

AGING MANAGEMENT WITH THE USE OF EXOSOMES, PRP/ PRF WITH ALBUMIN GEL (PLASMA GEL) AND ASSOCIATED TECHNIQUES IN OROFACIAL HARMONIZATION TREATMENT

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Abstract: Aging, it is a physiological process that involves a progressive decline in the function of the organs, with loss of homeostasis and increased likelihood of disease disease and death. This account focuses on the classic perspectives on the biogenesis of exosomes, and age-related associated changes. Due to its ability to transmit biological information between cells, this work also discusses the interaction of mesenchymal cell exosomes, as a potent adjuvant in the treatment of association of orofacial harmonization techniques. The demand for aesthetic and rejuvenating treatments is increasing in society, thus, each day, the demand for orofacial harmonization increases exponentially in order to slow aging. Orofacial harmonization is a set of procedures performed by the dentist, which aims at the aesthetic and functional balance of the face. Exosomes are membranous extracellular vesicles ranging from 30 to 200 nm in diameter. Exosomes has been found to be secreted by most cell types, including immune cells (B cells, T cells, mastocytes, dendritic cells), neuronal cells, epithelial cells, endothelial cells, embryonic cells, cancer cells and cells mesenchymal trunk (mscs). The search for youth and perfect skin is a natural desire for the human being. And in this way, collagen biostimulation stands out as a safe and effective option to rejuvenate the skin, fighting the signs of aging and promoting a firmer, toned and radiant appearance. Research in exosomes therapies continues to prosper. Subsequent data on indications, dose response, safety, effectiveness and ability to combine therapy with exosomes as a “skin primer” for biostimulation techniques, such as calcium hydroxylapatite

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(CAHA), platelet rich plaketers (PRP) and fibrin matrix Platelet plasma, (PRFM) is growing rapidly.

Keywords: exosomes, facial rejuvenation, orofacial harmonization, collagen bio -stomulator, PRP - plaquette plasma.

INTRODUCTION

Facial aging is a multifactorial process that has been widely studied, changes in the skin in the facial skeleton and soft tissues are considered the pillars of aging. (LUVIZUTO; QUEIROZ., 2019).

The intrinsic process of aging is characterized by decreased skin collagen, decreased elastin and hyaluronic acid (AH), which generates a decreased thickening of the skin and loss of elasticity. (MASO, TRAMONTINI, 2023)

The discovery of extracellular vesicles (EVs) or exosomes dates back to the 1940s, and these small vesicles were ignored as cellular trash bins for a long time (Théry et al., 2002)

Significant attention came only in the mid-2000s, after the rediscovery of exosomes as messengers of communication cells. Exosomes, and specifically MSC-EXOS, have great potential for promoting rapid and efficient wound healing. Exosomes can be applied directly to an injury, which in animal models has shown to promote collagen synthesis and proliferation and migration of fibroblasts and keratinocytes. These effects have been shown in part to the exosomic regulations of microorna levels and protease activities. (HADE et al., 2021)

Exosomes are derived from mesenchymal stem cells (CTMs) and can be potentially used as an alternative for cell therapy, wound treatment and angiogenesis aid. (Saheera et al., 2020)

Studies with treatments with exosomes continues to flourish. Subsequent knowledge around indications, dose response, safety, effectiveness and ability to combine treatment with exosomes as a “skin primer” - for bioestimulation modalities such as calcium hydroxylapatite (CAHA), platelet rich plaketers (PRP) and plasma rich in fibrin matrix (PRFM) is growing rapidly. (KALLURI et al., 2020)



Aging is a complex and natural biological process that involves several different pathways with genetic and environmental elements, which are studying with the decline of physical and mental abilities over the years. The effects of aging occur on various systems of the body, including the endocrine system, which is in the fall of various hormones, known as endocrinosenescence. (XU, 2012)

It is believed that the accumulation of molecular and stochastic cellular damage causes aging. Although there is no precise definition of the exact type of damage responsible for aging -related degeneration, it probably includes mitochondrial dysfunction, high levels of ros, telomeric friction, changes in nuclear structure, accumulation of genetic mutations or DNA, proteins and membrane damage. (Robbins, 2017).

Exosomes are involved in multiple physiological and pathological processes, including cell senescence. Exosomes mediate cross-signaling and play a critical role in cell communications. Exosomes have evolved as potential biomarkers for aging - related diseases.

Development

The skin

The skin is the largest organ in the human body, provides mechanical protection and plays an important role in thermoregulação, water control and exposure to external aggressions, as it is the largest external clod is in constant exposure to environmental conditions. Consisting of three interconnected layers, epidermis, dermis and hypodermis. (Perlingeiro, 2020).

In the skin, the aged aspect is represented by wrinkles and sagging and results from structural changes at the molecular level. Modifications in collagen, the most important protein of connective tissue, were responsible for these anatomical changes. (FARIA, et al 1995).

The dynamics of skin metabolism is controlled by hormonal automatic functions, such as hydration. In the skin, hormones are responsible for the synthesis of hyaluronic acid, and collagen production. Anti -aging therapies and hormone replacement has been a complementary Authore



used by the scientific environment for a better result in treatment, according to studies the defense of hormones at ideal levels, have a negative response to both health and individual's skin and skin (MASO, TRAMONTINI, 2023)

Epidermis

It originates in the Ectoderm embryonic leaflet, its main function is coating and protection, creating a selective barrier between the external environment and the adjacent connective tissue. Can be divided into 4 strata or layers:

- Corneal layer,
- Granular layer
- Thorny layer
- Basal layer (LUVIZUTO, 2019).

The outermost layer of the skin, the epidermis of multiple cell layers, protects the skin from toxins, bacteria and liquid loss through the corneal layer. Although the fundamental structure of the skin is the same in all humans, there are significant differences in epidermic architecture of the face between different genres and ethnicities. (PERLINGERO, 2020).

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Dermis

The dermis is the second main part of the skin, aging changes are affected in this layer, it is a



highly wear -elastic elastic fabric, it is located just below the epidermis, consists of cellular and chard elements. It is in this layer that we find from 70 to 80% of collagen fibers. (PERLINGERO, 2020).

Fibroblast is the main cell present in the dermis, which is responsible for the synthesis of the components of the extra cellular matrix (MEC), such as collagen, elastic and reticular fibers. Plays a fundamental role in tissue regeneration. (LUVIZUTO, 2019).

The dermis is divided into three portions:

- Papillary, outermost.
- Reticular, more internal and dermis perianexial. (LUVIZUTO, 2019).

Hypodermis

The hioperm, the deepest layer of the skin, has a thickness that can range from a few millimeters to several centimeters, and its thickness is extremely important in the analysis of facial aging from the volumetric point of view. (Perlingeiro, 2020)

The subcoune tissue, a mesodermic product, is just below the skin. Hypodermis, which is defined by microscopic anatomy as a subcutaneous fascia, is not part of the skin. Instead, it serves as a link between the skin and other muscles and organs. (LUVIZUTO, QUEIROZ, 2019).

The subcutaneous screen is composed of a dense connective tissue fiber network within it, which connects the skin mime muscles to the skin, is divided into deep and superficial planes by the aponeurotic muscle system. (Perlingeiro, 2020)

Microscopically, the hypodermis is composed of a lobby -like adipose tissue, which serves as a thermal insulator and maintains caloric homeostasis. (LUVIZUTO, QUEIROZ, 2019)

Platelet aggregates: PRP/PRF for rejuvenation of skin

Platelet rich plasma (PRP) is an autologous biological product that It involves the injection of



activated platelets, which stimulate the release of growth factors, triggering fibroblast proliferation and healing through the formation of new collagen, elastin and extracellular matrices. (Phoebe et al., 2024)

Platelet -rich fibrin (PRF) is an autologous membrane proposal that while imprisoning growth factors, offers advantages in accumulating platelets and leukocytes in the host. But its faster resorption properties (2 weeks) are limitations. Recent studies have shown that heating a poor platelet liquid plasma layer (PPP) may extend the heated albumin resorption properties (albumin gel) from 2 weeks to more than 4 months (E-PRF). (Fujioka, 2020)

Marx defines that platelet rich plasma (PRP) is an autologous plasma volume that has a platelet concentration above the basal values. (MARX, 2001).

Platelets have a variety of growth factors, and seven growth factors were described by Marx in 2001. Since then, more than 1500 growth factors and regulatory proteins are responsible for the effects of PRP. (Marx., 2001).

By producing platelet gel, the centrifugation of autologous venous blood results in a high concentration of platelets in a relatively small volume of plasma, resulting in the formation of platelet -rich plasma. This is a thrombin and calcium composed of platelet activation and at the beginning of the coagulation step, resulting in platelet gel formation, rich in growth factors such as PDGF, TGF-BETA, EGF and VEGF besides IGF3-6.8 . (EPLEY, 2004)

Kolster reports that the mechanism of action happens due to some platelets to be activated during the mechanical effect of centrifugation. A Liberation of growth factors occurs after endogenous or exogenous activation of platelets and have a chemotatic effect as well as a direct and indirect effect on tissue regeneration. Mononuclear leukocyte fibroblasts and mesenchymal stem cells are attracted to PRP, and their proliferation is stimulated. (Kolster., 2020).

The literature provides indications that the ideal platelet concentration is approximately 2.5 times higher than basal values, and the higher secretion of endogenous hyaluronic acid, and type 1 procollagen by skin fibroblasts was described in a concentration in this range. (Anitu et al., 2009).



Exosomes

Exosomes are produced through the formation of intracellular multivesicular bodies with intraluminal vesicles and double invagination of the plasmatic membrane. Exosome may contain membrane proteins, cytosolic and nuclear proteins, extracellular matrix proteins, metabolites and nucleic acids, namely mRNA, non -coding RNA and DNA species. (Kalli et al., 2020).

Exosomes are a type of extracellular vesicles (EVs) of nanometric size released by almost all eukaryotic cells, which serve as mediators for intercellular communication and can be used as cell free therapies. (DING et al., 2019)

Exosomes derived from mesenchymal cells (MSC) play a crucial role in modulating inflammatory and immunological response. Increasing evidence indicates that these exosomes promote polarization of M1 phenotype macrophages, associated with pro-inflammatory responses, to the M2 phenotype, which is characterized by the secretion of anti-inflammatory factors such as IL-10 and TGF- β . (Cunnane et al., 2018)

Mesenchymal trunk cells, which have the capacity for differentiation and self -renewal, are being studied in order to find a clinical application in regenerative medicine.

Previous studies have shown that mesenchymal stem cells (CTMs) are capable of self-renewal and multipotential differentiation capacity, which demonstrates promising therapeutic potential for tissue regeneration and skin function recovery. (McFarlin; et al 2006). Exosomes released from different cell types contain different lipids and proteins. The lipid composition of exosomes comprises lipids that are part of the plasma membrane and golgi, and are enriched in glycoesfingolipids, phosphatidilserine cholesterol and ceramide. (Friendrana, 1998) Skin wound healing is characterized by the repair of injured tissue, being the regeneration orchestrated by multiple cells to restore a protective barrier (Singer, 1998)



Case report

Female patient, 78 years old leucoderm, presenting a skin with wrinkles, sagging, dehydrated and tired appearance.

It sought orofacial harmonization treatment to improve the skin in general.

Main complaint wrinkles on the face and “aged and fallen”

Anamnesis, clinical examination, physical examination and evaluation of inflammatory parameters, and the falls of the face was performed.

In physical examination there was a flabby, dehydrated skin with the presence of sharp wrinkles in orrobital orrobial region.

Treatment

The treatment proposed and performed on the patient was a facial harmonization with various procedures joined with exosomes.

Among them, botulinum toxin, lip filling with hyaluronic acid, biorevitalization of the skin with exosomes, and alb-PRF collagen bio-stimulation associated with exosomes were performed.

After anamnesis and clinical examination, the diagnosis of starting the procedures was closed.

To perform the procedures, we divide the steps. At first we performed the treatment with botulinum toxin, did the hygiene of the skin with chlorhexidine, and apply at specific points to relax the muscles.

After the 10th day, the biorevitalization of the skin was performed through microagulating with the use of exosomes. Exosomes were applied in two ways, through microagulating and in conjunction with the PRF and ALB PRF (plasma gel).

To obtain the PRP/PRF, the patient’s blood was collected, the full blood collected was from peripheral region, in 9 ml plastic tubes and centrifuged at 1600 rpm for 5 minutes to a force g 200. The



sedimentation centrifugation In compact disc (CDC) uses a relatively low G force (about 200-500 g).

After that, the plasma layer was heated at 80 ° C for 10 minutes to create denatured albumin (albumin gel). The remaining cells and the growth factor found in the leukocyte layer (liquid PRF) were later mixed again with the cooled albumin gel to form ALB-PRF, and the same mixed with reconstituted and injected exosomes on the facing face in specific regions using cannulas, thus aiming an improvement in dermal thickness.

FINAL CONSIDERATIONS

Many fields of regenerative medicine use platelet concentrates because they can provide supraphysiological concentrations of autologous platelets, leukocytes and growth factors. To accelerate the formation of hard or soft tissues, regenerative medicine has used a variety of biomaterials, surgical procedures and growth factors.

Exosomes, and specifically mesenchymal cells, have great potential for promoting rapid and efficient wound healing when associated.

Authors report that platelet-rich fibrin (PRF) is a regenerative biomaterial that is fully reabsorbed in about 2 to 3 weeks. However, it has recently been shown that a new heating process prolongs PRP/PRF working properties from 2 to 3 weeks to 4 to 6 months.

Entlyam, many authors report that, platelet-rich fibrin (PRF) has been characterized as a regenerative biomaterial that is fully reabsorbed in a typical period of 2 to 3 weeks, but reports that a new heating process has recently been demonstrated extends the properties. of the PRP/PRF work of a standard period of 2 to 3 weeks for a duration of 4 to 6 months.

In order to have a good result and a good response and maintenance of aesthetic procedures that it aims to achieve and maintain for longer, it is of fundamental importance to manage aging with the use of safe and advanced techniques, guiding the patient as to the lifestyle and adequate feed and supplementation.



Taking into consideration of the articles and findings in the present report, we can see the importance of approaching the patient as a whole, and of emphasis that exosomes have also gained wide attention in the field of biomarkers research and are now seen as a strategy Alternative to regenerative therapies based on stem cells.

Although exosomes have achieved significant achievements in various therapies, the challenges remain, as we find in the literature numerous articles that report the use of exosomes and their relationship with the skin, however, we need to perform more studies with this type of treatment

Clinical result before and after



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