

Current perspectives on the use of stem cells in plastic surgery

Perspectivas atuais sobre o uso de células tronco na cirurgia plástica

Perspectivas actuales sobre el uso de células madre en cirugía plástica

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Abstract

Adult stem cells, especially mesenchymal ones, have the ability to multiply and differentiate into other tissues, which is promising when dealing with the area of cell therapy. Furthermore, stem cells derived from adipose tissue (ASCs), which are multipotent and have the ability to differentiate into mesenchymal cells, are highly efficient in repair and aesthetic surgeries, mainly due to their high healing process, as they have anti-inflammatory effects. -inflammatory and immunosuppressive. In addition, adipose tissue presents itself as the best way to deal with this subject, as it has minimal morbidity and has high capacity for in vitro cell production. Despite being a great advance in aesthetic and restorative medicine, there are controversies regarding the use of this procedure, such as the safety of the material used. Thus, more comprehensive studies with scientific evidence are still needed.

Keywords: Stem cells; Plastic surgery; Graft.

Resumo

As células-tronco adultas, principalmente as mesenquimais possuem a capacidade de se multiplicarem e de se diferenciarem em outros tecidos, o que é promissor ao se tratar da área de terapia celular. Ademais, as células-tronco derivadas do tecido adiposo (ASCs), que são multipotentes e que possuem capacidade de diferenciação

em mesenquimais, apresentam alta eficiência em cirurgias de reparos e estéticas, principalmente, devido ao seu alto processo de cicatrização, pois apresentam efeitos anti-inflamatórios e imunossupressor. Além disso, o tecido adiposo apresenta-se como a melhor forma ao se tratar desse assunto, pois apresenta mínima morbidade e possui alta capacitação para produção de células *in vitro*. Apesar de ser um grande avanço na medicina estética e reparadora, há controvérsias quanto ao uso desse procedimento, como a segurança do material utilizado. Dessa forma, ainda se faz necessário estudos mais abrangentes e com comprovações científicas.

Palavras-chave: Células tronco; Cirurgia plástica; Enxerto.

Resumen

Las células madre adultas, especialmente las mesenquimales, tienen la capacidad de multiplicarse y diferenciarse en otros tejidos, lo cual es prometedor cuando se trata del área de la terapia celular. Además, las células madre derivadas de tejido adiposo (ASC), que son multipotentes y tienen la capacidad de diferenciarse en células mesenquimales, son altamente eficientes en cirugías reparadoras y estéticas, principalmente debido a su alto proceso de cicatrización, ya que tienen efectos antiinflamatorios...-inflamatorias e inmunosupresoras. Además, el tejido adiposo se presenta como la mejor forma de abordar este tema, ya que presenta una mínima morbilidad y una alta capacidad de producción celular *in vitro*. A pesar de ser un gran avance en la medicina estética y reparadora, existen controversias en cuanto al uso de este procedimiento, como la seguridad del material utilizado. Por lo tanto, aún se necesitan estudios más completos con evidencia científica.

Palabras clave: Células madre; Cirugía plástica; Injerto.

1. Introduction

This article proposes a discussion about the perspectives of the use of stem cells in plastic surgery, through a very detailed bibliographic review. Stem cells (SC) are characterized by being undifferentiated or unspecialized, having the ability to self-renew and differentiate into various cell types (multilineage), from the same tissue and from different tissues with different functions. Thus, they are divided into two main groups, embryonic and adult stem cells. Embryonics are obtained from embryoblasts and can be totipotent (forming tissues, placenta and embryonic annexes) or pluripotent (forming tissues). The adult or somatic cells are already developed organism cells and can be multipotent, oligopotent and unipotent, they are isolated and defined in different tissues of the body, among them the placenta, the umbilical cord, the dental pulp, the brain, the adipose tissue. and red bone marrow (Nayar et al. 2014).

In addition to the above, among the acceptable adult SC, the so-called mesenchymal stem cells are highlighted in research and clinical studies due to their easy obtainment, as they can be found in various biological sources, such as adipose tissue, they have a high capacity for proliferation, and circumvent ethical issues, however, are restricted to the resident lineage. Above all, it is important to emphasize that the use of SC is limited, embryonic SCs, for example, despite having greater regenerative potential and efficiency, present obstacles involving their origin and isolation, safety, immunocompatibility and tumorigenicity issues, in addition to ethical barriers, which makes its clinical applicability difficult. Adults, on the other hand, are more useful in medicine due to greater applicability, ease of isolation and differentiation into various lineages (Saliban et al. 2013).

In addition, recently induced pluripotent stem cells have great relevance, through cellular reprogramming techniques they can be created from various types of cells, have a great capacity for differentiation and circumvent ethical issues, although they still have challenges regarding the its use. Thus, the biological and functional properties of stem cells make them very relevant in the field of plastic and reconstructive surgery (McArdle et al. 2014). Its use has the main advantage of providing an effective treatment to patients, potentially avoiding very invasive surgical procedures and possible complications, in addition to reducing morbidity and surgical risk, especially in elderly patients. Therefore, the relevance of the use of stem cells in medicine, whether for aesthetic, repair and regeneration purposes, as well as its advances and applications in tissue bioengineering, is a potentially promising tool (Nowacki et al. 2017).

Therefore, the present review aims to present and discuss the potential of stem cells and their derivations in the contexts mentioned above and provide information on their safe use in effective therapies such as: healing of chronic wounds,

skin ulcers and fistulas, scar treatment, burns, bone and soft tissue defects. In addition, highlight its main uses in plastic surgery and applied future perspectives, in tissue aesthetic and functional restoration, as well as possible challenges in this field of science. Finally, contextualize the importance of stem cells in the quality of life of patients as social reintegration and gather evidence and the progress of studies in this area of constant discoveries.

2. Methodology

The present study consists of an integrative literature review on the relationship between the use of stem cells and the prospects in plastic surgery. From the establishment of the research keywords, the descriptors “stem cells” and “plastic surgery” were crossed; in the following databases: Virtual Health Library (VHL); National Library of Medicine (PubMed MEDLINE), Scientific Electronic Library Online (SCIELO), EbscoHost.

The search was carried out in July 2021. Studies published between 2009 and 2021 were considered. The article selection strategy followed the following steps: search in selected databases; reading the titles of all articles found and exclusion of those that did not address the subject; critical reading of the abstracts of the articles and full reading of the articles selected in the previous steps. Thirty articles were found, of which the titles and abstracts published were read. As inclusion criteria, original articles that addressed the researched topic and allowed full access to the study content were considered, excluding those studies that did not meet the aforementioned inclusion criteria. After a careful reading of the publications, 6 articles were not used due to the exclusion criteria. Thus, 21 articles were selected for the final analysis and construction of the literature review on the topic.

3. Results and Discussion

After the selection of articles, a table (Table 1) was prepared containing the main information on the perspectives of the use of stem cells in plastic surgery.

Table 1 - Studies used in the Integrative Review and main findings.

AUTHORS AND YEARS	MAIN FINDINGS
Moraes et al. 2021	There are obstacles that involve the use of mesenchymal stem cells, for example, the safety of the biological material used, pre-existing comorbidities of the patient and the cost of the procedure.
Agrawal et al. 2019	Fat grafts are indicated for procedures such as: scar correction surgeries, aesthetic augmentation of the buttocks, aesthetic and reparative surgeries, treatment of tissues damaged by radiotherapy, facial rejuvenation and hand rejuvenation, among others.
Boháč et al. 2016	Currently, fat autotransplantation is widely used in breast reconstruction surgeries. This lipotransfer is characterized by the removal of fat from one part of the patient's body to be applied to another.
Garcia et al. 2016	Fibrin gel, made up of thrombin and fibrinogen, when used together with mesenchymal stem cells to treat burn patients, is capable of accelerating healing, as it resembles the skin.
Gomes, 2011	Among the routes of inoculation of stem cells (SC), the intravenous (IV) is the least invasive, since the route of local infusion can result in unsatisfactory healing, in addition to not being suitable in organs such as the brain and heart, as it consists of in a very invasive procedure. Furthermore, migration to target tissues is more efficient when it results from inflammatory processes or trauma.
Eun, 2014	ASCs have potential for cell therapy in the case of excess scarring because they have anti-inflammatory and immunosuppressive effects, enabling healing-like regeneration without scarring.
Mizuno, 2013	After being transplanted, the fat graft tends to lose about 20 to 90% of its original volume, due to tissue resorption.
Meruane et al. 2011	Healing involves 3 phases: inflammation, proliferation and remodeling. Therefore, MSCs migrate to the inflamed site and act on cell proliferation and differentiation, also promoting anti-inflammatory and immunomodulatory effects.
Plock et al. 2013	There are data that support that mesenchymal stem cells have several mechanisms of action, including paracrine communication.
Naderi et al. 2017	Vascularized tissue allotransplantation is currently widely used in the reconstruction of complex tissues because, among other factors, it does not cause morbidity at the donor site. However, immunosuppression may be necessary throughout this patient's life.
Nayar et al. 2014	The ethical question about the use of stem cells in cosmetic surgery has worried surgeons and patients due to the romanticized way in which this procedure has been publicized by the media.
Salibian et al. 2013	The transplantation of BMSCs in cases of limb ischemia proved to be efficient, but it can cause unwanted effects on angiogenesis.
McArdle et al. 2014	The application of stem cells clinically is worrying due to the lack of regulation of the same, therefore, it is a practice that can present risks, requiring further studies and scientific evidence about the case.
Nowacki et al. 2017	Plastic surgery must have a social commitment to patient satisfaction and possible side effects, therefore, the latter needs to be considered before surgery, so that treatment lines can be traced.
franck et al. 2017	The use of ADSCs in burns is very favorable due to their ability to accelerate the healing process, releasing anti-inflammatory and immunosuppressive substances, facilitating neovascularization and giving a better appearance to the scar itself.
Oliveira et al. 2010	Stem cells (CTs) are divided into totipotent CTs (present only in the first days of embryogenesis and capable of differentiating into any type of tissue), CTs pluripotent or multipotent (differentiate in almost all tissue types, with the exception of placenta and embryonic appendages), CTs oligopotent (found in the intestine) and CTs unipotent (they differ in only one type of tissue).
Yarak et al. 2010	Stem cells derived from adipose tissue have the ability to differentiate into mesenchymal cells, such as osteocytes and adipocytes, or non-mesenchymal cells, such as hepatocytes and neurons.
Gianotti, 2011	MSCs promote healing because they have the ability to release cytokines that will repair the injured tissue, in addition to the attribute of differentiating into different types of tissues and integrating them.
Silva et al. 2009	Fat grafts combined with mesenchymal stem cells give very satisfactory results with low risks of clinical complications in breast augmentation surgeries.
Martins et al. 2011	In studies on stem cells, it was possible to see that fetal healing is better than in adults.
Andrade et al. 2013	Autologous adipose tissue stem cell transplantation is one of the most reliable methods of cell therapy, as the risks of rejection and disease transmission are low.

Source: Own authorship (2021).

Stem cells are important for the composition and maintenance of tissues, as they are undifferentiated cells, therefore, they have the ability to multiply and form other stem cells or to differentiate into other types of cells. That said, they are essential not only for human development but also for the restoration of damaged tissues.

Adult stem cells (ASCs), mainly mesenchymal ones (MSCs), because they have the ability to maintain tissue homeostasis, have high differentiation power, great effectiveness in replacing their cells and are easy to isolate, are promising in the use of therapy cell phone (Gianotti, 2011). In addition, the main advantage of using them in this type of procedure is the possibility of avoiding potentially harmful surgeries to patients. In this bias, adipose tissue-derived stem cells (ASCs) are multipotent, capable of differentiating into several other tissues, so the use of this cell type is through grafts, being very

efficient in aesthetic and reparative surgeries. In this context,) points out that adipose tissue-derived stem cells (ADSCs), when grafted, also favor angiogenesis, accelerating the healing process and increasing the success rate of the procedure, especially in these types of surgeries.

According to, the application of MSCs may be the most efficient option in scar correction surgeries because their cells have the potential to mobilize and stimulate collagen production. Another application is in patients who have suffered serious facial trauma, using cell therapy right after surgery to avoid initial scarring. In addition, a study by Franck et al. (2017) also reinforces the importance of treating burns with ADSCs, as they accelerate the healing process, helping to repair the damaged region, favoring the functioning of the immune system.

A study by Gomes (2011) points out three sources of CSM: umbilical cord blood (UCB), which, however, is only possible to remove the substance in this single stage of life; the bone marrow (BM), which, until then, was the main point of removal of mesenchymal stem cells, in an invasive, painful way and subject to loss of differentiation potential throughout life; and, finally, adipose tissue (AT), which has been the subject of research for use in plastic surgery, which has a less invasive method than the previous one, liposuction. In this context, the removal of MSCs should be performed in the least invasive way possible and that, among the options of sites, adipose tissue is the best, because it can be removed with minimal morbidity, therefore, capable of having greater production of cells. *in vitro* than when taken from other sites (Naderi et al., 2017; Nowacki et al., 2017).

Furthermore, Mizuno (2013) points out that, despite the benefit of ASCs having higher yields when compared to other cells, it is necessary to be careful with the place where they will be removed, as deposits collected from abdominal regions have a better long-term response in compared to other fat grafts. Furthermore, these cells can differentiate both *in vitro* and *in vivo*. Therefore, the percentage of surviving and implanted fat cells, as well as the reduction of fibrosis and cysts, may be higher when a technique called Cell-Assisted Lipotransfer (CAL) is used, which associates ASCs with aspirated fat so that there is a higher concentration. of ASC, therefore, a high quality tissue regeneration (EUN, 2014).

Furthermore, Plock et al. (2013) claim that the *in vitro* differentiation process of mesenchymal stem cells can result in various cell types, such as osteocytes, chondrocytes, adipocytes, Schwann cells, etc. However, Meruane et al. (2011) brought studies that show the need for care when handling and applying ASCs. Thus, these cells can duplicate in a period between 2 and 4 days, but in manipulations that lasted more than 4 months, they could show a malignant character, in addition to karyotypic abnormalities.

Research by Nayar et al. (2014) was carried out with a group of plastic surgeons from the United States of America, about the ethical perception of the use of stem cells in cosmetic surgery. In this case, most of the interviewees claimed not to be confident that the knowledge of the pros and cons on this subject is already mastered enough to be indicated to their patients and, therefore, regardless of the patients' will, the practice should not be made available in the country; however, many also claim that restricting this technique to cosmetic surgery violates their right as physicians. By the way, McArdle et al. (2014) reiterate the concern with untrained professionals performing this type of procedure both surgically and clinically, which aim only at profit and have no commitment to patient safety or even to the technology used.

According to a study by Salibian et al. (2013), stem cell treatments can be effective in repairing peripheral nerve injuries, especially by replacing supporting cells with bone marrow-derived stem cells (BMSCs) or even the more easily accessible ones, ADSCs. Despite being a mechanism not yet explored, this transplantation with adipose tissue cells proved to be very efficient, being possible the excretion of many neurotrophic factors necessary for the success of the procedure (Andrade et al. 2013). Furthermore, mesenchymal stem cells derived from adipose tissue, when used in liposculpture procedures, increase the chance of graft success, since the presence of adipocytes is a very important factor for soft tissue enlargement (Silva et al., 2009).

4. Final Considerations

In view of the analyzed studies, we understand that stem cells derived from adipose tissue are an advance in plastic surgery, since they are capable of differentiating into several other tissues, being very efficient in aesthetic and reconstructive surgeries. It was found that when grafted, they also favor angiogenesis, accelerating the healing process and increasing the success rate of the procedure. Furthermore, as it is an autologous transplant, it has a low risk of rejection and disease transmission compared to possible sources of exogenous stem cells. However, it was discussed by several professionals in the area about the importance of using this technique by trained professionals, demonstrating the need for study and knowledge of the technique by plastic surgeons, so that confidence and success in the procedure are established.

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