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ROLE OF BIOMATERIALS IN CARDIAC REPAIR AND REGENERATION: THERAPEUTIC INTERVENTION FOR MYOCARDIAL INFARCTION

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Abstract: Objective: To evaluate the current status and recent advances in cardiac tissue engineering for the treatment of myocardial infarction, focusing on manufacturing methods, therapeutic efficacy, challenges and potentials for cardiac tissue regeneration and restoration of cardiac function. Methodology: Bibliographic review conducted using the PubMed database. Search terms included "myocardial infarction", "treatment", "tissue engineering", "regenerative medicine", "biomaterials", "bioimpression", "scaffolds", "stem cells" via search strategy: (myocardial infarction) AND (treatment) AND (tissue engineering) OR (regenerative medicine) OR (biomaterials) OR (bioimpression) OR (scaffolds) OR (stem cells). A total of 26 articles were selected for detailed analysis after applying the selection criteria. Review: The benefit of using tissue engineering to recover cardiac function after AMI was demonstrated. Several techniques were detailed within the selected articles, among them the use of stem cells, which had an important response to improving electrical conductivity and restoring cardiac function, but with the risk of predisposing arrhythmias and tumors, in contrast, the use of acellular electroconductive biomaterials showed have responses as favorable as the use of stem cells, and with less risk for the patient. Final Considerations: Post-MI patients suffer from high cardiac morbidity, loss of function and irreversible injuries. Tissue engineering using stem cells or biomaterials is proving to be a promising means of treating this complication caused by AMI. More studies are still needed to stratify the best technique taking into consideration, the resolution of the problem and less risk for the patient.

Keywords: Myocardial infarction, tissue engineering, biomaterials, stem cells.

INTRODUCTION

Cardiovascular diseases are one of the main causes of death globally, with acute myocardial infarction (AMI) contributing significantly to this scenario. AMI results in myocardial necrosis and, given the regenerative incapacity of myocardial cells, there is a significant cardiac functional loss due to tissue scars that form after the injury (Tajabadi et al., 2022; Saito et al., 2023).

Several regenerative therapies using different types of cells, such as mesenchymal stem cells, cardiac stem cells and pluripotent stem cells, have demonstrated benefits in the treatment of AMI (Smagul et al., 2020; Bolli et al., 2022; Sun et al., 2023). However, according to Zhu et al. (2021), despite their high efficacy, these therapies are challenging to apply to the heart, due to their high cost and invasiveness. In response to these challenges, other methods such as therapeutic cardiac patches are being explored. Currently, therapies for myocardial restoration are focused on both exogenous cell transplantation and endogenous regeneration, stimulating the differentiation of multipotent cardiac stem cells through growth factors, extracellular vesicles and miRNAs (Gil-Cabrerizo et al., 2021; Bolli et al., 2022). Other approaches include the use of biocompatible hydrogels implanted in the pericardial cavity, which allow the continuous release of substances that benefit cardiac repair (Zhu et al., 2021; Saito et al., 2023; Sun et al., 2023; Zheng et al., 2021).

Given the diverse treatment possibilities for the recovery of the mechanical and electrophysiological functions of the heart, it is crucial to evaluate the current state and recent advances in cardiac tissue engineering. This field encompasses manufacturing methods, therapeutic efficacy, challenges, and potentials for cardiac tissue regeneration and restoration of cardiac function. It is observed that AMI is a preponderant cause of mortality, representing a significant threat to public health.

In this context, interventional therapies, particularly those based on biomaterials, are being intensely studied. These biomaterials not only provide a favorable environment for cell growth, but also promote cell regeneration and differentiation through therapeutic factors (Wang et al., 2023). Faced with this scenario, the objective of the present study is to evaluate the current state and recent advances in cardiac tissue engineering for the treatment of myocardial infarction, focusing on manufacturing methods, therapeutic efficacy, challenges and potential for cardiac tissue regeneration and restoration of heart function.

METHODOLOGY

The bibliographic review developed according to the criteria of the PVO strategy, an acronym that represents: population or research problem, variables and outcome. Used to develop the research through its guiding question: “How can cardiac tissue engineering be applied in the treatment of myocardial infarction to improve cardiac function and reduce morbidity?”. The searches were carried out through searches in the PubMed - MEDLINE (Medical Literature Analysis and Retrieval System Online) database. The search terms were used in combination with the Boolean terms “AND” and “OR” through the following search strategy: (myocardial infarction) AND (treatment) AND (tissue engineering) OR (regenerative medicine) OR (biomaterials) OR (bioimpression) OR (scaffolds) OR (stem cells). From this search, 2037 articles were found, subsequently submitted to the selection criteria. The inclusion criteria were: articles published in the period from 2019 to 2024 and that addressed the issues. themes proposed for this research, studies such as literature review, systematic review, meta-analysis, observational studies, experimental studies and clinical trials, available in full. The exclusion criteria were: duplicate articles, available in abstract form, which were not available. directly addressed the proposal studied and did not meet the other inclusion criteria. After applying the search strategy in the searched database, a total of 2037 articles were found. After applying the inclusion and exclusion criteria, 26 articles were selected to form the collection of this study.

DISCUSSION

The biomaterials play a crucial role by offering a controlled and sustained release of growth factors and cytokines, making them an essential tool to overcome challenges associated with repairing necrotic cardiac tissue and preventing adverse ventricular remodeling post-myocardial infarction (MI), (Smagul et al., 2020). The research highlighted by Shilo et al. (2021) highlights the potential of biomaterials enriched with growth factors/cytokines and stem cells to facilitate cardiac tissue regeneration, pointing out the challenges of direct administration of growth factors and the importance of controlled delivery by biomaterials.

On the other hand, Gil-Cabrerizo, Scacchetti, Garbayo and Blanco-Prieto (2021) explore therapeutic strategies, both exogenous and endogenous, to promote the regeneration of damaged myocardium, highlighting the inability to regenerate cardiac tissue under physiological conditions and the need of therapeutic interventions to increase the proliferation and differentiation of resident cardiac stem cells.

These studies collectively highlight the importance of continued research and development of innovative approaches to treat AMI and improve clinical outcomes in patients with cardiovascular disease (Abouleisa et al., 2022). Significant advances in cardiac therapy include the use of hydrogel-encapsulated cardiac implants with gold nanoparticles, which show promise for treating myocardial infarction and other cardiac conditions (Shilo et al., 2021; Pan et al., 2021; Zheng et al., 2021; al., 2021). The ability of these implants to reduce the accumulation of reactive oxygen species (ROS), preserve cardiac tissue morphology, and improve cardiac function after infarction represents an innovative approach, although it is essential to discuss the challenges associated with their long-term effectiveness, including safety issues and the need for more robust clinical studies to gain a deeper understanding of the mechanisms underlying its therapeutic action.

Furthermore, the use of bone marrow-derived progenitor cells is a promising alternative approach for post-infarction cardiac repair. Although the results of clinical studies have been mixed regarding the improvement of cardiac function, intracoronary administration of these cells is considered a promising technique, despite limitations such as the possible low retention of the infused cells (Peregud-Pogorzelska et al., 2020). Better understanding the mechanisms by which these cells contribute to cardiac repair and improving delivery strategies are essential to maximizing their clinical efficacy. Comparison of these therapeutic approaches illustrates the complexity of treating myocardial infarction and emphasizes the importance of a multidisciplinary and innovative approach to address this significant medical challenge.

Cardiac tissue engineering has stood out especially in the use of Biomaterials and Scaffoldings for treatment and myocardial regeneration after AMI. Recent research, such as that by Beleño Acosta, Advincula, and Grande-Tovar (2023), shows that biomaterial scaffolds can not only promote cardiac restoration and improvement of the heart's electrical conductivity, but also stimulate stem cell differentiation. This highlights the relevance of discussing progress in myocardial repair, including the use of cardiac adhesives and scaffoldings based on biopolymers and conductive biomaterials (Dai; Mu; Zhou, 2021).

The development of cardiac patches through decellularized placenta (BCP) bioengineering represents an innovative technique with potential for myocardial restoration. Studies indicate that BCP, derived from decellularized rat placenta, facilitates the maturation of cardiomyocytes generated from human induced pluripotent stem cells (hiPSC-CMs), thanks to the pro-angiogenic and growth factors contained therein (Yeung et al., 2023; Jiang et al., 2021).

Patino-Guerrero et al. (2020) complement this by suggesting that the use of decellularized placenta (DP) as a natural support for BCP using hiPSC-CMs can offer paracrine and pro-angiogenic benefits, essential for myocardial repair and reducing the size of the infarcted area. In line with this position, Jiang et al. (2021) propose a bioengineered adhesive graft using decellularized placenta and stem cells, observing the development of pro-angiogenic factors that improve graft survival and stimulate paracrine secretion.

Esmaeili et al. (2022) point out that although cell therapies have shown beneficial effects, concerns about the maturation of injected cardiomyocytes, potential immunological rejection and tumor formation must be considered. A promising alternative is the use of electroconductive acellular biomaterials, such as gold nanoparticles, carbon-based nanomaterials or electroconductive polymers (Shi et al., 2022; Yin et al., 2023). These materials can regenerate the ischemic area by maintaining and propagating electrical conductivity in cardiac tissue, offering a safe solution compared to stem cell-based therapies (Pan et al., 2021; Shi et al., 2022). The integration of acellular electroconductive structures, whether through injection or implantation, is an innovative approach in myocardial repair (Dai; Mu; Zhou, 2021).

Raziyeva et al. (2020) highlight that treatment with multipotent adult stem cells (MSCs) has shown promising results in the regeneration of cardiac tissue. Interestingly, the benefit arises not from the differentiation of these cells into cardiomyocytes, but rather from their paracrine ability to release trophic factors that activate the resident cells of the cardiac tissue. Opposing this point, Ostovaneh et al. (2021) report that, although the use of stem cells from the ALLSTAR study did not significantly increase the left ventricular ejection fraction, they benefit the circumferential deformation of the left ventricle, a crucial factor associated with mortality and hospitalizations after a myocardial infarction.

Additionally, Guo et al. (2020) criticize the direct in situ injection technique used in the ALLSTAR study, as it presents risks of graft aggregation and necrosis, suggesting the use of cell sheet technology that has been shown to improve angiogenesis and ejection fraction. In turn, Soma et al. report that stem cell patches, when electromechanically stimulated, may be more successful than in situ injection, despite presenting high risks of arrhythmias due to differences in electrical properties between the myocardium and the patch. Sadahiro (2019) warns of the risks associated with allogeneic pluripotent stem cell therapy, including arrhythmias and tumor formation, suggesting that stimulating the conversion of resident fibroblasts into cardiomyocytes may be a safer approach.

Finally, Peregud-Pogorzelska et al. highlight that cell administration via catheter in the coronary artery affected by the infarction reduced the levels of biomarkers such as BNP, CK-MB and Troponins, and increased the left ventricular ejection fraction by 10%, pointing to the effectiveness of this method in recently ischemiated patients., in contrast to the ALLSTAR study, which required a minimum post-infarction interval of four weeks for patient inclusion.

FINAL CONSIDERATIONS

The AMI is an important cause of cardiac morbidity worldwide, leading to irreversible consequences for the heart. As a result, several studies report the use of cardiac tissue engineering, through biomaterials, as promising treatments for the recovery of cardiac function and the reversibility of the sequelae caused by AMI. There are several documented strategies, from the use of stem cells, cardiac implants encapsulated in hydrogel with gold nanoparticles, cardiac patches made from bioengineering decellularized placenta, scaffoldings, among others. Some authors indicate the need to carry out more studies using stem cells, which although they have beneficial results with an improvement in the left ventricular ejection fraction and good cardiac remodeling, there are still risks of arrhythmias, tumor formation, and graft necrosis. In order to overcome such risks, some studies present as an alternative the use of cardiac implants encapsulated in hydrogel with gold nanoparticles or the use of scaffoldings, which showed positive results regarding the restoration of the necrotic cardiac area, increased electrical conductivity and stimulation of differentiation. of stem cells, in addition to being safer when compared to the use of stem cells. It is still necessary to carry out more experimental and interventional studies on each technique, mainly comparing their effectiveness and safety in order to determine the clinical feasibility and safety of large-scale use of this promising technology in the area of post-AMI cardiac recovery.

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