



The use of platelet-rich plasma is dynamically developing technique used in many fields of medicine.

## The Use Of Platelet-Rich-Plasma In Aesthetic And Regenerative Medicine

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**RUNNING TITLE** The use of PRP in medicine

**KEYWORDS** platelet-rich plasma, growth factors, orthopedics, wounds, scars, alopecia, skin rejuvenation

**WORD COUNT** 4 987

**CONFLICT OF INTERESTS** no conflicts of interest

**ABBREVIATIONS**

- PRP - platelet-rich plasma
- PAF - platelet-activating-factor
- IL-8 - interleukin 8, CCL5 - chemokine ligand 5
- RANTES - regulated on activation, normal T-cell expressed and secreted
- MIP-1 - macrophage inflammatory protein
- PMPs - platelet microparticels
- VEGF - Vascular Endothelial Growth Factor
- TGF- $\beta$  - Transforming Growth Factor beta
- EGF - Epidermal growth factor
- FGF - fibroblast growth factor
- HGF - hepatocyte growth factor
- WBC- white blood cells
- TOT- turnover time
- DNA - deoxyribonucleic acid
- ROS - reactive oxygen species
- UVA - ultraviolet A
- ACR - Autologous Cell Regeneration
- DHT - dihydrotestosterone
- PDGF - Platelet-derived growth factor
- Bcl-2 - B-cell lymphoma 2
- V.A.C. - Vacuum-Assisted Closure
- CDK-4 - Cyclin-dependent kinase 4
- NPWT- Negative-pressure wound therapy
- IL-1- interleukine 1
- WOMAC - The Western Ontario and McMaster Universities Arthritis Index

## ABSTRACT

The use of platelet-rich plasma, which is concentrated blood plasma enriched with platelets, is a relatively young but dynamically developing technique used in many fields of medicine. Growth factors released from platelets promote tissue regeneration and constitute an important part of tissue repair. There are several techniques to obtain PRP such as double spin method, which gives an opportunity to receive various concentrations of thrombocytes and leucocytes, and hence- various content of growth factors. Due to great regenerative potential with its high content of growth factors and other biologically active substances, PRP could be used in medical treatment aimed at skin rejuvenation and mesotherapy of head's skin in the case of alopecia. There are also a number of reports confirming positive effects of PRP usage in scar reduction and minimization, improving results of wound therapy and in treatment of diabetic foot ulcer. Recent studies show that platelet-rich plasma could be used in orthopedics in bone regeneration, osteoarthritis and tendinopathy. Autologous platelet rich plasma does not stimulate immune response, which translates into minimal therapeutical side effects. Therefore it is probably one of the safest available methods of treatment in many cases. The aim of this publication is to present the outcomes of platelet-rich plasma usage in aesthetic and regenerative medicine.

## INTRODUCTION

The use of platelet-rich plasma, which is concentrated blood plasma enriched with platelets, is a relatively young but dynamically developing technique used in many medical fields such as orthopedics, dentistry, surgery or dermatology. PRP (platelet-rich plasma) has also drawn attention of regenerative and aesthetic medicine. Platelets are an important component of inflammatory cascades due to their significant number of cell surface antigens and granules, which store mediators. PAF and IL-8 are involved in leukocytes chemotaxis. CCL5, also known as RANTES, is chemotactic for eosinophils, basophils and T-cells, and MIP-1 alfa has a role in antiviral response. Thrombocytes contain PMPs, which evoke direct antibacterial effects and stimulate white blood antimicrobial properties. Moreover, they have the ability to phagocyte small pathogens and internalize. Platelets are an important part of wound healing and tissue repair. Growth factors released from platelets granules promote tissue regeneration. PDGF induces formation of granulation tissue through the chemotaxis and mitosis stimulation, VEGF, TGF-beta, EGF stimulate angiogenesis. Growth factors concentrated in platelets stimulate the fibroblasts and osteoblasts to produce proteins (TGF-beta strongly induces collagen and fibronectin synthesis) and stimulate tissue regeneration and organization (FGF, HGF). In practice, PRP injection has already been used in the event of both problematic, poorly healing wounds and bone fractures and ineffectiveness of other therapeutic methods, as it will be discussed below. (1, 2)

### PREPARATION OF PLATELET-RICH PLASMA

Platelet-rich plasma is an autologous preparation of high number of platelets in a relatively small quantity of plasma. There are no explicit criteria assessing how high the concentration of platelets should be. In current literature, there are reports suggesting that the optimal concentration of PRP is at least 1mm<sup>3</sup>/microliter. (3)

There are several techniques to obtain platelet-rich plasma. They give an opportunity for receiving plasma with various concentrations of thrombocytes and leucocytes and hence with various content of growth factors, which may induce different biological effects. Regardless of the procedure type, the diagram of obtaining platelet-rich plasma is the same:

1. Extraction of blood samples into the tube containing anticoagulant, for example sodium citrate.
2. First centrifugation, after which plasma is divided into 3 layers. It is a result of specific gravities taking place in the upper layer, which mainly contains leucocytes and platelets; whereas middle buffy coat layer and down layer contain erythrocytes.
3. Pipetting upper layer (or upper and middle) to the second tube for the next centrifugation.
4. Second centrifugation, after which sample is separated into two layers.
5. Superior plasma supernatant is aspirated away (poor-rich plasma).
6. Obtaining platelet-rich plasma.

This technique is called a double spin method. There are also other techniques such as single centrifugation or automatic methods, however that last one is much more expensive than the others, and is rarely used in practice. Factors, which can influence the platelets integrity and the effectiveness of PRP, are for example the sedimentation coefficient or centrifugation protocols (4). There are many commercial systems which not only differ in centrifugation parameters, but also in the used anticoagulant or type of tube for patient blood sample. They allow obtaining various concentrations of platelets and it is possible to have an even 11 times higher level compared to the original amount (5). Parameters, which are possible to be evaluated ambulatorily, are the percentage of platelet recovery and level of concentration, which translates into the quantity of plasma in the PRP sample. The percentage of platelet recovery

is a basic ratio, which should be taken into a careful consideration during the effectiveness evaluation of each system to obtain PRP. The effectiveness of platelet-rich plasma depends not only on platelet concentration, but also on the content of growth factors. However, determining their concentrations requires special markings. Growth factors are released from activated thrombocytes. There are different ways of activations, which depend on the type of activator. Thrombin is a fast activator of degranulation whereas collagen needs time to stimulate platelets to release mediators. In practice, we can also use calcium chloride. There are contradictory reports about the influence of leucocytes presence in PRP. Supporters of PRP having high concentration of WBC believe that the presence of white blood cells stimulates patients' natural immune to respond to infections and allergens. Other researchers believe that high level of leucocytes may negatively affect the surrounding tissue, even if it is not damaged. The reason is that WBC produces nonselective and toxic oxides, e.g. peroxides and chlorine monoxide (6). Moreover, the concentration of WBC is directly correlated with the genes expressions, which are responsible for producing catabolic enzymes interacting with tendons and ligaments, furthermore such genes products may slow down tissue healing and regeneration. (7)

#### THE USE OF PLATELET RICH PLASMA IN THE AESTHETIC FIELD FOR SKIN REJUVENATION.

First visible signs of skin aging appear in the third decade of life. Fibroblasts activity, collagen and elastin production in dermis decrease with age. Stem cells proliferate slower as compared to young skin, TOT prolongs from 28, even up to 60 days and the border between epidermis and dermis becomes thinner. As a result of vascular integrity deterioration, skin is less oxygenated and nourished. Melanin production is irregular, which is manifested by pigmentation spots and lentigines. Factors determining the rate of aging are mostly genetic, yet they might also be environmental. Factors that accelerate aging mainly induce the production of free radicals, which leads to the cell membrane destruction mostly in a mechanism of lipid peroxidation. However, this may result in enzymes destruction, interference with nuclear and mitochondrial DNA and may cause a lot of mutations. Another effect is photo-aging, mainly caused by the exposure to UVA radiation, which leads to formation of ROS and a large number of collagenases production. In aging skin, endogenous antioxidants and regeneration are insufficient and cannot protect it from destructive effects of free radicals activity. (8, 9)

By understanding the aging mechanisms better, we can prevent it more effectively. There are a lot of new methods that give increasingly good rejuvenation effects. They are based on the stimulation of natural regeneration, i.e. cell division, stimulating fibroblasts to produce proteins (collagen, elastin) and enhanced skin blood supply. One of such methods is mesothe-

rapy performed through the use of platelet rich plasma. Due to the great regenerative potential, PRP could be applied in medical treatment which is aimed at rejuvenation. The use of platelet rich plasma in procedures results in the reduction of furrow and wrinkles, therefore improving the skin structure, tone and density, but also accelerating regeneration after other procedures such as removal of acne scars and striae- all of these in the mechanism of ACR, which is autologous cell regeneration(10). The preparation of PRP is performed on the day of the procedure, and then PRP is administrated to the patient in needle mesotherapy. The procedures should be repeated for one year, every 4-6 months and then, as a maintenance therapy, once a year. (6) Recent available studies show that PRP has a positive impact on the skin restoration and regeneration. In a study by Kim DH et al, it was showed that PRP, due to great number of growth factors, induces production of collagen type I and stimulates fibroblasts to multiply. Moreover, it has an impact on tissue remodeling by stimulating collagenases to remove collagen remains and thus provides optimal condition for the production of new molecules. (3) Using PRP brings very good results in improving the condition and flexibility of the skin, furrows and wrinkles reduction, while no significant or lasting side effects are observed. (11) Apart from the use of platelet-rich plasma on its own, it can be used as supplement to enhance the effects of anti-aging procedures. The use of PRP as an additive to fractional laser therapy was described. Results were significantly better in comparison to the group of patients who were treated with the application of fractional laser only. (12) The usage of PRP as a supplement in case of graft tissue transplantation has a positive influence on therapy outcomes. It should be mentioned, that the trial comparing results in a group of patients after fat tissues transplantation and a group where PRP was used, also showed that the recovery time was significantly shorter in the second one. (13)

#### ALOPECIA AND EXCESSIVE HAIR LOSS

Alopecia is a process that consists of progressive atrophy of hair production in a follicle. It affects both men and women and can appear at any age. There are a lot of reasons for the emergence of alopecia and excessive hair loss. This process can be caused by congenital defects, drugs side effects, hormonal changes (caused by pregnancy or lactation) or dermatological diseases, but also slimming and stress. Alopecia can be divided into different types, e.g.: alopecia areata, androgenic alopecia, scarring alopecia, telogen alopecia, total alopecia, post chemotherapy or radiotherapy, post pregnancy or neurotic, and many others. The most common type is androgenic alopecia (90% of all cases). The reason is conditional upon genetic hypersensitivity on dihydrotestosterone (DHT), which leads to the miniaturization of follicle, hair thinning down to atrophy. Men are mostly affected by the disease, but it can also affect women



suffering from hormonal disturbance e.g. in polycystic ovary syndrome. The treatment depends on the reason of hair loss and as far as the most common cause, androgenic alopecia is concerned, currently available methods are nutritional components supply, treatment with oestradiol, minoxidil, finasteride, mesotherapy, laserotherapy and transplantation. One of the most effective ways of hair growth stimulation is mesotherapy of the head skin with platelet-rich plasma. It can be applied providing that there is no follicle atrophy – otherwise the hair transplantation is necessary. For the patients with alopecia areata, androgenic alopecia or alopecia as a consequence of hormonal imbalance, circulatory insufficiency or inadequate diet, mesotherapy of the head skin with platelet-rich plasma is more than a perfect solution. The procedure consists of injections in the guise of small head skin deposits. Platelet-rich plasma has been designed to stimulate follicle to produce new hair – subcutaneous application of preparation should stimulate regenerative processes. The growth factors have an influence on hair growth cycle. Some of the most important factors connected with hair cycle regulation are vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), insulin 1-like growth factor and fibroblast growth factor (FGF). Platelet-rich plasma contains a whole range of growth factors and for that reason beneficially affects the hair cycle regulation and re-establishing of adequate hair cycle. Platelet-derived growth factor (PDGF) stimulates mitosis, whereas VEGF is supposed to stimulate angiogenesis, which is increase of follicle blood supply and, as a result, its nourishment and oxygenation. FGF found in platelets was tested in vitro and turned out to be one of the most important factors stimulating the differentiation of hair follicles stem cells, longer growth phase, and thus lengthening hair. (14) PRP therapy affects also the apoptotic pathways, inhibiting it by influencing on Bcl-2 activity and improving the survival of hair papilla, thereby the hair growth cycle is prolonged. As a result, an excessive hair loss should be stopped. Multiple hairs may grow in one hair follicle, which leads to hair thickening. The growth of brand new hair takes about 3 months and to achieve lasting results the procedure should be repeated. It is recommended to carry out 3-6 procedures every two or three weeks. In some cases it is necessary to carry out a series of procedures or the maintenance therapy every few months. Mesotherapy of the head skin with platelet-rich plasma is one of the best methods of treatment, because of the minimal number of side effects in comparison to steroids or hormone therapy. (15) Autologous platelet-rich plasma does not stimulate the immune system response and thus it is one of the safest available methods of treatments. More and more positive studies appear, evaluating the effects of the therapy for the treatment of alopecia and excessive hair loss. (16) In patients from a group that formerly underwent the procedure with the application of PRP and was treated with hair transplantation, statistically better

results were observed in comparison to the group where PRP was not applied. (17) Preservation graft in platelet-rich plasma before transplantation also had an impact on its long-term function. (16) Moreover, the treatment that uses PRP containing leucocytes (L-PRP) has positive results in patients suffering from alopecia. (18) The majority of available literature describes the treatment that uses PRP mostly in the event of androgenic alopecia emergence. This is probably a result of androgenic alopecia being the most common type of alopecia. It is worth mentioning Trink A et al. study, where PRP was used for the first time in the event of alopecia areata. The study was randomized, double-blind and showed that treatment that uses platelet-rich plasma gives good results in the event of patients suffering from alopecia areata and provides the greatest application comfort. It is also the safest method, due to autologous nature of PRP. (19)

#### THE USE OF PLATELET-RICH PLASMA IN THE REDUCTION AND REMOVAL OF SCARS AND STRIAE

Surgery, traumatic and acne scars especially on the face or exposed parts of the body are associated with a great mental discomfort in patients and thus are one of the most frequent causes of visiting dermatologist or aesthetic medicine specialists. The use of fractional laser, graft tissue transplantation, platelet-rich plasma and stem cells therapy brings increasingly better results in such patients. There are number of reports confirming a positive effect of using PRP in scars reduction and their minimization. In patients with scars of different etiology and localization, who are treated with graft tissue transplantation connected with fractional laser and platelet-rich plasma, the results were satisfactory. Significant skin lesion regression and high level of patients' satisfaction were obtained, as well as the minimization of side effects and shortening of the recovery time. (7). A similar combination was used in the other study, in which 20 of 60 patients with traumatic scars were treated. Consequently, in this group of 20 patients, where PRP was used, therapeutic effects were the best of all. (20) Combination therapy was also applied in patients with post-burn scars, where platelet-rich plasma was used with graft tissue transplantation. In comparison to the use of only graft transplantation, the therapy with PRP resulted in better outcomes. (21) Platelet-rich plasma could be mixed as well with skin graft. In patients with severe non-healing wounds after skin burn, the therapeutic effect was achieved faster in that group where transplantation was connected with PRP application. (22) In addition to the scars that cause physical and mental discomfort and skin lesions, which are a big aesthetic problem, there are also the stretch marks. They are red, evolving in white and shimmering lines, most frequently located on buttocks, abdomen, thighs and breasts. Stretch marks are the result of rapid stretching of the skin, which can be associated with growth, weight changes, pregnancy or intensive exercises leading to the

muscle growth. There are a lot of methods used to reduce this kind of skin lesions, but results are not satisfactory. One of the new, promising methods that give good results is the procedure involving the radio waves mixed with platelet-rich plasma. The use of this method resulted in observable improvement in study groups. It should be mentioned that there no deterioration of the skin appearance was observed. Patients evaluated results as excellent, with at least mild improvement of the skin condition. (23,24)

#### THE USE OF PLATELET- RICH PLASMA IN PATIENTS WITH ACNE SCARS

Acne can occur in any area with sebaceous glands, but is mostly localized on the face, back or neck. Inflammation around the acne lesions could damage collagen and elastin, which may result in forming permanent scars. According to the literature, severity of acne scars is correlated with severity of acne. (25) Acne scars are very common and very difficult to treat. There are a lot of methods to fight acne, i.e. chemical peelings, dermabrasion, microdermabrasion, cryotherapy or fractional laser therapy. The last one is very effective when applied on shallow scars – it removes tough epidermis by evaporation and stimulates collagen regeneration and skin remodeling. However, it is associated with the occurrence of erythema and edema, which can last for even 5 - 10 days. Another effective way to minimize acne scars is the therapy that uses platelet rich plasma. PRP accelerates wound healing, stimulates regeneration and rebuilds its structure through stimulating fibroblasts and keratinocytes proliferation and accelerating hyaluronic acid, collagen, elastin synthesis, by the release of a lot of growth factors from platelet alpha granules. Monotherapy of acne scars that uses PRP brings good results (26), but the best ones are observed when PRP is combined with fractional laser (25) and, as a result, is connected with a very high level of patient satisfaction. Similar results were obtained in a study by Lee et al., when using PRP significantly shortened the occurrence of oedema and erythema and in several months of follow up the improvement of skin condition was clearly noticeable. (27) The use of platelet-rich plasma mixed with fractional laser not only accelerates the regeneration and minimizes the side effects like oedema and erythema, but also stimulates the neogenesis of collagen. (28) In conclusion, in patients with acne scars the use of platelet-rich plasma combined with fractional laser brings excellent results, shortens the healing time and is considered to be a well tolerated therapy.

#### THE USE OF PLATELET-RICH PLASMA IN WOUND CARE TREATMENT

In many patients the poorly healing wounds are a therapeutic challenge and a great problem. In the event of the chronic non-healing wounds, there is even a risk of developing squamous cell carcinoma. Despite the great progress in this area in a last few years and the development of new techniques such

as V.A.C. therapy, there are still a lot of cases, where full therapeutic success could not be achieved. The best example is diabetic foot ulcer. Moreover, the chronic non-healing wounds may occur in the chronic venous insufficiency and in patients who are immobile in the pressure ulcers. In such diseases, cell proliferation index is reduced; keratinocytes do not proliferate and migrate properly, which destabilizes wound healing by inhibiting epidermalization. (29) One of the methods, which may improve the results of wound therapy, is the use of PRP. PRP contains a lot of growth factors and other biologically active substances that may accelerate wound healing and tissue regeneration. In the current literature, there are a number of studies evaluating usefulness of the therapy that uses platelet-rich plasma in the event of poorly healing wounds, tissue damage after trauma or surgery. PRP is administered directly to the wound in the form of gel or liquid. (30, 29) It is also possible to inject it directly into the wound. (31) There is evidence of lower number of wound site infections in a group of patients treated with PRP. (30) The supply of PRP to the wound in the case of non-healing wounds is an effective therapeutic method. (32) It has been proved that platelet-rich plasma accelerates keratinocytes proliferation and migration by stimulating the cell cycle regulatory proteins, such as cyclin A or CDK4, which is crucial to the correct skin formation, and which is disturbed in patients with chronic ulcers. (29) In a study by Carter MJ. et al. it was showed that the use of PRP in case of non-healing wound with no response for any other treatment led to the significant reduction in the surface and depth of the wounds. (33) The same therapeutic effect was observed in other study, where the use of PRP in a group of patients with multiple comorbidities and with bad results of laboratory tests is the only method, which brings good results. Moreover, the use of PRP in a combination with vacuum patch could shorten the healing process and reduce the costs of therapy. (34) The available literature describes the use of a combination of platelet-rich plasma, fibrin glue and matrix collagen in patients with severe, non-healing and life-threatening ulcers. In a group of 10 patients, in serious medical condition and with no response to any other treatment, the use of this combination resulted in complete healing in 9 patients, and in 1 patient the definite improvement was observed. No complications were observed in both systemic and local of the treatment. Using this noninvasive method made it possible not only to heal the wound, but also led to significant improvement of the general condition of patients (35). PRP could also be used as adjuvant therapy before planned, reconstruction procedures. (31)

#### THE USE OF PLATELET-RICH PLASMA IN PATIENTS WITH DIABETIC ULCERS

Diabetic foot ulcer is a complication affecting of 15% of patients who suffer from diabetes mellitus type 2. Charcot arthropathy is a disease where apart from ulcer occurs bone and articular damage. Progress-

ing tissue destruction can lead to such advanced damage, and amputation might be the only remedy. Treatment is long-term and complicated, and achieving good therapeutic effects is difficult. Treatment is based on disinfection, surgery and enzymatic substances. In the treatment there are used disinfectants, surgical or enzymatic, necrosis removal and treatment of infection. The proper solution in severe cases is i.e. NPWT (negative pressure wound therapy). Recent studies assess the suitability of PRP in the event of diabetic foot ulcer. (36) In the study done by Saad Setta H. et al. in diabetic patients with chronic ulcers, PRP was applied in gel form directly to the ulcer, after cleaning the wound. In comparison with the control group wound, healing was faster and complete. (37) Platelet-rich plasma could also be used in combination with other methods. In the study done by Tzen YS. et al. PRP was mixed with skin graft in therapy of persons with vast, non-healing ulcers in diabetes foot ulcer. Firstly, PRP was applied, and then skin transplantation was made. Procedure had good tolerance, in 8 out of 9 patients wound was completely healed and no reactivation was observed. (38) The use of PRP accelerates wound healing and leads to the complete ulcer healing. This is a promising and effective method of therapy of diabetic food ulcer, significantly enhancing the quality of life, and in many cases preventing from amputation and lowering the costs and duration of treatment. (32, 39, 40) It is scientifically proven that PRP is effective in the treatment of diabetic foot ulcer, which is shown by the present systematic review and meta-analysis. (41) Treatment of pressure ulcer is mostly based on the application of dressings and surgery. Effects are not satisfactory. That is why novel methods are required. In current studies there are reports referred to the use of PRP in case of patients with comorbidities and pressure ulcers, not responding to any other types of medication. (42, 43, 44) The use of platelet-rich plasma is a new and non-invasive type of treatment of poorly healing wounds. It accelerates recovery after surgery, through wound healing stimulation. Due to the efficiency of the therapy, the cost of treatment is lower, especially in case of chronic wounds and the quality of life is improved. In general, platelet-rich plasma used as a last method of therapy brings excellent results in patients not responding to any other methods.

#### THE USE OF PLATELET-RICH PLASMA IN ORTHOPAEDICS.

The next medical field, where platelet-rich plasma could be used is orthopaedics. PRP is a reservoir of great number of growth factors and biologically active substances. Some of them are actively involved in many biological processes taking place in the skeletal system. TGF- $\beta$  inhibits the synthesis of inflammatory IL-1 mediator and the cartilage glycoprotein mulin. (45) Platelet-derived growth factor and epidermal growth factor stimulate osteoblast precursors to proliferation. Transforming growth factor  $\beta$  induces the development of the intercellular

matrix through the collagen type I stimulation and vascular endothelial growth factor stimulates angiogenesis. (42) Platelet-rich plasma contains fibronectin and vitronectin, which stimulate osteoblasts adhesion and migration. (46) Bone tissue has enormous regenerative potential, but in some cases, when trauma is colossal, regeneration may be difficult or even impossible. In this situation, bone grafting could be proper solution. Anyway, it is a big surgery, burdened with many complications, especially in case of allo- and xenotransplantation. The use of PRP was described as a supplement to the bone transplantation. Due to the high content of growth factors, PRP has some osteoinductive and accelerative properties. (47) In the study by Latalski et al. PRP was used in patients after distraction osteogenesis surgery. The recovery time was significantly shorter, which was clearly associated with high level of patient's satisfaction. (48) In that study another method was also described, where PRP was mixed with the stem cells previously acquired from umbilical cord blood as a potential combination, which could positively influence bone tissues regeneration. Stem cells are the basis of tissue regeneration (49) and its combination with PRP could be a promising possibility in bone regeneration. (50) In spite of many studies considering positive influence of PRP, there are also many studies denying positive effects of PRP in bone regeneration. Due to the low level of evidence, small group of patients and variety in treatment, further research is needed.

#### THE USE OF PLATELET-RICH PLASMA IN ARTICULAR CARTILAGE REGENERATION

In contrast to the bone tissue, articular cartilage has a low regenerative potential. That is the reason why new strategies are needed. Osteoarthritis is a great therapeutic problem, because there is lack of casual treatment. In the early stage of a disease treatment, it is based on pain prevention and improvement of life quality. In later stages ednoprotheses are used. PRP contains growth factors, which accelerates chondrogenesis that could possibly be used in cartilage regeneration. (51) In a study by Cavallo C. et al. it was shown that PRP, also enhanced with leucocytes, stimulates chondocytes proliferation. (52) PRP, by stimulation of cell and intercellular matrix proliferation, leads to cartilage regeneration and additionally inhibits catabolic processes responsible for its degeneration. Intra-articular injection in patients with osteoarthritis also resulted in pain reduction and improvement of physical function. (2) In the study of the use of PRP in patellofemoral arthritis of the knee, there were observed positive results in a group of young patients, in the early stage of the disease. The mean duration of therapeutic effect was 8.8 months. (53) Similar results were obtained in prospective, randomized, double-blind study, in a group of 78 patients with early stage of knee osteoarthritis. The results were compared using WOMAC score, which contains parameters such as pain, joint function and stiffness. After PRP intra-articular injection a significant improvement was observed in comparison to the



group of patients where injection of saline was made. (54) In the study by Aggarwal et al. PRP was used in combination with knee joint arthroplasty. Short-term results in group of patients treated with PRP were better and after the procedure a hemoglobin decrease was significantly smaller, patients needed fewer transfusions, pain as well as analgesic needs were reduced. (55) Tietze DC et al. made a review of studies evaluating efficacy of PRP in knee and hip osteoarthritis treatment. PRP therapy in comparison to hyaluronic acid had significantly better results and the therapeutic effect was noticed up to 1 year after the procedure. In the event of the use of PRP in orthopaedic diseases there is a low level of evidence of efficacy of the treatment. However, the results of the PRP use are promising and could be an alternative for current methods. Platelet-rich plasma is an autologous substance, which is the reason for its safeness and does not cause immunological reactions, which are common in other methods, i.e. steroids or hyaluronic acid. (56)

#### THE USE OF PLATELET-RICH PLASMA IN TENDINOPATHY

The next field in orthopaedics, where PRP was used is tendinopathy. Recent studies have shown that there are positive effects of using platelet-rich plasma in some kind of diseases, where tendons are damaged. The full-thickness rotator cuff is one of the most common pathologies, especially in elderly patients. There are many therapeutic options for these patients, but they are still not sufficiently satisfying. One of the new ideas is the use of PRP in patients. In one study, which was randomized, prospective double-blind and controlled, patients had a localized injection of PRP after arthroscopy. PRP influenced positively on the short term outcomes, i.e. early healing and reducing pain in comparison to the control group. (57) Similar results were observed in patients with recalcitrant Achilles tendinopathy. Significant complications after using PRP were not observed. Clinical outcome was satisfactory, only in 3 out of 27 patients therapy did not work, where a clinical improvement was observed with the remaining patients. (58) In case of a patellar tendinopathy, the use of PRP has positively affected the clinical outcome, in both short and long-term observation in many studies. However, thorough investigation on bigger population and more objective and standardized protocols of its use are still needed. (59)

#### SUMMARY

In conclusion, platelet-rich plasma is successfully used in many fields of medicine. It brings very good results both as a method for skin rejuvenation and as a treatment in the event of poorly healing wounds or cartilage damage. PRP contains many biological activity substances and growth factors, which modulates the processes of reconstruction and tissue regeneration. It also results in many possibilities of using PRP in many fields of medicine. Depending on the way of application, this method is less or even noninvasive, which provides high level of comfort for pa-

tients. PRP could be used in monotherapy, but also in mixed therapy, i.e. with fractional laser, fat tissue transplantation, skin graft and many others. Due to the completely autologous nature, it does not bring a risk of immune system reaction or the transmission of viruses (HIV, hepatitis B and C virus). This method is simple and cheap, due to the fact that it can be used in all medical institutions without requiring large amounts of money and complicated technical training. With so many advantages, PRP is a novel and an attractive medical possibility, capable of becoming a basic therapeutic method in the poorly healing wound treatment, osteoarthritis, alopecia or skin aging.

#### CITE THIS AS

MEDtube Science 2015, Mar 3(1), 8 – 15

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