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The Use of L-PRF in Autogenous Tooth Transplantation

Silvia Fernández

Dissertação conducente ao Grau de Mestre em Medicina Dentária (Ciclo Integrado)

—

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Trabalho realizado sob a Orientação de **Prof. Doutor Paulo Miller e Coorientação do Professor Dr. António Ferraz**

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``O futuro pertence àqueles que acreditam na beleza de seus sonhos´´

Eleanor Roosevelt

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RESUMO

Introdução: O autotransplante dentário é definido como a transferência de um dente de seu alvéolo para um alvéolo pós-extração ou alvéolo feito cirurgicamente na mesma pessoa. O prognóstico da técnica melhorou graças aos avanços na compreensão da cicatrização óssea, periodontal e pulpar. O L-PRF tem um grande potencial de regeneração natural, atuando como barreira biológica, facilitando o fechamento primário do leito cirúrgico e protegendo-o das agressões externas e acelerando a cicatrização.

Objetivos: O objetivo desta revisão sistemática integrativa foi pesquisar a literatura atual relevante e analisar os efeitos do uso de L-PRF no Transplante Autógeno de Dentes.

Materiais e Métodos: Foi realizada uma pesquisa nas bases de dados PUBMED, EBSCO e SCIENCEDIRECT e foram aplicadas combinações de vários termos de pesquisa para encontrar os estudos incluídos.

Resultados: Selecionámos 17 artigos com informação pertinente para os objetivos propostos.

Discussão: Segundo a literatura, a utilização de L-PRF demonstrou ter efeitos positivos na regeneração do tecido, aumentando a proliferação de fibroblastos e células estaminais, proporcionando uma rápida hemostasia e liberação de de fatores de crescimento, citoquinas e proteínas, que atuam em conjunto no processo de regeneração, impulsionando e acelerando a resposta biológica natural do organismo.

Conclusão: Podemos concluir que os resultados obtidos não mostram diferenças significativas que permitam uma comparação directa entre a técnica L-PRF e as técnicas convencionais. Assim, é necessária mais investigação para comparar os resultados de ambas as técnicas neste contexto específico.

Palavras-chave: *``reimplanted tooth´´; ``avulsed tooth´´; ``tooth transplantation´´; ``cells of the periodontal ligament´´; ``prf´´; ``leukocyte platelet-rich fibrin´´; ``L-PRF´´.*

ABSTRACT

Introduction: The dental autotransplantation is defined as the transfer of a tooth from its socket to a post-extraction socket or a surgically created socket in the same person. The prognosis of the technique has improved thanks to advances in understanding bone, periodontal, and pulp healing. L-PRF has great potential for natural regeneration, acting as a biological barrier, facilitating primary closure of the surgical site and protecting it from external aggressions and accelerating healing.

Objetives: The objective of this integrative systematic review was to research current relevant literature and analyze the effects of using L-PRF in Autogenous Tooth Transplantation.

Materials and Methods: A Search was conducted in PUBMED´s, EBSCO´s and SCIENCEDIRECT´s databases and combinations of various search terms were applied to find the included studies.

Results: We have selected 17 articles with relevant information for the proposed objectives.

Discussion: According to the literature, the use of L-PRF has been shown to have positive effects on tissue regeneration by increasing fibroblast and stem cell proliferation, promoting rapid hemostasis, and releasing growth factors, cytokines, and proteins that work together in the regeneration process, boosting and accelerating the organism's natural biological response.

Conclusion: We can conclude that the obtained results do not show significant differences that allow for a direct comparison between the L-PRF technique and conventional techniques. Therefore, further research is needed to compare the results of both techniques in this specific context.

Keywords: *``reimplanted tooth´´; ``avulsed tooth´´; ``tooth transplantation´´; ``cells of the periodontal ligament´´; ``prf´´; ``leukocyte platelet-rich fibrin´´; ``L-PRF´´.*

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LIST OF ABBREVIATIONS:

ATT: Autogenous Tooth Transplantation

BMSTs: Bone Mesenchymal Stem Cells

BMMSCs: Bone Marrow Mesenchymal Stem Cells

DFDBA: Demineralized Freeze Dried Bone Graft

I-PRF: Injectable Form of Platelet-Rich Fibrin

L-PRF: Leukocyte Platelet-Rich Fibrin

PDL: Periodontal Ligament

PDLSCs: Periodontal Ligament Stem Cells

PPP: Platelet-Poor Plasma

PRF: Platelet-Rich Fibrin

TDM: Treated Dentin Matrix

1- INTRODUCTION

Autogenous Tooth Transplantation (ATT) is the surgical movement of a maturely or immaturely formed tooth from its original site to another extraction site or a surgically prepared socket in the same individue[1].

Auto-transplantation was first tried by Widman in 1915 in impacted canines[2].

There are other types of autotransplantation, including intra-alveolar transplantation, which is when the position of the tooth is changed within the original cavity, for example, surgical realignment and intentional replantation, and when the tooth is replanted in the original cavity after intentional extraction for the treatment of endodontic lesions[1].

Autotransplantation is typically viewed as a final option for preserving a tooth with a poor prognosis, as dental treatment generally focuses on the most minimally invasive approach that meets the patient's cosmetic and functional needs[3].

The success rate of autotransplantation has increased in recent studies, thanks to an improved understanding of how the periodontal tissues heal[4].

That success lies in the ability of periodontal ligament (PDL) cells to differentiate and prompt the formation of dentin and cementum. PDL cells possess the ability to differentiate into osteoblasts and stimulate the development of bone. Andreasen and colleagues demonstrated that the presence of viable and intact PDL cells is regarded as the primary determinant for achieving a successful healing outcome following autotransplantation[1].

L-PRF, which was introduced by Choukroun et al. in 2001, is considered a second-generation platelet growth factor. L-PRF has a fibrin network appearance and promotes cell migration and proliferation, leading to faster healing. Its distinct structure may also serve as a means of transporting essential cells for tissue regeneration[3].

The formation of a clot results in the creation of a robust and innate fibrin matrix. This matrix has a complex architecture that serves as a healing framework and concentrates the majority of platelets and growth factors found in the harvested blood. In addition, it possesses mechanical properties that are unmatched by any other platelet concentrate. PRF can stimulate cell proliferation of osteoblasts, gingival fibroblasts, and PDL cells. These cell type–specific actions of PRF may be beneficial for periodontal regeneration[5].

This biomaterial has also been tested as a matrix in the regeneration process of the reimplantated tooth periodontum, and describes it as a biocompatible and specific matrix for the delivery of therapeutic films that would improve clinical efficacy and support cells in the space between the alveolar bone and cement[6].

1.1- THE PRIMARY GROWTH FACTORS PRESENT IN L-PRF AND THEIR ROLES

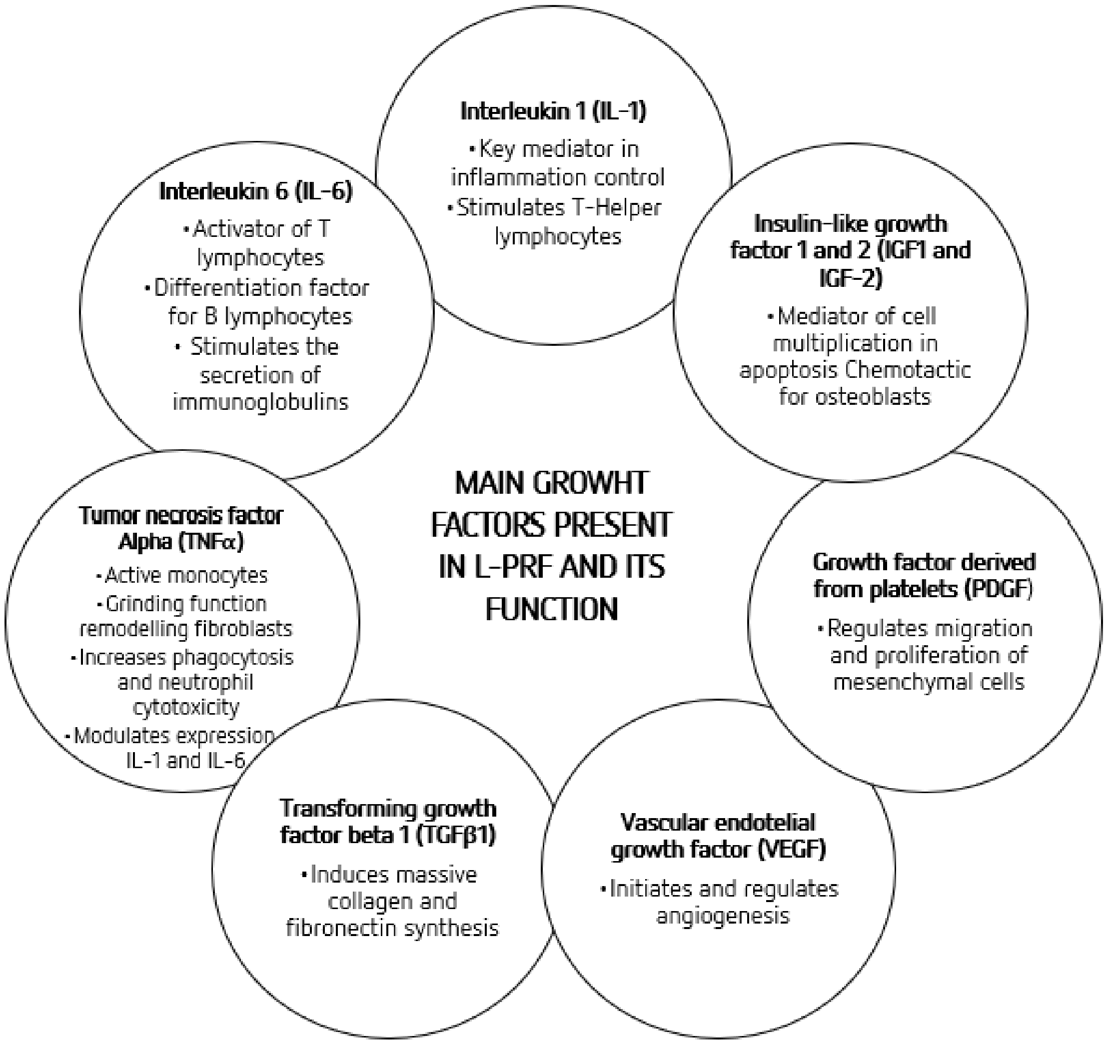

Figure 1. Main growht factors present in L-PRF and its function

1.2- ADVANTAGES OF USING L-PRF

The effects of PRF on periodontal regeneration have been proved by animal models and human clinical applications. After tooth replantation, the key requirement for successful periodontal healing is that sufficient PDL cells occupy tooth surface rather than osteoblasts or epithelial cells[7].

PRF have been widely used in oral, maxillofacial, and plastic surgery, as well as new tissue-engineering paradigms. The advantages of PRF are, but not limited in, its low cost and high efficiency and the significant ease of the procedure, which does not require chemical or unnatural conditions[8].

Compared to other platelet aggregates, PRF offers several advantages such as a single-step preparation process that involves natural blood products without the use of anticoagulants. Furthermore, PRF results in a three-dimensional structure that facilitates the delivery and support of cell sheets in tissue areas that have been damaged or destroyed[6].

PRF is not only characterized by its functional three-dimensional structure but also possesses diverse beneficial local properties including the ability to promote cell migration, attachment, proliferation, and differentiation. Consequently, PRF has been identified as an optimal biomaterial[2].

On the other hand, the literature indicates the advantages of using PRF alone or combined with other biomaterials, without reporting any drawbacks[9].

2- OBJECTIVES AND HYPOTHESES

2.1- OBJECTIVES

The main objective of this thesis was to carry out an integrative systematic review on the benefits of using L-PRF in Autogenous Tooth Transplantation, comparing the different protocols for its implementation, the rate of occurrence of treatment, as well as it applicability and importance in clinical practice.

2.2- HYPOTHESES

H0 (Null hypothesis) = There is no difference between the results of autologous tooth transplantation with the L-PRF technique compared to the conventional technique.
H1 (Hypothesis 1) = There is a significant difference between the results of autologous tooth transplantation with the L-PRF technique compared to the conventional technique.

3- METHOD

3.1- SEARCH STRATEGY

A bibliographic search was performed in PUBMED, EBSCO and SCIENCEDIRECT until 20 February 2022, using the following combination of search terms:
``reimplanted tooth´´ AND ``PRF´´; ``avulsed tooth´´ AND ``PRF´´; ``tooth transplantation´´ AND ``PRF´´; ``cells of the periodontal ligament ´´ AND ``leukocyte platelet-rich fibrin´´ OR ``L-PRF´´ AND ``reimplanted tooth´´.
Boolean operators were used to combine the different searches in a way to gather to gather the most articles.

3.2- CRITERIA FOR STUDY SELECTION AND INCLUSION

Inclusion criteria considered articles published in English from 2013 to 2023, describing in vitro and case reports evaluating the effect of PRF on the prognosis of reimplanted and autotransplanted teeth. Articles for literature review, systematic review and meta-analysis, books and articles not published in English were used as exclusion criteria.

3.3- STUDY SELECTION

The search for literature resulted in a total of 231 articles: 79 articles from *PubMed,* 41 articles from *Ebsco Host* and 111 articles from *ScienceDirect.*
Following the collection of articles, 25 were withdrawn because they were duplicated, leaving a total of 206 articles.
A selection of articles was then made according to reading the title and abstract, leaving a total of 17 articles that were included because they seemed all relevant for the preparation of this integrative systematic review.

3.4- PICO QUESTION

Three independent authors (P.M., A.F., S.C.) analyzed the titles and abstracts of potentially relevant articles to determine their relevance to the question: "Does platelet-rich fibrin (PRF) have an impact on autogenous tooth transplantation?" Full-text articles were obtained if they answered the screening question with "yes," "uncertain," or "no." The selected articles were then individually assessed to determine their suitability for this study. Duplicate articles were removed using the Mendeley citation manager after compiling the total number of articles for each combination of key terms.
In this review, the authors considered several factors, including the names of the authors, the year of publication, the characteristics of the population, and the purpose and findings of each study.

Population	Patients with indication of autologous tooth transplantation as treatment option.
Interest	Evaluate the results obtained with the use of L-PRF.
Comparison	Autologous tooth transplantation technique with L-PRF VS Autologous tooth transplantation technique without L-PRF.
Outcomes	The results suggest that the technique using L-PRF is better in relation to the technique without L-PRF, in terms of regeneration of lost periodontal structure and tissue healing, without statistically significant differences in relation to the other parameters.

Table 1. PICO question

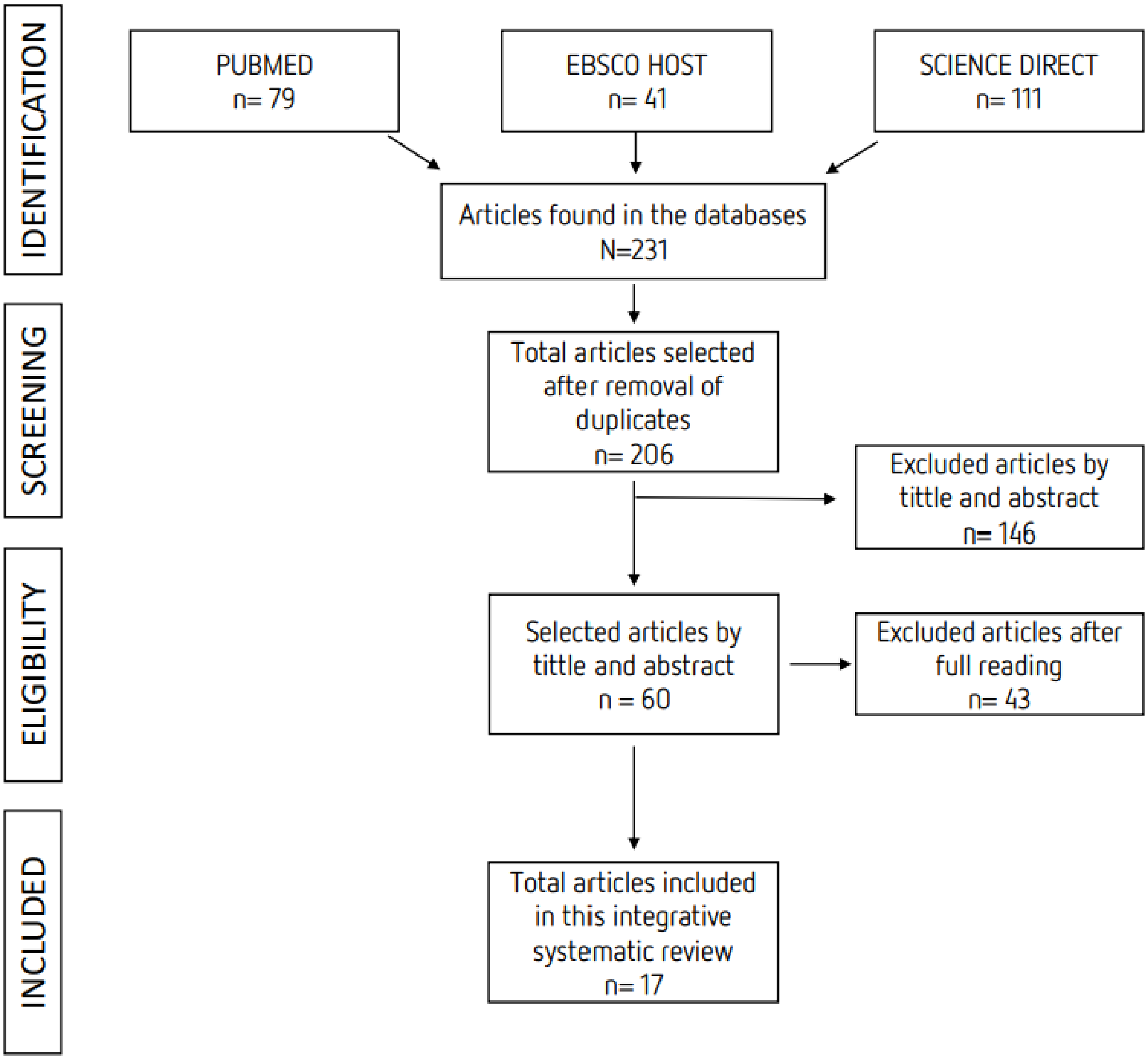

Figure 2. Flow diagram of Study Selection

4- RESULTS

It is crucial to differentiate between the results obtained "in vitro" and "case reports" because the conditions under which these studies are conducted can vary significantly. "In vitro" studies can provide valuable information on the efficacy of treatment in a controlled environment, identifying its mechanism of action and evaluating its activity in specific cells or isolated tissues. However, these studies may not fully reflect how the treatment will behave in a living organism due to the complexity of biological and physiological systems.
On the other hand, case reports provide a detailed description of a particular patient's clinical situation, which can provide valuable information on a treatment or condition, helping to identify patterns and trends. However, these reports have limitations in terms of fully evaluating treatment efficacy and applicability to a wider population.
In summary, the main difference between "in vitro" studies and case reports is that the former are conducted in a controlled laboratory environment, while the latter are based on observation and description of patients in real clinical situations. Both types of studies are important for research as they allow for advancing knowledge on specific treatments and provide valuable information about them.

4.1- IN VITRO

In vitro studies have demonstrated that PRF has the potential to reduce the risk of ankylosis by inhibiting the osteogenic differentiation of periodontal ligament stem cells. This is due to three factors. Firstly, PRF can stimulate cell proliferation to generate more fibroblasts and promote tissue repair using seed cells, rather than mobilizing bone stromal and bone-derived cells. Secondly, the collagen fiber present in PRF can act as a physical barrier, preventing direct contact between the tooth root and the alveolar socket's inner wall, thereby reducing bone repair between them. Finally, PRF can inhibit osteoclast generation by promoting the secretion of osteoprotectin, thereby reducing osteoclast activity and suppressing external resorption to some extent[10].
Although in vitro studies are useful for evaluating the effects of PRF on periodontal cells, they may not fully replicate the clinical conditions[11].

One of the studies aimed to analyze the effectiveness of L-PRF in the maintenance and recovery of cell viability of the periodontal ligament, obtaining as a result the proof that it helps in cell maintenance and recovery, providing greater cellular viability in relation to the different extraalveolar dry times analyzed ($p<0.001$)[6].

Another study has evaluated bone marrow mesenchymal stem cells in L-PRF with the objective of periodontal regeneration. To evaluate this new method of cell transplantation, this study aimed to design a L-PRF scaffold to determine the viability and function of BMMSCs in the manufactured scaffold. L-PRF was found to have significantly induced the proliferation of BMMSCs throughout the incubation period due to its growth factor secretion, demonstrating the result of scanning electron microscopy showed that BMMSCs could adhere firmly to the fibrin scaffold shortly after sowing. These data suggest that the BMMSCs/L-PRF construction has the potential to improve the clinical prognosis of re-implanted avulsed teeth in the future[12].

One study found that the use of L-PRF had a significant effect on the recruitment and proliferation of PDLSCs and BMSCs in an in vitro environment. When combined with treated dentin matrix (TDM), cell differentiation could be induced by increasing the expression of genes associated with bone sialoprotein mineralization and osteopontin after 7 days of coculture.

In an in vivo environment, autologous L-PRF and allogeneic TDM were transplanted into a fresh tooth extraction socket, resulting in successful tooth root regeneration after 3 months. Regeneration was characterized by the restoration of cement and periodontal ligament-like tissues with oriented fibers, suggesting functional regeneration.

These results suggest that it is possible to regenerate the connection of the tooth root to the alveolar bone through the use of L-PRF and TDM in a dental alveolar microenvironment, possibly by finding and stimulating BMSCs and PDLSCs. In addition, bioactive signals and inductive microenvironment were shown to be important factors for endogenous regeneration[7].

Another study was conducted with the purpose of developing a cell transplantation method that combines fragments of cell sheets of periodontal ligament stem cells (PDLSCs) and platelet-rich fibrin granules (PRF), in order to improve periodontal healing in the reimplantation of avulsed teeth. After eight weeks of reimplantation, it was observed that the group treated with PDLSCs/PRF presented a more effective periodontal healing, characterized by the regeneration of tissues similar to the periodontal ligament, and a decrease in ankylosis and inflammation compared to the other test groups. These findings suggest that the PDLSC/PRF cell transplant method could be a useful tool in alveolar surgery, and has the potential to improve clinical outcomes in future cases of avulsed tooth reimplantation[8].

The purpose of another study was to examine the impact of PRF application during late reimplantation of mature extracted teeth. After a period of 8 weeks, the animals were sacrificed and the histological sections were examined. The group that received PRF showed a significant decrease in inflammatory root resorption compared to the control group ($P = 0,031$). However, no significant differences were observed between the two groups in relation to new bone formation, inflammatory state, connective tissue healing and replacement resorption ($P > 0.05$). Although PRF was applied to the extracted alveolus prior to late reimplantation, no significant benefits other than reduced inflammatory root resorption were observed[9].

Another study aimed to investigate the impact of the use of platelet-rich fibrin (PRF) and platelet-poor plasma (PPP) as a means of autologous biological rejuvenation on periodontal ligament cell survival. The results indicated that the combination of PRF and PPP resulted in an increase in the number of viable PDL cells, suggesting that this combination may be an effective means of biological rejuvenation for avulsed teeth[11].

4.1.1- L-PRF VS OTHER BIOMATERIALS

In recent times, there has been a shift in the way regenerative procedures are approached, with a focus on growth factors. These are a set of biological mediators that occur naturally and play a critical role in regulating essential cellular processes involved in tissue regeneration. These processes include cell proliferation, chemotaxis, differentiation, and matrix synthesis[3].

Platelet-rich fibrin (PRF) is a platelet concentrate that belongs to the second generation of such products. It is prepared using a one-step centrifugation process and the patient's own blood, without the use of anticoagulants. PRF can be categorized as L-PRF or PRF based on its leukocyte content. Additionally, the classification can be further divided into standard PRF and advanced PRF based on the centrifugation process used. The final form of PRF can either be a membrane or an injectable substance, depending on the consistency of the centrifuged product[10,13].

PRF has several advantages over other platelet aggregates. It is prepared in a single step without the use of anticoagulants, resulting in the production of natural blood products. Additionally, PRF forms a three-dimensional structure that supports the delivery and maintenance of cell sheets in damaged tissue areas. The fibrin matrix closely mimics the extracellular matrix in terms of structure, creating an optimal environment for cell function. Furthermore, PRF contains glycosaminoglycans, such as heparin and hyaluronic acid, which have a strong affinity for small circulating peptides like cytokines and platelets. Platelet aggregates, such as platelet-rich plasma (PRP) and platelet-rich fibrin (PRF), have been utilized in a range of dental and medical regenerative procedures to aid in wound repair, act as scaffolding, promote angiogenesis, and enhance immunocompatibility[6].

Compared to platelet-rich plasma (PRP), PRF offers several advantages, including easy application, low cost, and no need for biochemical modification. Additionally, PRF forms an elastic fibrin mesh that allows for the entrapment of various cytokines and preserves growth factors from proteolysis[12]. The release of growth factors by PRP reaches 81% on the first day, leading to a notable yet brief effect. Additionally, the use of anticoagulant and activator agents required by PRP poses a risk of potentially fatal coagulopathies, making it less favorable compared to PRF[9].

Research conducted in laboratory settings has demonstrated that PRF gradually releases self-derived growth factors over a span of at least one week and up to 28 days. The utilization of PRF together with bone grafts provides numerous benefits such as enhanced wound healing, bone development and maturation, graft stabilization, wound closure and prevention of bleeding, as well as improving the manageability of graft materials[2].

Author Publication Year	Population	Parameters recorded	L-PRF Preparation Protocol	Comparison/Control	Findings/Conclusion
Navarro L.B. et al. 2019 (6)	45 extracted teeth	Analyzed the eficacy of autologous platelet-rich fibrin (PRF) in maintaining and recovering cell viability of the periodontal ligament (PDL).	9 ml-18 ml, according to the number of teeth extracted from each donor, for 8 min at 2100 rpm	A total of 45 teeth were analyzed in 6 groups. Each group was kept dry for a different time than the other groups and each group was placed in PRF for a different period of time.	The statistically significant difference between groups confirms that PRF provided and increased cell viability in relation to the different dry extra-alveolar times analyzed.
Moradian H. et al. 2017 (12)	N/A	Evaluate bone marrow mesenchymal stem cells (BMMSCs) culture in PRF for periodontal regeneration.	10 ml for 10 min at 400xg	N/A	It was found that PRF significantly induced BMMSCs proliferation throughout the incubation period due to its growth fator secretion. These data suggest that the BMMSCs/PRF construct has the potential to improve the clinical prognosis of replanted avulsed teeth in future.
Behnaz M. et al. 2021 (9)	16 teeth intentionally extracted in two mature Beagle dogs	The aim of this study was to evaluate the effect of platelet-rich fibrin (PRF) placed on late reimplantation of mature extracted teeth	10 ml for 12 min at 2700 rpm	Extraction sockets with and without PRF prior to replantation.	In the PRF group was noted less inflammatory root resorption compared to the control. However, there was no significant difference between the two groups with regard to inflamatory status, connective tissue healing, new bone formation and replacement resorption.
Hiremath H. et al. 2014 (11)	30 human premolar teeth	The purpose of this research was to evaluate the effect of platelet-rich fibrin (PRF) and platelet poor plasma (PPP) as an autologous biologic rejuvenating medium on the survival of PDL cells.	10 ml of venous blood were collected from 10 healthy volunteers from whom teeth had been extracted for the study. PRF and PPP were obtained by centrifugation of the collected blood at 705.6 g for 12 min.	Teeth immersed in a combination of platelet-rich fibrin and platelet-poor plasma (PRF+PPP) vs teeth immersed in platelet-poor plasma (PPP) vs untreated teeth.	It was foud that PDL ligament cells could benefit after immersing the tooth in PRF+PPP for 45 min.
Ji B. et al. 2014 (7)	Beagle dogs were used as an orthotopic	The biological effects of canine PRF and treated dentine matrix (TDM) on periodontal ligament stem cells (PDLSC) and mesenchymal bone	5 ml for 10 min at 400 g	Allogeneic TDM with PRF membrane vs Autoclave-treated allogeneic TDM with PRF membrane vs TDM without PRF membrane	It was concluded that PRF is useful in the emission of bioactive signals and that TDM serves as inductive scaffolding. This coupled with the microenvironment of the tooth

	transplant model.	marrow stem cells (BMSC) were evaluated respectively.		vs PRF and TDM implanted in the tooth socket after healing.	socket is indispensable to achieve endogenous regeneration of the tooth root in this study.
Zhao Y.H. et al. 2013 (8)	36 incisors were extracted from 6 dogs.	The aim of this study was to construct a cell transplantation method consisting of fragments of cell sheets of periodontal ligament stem cells (PDLSC) and platelet-rich fibrin granules (PRF) to improve periodontal healing in the reimplantation of avulsed teeth	10 ml for 10 min at 400 g	Teeth reimplantated with the use of autologous construction of PDLSC/PRF (cell lamina fragments in combination with PRF granules) vs reimplantated teeth with the use of autologous PDLSC or PRF alone vs without adjuvant use of PRF or PDLSC.	The results suggest that PDLSCs/PRF construction may be a useful tool for alveolar surgery that has the potential to improve clinical outcomes in future avulsed tooth reimplants.

Table 2. In vitro results

4.2- CASE REPORTS

Based on results from clinical trials, it appears that using both bone grafts and growth factors found in PRF may be effective in improving bone density. PRF can also be obtained as a membrane by extracting the fluids from the fibrin clot, making it a healing and interpositional biomaterial. As a healing material, it speeds up the process of wound closure and mucosal healing by providing a fibrin bandage and releasing growth factors. As an interpositional material, it prevents the early infiltration of unwanted cells, serving as a barrier between desired and undesired cells[2].

In a recent article, a case study was presented involving a 16-year-old male patient who suffered from extrusive luxation of his left central incisor (tooth 21). The article details the treatment plan, which involved intentional replantation using L-PRF in an effort to regenerate the lost periodontal structure.

After a six-month follow-up, the treatment has proven to be successful both aesthetically and functionally. The patient's tooth has been restored to its normal position and the periodontal structures have regenerated to a satisfactory level[3].

A different article describes how platelet-rich fibrin was utilized in the emergency and rehabilitation treatment of a maxillary anterior tooth that had been completely displaced from its socket. The properties of platelet-rich fibrin, which are known to promote the growth of new bone and tissue, were harnessed to stimulate regeneration of both the pulp and periodontal tissues.

Over the course of several follow-up appointments, there were no indications of any negative clinical signs or symptoms. Additionally, after an initial period of six months, no further loss of bone or attachment was observed. The tooth remained functional and also maintained an aesthetically pleasing appearance[5].

In one of the case reports included in this study, the amalgamation of platelet rich fibrin (PRF) and demineralized freeze dried bone graft (DFDBA) with the use of PRF membrane during auto transplantation of an impacted central incisor has shown promising results. The placement of DFDBA in the extraction socket provided a scaffold for bone remodeling around the tooth, while the addition of PRF clot allowed for rapid healing. The use of a PRF membrane further optimized periodontal healing through guided tissue regeneration, allowing for recolonization of periodontal cells into the extraction site. After a 1 year follow-up, there were no signs of bone loss, root resorption, or ankylosis, indicating the success of this approach. Overall, this amalgamation of DFDBA and PRF products offers a promising solution for auto transplantation of impacted teeth[2].

Another article presents a case of traffic accident involving dental avulsion of maxillary incisors. Avulsed teeth, 11 and 12, had closed apices and intact crown and root surfaces. After extraoral endodontic therapy, immediate replanting was scheduled. Subsequently, the socket were irrigated with saline to remove the clot and any coarse remnants present. The teeth were re-implanted in the alveolus after the placement of a L-PRF membrane around the root surface. The evaluation carried out after one year revealed the absence of clinical symptoms and a satisfactory cure without signs of radiographic reabsorption[14].

In a different case study the effectiveness of the L-PRF is demonstratedduring immediate transplantation of a third molar with unformed roots into the extraction socket of a first molar. Two years of radiographic monitoring revealed ongoing root development, which was further confirmed by a periapical radiograph taken during a 3-year follow-up examination, along with other positive clinical indicators[1].

Another case study reports the effective reattachment of a permanent tooth that had been completely knocked out, despite a longer than usual period of time outside of the mouth, thanks to the use of an injectable form of platelet-rich fibrin (i-PRF). The patient's progress will be closely observed for indications of root resorption, infection, or ankylosis[13].

A different instance sought to illustrate the use of intentional replantation, with the aid of biomaterials such as mineral trioxide aggregate (MTA) and platelet-rich fibrin (L-PRF), as a final option to salvage a premolar that was otherwise deemed hopeless due to perforated internal resorption and root fracture. After a 2-year monitoring period, the tooth demonstrated adequate healing and continued to be free of symptoms[15].

A successful intentional replantation case report is presented in which a mandibular first molar with an endodontic mishap was replanted into the socket using digital finger pressure. To aid in periodontal regeneration and prevent ankylosis, PRF was packed into the alveolar socket wall. The patient was subsequently followed up after 1, 3, 6 months, 1 year, and 2 years, and healing was uneventful. The tooth exhibited normal mobility and probing depth, and the patient was asymptomatic at the 1-year follow-up. Clinical examination revealed no response to percussion or palpation, and probing depths and mobility were within normal limits. Radiographic findings at all recall visits showed a normal PDL space and continuous lamina dura around the tooth[16].

A rare case of autotransplantation of an impacted tooth in a post-odontoma site is described in another article. The procedure was performed in two stages using synthetic bone granules (Biograft) and PRF. The patient was followed up weekly for one month, and then at 2 and 6 months, and every 6 months thereafter. Throughout the follow-up period, there were no signs of infection. The slight mobility and tenderness on percussion observed at the time of splint removal gradually normalized. At the 6-month follow-up, there were no radiological signs of root resorption or bone loss[4].

A different article details how two patients had their incisors re-implanted following the avulsion of their sockets. Autologous PRF was used during the reimplantation procedure, and upon subsequent follow-up examinations at 3, 6, and 12 months, no symptoms of inflammatory root resorption or ankylosis were observed in the reimplanted teeth[10].

A case report is presented in which a 23-year-old male patient with a periodontally hopeless left maxillary central incisor is treated with a novel approach. The patient had experienced bone loss beyond the root apex, making conventional treatments difficult. The tooth was extracted gently and replanted using root conditioning and combined regenerative therapy, which included the use of Xenograft, PRF, and Type I Collagen Membrane.

After nine months, surgical re-entry showed evidence of bone formation in the apical third of the tooth. At one year, radiographic analysis revealed an 87% increase in bone gain. This innovative approach may offer new options for the treatment of periodontal disease, particularly in cases where traditional treatments may not be effective[17].

4.2.1- ADVANTAGES OF AUTOGENOUS TOOTH TRASPLANTATION

Autogenous tooth trasplantation can serve as a permanent solution for patients who are not suitable for dental implants or fixed prosthesis[1]. It is a faster and more economical treatment option that uses the patient's own tooth, providing a highly esthetic outcome[2]. The procedure also allows for future orthodontic movement of the transplanted tooth if necessary. Additionally, ATT preserves normal chewing and arch integrity, pulpal viability, and periodontal ligament health while maintaining normal proprioception reflexes, stimulating eruption in growing patients, and preventing loss of alveolar bone height[1]. Moreover, the success rate of auto-transplantation is over 90% based on a long-term review of cases ranging from 17 to 41 years, which is similar to dental implant-supported restorations[2]. The procedure is non-invasive, providing better access and visualization of the roots and greater patient comfort, making it a cost-effective option for patients[16].

4.2.2- INDICATIONS AND CONTRAINDICATIONS FOR AUTOLOGOUS TOOTH TRANSPLANTATION

The most important factor for successful replantation is the viability of periodontal ligament (PDL) cells[9].

Autotransplantation has gained popularity in recent times due to a better comprehension of its scientific basis, after years of being overshadowed by dental implants. The success of autotransplantation mainly relies on the availability of a sound alveolar bone at the transplant location and the regeneration of a functional periodontal ligament. The ultimate goal of autotransplantation is to replace a lost or irreparable tooth with a natural tooth having a normal periodontium within a short treatment duration[4].

There are several preoperative and postoperative factors that can affect the success rate of auto-transplantation. These factors include the age of the patient, any trauma to the alveolar bone or periodontal cells, the type of tooth being transplanted, contamination at the recipient site, timing of endodontic treatment, and the duration and method of splinting after transplantation[2].

Auto-transplantation of teeth can help preserve bone levels and stimulate the formation of alveolar bone, which is essential for ensuring the long-term success of dental implants, even in cases where implants have failed. This procedure is particularly useful for replacing congenitally missing teeth, as well as for restoring upper maxillary incisors lost due to traumatic injury. Additionally, auto-transplantation can be used in conjunction with orthodontic treatment to reconstruct the mandibular margin. In cases where caries and periodontal disease lead to first molar loss in a pubertal patient, auto-transplantation can successfully replace removable dentures, as dental implants cannot be placed until skeletal maturity is reached[1].

Several crucial factors play a significant role in promoting healing after tooth extraction and reinsertion, including gentle handling of the tooth during the process, the use of a root hydration medium, prevention of any damage to the tooth roots, minimizing the time the tooth is outside of the mouth, achieving an adequate apical seal with appropriate material compaction, and ensuring suitable case selection. Additional factors that can affect the success of the treatment include the use of preoperative antibiotics and disinfection, as well as the number of operators involved in the procedure.

Although teeth with flared or curved roots, periodontal involvement, vertical root fracture, or nonrestorable teeth are generally considered contraindications, recent evidence suggests that this treatment can still be successful in periodontally compromised hopeless teeth and can serve as a means of preserving natural dentition[16].

Author Publication Year	Population	Aim	L-PRF Preparation Protocol	Healing period/ Follow up	Comparison/Control	Findings/Conclusions
Chaudhary Z. et al. 2015 (2)	1 patient, 22-year-old patient	Evaluate the effect unique amalgamation of platelet-rich fibrin (PRF), demineralized freeze-dried bone graft (DFDBA) with use of PRF membrane during auto-transplantation of an impacted central incisor.	20 ml for 10 min at 3000 rpm	1 year	N/A	Placement of DFDBA in the extraction socket provided a scaffold for bone remodeling around the tooth. PRF clot mixed with the DFDBA allowed rapid healing. The graft was covered with a PRF membrane, which permitted recolonization of the periodontal cells into the extraction site and optimized the periodontal healing, based on the concept of guided tissue regeneration. A 1-year of follow-up revealed no signs of bone loss, root resorption, or ankylosis which confirmed the promising results of the amalgamation of DFDBA and PRF products.
Parthasarathy R. et al. 2022 (14)	1 patient 30-year-old patient	Describe the interdisciplinary management of two avulsed and reimplantated teeth after 2 hours of extraoral time.	Non disclosed	1 year	N/A	The 2 avulsed teeth, after undergoing extraoral endodontic therapy, place a PRF membrane around the surface of their roots and be implanted in their respective alveolar sockets (previously irrigated with saline) and then performed the interdisciplinary approach to correct the bone defect, were evaluated after a year and did not present clinical symptoms or resorption and had a satisfactory healing.
Alkofahi H. et al. 2020 (1)	1 patient 16 year-old patient	Describe the autotransplantation of a third molar to the alveolar socket of a first molar, introducing PRF into the recipient alveolar socket.	10 cc for 10 minutes at 3000 rpm.	1 year	N/A	The benefits of including PRF in autotransplantation of teeth with immature roots acts positively during the inmediate and late regeneration process. PRF can eliminate the risk of arrested root formation and the need for pulpal treatment and can decrease the risk of complications.
Yang Y. et al. 2021 (15)	1 patient 20 year-old patient	Describe the intentional replantation as a last resort to save an otherwise hopeless premolar with perforated internal resorption and root fracture, with the application of biomaterials	Not disclosed	2 years	N/A	The successful outcome of the case suggests that intentional replantation could preserve a fractured tooth caused by internal root resorption. Incorporated application of biomaterials, such as

		including mineral trioxide aggregate (MTA) and platelet-rich fibrin (L-PRF).				MTA and L-PRF, might as well improve the chances of saving this otherwise hopeless tooth.
Patel G.K. el al. 2013 (3)	1 patient 16 year-old patient	Describe the case of a patient, where management of extrusive luxation of the left central incisor was done by intentional replantation using benefits of platelet rich fibrin (PRF) in attempt to regenerate lost periodontal structure.	10 ml at 3000 rpm	6 months	N/A	Intentional replantation with PRF can be an alternative and effective modality of treatment for management of a tooth with hopeless prognosis.
Johns et al. 2013 (5)	1 patient 15 year-old patient	Describe the reimplantation o fan avulsed maxillary anterior tooth using platelet-rich fibrin. The osteoconductive and osteoinductive properties of PRF were used to stimulate periodontal and pulpal regeneration.	12 ml for 10 min at 3000 rpm	2 yers	N/A	No clinical symptoms and signs were present during a 24 months follow up. After 6 months, no further bone loss attachment loss were observed. The tooth was aesathetically acceptable and remained functional.
Singh W.R. et al. 2015 (4)	1 patient	We present the case of an autotransplant of a central incisor included in a post-odontoma site in which a surgical procedure is performed in two stages using synthetic bone granules (Biograft) and PRF, with the aim of improving prognosis and shortening treatment time.	10 ml for 10 min at 3000 rpm	6 months	N/A	An absence of infection, a normal pocket depth and a lack of pathological tooth mobility and radiographic absence of periodontal bone loss or root resorption were observed at 6 months follow up.
Yang Y. et al. 2023 (10)	2 patients	The aim of this work was to improve the success rate of avulsed teeth after late reimplantation using autologous platelet-rich fibrin.	10 ml for 10 min at 400xg (3000 rpm)	1 year	N/A	After simultaneous reimplantation of avulsed teeth with autologous PRF, reimplantated teeth showed no symptoms of inflammatory root reabsorption or ankylosis in both cases, suggesting that the application of PRF may offer new therapeutic opportunities for "hopeless" avulsed teeth.
Ryana H.K. et al. 2016 (17)	1 patient 23 year-old patient	Describe the reimplantation of a left maxillary central incisor with periodontally hopeless, having bone loss extending beyond root apex. The tooth was extracted and replanted utilizing root conditioning and	5 ml for 10 min at 3000 rpm	1 year	N/A	The case indicates intentional reimplantation as a promising treatment option that lays the foundation for future research, concluding that is not necessarily contraindicated in periodontally compromised teeth

		combined regenerative therapy (Xenograft, PRF and Type I Collagen Membrane).				
Suresh N. et al. 2021 (13)	1 patient 21 year-old patient	Discuss the successful replantation of an avulsed permanent tooth with an increased extraoral dry time using Injectable form of Platelet rich fibrin.	5 ml for 3 min at 700 rpm	1 year	N/A	After a year of follow-up, no signs of root resorption, infection or ankylosis were detected in the transplanted tooth.
Despande N.M. et al. 2019 (16)	1 patient 23 year-old patient	This report presents a successful case of intentional reimplantation of a first mandibular molar whose procedure served as a means to remove a fractured endodontic instrument. Platelet-rich fibrin was placed in the alveolar cavity to improve reinsertion of PDL cells and prevent ankylosis.	10 ml for 10 min at 3000 rpm	2 years	N/A	Radiographic findings revealed a normal PDL space and a continuous hard lamina around the tooth at all revision visits.

Table 3. Case report results

5- DISCUSSION

In the Chaudhary *et al.*[2] article from 2015, a combination of DFDBA, PRF gel, and PRF membrane was used to autotransplant an impacted central incisor, resulting in synergistic benefits. This is one of the few cases in which such a combination has been used. Based on this case, the authors suggest that allogenic bone graft and PRF products could be used in other types of bony defects as well.

Extraoral drying time plays a vital role in determining the result, since excessive drying would have harmful effects on the cells of the periodontal ligament, reducing their regenerative capacity and increasing the probability of root resorption.

In his article from 2022, Parthasarathy *et al.*[14] emphasize stresses the significance of taking an interdisciplinary approach in the re-implantation of avulsed teeth, even in cases where the tooth has been outside the mouth for up to two hours. They concluded that the knowledge and management of the patient in cases of avulsion is of paramount importance, directly influencing the outcome of the treatment.

In 2020 Alkofahi *et al.*[1] reported a case where they performed immediate autotransplantation of a third molar with underdeveloped roots into the extraction site of a first molar. To enhance the healing and regeneration of periodontal tissues and pulp formation, they employed platelet-rich fibrin (PRF). The results of their study indicated that incorporating PRF in the autotransplantation of teeth with immature roots, even with less than 25% root development, positively affected both the immediate and long-term regeneration process. The use of PRF could potentially prevent arrested root development, reduce the need for pulpal treatment, and lower the risk of complications.

The 2021 study conducted by Suresh *et al.*[13] highlights the successful use of Injectable form of Platelet rich fibrin (i-PRF) in the replantation of an avulsed permanent tooth, even with an increased extraoral dry time. While delayed replantation is not considered as an ideal conventional treatment option, the use of advanced biomaterials like i-PRF can promote physiological events of regeneration, leading to improved survival rates for such treatments. However, the authors also note that further studies are needed to establish the long-term prognosis of late PRF re-implantation. It is important to continue exploring and refining the use of biomaterials in dental treatments to improve outcomes and provide better options for patients who have suffered dental trauma.

Yang *et al.*[15] presented a case in 2021 that illustrated the utilization of intentional replantation as a final option to rescue a premolar suffering from internal resorption with root fracture. The positive outcome of this case indicates that intentional replantation might be an effective solution for preserving a broken tooth due to internal root resorption. The integration of biomaterials, including MTA and L-PRF, could also potentially enhance the probability of saving such a tooth that would otherwise be deemed hopeless.

Deshpande *et al.*[16] reported in 2019 a successful case of intentional replantation used to address an endodontic complication in the mandibular first molar. Specifically, an endodontic instrument had become separated in the apical third of the root canal and extended beyond the mesiobuccal root apex. To remove the separated instrument, intentional replantation was performed. Throughout the endodontic treatment, the viability PDL cells was maintained using a distinctive technique, which involved using a preoperative impression for continuous wetting with saline. Furthermore, L-PRF was shredded and placed in the alveolar socket to enhance PDL cell reattachment and prevent ankylosis. The successful 2-year follow-up of the case supports the use of intentional replantation as a viable option for removing separated instruments that extend beyond the root apex. Moreover, employing these techniques to maintain PDL cell viability and using L-PRF can aid in preventing ankylosis.

Patel *et al.*[3] described in 2013 a case involving a 16-year-old patient who underwent intentional reimplantation for the management of an extrusive dislocation of their left central incisor. They utilized L-PRF to regenerate lost periodontal structure and observed promising results. The authors concluded that intentional reimplantation with PRF may offer an alternative and effective treatment option for teeth with a poor prognosis. This procedure is relatively conservative and cost-effective. However, further studies and long-term follow-up are necessary to establish the efficacy of this treatment modality.

Jonhs *et al.*[5] described in their article from 2013 the use of platelet-rich fibrin for the emergency treatment and rehabilitation of an avulsed anterior maxillary tooth. They utilized the osteoinductive and osteoconductive properties of this substance to encourage regeneration of the pulp and periodontal tissue. Based on their findings, the authors stated that as long as the periodontal ligament that remains attached to the root surface does not dry out, the effects of tooth avulsion are typically not severe.

In 2015, Singh *et al.*[4] conducted a two-stage surgical procedure with the assistance of synthetic bone granules (Biograft) and PRF to improve prognosis and reduce treatment time for a rare case of self-injury to an impacted tooth at a post-odontoma site. The results of clinical and radiological assessments after a 6-month follow-up period demonstrated promising outcomes with no signs of infection, normal pouch depth, absence of pathological dental mobility, and no radiographic evidence of periodontal bone loss or root resorption.

In 2023, Yang *et al.*[10] aimed to enhance the success rate of late reimplantation of avulsed teeth by utilizing L-PRF. They concluded that enriching L-PRF with growth factors and leukocytes may decrease pathological resorption, facilitate the healing of periodontal wounds, and promote the regeneration of the periodontal ligament after late reimplantation of avulsed teeth. Although further demonstration of treatment efficacy is necessary, the utilization of L-PRF could potentially provide novel therapeutic possibilities in similar cases.

In a case report from 2016, Ryana *et al.*[17] documented the successful treatment of a 23-year-old male patient with a periodontally hopeless left maxillary central incisor. The patient had extensive bone loss beyond the root apex, and the tooth was extracted with care and replanted using a combination of regenerative therapies, including Xenograft, PRF, and Type I Collagen Membrane, along with root conditioning. Follow-up assessments using clinical and radiographic parameters showed significant improvement, which was further reinforced by the findings of re-entry surgery. These results suggest that intentional replantation may be a more cost-effective alternative to implants or tooth-supported prostheses when conventional periodontal therapy may yield compromised outcomes.

In their study from 2019, Navarro *et al.*[6] assessed the effectiveness of autologous platelet-rich fibrin (PRF) in preserving and restoring the viability of periodontal ligament (PDL) cells. Their findings demonstrated that autologous PRF was successful in sustaining and restoring PDL cell viability in extracted teeth, even after being left dry for a period of up to 2 hours.

In 2017, Moradian *et al.*[12] suggested the development of a scaffold based on PRF to evaluate functionality and viability of BMMSCs within the scaffold. In vitro experiments were conducted using human BMMSCs that were isolated and characterized based on their surface markers and their potential for differentiation into osteogenic or adipogenic lineages. The impact of the PRF scaffold on BMMSCs was assessed by measuring cell proliferation. The findings indicated that using PRF scaffolds with fragments of BMMSC cell laminae was effective, and that PRF growth factors could enhance the prognosis of avulsed teeth that are stored dry.

Ji *et al.*[7] conducted an in vitro study in 2015 to examine the impact of canine platelet-rich fibrin (PRF) and tissue-derived matrix (TDM) on periodontal ligament stem cells (PDLSC) and bone marrow stem cells (BMSC). The findings indicated that PRF and TDM can promote regeneration of the root of a tooth attached to the alveolar bone via the cementum-periodontal ligament complex. This regeneration is believed to be facilitated by the recruitment of PDLSC and BMSC in the microenvironment of dental socket. Moreover, creating a bioactive environment and inducing a microenvironment are crucial factors in the natural regeneration process.

Zhao *et al.*[8] carried out a study in 2013 with the objective to developing a cell transplantation technique that utilized cell sheet fragments of periodontal ligament stem cells (PDLSCs) and platelet-rich fibrin (PRF) granules, in order to enhance the healing of periodontal tissues in cases of re-implantation of avulsed teeth. The study demonstrated that the transplantation method was effective in promoting the healing of periodontal wounds and regeneration of PDL tissues following delayed re-implantation of avulsed teeth.

In 2021, Benhaz *et al.*[9] conducted a study with the objective of assessing the impact of L-PRF on the late reimplantation of teeth in two fully-grown Beagle dogs. Their findings indicate that while the application of PRF in the extraction socket prior to late reimplantation did result in a reduction in inflammatory root reabsorption, no significant advantages were otherwise observed.

In 2014, Hiremath *et al.*[11] carried out a research aimed at evaluating the viability of periodontal ligament (PDL) cells after immersion in an autologous rejuvenating medium following 40 minutes of extraoral dry time. The results of the study suggest that the use of a combination of L-PRF and PPP resulted in a higher number of viable PDL cells. This finding indicates that this approach could be a useful method of biological rejuvenation for teeth that have been avulsed.

5.1- L-PRF COLLECTION

To prepare platelet-rich fibrin (PRF), 20 ml of blood was withdrawn from the patient's antecubital vein and centrifuged for 10 min at 3000 rpm (approximately 400 g) per minute[1-3] or at 2700 rpm for 12 min[9]. The blood was collected without anticoagulant and transferred into two sterile vacutainer tubes, each containing 9 mL[6,9]. The tubes were symmetrically placed in a centrifuge device[9].

After the centrifugation process, the PRF formed as a fibrin clot. By compressing the fluids contained within the fibrin matrix, a semi-transparent and durable autologous fibrin membrane was obtained. Analysis of the microstructure indicated that the upper region of the PRF contained no cells, while the lower region contained mostly leukocytes and some red blood cells that accumulated at the junction between the red corpuscles and the PRF clot. The fibrin clot was found in the middle of the tube and was easily separated from the red corpuscles at the bottom. After compression with sterile dry gauze, the trapped fluids were expelled from the fibrin matrix, resulting in a highly durable autologous fibrin membrane[8].

5.2- THE L-PRF ROLE IN WOUND HEALING AND TISSUE REGENERATION

The regeneration of tissues after surgery requires the mobilization of progenitor/stem cells to differentiate into committed cells, as well as the presence of growth and differentiation factors that act as necessary signals for cell adhesion, migration, proliferation, and differentiation. In addition, local microenvironmental signals are required, such as adhesion molecules, extracellular matrix, associated non-collagenous protein molecules, and others[2,6].

PRF can stimulate cell proliferation of osteoblasts, gingival fibroblasts, and periodontal ligament cells while suppressing oral epithelial cell growth, making it a promising biomaterial for periodontal regeneration and pulp-dentin complex regeneration[5,13,15].

L-PRF is composed of an autologous matrix rich in leukocytes and platelets, which contains various mitogenic factors such as platelet-derived growth factor, vascular endothelial growth factor, and transforming growth factor released from the α-granules[1].

The α-granules within the platelets store proteins essential for wound healing, such as PDGF, TGF-b, IGF, EGF, and VEGF, which are released upon activation and degranulation of the α-granules[8].

Beta-transforming growth factors (TGF-β1) induce collagen I synthesis, while insulin-like growth factors (IGFs) protect cells by increasing their survival potential[6].

L-PRF stimulates angiogenesis through the migration, division, and phenotypic changes of endothelial cells, promoting cell mitosis and inducing osteogenesis without causing inflammatory reactions[1].

Thus, many growth factors, such as platelet-derived growth factor, transforming growth factor-β, insulin-like growth factor, epidermal growth factor, and vascular endothelial growth factor, can be released for at least a week and up to four weeks. Therefore, PRF supports the regenerative and remodeling environment for a certain period of time. These growth factors increase the mitotic activity of periodontal fibroblasts by 20%-37%, thereby improving the proliferation and periodontal differentiation of target cells and further promoting periodontal healing. When a variety of growth factors act together, synergistic or even antagonistic effects among them cannot be ruled out. Therefore, the natural proportion of various growth factors is particularly important[10].

Previous studies with PRF have shown faster healing and increased bone regeneration when used in the treatment of cystic cavities, maxillary sinus lift procedures, alveolar preservation, palatal bandaging, and grade II furcation defects in the mandible[3].

In dentistry, PRF has shown favorable results in recovering and repairing soft and hard tissues, particularly in implant dentistry and periodontal applications. It has also been used as a biocompatible matrix for delivering therapeutic agents to improve clinical efficacy and sustain cells between the alveolar bone and cementum[6].

PRF has also been demonstrated to stimulate osteogenic differentiation of human dental pulp cells by up-regulating osteoprotegerin and alkaline phosphatase expression[5].

Furthermore, PRF has demonstrated successful outcomes as a sole agent in periodontal regeneration, including clinical attachment loss and intrabony defects. It has also proven effective in regenerative endodontics, where it increases the thickness of dental-associated mineral tissue[1].

5.3- THE ROLE OF L-PRF IN THE INHIBITION OF OSTEOGENIC DIFFERENTIATION AND REDUCTION OF ANKYLOSIS

The root is the most essential part of the tooth for maintaining its functions. Loss of periodontal tissue, which serves as the functional interface between the root and alveolar bone, can compromise tooth function and even lead to tooth loss[7].

When a tooth is harvested for transplantation, two main tissues are primarily injured: the dental pulp and periodontal ligament. Poor healing of these tissues can lead to two major complications: inflammatory root resorption and replacement root resorption or ankylosis[2,9,10].

Preventing damage to the cementum and pulpal infection is crucial in avoiding replacement resorption and inflammatory resorption of the root, respectively. Among the criteria for success, the absence of chronic root resorption is the most important[4].

In cases where the root canal becomes infected, microbial toxins can migrate to the root surface via dentinal tubules, resulting in root resorption. Timely removal of the etiological cause, such as root canal intervention, can prevent or control inflammatory root resorption on the outer surface[2,9,10].

The high density leukocytes in the PRF could produce an anti-inflammatory and immunoregulatory effect to promote healing and reduce inflammatory resorption[8].

When cementoblastic cells move slowly and cannot cover the entire surface of the root in time, bone cells can come into direct contact with the root surface, which may lead to replacement root reorption or ankylosis[5].

To prevent osseous replacement or ankyloses, it is recommended to remove any remaining periodontal ligament (PDL) that may act as a source of infection[13].

The same way is immediate replantation or storage of the tooth in an appropriate storage medium[10]. Replacement root resorption/ankylosis occurs when the damaged periodontal ligament fails to heal, and these complications typically manifest within six months to one year after treatment[2].

The pulp necrosis is also an inevitable consequence of avulsion injuries, which requires endodontic procedures[5].

Several factors are crucial to achieve a successful autotransplantation of teeth. Atraumatic extraction should be performed to preserve the Hertwig's epithelial root sheath, which is responsible for future root growth. The duration of the tooth outside the socket should also be minimized, and the dimensions of the apical foramen should be more than 1 mm to increase the chances of postoperative revascularization. Additionally, maintaining good alveolar bone support during the procedure is important.

While ATT of mature and immature teeth has a high success rate, endodontic treatment is usually required in mature teeth within four weeks to prevent the development of pulp-associated lesions[1].

6- CONCLUSION

The use of L-PRF in autotransplantation of teeth with immature roots has shown positive impacts on the regeneration process and eliminated the risk of arrested root formation, decreasing the need for pulpal treatment and reducing the risk of complications. Additionally, L-PRF has been shown to be a suitable scaffold material due to its biodegradability, mechanical properties, and ability to prevent infections. The use of L-PRF as an adjunctive treatment modality in periodontal defects has also shown faster healing and bone fill. In general, potential benefits of using L-PRF in various dental procedures have been demonstrated.

In response to the hypotheses raised at the beginning of this review:

H0 (Null hypothesis) = There is no difference between the results of autologous tooth transplantation with the L-PRF technique compared to the conventional technique.

H1 (Hypothesis 1) = There is a significant difference between the results of autologous tooth transplantation with the L-PRF technique compared to the conventional technique.

We can conclude, whitin the limitations of this study, that we accept the null hypothesis, as the results obtained do not show significant differences in the specific case of autologous tooth transplantation, the provided data does not allow for a direct comparison between the L-PRF technique and conventional techniques.

Therefore, further research is needed to compare the results of both techniques in this specific context.

7- REFERENCES

1. Alkofahi H, Maghaireh A, Fnaish M, Jarrah M, Bataineh M. Application of Platelet-Rich Fibrin as Regeneration Assistant in Immediate Auototransplantation of Third Molar with Unformed Roots: Case Report and Review of Literature. Case Rep Dent. 2020 Jan 21.

2. Chaudhary Z, Kumar YR, Mohanty S, Khetrapal A. Amalgamation of allogenic bone graft, platelet-rich fibrin gel, and PRF membrane in auto-transplantation of an impacted central incisor. Contemp Clin Dent. 2015 Apr 1;6(2):250–3.

3. Patel GK, Gujjari SK, Annapoorna BM, Veerendra Kumar SC. Management of chronic luxated central incisor with hopeless prognosis. J Indian Soc Periodontol. 2013 Sep;17(5):670–5.

4. Robindro Singh W, Aheibam K, Nameirakpam A. Post-Odontoma autotransplantation of an impacted tooth: A case report. J Oral Biol Craniofac Res. 2015 May 1;5(2):120–3.

5. Johns DA, Shivashankar VY, Maroli RK, Vidyanath S. Novel management of avulsed tooth by pulpal and periodontal regeneration. J Endod. 2013 Dec;39(12):1658–62.

6. Navarro LB, Barchiki F, Navarro Junior W, Carneiro E, da Silva Neto UX, Westphalen VPD. Assessment of platelet-rich fibrin in the maintenance and recovery of cell viability of the periodontal ligament. Sci Rep. 2019 Dec 1;9(1).

7. Ji B, Sheng L, Chen G, Guo S, Xie L, Yang B, et al. The combination use of platelet-rich fibrin and treated dentin matrix for tooth root regeneration by cell homing. Tissue Eng Part A. 2015 Jan 1;21(1–2):26–34.

8. Zhao YH, Zhang M, Liu NX, Lv X, Zhang J, Chen FM, et al. The combined use of cell sheet fragments of periodontal ligament stem cells and platelet-rich fibrin granules for avulsed tooth reimplantation. Biomaterials. 2013 Jul;34(22):5506–20.

9. Behnaz M, Izadi SS, Mashhadi Abbas F, Dianat O, Sadeghabadi S, Akbarzadeh T, Haeri A, Kazem M, Younessian F. The impact of platelet-rich fibrin (PRF) on delayed tooth replantation: A preliminary animal study. Aust Endod J. 2021 Dec;47(3):457-466.

10. Yang Y, Liu YL, Jia LN, Wang JJ, Zhang M. Rescuing "hopeless" avulsed teeth using autologous platelet-rich fibrin following delayed reimplantation: Two case reports. World J Clin Cases. 2023 Jan 26;11(3):635–44.

11. Hiremath H, Kulkarni S, Sharma R, Hiremath V, Motiwala T. Use of platelet-rich fibrin as an autologous biologic rejuvenating media for avulsed teeth - an in vitro study. Dent Traumatol. 2014 Dec;30(6):442-6.

12. Moradian H, Rafiee A, Ayatollahi M. Design and Fabrication of a Novel Transplant Combined with Human Bone Marrow Mesenchymal Stem Cells and Platelet-rich Fibrin: New Horizons for Periodontal Tissue Regeneration after Dental Trauma. Iran J Pharm Res. 2017 Fall;16(4):1370-1378.

13. Suresh N. Entitled "THE MAGIC WAND": A novel treatment option for delayed replantation of an avulsed permanent tooth using injectable platelet-rich fibrin. J Indian Soc Periodontol. 2021 May 1;25(3):262–6.

14. Parthasarathy R, Srinivasan S, C V, Thanikachalam Y, Ramachandran A. An Interdisciplinary Management of Avulsed Maxillary Incisors: A Case Report. Cureus. 2022 Apr 6;14(4).

15. Yang Y, Zhang B, Huang C, Ye R. Intentional Replantation of a Second Premolar with Internal Resorption and Root Fracture: A Case Report. J Contemp Dent Pract. 2021 May 1;22(5):562-567.

16. Deshpande NM, Shah D, Wadekar S. Maintenance of cell viability in extraoral conditions for a case of intentional replantation to retrieve a separated endodontic instrument. J Conserv Dent. 2019 Mar-Apr;22(2):207-212.

17. Ryana HK, Srinath R, Prakash S. Surgical Re-entry of an Intentionally Replanted Periodontally Compromised Tooth Treated with Platelet Rich Fibrin (PRF): Hopeless to Hopeful. J Clin Diagn Res. 2016 Jun;10(6): ZD01-4.