A SYSTEMATIC REVIEW OF THE USE OF PLATELET-RICH FIBRIN IN THE HEALING IN ADULTS IN ORAL SURGICAL PROCEDURES

Master’s Thesis

Dr. Marijus Leketas
D.D.S. Oral Surgeon

Kaunas, 2017
A SYSTEMATIC REVIEW OF THE USE OF PLATELET-RICH FIBRIN IN THE HEALING IN ADULTS IN ORAL SURGICAL PROCEDURES

Master’s Thesis

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Kaunas, 2017
# EVALUATION TABLE OF THE MASTER’S THESIS
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*In total (maximum 10 points):

**Remark:** the amount of collected points may exceed 10 points.

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SUMMARY

Aims: To evaluate the effect of platelet-rich fibrin (PRF) in the healing in adults in oral surgical procedures by comparing the use of PRF to traditional treatments.

Objectives: To search the literature for randomised controlled trials involving the use of platelet-rich fibrin in adults in oral surgical procedures. To perform a screening process of the literature and to analyse the included studies.

Methods: An electronic search was conducted on PubMed MEDLINE and the Cochrane Central Register of Controlled Trials database to identify randomised controlled trials published between March 2012 and March 2017. The keywords used during the search were “platelet rich fibrin”. A manual search was performed in bibliographies of included articles, and in relevant journals.

Results: The electronic search yielded 1369 articles, nine articles matched the inclusion criteria. The articles included 197 patients and 394 treatment sites, involving four oral surgical procedure types. Four articles evaluated healing after bilateral contralateral impacted third molar extractions, two studies evaluated alveolar ridge preservation and socket preservation after bilateral contralateral tooth extractions, two studies evaluated bilateral Miller Class I or Class II gingival recession defect treatment, and one study evaluated bilateral gingival recession treatment. Five of the nine studies presented statistically significant results, favouring PRF.

Conclusion: The use of PRF in oral surgical procedures may be an effective method in healing in adults in oral surgical procedures, such as after impacted third molar extractions, simple tooth extractions, Miller Class I or Class II gingival recession defect treatment, and in gingival recession treatment.
INTRODUCTION

An oral surgical procedure begins with the initial patient consultation and ends with the post-surgical healing of the clinically induced wound. Various treatments are used to aid the healing in socket preservation, and bone defect and gingival defect treatment. Treatments include bone grafts and substitutes, connective tissue grafts, and membranes. Autologous blood products have been used in dentistry for at least thirty years. The most recent protocols include platelet-rich plasma (PRP) (1998) (1) and plasma rich in growth factors (PRGF) (1999), that have been used in the healing phase, guiding the growth and healing of new tissue. (2) Platelet-rich fibrin (PRF) has also been in use in dentistry since 2001. Unlike the other protocols, PRF requires no chemical additives to the collected blood. (3) Wound healing presents as inflammation such as pain and swelling, and proliferation and repair such as neoangiogenesis, osteogenesis, and gingival attachment. (4) These mechanisms are thought to be of various effectiveness, depending on the patient’s own immune system, the particular conditions of the surgery, as well as the type of adjunctive treatment used for healing. It is to the author’s best knowledge that no systematic review exists that does not limit the type oral surgical procedure in the inclusion criteria.

SELECTION CRITERIA OF THE STUDIES. SEARCH METHODS AND STRATEGY

PROTOCOL

Objective: The purpose is to systematically review the current literature as to whether PRF is effective in healing in oral surgical procedures, in adults in comparison to a control of traditional treatment.


Study selection: only randomised controlled trials with a split mouth study design and a suitable control, published within the past 5 years (March 2012 – March 2017), human studies, clinically evaluated outcomes, PRF usage in healing in oral surgical procedures in adults were included. Only articles published in the English language were included.

Data extraction: Data extraction was performed for studies that fulfilled the inclusion criteria. Data extraction included participant and intervention characteristics, reported data on the efficacy of the outcomes using standard data extraction templates.

Data Synthesis: The databases PubMed MEDLINE and the Cochrane Central Register of Controlled Trials were searched. A manual search was also performed. Studies that met all the requirements of the inclusion criteria set for this systematic review were selected.

Results: Five of the nine studies presented statistically significant results, favouring the intervention of PRF.

Conclusions: The literature appears inconclusive regarding the effectiveness of PRF compare to traditional treatment, in the healing in oral surgical procedures in adults.
ELIGIBILITY CRITERIA

In this systematic review, studies with evidence level I were included (randomised controlled trials (RCT)). Articles were selected according to the criteria listed below. Articles older than five years were included.

Types of study designs: Only evidence level I studies (RCTs), with the additional requirement of a split-mouth, bilateral design, were included. Other study designs such as randomised controlled trials without a split-mouth design, case reports, case series, review articles, abstracts, discussions, interviews, editorials and opinions will be excluded. Only in-vivo studies and articles published in the English language will be included.

Types of participants: Studies involving the treatment of adult humans (18 years and older) will be included. Non-human studies will be excluded.

Types of Intervention: PRF prepared according to the protocol by Choukroun et al., in oral surgical procedures, such as extractions, and bone defect and gingival defect treatment. The protocol involves taking peripheral blood samples in glass coated plastic tubes, with no additional clotting factors, centrifugation at 3000rpm for 10 minutes, then compressing the platelet rich fibrin layer to obtain a platelet-rich fibrin membrane (3).

Types of comparator: The control group will be either no use of PRF, or using the traditional treatment for a particular procedure.

Types of outcomes: The main outcomes were clinical and radiographic evaluation of soft and hard tissue healing, and pain evaluation. The outcome measurements were separated according to the type of oral surgery performed. Due to the possible variety of the potential studies, it is likely that the exact nature of each study will have different outcomes. As a result, the outcomes were not limited as otherwise a very limited number of studies could be included. There was not limit to the duration of the follow-up time of the studies.
INFORMATION SOURCES

Information sources included PubMed MEDLINE, the Cochrane Central Register of Controlled Trials database and a manual search of bibliographies of included articles and of relevant journals.

ELECTRONIC SEARCH STRATEGY

The search strategy will include searching electronic databases and conducting a manual search. An electronic literature search will be conducted on the PubMed MEDLINE database (https://www.ncbi.nlm.nih.gov/pubmed) and the Cochrane Central Register of Controlled Trials database (http://onlinelibrary.wiley.com/cochranelibrary/search). Additional manual searches will be performed in bibliographies of included articles and relevant journals.

The electronic search was conducted on the 4th of March 2017.

1. PubMed MEDLINE search
   Filters applied:
   1. Publication dates: 5 years (6th March 2012 - 4th March 2017)
   2. Species: Humans
   3. Article types: Randomized Controlled Trial
   4. Languages: English

2. Cochrane Central Register of Controlled Trials search
   Filters applied:
   1. Trials only
   2. Publication year between 2012 and 2017

3. Manual search of bibliographies of included articles and related journals

SELECTION SCREENING PROCESS

The titles and abstracts yielded by the electronic search were evaluated against the inclusion criteria. During screening of articles, full texts were analysed. Reasons for excluding articles were
included. The author and the supervisor were not blind to the journal titles, nor to the study authors or institutions.

1. PubMed MEDLINE search
   1287 articles at first search
   34 articles screened after filters applied
   32 articles excluded:
   1. n = 10 inaccessible
   2. n = 8 not oral surgery
   3. n = 1 in vitro - non clinical study
   4. n = 2 PRF preparation protocol not according to Choukroun
   5. n = 8 no control or unsuitable control
   6. n = 1 not adults
   7. n = 2 not split mouth studies
   Studies included in data synthesis: n = 2

2. Cochrane Central Register of Controlled Trials search
   76 articles title and abstract screened
   68 articles after 8 duplicates removed
   37 suitable articles
   31 articles excluded
   1. n = 7 not split mouth study
   2. n = 8 inaccessible
   3. n = 2 PRF preparation protocol not according to Choukroun et al.
   4. n = 4 no control or unsuitable control
   5. n = 1 not oral surgery
   6. n = 1 additional variable
   7. n = 2 not randomised controlled trial
   Studies included in data synthesis: n = 4

3. Additional records identified through other sources (hand search of journals): n = 6

Total number of articles included in the systematic review data synthesis n = 9
DATA EXTRACTION METHOD

Data extraction will be performed by the author based on the Cochrane Consumers and Communication Review Group’s data extraction template.

RISK OF BIAS EVALUATION

The risk of bias of the articles was assessed according to the Cochrane Risk of Bias Tool. A total of seven domains were evaluated: random sequence generation, allocation concealment, blinding of patients and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting risk and other potential threats to validity. The risk of bias was evaluated both at the study level and outcome level. Five studies had random sequence generation, the remaining studies did not mention the method of sequence generation. Only one study had and mentioned allocation concealment. Only one study mentioned blinding of participants and personnel. Four studies mentioned blinding of outcome data, the others did not. All studies had no issues relating to incomplete outcome data and all articles discussed patient attrition where relevant. Four studies had pre-specified outcomes, meaning a low risk regarding selective outcome reporting. Seven studies had low risk of other potential threats to validity.

RISK RATIO, DIFFERENCES IN MEANS

The risk ratio and differences in means are not available because a meta-analysis is not being performed. This systematic review is analysing continuous outcomes, not dichotomous outcomes.

SYSTEMISATION AND ANALYSIS OF DATA

NUMBER OF STUDIES SCREENED FOR ELIGIBILITY

A total of 9 randomised clinical trials were identified for inclusion in this systematic review. The electronic search of PubMed MEDLINE, the Cochrane Central Register of Controlled Trials database and the manual search provided a total of 1369 articles. After adjusting for duplicates, 1358 articles remained. After the application of filters on the PubMed search, 105 articles were screened, with 31 articles excluded due to irrelevant abstracts and 26 articles excluded due to inaccessible full articles. The full text of the remaining 48 articles was examined and 39 articles did
not meet the inclusion criteria. Nine articles met the inclusion criteria. No unpublished relevant studies were obtained.

1. PubMed MEDLINE search
   Initial number of articles: 1287
   Final number of articles for title and abstract evaluation after application of filters: 34

2. Cochrane Central Register of Controlled Trials database search
   Initial number of articles: 76
   Final number of articles for title and abstract evaluation after removal of duplicates: 68

3. Manual search of bibliographies and relevant articles
   Initial number of articles: 6
   Final number of articles for title and abstract evaluation after removal of duplicates: 3
The following flowchart illustrates the search, keyword search and the retrieved results:

Papers identified through electronic database search (PubMed MEDLINE and Cochrane Central Register of Controlled Trials database) (n = 1363)

Additional records identified through a manual search of bibliographies and relevant journals (n = 6)

Total articles (n = 1369)

Duplicates removed (n = 11)

Papers after duplicates removed (n = 1358)

Records removed after application of filters (n = 1253)

Papers screened (n = 105)

Records excluded abstracts not relevant (n = 31)

Articles assessed for eligibility (n = 74)

Inaccessible records excluded (n = 26)

Full text articles assessed for eligibility (n = 48)

Full-text articles excluded, with reasons (n = 39)

1. n = 9 not oral surgery
2. n = 1 in vitro-non clinical study
3. n = 4 PRF preparation protocol not according to Choukroun et al.
4. n = 12 no control or unsuitable control
5. n = 1 not adults
6. n = 9 not split mouth study
7. n = 1 additional variable
8. n = 2 not randomised controlled trial

Studies included in the qualitative systematic review (n = 9)
CHARACTERISTICS OF THE ARTICLES

The nine articles included were from six different countries. Three articles were from Turkey, two from India, and the remaining articles were from Thailand, Cyprus, Serbia and Belgium. All articles were randomised controlled trials with bilateral treatment in adult subjects. Eight of the nine included studies performed treatment in one session, with one study waiting at least 21 days between the bilateral extractions of impacted third molars. Outcome measurements were performed by blinded clinicians in four studies and the remaining studies did not mention the nature of the blinding.

RESULTS

Bilateral impacted third molar extraction

Four articles evaluated the use of PRF in the healing of post-extraction sockets after impacted third molar extractions. Two of the four studies found statistically significant differences between the intervention and the control group.

Ozgul et al. found PRF to be efficient in postoperative horizontal swelling after impacted third molar extraction. The postoperative horizontal swelling, measured between the ear tragus and the buccal comissura, was measured at the baseline, and on the 1st day, 3rd day and 7th days postoperatively. The 1st day and 3rd day showed statistically significant results favouring the intervention group (mean ± standard deviation) (mm) (3.28 ± 3.02 vs. 4.64 ± 4.27) (p = 0.041) and (1.83 ± 2.52 vs. 3.63 ± 3.51) (p = 0.001). Of the 56 subjects requiring bilateral impacted third molar extractions (a total of 102 treatment sites), 20 subjects had horizontally positioned teeth, 15 subjects had “mezioangularly” positioned teeth and 21 subjects had vertically positioned teeth. All the included subjects had the removal of both impacted third molars during one session. (5) In a randomised controlled trial by Baslarli et al., which evaluated hard tissue outcomes, it was found that PRF had no effect on the healing of the extraction socket. The 20 included subjects with 40 treatment sites, had their bilateral vertically and/or mildly mesio-angularly positioned impacted third molars extracted during the same session. The study evaluated osteoblastic activity in the sockets using a scintigraphic study and grey values from orthopantomograms. (6) According to Uyanik et al., the use of PRF was found to significantly reduce pain and decrease trismus 24 hours postoperatively when compared to the control, which was a blood clot. The 20 included subjects
had a minimum of 21 days between the two extractions. The pain parameter, “visual analog scale” (VAS), was the sum of the measurements on the 1st, 2nd, 3rd and 7th days postoperatively. The trismus parameter was measured at baseline, prior to surgery, and on the 1st, 2nd, 3rd and 7th days postoperatively. The pain scores were found to be statistically significantly less in the PRF group compared to the control group (mean ± standard deviation) (VAS score) (25.00 ± 18.99 vs 74.60 ± 35.21) (p = 0.001). The 24 postoperative trismus, was found to be statistically significantly less in the PRF group than in the control (mean ± standard deviation) (%) (4.50 ± 9.03 vs 25.61 ± 16.65) (p = 0.011). (7) Kumar et al. found that PRF had a positive effect on both hard tissue and soft tissue healing. The 34 subjects (from an original 66 subjects) and 68 sites in the study had their bilateral impacted mandibular third molars removed in one session. Median pain scores were evaluated 1 day, 3 days, 1 week and 4 weeks postoperatively, a parameter reflecting soft tissue healing. Statistically significant differences were found in the median pain scores, between the intervention group and the control group, favouring the intervention group at 1 day, 3 days and 1 week postoperatively (median (interquartile range)) (3.0 (2.0 to 3.25) vs 6.0 (5.7 to 7.0)); (1 (0 to 2) vs 4 (3 to 5)); (0 (0 to 0) vs 1 (1 to 2)). Fractal analysis evaluating bone growth was measured at 2 months, 4 months and 6 months postoperatively. No statistically significant differences were found between the two groups in fractal analysis. (8)

Alveolar ridge preservation after bilateral tooth extraction

Suttapreyasri et al. found that PRF was not more effective than the control (blood clot) in preserving the alveolar ridge, and, was not found to enhance bone formation in the extraction socket compared to the control. The 8 subjects and 20 sites included in the study had bilateral premolar extractions performed in one session. All outcome parameters were measured at the baseline, and 1 week, 2 weeks, 4 weeks, 6 weeks, and 8 weeks postoperatively. The use of PRF was found to encourage soft tissue healing, at the mesio-distal and bucco-lingual widths of the socket orifices, although no statistically significant differences were found between the groups at any of the measurement times. Similar results were found in the mesial and distal marginal bone of the extraction sites as well as the buccal and lingual tissue contour changes. The buccal marginal bone resorption was found to be statistically significantly less in the intervention sites compared to the control sites, at the first week (p = 0.031). (9) Temmerman et al. found that the use of PRF in incisor or premolar sockets was effective three months postoperatively in outcomes regarding bone crest dimension changes. The 22 subjects, equating to 44 treatment sites, all had their extractions performed during the same session. All outcome parameters in the study were evaluated at baseline,
and 3 months postoperatively, except for the postoperative pain questionnaire, which was filled in by the subjects, commencing on the day of the surgery, every four hours until day seven postoperatively. Statistically significant differences were found between the intervention sites and control sites regarding buccal vertical dimension changes (mean ± standard deviation) (mm) (0.5 ± 2.3 vs -1.5 ± 1.3) (p = 0.0002), buccal horizontal changes 1mm and 3mm below the bone crest (mm) (-0.8 ± 2.5 vs -2.9 ± 2.7) (p = 0.003) and (mm) (-0.4 ± 1.5 vs -1.0 ± 1.1) (p = 0.04), and lingual horizontal changes 1mm below the bone crest (mm) (-0.8 ± 2.5 vs -2.9 ± 2.7) (p = 0.004). Total horizontal changes were statistically significant between the two groups at 1mm, 3mm and 5mm, with smaller changes in the intervention group (mm) (-22.84 ± 24.28 vs -51.92 ± 40.31) (p = 0.004), (mm) (-5.42 ± 6.16 vs -14.51 ± 19.6) (p = 0.007) and (mm) (-2.91 ± 4.54 vs -4.47 ± 4.89) (p = 0.02). Socket fill percentage, as well as postoperative pain differences between the groups were found to be statistically significant, favouring the intervention group (p = 0.0004), (p < 0.005). Buccal bone plate changes and lingual vertical dimension changes between the two groups were not found to be statistically significant different. (10)

**Miller’s Class I or Class II gingival recession defects**

According to Shivakumar et al., in a study of ten patients and twenty treatment sites, the use of PRF with a coronally advanced flap (CAF) was reported to be effective than a subcutaneous connective tissue graft (SCTG) with a CAF in the treatment of gingival recession defects classified as Miller’s Class I or Class II in the gingival thickness outcome at 1, 3 and 6 months postoperatively. However, no statistically significant differences were found between the intervention group and the control group at 1, 3, and 6 months postoperatively, in the almost all parameters, including width of keratinised gingiva, clinical attachment level, pocket probing depth, recession width and recession depth. Nevertheless, statistically significant differences were found between the intervention group and the control group for the gingival thickness at 1 month, 3 months and 6 months postoperatively (mean ± standard deviation) (mm) (1.39 ± 0.09 vs 1.24 ± 0.08) (p = 0.0036); (1.51 ± 0.13 vs 1.28 ± 0.10) (p = 0.0013); (1.58 ± 0.12 vs 1.31 ± 0.07) (p = 0.0004), favouring the intervention group. (11) Eren et al. found no difference between the use of PRF with CAF versus SCTG with CAF. The study suggested that PRF with CAF may decrease postoperative patient discomfort due to avoiding the need of a donor site. Nevertheless, a statistically significant difference was found between the intervention group and the control group in the probing depth parameter, at 6 months postoperatively, favouring the intervention group (mean ± standard deviation) (mm) (1.09 ± 0.29 vs 1.45 ± 0.60) (p = 0.017). (12)
Gingival recession

In the study by Jankovic et al., including fifteen subjects and thirty sites, it was found that PRF was less effective than a connective tissue graft (control group) in root coverage (88% vs 91%) and in complete root coverage (75.85% vs 79.56%). Nevertheless, PRF was found to encourage tissue healing during the first two weeks postoperatively, as well as decrease pain during the first week postoperatively. Statistically significant differences were found between the intervention group and the control group regarding the apicocoronal width of keratinised tissue, favouring the control group (mean ± standard deviation) (mm) (0.88 ± 0.71 vs 1.44 ± 0.63) (p = 0.013). Statistically significant differences were also found in the healing index between the two groups, at the first week and second week postoperatively, favouring the intervention group (mean ± standard deviation) (3.11 ± 0.32 vs 2.25 ± 0.54) (p < 0.05) (4.20 ± 0.27 vs 3.05 ± 0.38) (p < 0.05). Regarding postoperative pain, there was one case of severe pain in the PRF group and there were seven cases of severe pain in the control group. All fifteen patients experienced greater pain in the control sites than in the intervention sites. Statistically significant differences regarding pain during the first seven days postoperatively were noted between the groups, favouring the intervention group (p < 0.05). It appears that PRF may be effective in short term parameters such as pain, though long term effectiveness is unclear as healing index results favour the intervention group whereas root coverage and complete root coverage favour the control group. (13)

All the included studies were bilateral randomised controlled trials, where the number of intervention and control subjects was equal, as each patient was both in the intervention group and the control group. The model of bilateral studies could be regarded as an ideal in research as it evaluates both the intervention and control in one subject, as such decreasing possible risk of influence of genetic and environmental factors on the parameters. This is relevant as PRF involves the activation of the immune system, so having both the intervention and control in the same subject i.e. the same immune system, is beneficial in evaluating the effectiveness of PRF. However, as the two sites are not completely isolated, it is possible for either side to have an effect on the opposing side, such as due to the phenomenon of referred pain.

DISCUSSION

Of the nine included articles, four articles involved bilateral impacted third molar extractions, three articles explained gingival defect treatment, one article involved premolar extractions, and one
article studied incisor and premolar extractions. The articles included in this systematic review appear to not be associated with the originator of the PRF protocol.

The literature reports various possible applications of PRF, such as for treating periodontal bone defects, localised osteitis and in pulp revascularisation procedures of necrotic immature permanent teeth. PRF can also be used after multiple extractions to preserve the height of the alveolar ridge, for bone regeneration around immediate implants, and for the reconstruction of large bone defects after cancer surgery. (14) Other applications include treatment of intrabony defects, recession defects, furcation defects, sinus floor elevation, closing oro-antral fistulas, and the treatment of bisphosphonate-related osteonecrosis of the jaw (BRONJ). (15) Possible non-dental applications could include plastic surgery and otolaryngology. (16) However, as for any blood and immune system related treatment, PRF use would be contraindicated in immunocompromised patients, patients with arthritis, haemophilia, thrombocytopenia, low blood cell count, and other diseases relating to blood and uncontrolled bleeding. Other contraindications may include needle phobia or blood phobia.

PRF was first introduced in 2001 by Choukroun et al. (6) PRF is produced without biochemical polymerisation of the patient’s blood. (16) Choukroun’s protocol allows for a greater chance of reproducible and reliable results to be obtained as it consists of a single centrifugation step. (17) As PRF preparation uses only the patient’s own blood, the possible risk of interspecies disease transmission is eliminated. (18)

Venous peripheral blood is collected into 9ml glass coated plastic tubes and then centrifuged at about 400g (3000 rpm) for 12 minutes. The fibrinogen in the blood is polymerised by centrifugal forces. Three layers are formed in the tube: red blood cells at the bottom, a PRF clot, and an acellular plasma on the surface. (16) The PRF clot is removed and compressed to form a platelet-rich fibrin membrane. Delayed preparation of the blood sample may result in diffuse polymerised fibrin within the glass tube and produce only a small clot. (17)

There are various methods of PRP production mentioned in the literature though it is frequently not possible to determine whether the protocol is producing pure platelet-rich plasma or leucocyte-rich platelet-rich plasma. The most basic outline of the PRP protocol includes centrifugation twice, at two different centrifugation forces. The centrifugation forces for the first centrifugation step vary from 160g to 3000g from 3 to 20 minutes, producing three layers: red blood cells followed by a “buffy coat”, and a platelet-poor plasma layer on the surface. The platelet-poor plasma layer and the
“buffy coat” are transferred to a second tube and are centrifuged at a high centrifugal force. Most of the platelet-poor plasma is discarded. The fibrinogen polymerisation is aided using bovine thrombin and calcium chloride. (2)

The PRGF protocol involves centrifuging the collected venous blood from the patient, in small tubes, producing three layers: red blood cells, a “buffy coat” and an upper layer of acellular plasma. The uppermost layer of acellular plasma is discarded using a pipette. The remaining plasma in the tube is removed using eyeballing as a method of measurement. The polymerisation of the fibrin in the obtained PRGF is chemically induced with a 10% calcium chloride solution. (2)

The PRF clot forms a strong natural fibrin matrix, which concentrates almost all the platelets and leucocytes from the patient’s blood sample. (16) PRF is a reservoir of platelets, leukocytes, cytokines and immune cells. (17) It has been found that PRF releases growth factors for at least seven days, (16) (19) (20) as well as cytokines over seven days. (21) It has also been found that PRF contains heparin and hyaluronic acid. (21) The increased density of fibrin fibres found in PRF (100 times the normal amount), may provide additional stability of the wound and promote rapid neoangiogenesis. (13)

PRF contains platelets contain α-granules which release growth factors such as platelet derived growth factor (PDGF), transforming growth factor-β (TGF-β), vascular endothelial growth factor (VEGF) and epidermal growth factor which are thought to play a vital role in angiogenesis and tissue healing. PDGF receptors are present on the gingival, the periodontal ligament and cementum. Upon activation, these receptors activate fibroblasts and osteoblasts. PRF also contains cytokines such as Interleukin-1 (IL-1), Interleukin-4 (IL-4), Interleukin-6 (IL-6) and tumor necrosis factor (TNF-α). (13) (17) It has also been reported that PRF enhances angiogenesis and supports immunity. (17) (22) The growth factors present in platelet-rich fibrin stimulate stem cells and attract them to the injury site, inducing angiogenesis and osteogenesis. (14) PRF traps stem cells that are circulating in the blood. The low level of thrombin in PRF allows for optimal migration of endothelial cells and fibroblasts, promoting angiogenesis. (20)

PDGF induces migration and proliferation of mesenchymal stem cells, and an angiogenic effect. TGF-β stimulates osteoblast proliferation, the production of collagen type 1 and woven bone, and stimulates angiogenesis. Insulin like growth factor (IGF-1) and fibroblast growth factor (FGF) both encourage the proliferation of osteoblasts and enhance wound healing. PDGF originates from
platelets and macrophages, TGF-β originates from platelets and lymphocytes, and IGF-1 originates from osteoblasts and macrophages. (21)

CONCLUSION

Five out of nine studies reported a positive effect of PRF in the healing of soft and hard tissues in oral surgical procedures in adults. It appears that the literature is inconclusive regarding the effectiveness of PRF in healing in various oral surgical procedures such as after impacted third molar extractions, simple tooth extractions and gingival defect treatment, compared to traditional treatment such as blood clots and connective tissue grafts respectively. Nevertheless, in order to evaluate the true effectiveness of PRF in a clinical setting, further randomised controlled trials with split-mouth designs and larger sample sizes in a broader range of oral surgical procedures are recommended to validate PRF in the healing in oral surgical procedures.

PRACTICAL RECOMMENDATIONS

The literature appears to be inconclusive regarding the use of PRF with five out of nine studies finding statistically significant results, favouring the use of PRF, and the remaining four studies finding no statistically significant results. Nevertheless, PRF may be used to aid healing in place of a blood clot, or a soft tissue graft, as a relatively painless and renewable regenerative source.
REFERENCES


17. Al-Hamed FS, Tawfik MA-M, Abdelfadil E. Clinical effects of platelet-rich fibrin (PRF) following surgical extraction of lower third molar. Saudi J Dent Res [Internet]. The Authors; 2016; Available from: http://dx.doi.org/10.1016/j.sjdr.2016.05.002


INDIVIDUAL DEVELOPMENT PLAN FOR THE MASTER’S THESIS

Graduate student Ugne Vijeikyte of the year V and the group 15 of the integrated study programme of Odontology.

Duration of studies from September 2012 till June 2017

Supervisor: D.D.S. Oral Surgeon, Dr Marijus Leketas

MT Title: A systematic review of the use of platelet-rich fibrin in the healing in adults in oral surgical procedures.

MT annotation: A systematic review of the literature on PubMed MEDLINE, the Cochrane Central Register of Controlled Trials database and a manual search.

Aim of the work: To evaluate the effectiveness and efficacy of platelet rich fibrin in the healing in minor oral surgery and dental procedures.

Tasks of the work: To evaluate the results from each of the 9 articles found and to provide a conclusion.

Schedule of the works

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