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Source / Izvornik: **Australasian Medical Journal, 2017, 10, 497 - 501**

Journal article, Published version

Rad u časopisu, Objavljena verzija rada (izdavačev PDF)

<https://doi.org/10.21767/AMJ.2017.3000>

Permanent link / Trajna poveznica: <https://um.nsk.hr/um:nbn:hr:127:212728>

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Download date / Datum preuzimanja: **2024-11-27**



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Plasma rich in growth factors in dentistry

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REVIEW

Please cite this paper as: Glavina A, Vucicevic Boras V, Gabric D, Susic M, Granic M, Pelivan I. Plasma rich in growth factors in dentistry. AMJ 2017;10(6):497–501. <https://doi.org/10.21767/AMJ.2017.3000>

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ABSTRACT

Background

Plasma rich in growth factors (PRGF) has wider use in many fields of dentistry due to its endogenous biocompatible regenerative potential i.e., their potential to stimulate and accelerate tissue healing and bone regeneration.

Aims

This review shows the increasing use of PRGF technology in various fields of dentistry.

Methods

In the last nine years PubMed has been searched in order to find out published articles upon PRGF in dentistry and 36 papers have been included.

Results

PRGF technology has many advantages with positive clinical and biological outcomes in tissue healing and bone regeneration.

Conclusion

In order to determine the most effective therapeutic value for patients, further research is required.

Key Words

Endodontics/PRGF, oral medicine/PRGF, oral surgery/PRGF, osteonecrosis/PRGF, periodontics/PRGF

What this review adds:

1. What is known about this subject?

Plasma rich in growth factors (PRGF) has potential to stimulate and accelerate tissue healing and bone regeneration.

2. What new information is offered in this review?

This review provides an overview of the advantages and disadvantages of PRGF therapy on humans in the last nine years.

3. What are the implications for research, policy, or practice?

PRGF technology has many advantages with positive clinical and biological outcomes when compared to standard therapy protocols.

Introduction

The main goal of the modern surgery is low invasiveness and a high rate of clinical healing which is known as "regenerative surgery".¹ PRGF releases growth factors as well as bioactive proteins. The concentration of growth factors at localized injected sites is higher than their concentration in the blood, a mechanism which stimulates tissue regeneration. PRGF technology is becoming more popular in various fields of dentistry (endodontics, implantology, oral medicine, oral surgery, and periodontics) during the last decade. This is a 100 per cent autologous technology with no reported side effects. This technology uses the patient's venous blood and after the centrifugation process, various growth factors are derived from platelets. Platelet α -granules contain a large number of Platelet-Derived Growth Factors (PDGFs): transforming growth

factor β (TGF- β , including isomers of TGF- β 1 and TGF- β 2), vascular endothelial growth factor (VEGF), epidermal growth factor from platelets (PD-EGF), insulin like growth factor (IGF-1).² Furthermore, PRGF increases epithelial to mesenchymal transition, and eliminates epithelial nests in the underlying connective tissue, therefore it adds to the restoration and function of original tissues.³ Platelets act as carriers of endogenous morphogens that may modulate cell fate and therefore affect tissue structure and function. PRGF might modulate the gene expression of many cells such as chondrocytes, synoviocytes, macrophages, mesenchymal stem cells, and thereby influence an anabolic microenvironment and reduce pain and improve the tissue functioning.⁴ PRGF might have neuroprotective, neurogenic and neuroinflammatory therapeutic modulator possibilities because some studies have shown positive results in enhancing the sensory and functional nerve and muscle recovery.⁵

Materials and Methods

In the last nine years a search has been conducted in PubMed in order to gather the published articles upon PRGF in dentistry and 36 papers have been included. The inclusion criteria were all papers published upon PRGF in dentistry on humans and the exclusion criteria were all other papers upon PRGF in dentistry performed on the animals and *in vitro*.

Results and Discussion

PRGF in dentistry

Endodontics

Studies upon the use of PRGF in endodontics are scarce. Study of Bakhtiar et al. demonstrated the positive result of PRGF in complete apex closure in two teeth and apical closure with continued increase of dentinal wall thickness in two other cases at 22 months of follow-up period.⁶

Oral medicine

The use of PRGF has been demonstrated as effective in the treatment of recurrent aphthous stomatitis (RAS).³ Recently, Piñas et al. has stated that PRGF was successful in the treatment of refractory oral lichen planus.⁷

Oral surgery

The use of PRGF technology in oral surgery belongs to a concept of "regenerative surgery". When the surface of the dental implant is soaked in PRGF, fibrin membrane is formed around the implant, which releases the growth factors and improves a process of osseointegration.⁸⁻¹⁰ Immediate dental implantation combined with the use of PRGF has been shown to be safe surgical procedure with

high success rate.¹¹ A total of 241 patients received 1.139 immediately loaded implants which were previously treated with PRGF.¹² Five implants were lost during the follow-up and no studied cofounder was significantly associated with implant failure.¹² The results of this five-year-retrospective study show that immediate loading of implants is safe and predictable if used under strict clinical protocols.¹² In the treatment of atrophic jaw PRGF in combination with block-graft improves the healing process, thus avoiding graft exposure and improving post-operative appearance of the patient.¹³ Transalveolar sinus floor augmentation in association with PRGF was performed in order to place 41 short implants in 26 patients.¹⁴ Stable augmented height bone was gained after three years' of the follow-up.¹⁴ It can be concluded that atrophic posterior maxilla could be treated by transalveolar sinus lift in association with PRGF and the placement of short implants.¹⁴ Anitua et al. evaluated dental implants combined with PRGF after transcresal sinus elevation performed by sequential bone drilling using a frontal cutting drill.¹⁵ The four year implant survival rate was 96.6 per cent, due to two implant failures.¹⁵ Implant failure did not correlate with the implant length.¹⁵ The same authors concluded that short implants and transcresal sinus elevation is effective in the treatment of posterior maxilla with a mean residual bone height <5mm.¹⁵ Cocero et al. compared fibrin glue with an autologous haemostatic PRGF in the controlled trial in patients with different blood disorders who underwent dental extraction procedures without hospitalisation (prior to the extractions, patients underwent systemic haematological evaluation).¹⁶ The bleeding rates in the study and control group demonstrated that PRGF works as well as fibrin glue as a local haemostatic agent.¹⁶ PRGF as a local haemostatic has many advantages because of its autologous origin, it does not require additional systemic treatment after tooth extraction to prevent severe bleeding (in patients with bleeding disorders) and is associated with an earlier onset of neo-angiogenesis.¹⁶ Surgical treatment of denture-induced fibrous hyperplasia with PRGF results in acceleration of wound re-epithelialization, the reduction of bleeding and oedema as well as in the decrease of duration and intensity of postsurgical pain.¹⁷ Pilot study of Taschieri et al. showed that PRGF may be helpful in reducing complications following sinus lift surgery.¹⁸ Eight maxillary sinuses were augmented in eight patients by making two small perforations of the Schneiderian membrane which were treated by use of the PRGF clot before grafting the site with PRGF and anorganic bovine bone.¹⁸ Another study demonstrated bilateral sinus lift augmentation in five patients in the following manner: on one side PRGF was combined with bovine anorganic bone and on the other side

biomaterial alone was applied.¹⁹ It was concluded that PRGF decreased inflammation, enhanced new bone formation and stimulated vascularization of bone tissue.¹⁹ Anitua et al. described lateral approach for sinus elevation by use of PRGF in 18 patients in whom 43 implants were placed.²⁰ They concluded that the sinus elevation with PRGF and implant installation was a successful and a safe treatment.²⁰ PRGF has positive clinical (reduced postoperative pain and facial swelling) and biological (interleukin (IL)-1 β and IL-6 induce fibroblast and keratinocyte proliferation) outcomes in the healing process after the extraction of an impacted mandibular third molars.²¹ Anitua et al. Analyzed the use of PRGF and solely blood clot which were placed in the sockets of 60 patients after molar tooth extraction in the mandible.²² Radiological findings and soft tissue healing were superior in patients treated with PRGF when compared to the ones treated only with blood clot.²² Pain and inflammation were lower in the PRGF group after three and seven, but not after 15 days when compared to the blood clot group.²²

Osteonecrosis

The results of various studies suggest that treatment with PRGF can reduce the risk of developing Bisphosphonate-Related Osteonecrosis of the Jaw (BRONJ) after tooth extraction in high-risk patients undergoing the treatment with bisphosphonates.²³ PRGF has shown to be effective in the management of patients with a history of head and neck radiotherapy, accelerating and fostering mucosal healing and avoiding postextraction bone exposure.²⁴ Anitua et al. reported a case of a patient with BRONJ whose symptoms included severe pain and hemimandibular paraesthesia.²⁵ The treatment included resection of necrotic bone and the application of PRGF.²⁵ One year postoperatively, mandibular sensitivity was totally recovered, the pain was absent and the bone was partially regenerated.²⁵ PRGF demonstrates positive results in the treatment of BRONJ by enhancing the vascularization and the regeneration of osseous and epithelial tissues. Clinical study carried out on the 32 patients treated with intravenous bisphosphonates due to the oncologic pathologies and affected by BRONJ has shown promising results.²⁶ All patients were treated by resection of the necrotic bone with primary closure of the mucosa over the bony defect by use of PRGF.²⁶ No intraoperative complications were observed, and all cases were treated successfully.²⁶

Periodontics

There are several studies upon the use of PRGF in periodontology. PRGF shows good results in masking the root surface, increasing the width of keratinized mucosa

and overlapping of gingival recession.^{27,28} Anitua et al. showed that PRGF might stimulate proliferation, migration and chemotaxis of osteoblasts and significantly enhance the autocrine expression of two relevant proangiogenic factors (vascular endothelial growth factor (VEGF) and hepatocyte growth factor (HGF)) as well as three markers of osteoblastic activity (procollagen I, osteocalcin, alkaline phosphatase).²⁹ Therefore, platelet derived growth factors support bone regeneration primarily via chemotactic and mitogenic effects on preosteoblastic and osteoblastic cells.³⁰ The increased levels of VEGF, thrombospondin 1, connective tissue growth factor (CTGF), HGF and procollagen type I were noticed.³¹ Only α 2 integrin expression was lower in PRGF treated cells when compared to the untreated cells.³¹ Anitua et al. concluded that PRGF has beneficial effects on the periodontal fibroblasts which may aid in the healing of periodontal tissues.³¹ PRGF has easier clinical handling than PRF and may represent alternative therapy to the materials used in the field of the mucogingival surgery.^{27,28} On the other hand, Gamal et al. showed that PRGF and PRF failed in augmentation of intrabony defects within teeth when compared to the xenograft alone.³² Lafzi et al. showed that although autogenous bone grafts, with or without PRGF, were successful in treating grade II furcation involvement of mandibular molars, no differences between the study and control groups were observed.³³ Khorshidi et al. compared the mechanical properties of early leukocyte- and platelet-rich fibrin (L-PRF) *versus* PRGF membrane.³⁴ The results of their study showed that early L-PRF membranes have stronger mechanical properties than membranes produced by PRGF.³⁴

Temporomandibular dysfunction (TMD)

The injection of PRGF following arthroscopy is more effective than the injection of hyaluronic acid (HA) with respect to the pain levels in patients with advanced internal derangement of the temporomandibular joint (TMJ).³⁵ On the other hand, Fernández Sanromán et al. showed that the injection of PRGF does not add any significant improvement to clinical outcomes at two years after surgery in patients with advanced internal derangement of the TMJ.³⁶

Conclusion

This overview of the literature on the use of PRGF technology in various fields of dentistry shows positive therapeutic results on tissue healing and bone regeneration in most studies. This is the reason of the increasing use of technology in various fields of dentistry. The disadvantage of this overview is that most studies were conducted on a small number of subjects and without clearly defined PRGF technology protocols. Since the quality of platelet

concentrates may vary according to the physical state of each individual, it is very difficult to compare the results of the so far published research. However, evidence is accumulating in both, preclinical and clinical settings, indicating that platelet-rich plasma products have an important therapeutic benefits. In order to determine the most effective therapeutic value for patients, further research is required.

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PEER REVIEW

Not commissioned. Externally peer reviewed.

CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

FUNDING

None