatory characteristics and its influence on angiogenesis, which justifies its effectiveness in the repair of muscle injuries when associated with microcurrent.

In studies by Bravo et al.[38] Ohno et al.[31] Fujiya et al.[23] and Zickri,[22] in which they used intensities between 10 µA , 20 µA , 60 µA , 100 µA , 500 µA and 900 µA , in turn, the application of microcurrent influenced the synthesis and proliferation of cells and proteins that participate and are essential in the repair of muscle tissue, among them, satellite cells. This fact is justified by the studies of Ohno et al,[44] Cheng et al.[45] and Junior Passarini et al.[46] in which they used different current intensities and concluded that MIC mimics the endogenous action potentials of cells, causing them to be attracted to the site of injury, since the physiological repair capacity is impaired.

According to some studies, to achieve these electrical potentials and cause a satisfactory effect, the ideal intensity must be measured. Therefore, Park, Kwon, and Moon[39] conducted two experiments using

different current intensities, one of 25 µA and the other of 5,000 µA , to compare their effects on the regeneration process. The conclusion was that the application of MIC at a low intensity (25 µA) was more effective than at a high intensity (5,000 µA). Other findings such as those by Kwon and Moon (2019), who used an intensity of 25 µA in the repair of rotator cuff tears; Cheng et al.[45] who applied an intensity of 1 to 30,000 µA to the skin of rats; and Lin et al.[32] with application of intensities between 0 µA , 50 µA , 100 µA , 500 µA , 1000 µA and 1500 µA in equine tenocyte culture , values similar to those found in the present study (graph 1), support the hypothesis that the lower the intensity, the greater the repair effect.



Graph 1 below shows the parameters used by the studies included in this review, with the variables intensity and time.

However, when very high intensities are applied and exceed approximately 1000 µA , according to Cheng et al.[45] therapeutic effects, such as protein synthesis and the generation of adenosine triphosphate (ATP), are reduced or even reversed, as they can cause protein denaturation. ATP is a fundamental factor in the tissue repair process and is used as a major source of cellular energy. With a large influx of ATP, greater control of primary cell functions is required , such as the entry and exit of mineral salts (sodium , potassium , magnesium , and calcium transport), thus favoring healing and tissue regeneration. Thus, currents of up to 500 µA increase ATP synthesis, and active transport of amino acids increases protein synthesis by 40%.[45]

In summary, the clinical applicability of microcurrent depends on the established intensity and the number of applications.[32] Furthermore, the application time can influence protein synthesis . In the study by Ohno et al.[31] when MIC was applied at an intensity of 10 µA for 15 or 60 minutes in a mouse cell culture, a significant increase in the proportion of myotube proteins was observed , as was the case when an intensity of 20 µA was used for 15 to 30 minutes. However, when it was applied for 120 or 60 minutes with intensities of 10 µA or 20 µA , there was no impact on this protein proportion. However, no studies were found to justify this intensity versus duration hypothesis.

In addition to these findings, Naclerio et al.[40] sought to demonstrate in their study the effectiveness of microcurrent before and after resistance training, using intensities between 50 and 400 µA , and concluded that MIC can help increase muscle thickness and reduce DOMS, a mechanism that can be triggered by muscle damage. Although this factor seems obvious after high-intensity exercise, Ohno et al.[44] and Curtis et al.[47] explain that MIC can maximize the effects of exercise and reduce DOMS due to its direct influence on the excitability of muscle membranes and its characteristics of being painless and not causing muscle contraction, which leads to increased protein synthesis and consequently faster recovery.

Finally, Zickri[22] and Fujiya et al.[23] who analyzed the area and arrangement of muscle fibers after the application of MIC on induced muscle injury, found that the cross-sectional area was increased with the presence of more regular fibers and centralized nuclei. This suggests, according to Chargé and Rudnick[11] and Morioka et al.[48] which is indicative of muscle regeneration.

However, there is still a significant shortage of studies available in the databases specifically reporting on muscle regeneration and discussing the ideal application parameters that will provide the most reliable results. Therefore, further studies on this therapy are needed to establish a consensus and a protocol for better clinical applicability.[30,49,50]

Conclusion

In conclusion, the application of microcurrent to injured areas has proven effective in muscle regeneration, as it acts at the cellular level, attracting cells, especially satellite cells, and influencing protein synthesis. This is due to its similarity to the physiological electricity of cells. It can increase the flow of endogenous current, allowing the affected area to recover its capacitance and enhance the regenerative process when applied at lower intensities and times , between 10 and 50 µA for 60 minutes . However, further studies are needed to elucidate the ideal parameters and durations to better support this assertion.

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None.

Conflicts of interest

Authors declare that there is no conflict of interest.

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