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Applications of Leucocyte-And Platelet-Rich Fibrin (L-Prf) – Literature Review

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ABSTRACT
This study aims to conduct an integrative literature review on state of the art and applications of leucocyte-and platelet-rich fibrin (L-PRF) in implant dentistry. Materials and methods. A bibliographic survey was carried out on the theme of L-PRF. For the literary search, we searched the following keywords in the databases PubMed, Google,Google Scholar and Academic Google: “Platelet-rich fibrins”, “dentistry”, “interventions”, and “implant dentistry". Results. L-PRF is an autologous biomaterial formed by an autologous fibrin matrix consisting of platelets, leukocytes, leukocyte cytokines, and growth factors collected from a simplified blood sampling. Conclusion. The use of L-PRF in implant dentistry brought real benefits to patients, such as an improvement in the quality of periodontal tissues in the region, especially in areas of immediate implantation, contributing to first-intention healing. This method accelerates the healing process of the patient, as well as makes the surgical procedure less invasive, as a consequence, the treatment is less traumatic and faster. In addition, the L-PFR technique is simple and economical, representing a promising option.

Keywords: Platelet-rich fibrins, implant dentistry, biomaterial, dentistry, interventions.

I. INTRODUCTION

One of the problems in science is the need to use biomaterials that enable the incorporation of autologous bioactive surgical additives with hemostasis-promoting functions, controlling inflammatory processes, accelerating healing procedures, and promoting a comfortable and safe postoperative. Research about tissue engineering, in which biomaterials are involved, isgrowing in dentistry and medicine, developing different techniques and biomaterials, highlighting leucocyte-and platelet-rich fibrin (L-PRF) (SÁ, 2013).

The L-PRF is the second generation of platelet aggregates developed by Choukroun et al. (2011), where a polymerized fibrin matrix in a tetramolecular structure involves platelets, leukocytes, cytokines, growth factors, and circulating stem cells.

The regenerative potential of platelets was exposed in 1974, demonstrating growth factors (GFs) isolated from peripheral blood. Factors in platelet alpha granules can stimulate cell proliferation, matrix remodeling, and angiogenesis. Platelets are fundamental components involved in the healing process through their coagulation and the release of GFs (RAJAet al., 2018).

Due to such indications, the L-PRF technique isan additive in dentistry to accelerate healing, reducing morbidities in tissue reconstructions (ALVES, 2011; Heggendorn et al., 2021). L-PRF is an autologous biomaterial with GFs enhancing bone regeneration and accelerating angiogenesis, cell proliferation, mitosis, and cell chemotaxis (SÁ, 2013).

In this context, L-PRF is indicated for different dental applications, such as maxillary sinus elevations combined with bone grafts, protection, and stabilization of grafting materials, the elevation of the bone crest, preservation of the socket after its extraction and root coverage of one or more teeth after tissue recession (BALBINO et al., 2015; Heggendorn et al., 2021; Araujo et al., 2022; De Nobregaet al., 2022).

II. OBJECTIVES

This study aims to conduct an integrative literature review on state of the art and applications of leucocyte-and platelet-rich fibrin (L-PRF) in implant dentistry.

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III. MATERIALS AND METHODS

A bibliographic survey was carried out on fibrin rich in platelets and leukocytes. For the literary search, we searched the following keywords in the databases PubMed, Google,Google Scholar and Academic Google: "Platelet-rich fibrins", "dentistry", "interventions", and "implant dentistry".

IV. RESULTS

4.1. What is L-PRF?

L-PRF is an autologous biomaterial harvested from venipuncture, produced by a natural polymerization process from the centrifugation of blood previously collected in the patient(SÁ, 2013).

The structure of L-PRFcan accelerate the healing process using an autologous fibrin matrix containing platelets, leukocytes, leukocyte cytokines, and platelet-rich fibrins. Developed in France by Dr. Joseph Choukroun, the L-PRF is classified as a second-generation platelet concentrate, produced naturally, without the usage of anticoagulants or any other gelling agents in the course of its manipulation, which represented an advance over the first-generation concentrate, the platelet-rich plasma (PRP) (SÁ, 2013).

This fibrin clot consists of three layers: a lower part, concentrating red blood cells; an upper part, the acellular plasma or platelet-poor plasma; and a central area of the clot, consisting of a yellowish portion of fibrin that constitutes the main body of the PRF clot, which is directly used after compression,forming the PRF membrane (CHOUKROUN et al., 2011).

The fibrin matrix is a determining part responsible for the therapeutic potential consisting of biochemical components such as cytokines, glycan chains,and glycoproteins involved in a network of finely polymerized fibrins (EHRENFEST et al., 2014). In this context, the concentration of platelets in the L-PRF triggers inflammatory regulations observed in surgical sites treated with PRF, resulting in aslow release of biochemical components captured in the fiber network during matrix remodeling (CARVALHO et al., 2010).

4.2 Protocols for obtaining the L-PRF

The preparation protocol is initially done by collecting blood, a procedure known as venipuncture, in 10 ml tubes without anticoagulant that are centrifuged at a speed of 2700-3000 rpm for 10 to 12 minutes. Thus, due to the absence of the anticoagulant, platelets ruptured by the shock against the walls of the tube trigger the coagulation cascade. The fibrinogen initially concentrated in the upper part of the tube, is affected by the effect of circulating thrombin, initiating the formation of the polymer network. Then the clot is removed from the tube, and the red blood cells, which are attached, are discarded(CHOUKROUN et al., 2019; Heggendorn et al., 2021; Araujo et al., 2022; De Nobregaet al., 2022).

The L-PRF clot is then placed in the grid of the PRF box and compressed. Therefore, the membrane is produced for about one minute. The concentrated exudate at the bottom of the box can still be used to hydrate the graft materials (CHOUKROUN et al., 2019; Heggendorn et al., 2021; Araujo et al., 2022; De Nobrega et al., 2022).

Part of the success of this process depends on the speed of blood collection and transfer because the delay of the centrifugation can lead to failures such as diffuse fiber polymerization, resulting in a reduced blood clot without consistency. The thrombin in this autologous process triggers polymerization by organizing the three-dimensional mesh of the fiber network, providing a resistant, elastic, and flexible membrane (DOHAN et al., 2016).

As in the healing process, this fibrin network acts as a barrier to prevent wound contamination and as a basis for the healing process, supporting cell migration and stimulating growth factors (SANAR, 2022).

4.3 Applications of L-PRF

The application of L-PRF in the surgical sites in the oral cavity is carried out with the expectation of increasing platelets so the concentration of GFs is also increased (FRIEDRINCH, 2022).

In the biology of this material, platelet and leukocyte cytokines play an important role in the matrix of fibers that support them, constituting the determining element for the therapeutic potential. Thus, L-PRF is indicated in treatments of periodontal plastic surgery, jawsosteonecrosis, bucco-sinusal communication, regeneration of infra-bone defects, alveolar preservation, maxillary sinus lifting techniques, rehabilitation of edentulous areas, maxillary sinus pneumatization, furcation lesions, gingival recession, and after dental extractions for implant installation, presenting itself as an excellent assistant in the regeneration process (MÉTHODOS, 2022; FACSETE, 2022).

4.4 Constituents of the fibrin matrix

Among the constituent cells of L-PRF, platelets are found, such as reduced, anucleated and megakaryocyte-derived cells. The platelets present

intracellular storage sets of proteins essential for healing, with a lifespan of 8 to 10 days, capable ofpreventing hemostasis and promoting tissue repair. The platelets are activated when they come into contact with the exposed endothelium, releasing healing factors and channeling macrophages through vascular growth (FACSETE, 2022).

Fibrin, on the other hand, is the activated form of fibrinogen, in plasma and platelets, with a fundamental role in the course of hemostasis. In contrast, fibrinogens are the final substrates of coagulation, as a soluble protein, and become fibrin insoluble by thrombin, being the first matrix of the injuredarea (MÉTHODOS, 2022).

Thus, fibrin behaves as a natural scaffold for angiogenesis, promoting the formation of new blood vessels in the lesion, favoring themigration of neutrophils, and causing monocytes to reach the lesion later. Consequently, the colonization of wounds by macrophages is controlled through fibronectin, as the fibrin matrix guides the coverage of injured tissues acting on the metabolism of epithelial cells and fibroblasts. During the phenomenon of hemostasis and healing, fibrin clots retain circulating stem cells from early neovascularization, enabling the cell differentiation of these cells (LEE et al., 2012).

Different proteins and polypeptides remain attached to this mesh of L-PRF fibers: cytokines, transforming growth factors β (TGF β-1), platelet-derived growth factors (PDGFs), insulin-like growth factors (VEGF/ECGF), fibroblast growth factors (FGF), and epidermal growth factor (EGF) (OLIVEIRA, 2014).

Cytokines are glycoproteins produced by numerous types of cells that modulate the cellular response. The L-PRF presents platelet cytokines, which play a primary role in the initial mechanism of healing, migration, and cell proliferation, inducing the remodeling of fibrin matrices and the secretions of scar collagens (OLIVEIRA, 2014).

Cytokines balance tissue homeostasis, so L-PRF is a platelet concentrate and an immune node that stimulates defense mechanisms. Anti-inflammatory regulations are observed in surgical sites treated with this biomaterial, resulting in cytokine control effects captured in the fiber network releasing during the remodeling of the initial matrix (HUGHES, 2013).

TGF β-1 can promote the proliferation of osteoblasts, considered the most potent agent of fibrosis, thus a transformer of inflammation, by inducing fibrous healing. TGF β-1 also performs in bone tissue formation(EHRENFEST, 2014).

PDGFs are key regulators for mesenchymal cell line migrations, proliferation, and survival, as they promote the development of cells, playing a key role in the mechanisms of tissue remodeling. On the other hand, Insulin-like growth factor type I and II regulatethe proliferation and differentiation of cells (CHOUKROUN et al., 2011).

VEGF/ECGF targets blood vessels for cell growth, migration, and initiation of angiogenesis. In FGF, the target cells are blood vessels, smooth muscles, skin, and fibroblasts with cellular purpose, angiogenesis, and proliferation of osteoblasts. On the other hand, EGFtargets blood vessels, external skin cells, and fibroblasts, stimulating cell growth and differentiation (CORREIA, 2015).

V. DISCUSSION

Tissue engineering aims to re-establish tissue functions, using biomaterials that promote the prolonged release of growth factors to achieve bone regeneration (PICHOTANO, 2019).

PRF membranes can be applied to exposed wound coverings, stabilizing and protecting graft materials, accelerating the healing process, providing a controlled release of growth factors, and aiding local hemostasis. Even when associated with other biomaterials, L-PRF accelerates the healing of the edges of the lesion, acting as a fibrin bandage and offering considerable postoperative protection, in addition to reducing the time in the integration and remodeling of grafted biomaterials (MARELLI, 2013).

The use of platelets associated with bone grafting materials offers valuable benefits, such as fibrin clots playing an essential role in the resistance of PRF membranes, maintaining the protection of the biomaterial and connecting bone particles, thus promoting a biomechanical force from the beginning of healing. The integrations of these fibrin networks with bone fragments favor cell migration, especially of endothelial cells, in promoting angiogenesis (RAJA et al., 2018).

Therefore, L-PRF can be considered a natural biomaterial consisting of a rich matrix of fibrins, favoring the development of a micro vascularization capable of guiding the migration of epithelial cells to its surface. The interests of such membranes are evident for the protection of open wounds and to accelerate healing (DOHAN et al., 2016).

Alves (2011) stated that L-PRF could be used as a membrane, gel, buffer, and as membranes cut into fragments, as applied in autonomous, additive,and combination therapies, presenting benefits in wound and bone healing. The anti-

inflammatory and antibacterial effects of L-PRF, associated with the reduced risk of its usage and easy preparation methods, increasingly encourage professionals to adopt this technology in dental practices to benefit patients.

Correia (2015) indicated the easy acquisition of L-PRF, as it requires only the patient's blood anddoes notpresent risks of cross-infection due to the absence of additives, demonstrating safety for use in oral and maxillofacial applications. The hemostatic and immune system supportive characteristics of L-PRF contribute to its success and real effectiveness in reducing morbidities in surgical procedures,given that they have wide possibilities of applications, with promising results in a short time.

Carvalho (2010) stated that using fibrin membranes is effective for interventions, showing no recurrence of lesions; in addition,fibrin membranes are an alternative for low-cost grafting. Also, other interventions are unnecessary, as the need for a second surgical site to collect autogenous material significantly reduces morbidity in procedures. The applicability of L-PRF in a procedure of total surgical excision of a pyogenic granuloma lesion recurrently associated with curettage of adjacent bones can avoid further recurrences, for example (CAMPOS, 2017). The use of L-PRF is satisfactory, with no signs of lesion recurrence, and its low cost (CAMPOS, 2017).

Dohan et al. (2016) concluded that the L-PRF showed efficacy as adjuvants in grafting surgical interventions with biomaterials in the elevation of the Schneider membrane by the lateral bone window access technique, satisfactorily favoring vertical bone gain for implant installations. Corroborating these facts, Oliveira (2014) reported the benefits of L-PRF in maxillary sinus lift surgeries, in the form of a membrane and when used as a filling material to treat membrane perforations, in addition to reporting its applicability as an adjuvant in guided bone regeneration.

Ehrenfest (2014) described the success ofapplying L-PRF in association with synthetic biomaterials in treating a periapical cyst. These approaches demonstrated the advantages of the association of L-PRF in oral surgeries, obtaining adequate healing and providing a gain in bone volume. The application of such a technique demonstrated favorable recovery, reducing the time of morbidity of inflammatory conditions and allowing the rehabilitation of the patient through implants in a shorter period (EHRENFEST, 2014).

Balbino et al. (2015) concluded that L-PRF is an excellent alternative to be used as an additive to biomaterials, favoring repair. In this context, the associations of this blood concentration with bone grafts favor the insertion of biomaterials in dental alveoli, allowing them to settle satisfactorily.

In surgical interventions of extraction of lower third molars, using L-PRF demonstrated positive results for bone healing, edema control, and soft tissue healing (CARVALHO et al., 2016). However, in the research by Hughes (2015), good results were indicated only for the quality of soft tissue healing, with no differentiation in relation to pain control and prevention of alveolitis.

With several techniques for improving the postoperative surgical period of extraction, PRF is also associated with other materials, such as hyaluronic acid; however, there is no statistically relevant difference when comparing the application of hyaluronic acid in isolation with the form associated with PRF (MARELLI, 2013). Lee et al. (2012) emphasized that although PRF is used in dental surgery, divergences regarding the indications and advantages of PRF in the literature should be carefully revised.

The use of pure L-PRF in infected sites and the survival of implants installed with immediate loads of tooth extraction presented lesions were evaluated (MAZOR et al., 2009). Significant results in the gingival aesthetic score on interproximal surfaces and the significant decrease in bone resorption led to accelerated bone regeneration during the initial post-extraction stage (Mazor et al., 2009).

VI. CONCLUSION

The use of L-PRF in implant dentistry has real benefits to patients, such as an improvement in the quality of periodontal tissues in the region, especially in areas of immediate implantation, contributing to healing in the first intention.

The great differential of this method is the acceleration of the healing period of the patient, as well as making the surgical procedure less invasive and the treatment less traumatic and faster. In addition, L-PRF isa simple and economical technique proving to be a promising option.

Although numerous authors present highly relevant results about the use of PRF, further research is still necessary to understand this technique's limitations and its real interaction with different biomaterials.

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