

## НОВІ МЕДИЧНІ ТЕХНОЛОГІЇ

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O.V. Pavlenko, R.Yu. Bida

### Using PRGF-Endoret Technique for the Regeneration of Soft Tissues Defects Applied in Regenerative Medicine

Institute of Stomatology of National Medical Academy of Postgraduate Education P.L.Shupyk  
rosya.bida@gmail.com

**Abstract.** The problem of diagnosis and treatment of patients with acute purulent inflammatory diseases of maxillofacial area remains relevant today. Despite the improvement of the quality of the dental care provision, improvement of the well-known and application of modern methods of diagnosis and treatment of this disease, the number of patients with odontogenic inflammatory processes of maxillofacial area continues to grow. The work deals with the study of methods of treatment of inflammatory processes of maxillofacial area soft tissues using plasma enriched with platelets. The use of platelet-rich plasma in the treatment of inflammatory processes positively influences the regeneration of soft tissues of maxillofacial area, especially in patients of young and middle age.

**Keywords:** *plasma rich in platelets, inflammation, soft tissue, maxillofacial area.*

Growth factor is a naturally occurring substance capable of stimulating cellular growth, proliferation, healing, and cellular differentiation. Usually it is a protein or a steroid hormone. Growth factors are important for regulating a variety of cellular processes. Growth factors typically act as signaling molecules between cells. Examples are cytokines and hormones that bind to specific receptors on the surface of their target cells. They often promote cell differentiation and maturation, which varies between growth factors. For example, bone morphogenetic proteins stimulate bone cell differentiation, while fibroblast growth factors and vascular endothelial growth factors stimulate blood vessel differentiation (angiogenesis). The system of PRGF stands for Plasma Rich in Growth Factor. It is a technology developed to promote the regeneration, repair and healing of the injured and damaged tissues. In the article below, we have elaborated the methods of PRGF-Endoret application to patients suffering from injuries or damages to soft tissue in the maxillofacial area. These clinical researches were held at the Department of Surgical Dentistry and Maxillofacial Surgery of Lviv National Medical University named after Danylo Halutsky, 2012-2014.

The scientific dossier summarises the series of international articles published over the last 10 years on the range of products and technologies developed by BTI Biotechnology Institute. It highlights the vast amount of scientific evidence that supports the biosafety and effectiveness of plasma rich in growth factors (PRGF-Endoret) in many fields of medicine, with a particular focus on oral and maxillofacial surgery. This autologous technology has revolutionised the field of regenerative medicine, as with the patient's blood we can obtain different therapeutic formulations rich in growth factors, the application of which encourages healing and tissue regeneration, reducing pain and inflammation.

Growth factors are a set of substances that carry out an important function in intercellular communication. They carry out a large number of biological functions among which cellular proliferation is important, though they also decisively affect cellular survival, migration, differentiation and even apoptosis.

Growth factors carry out their function at very low concentrations in body fluids and tissues.

The process of tissue regeneration includes a complex set of biological events controlled by the action and synergy of a cocktail of growth factors and cytokines.

Growth factors are also necessary to promote angiogenesis or the formation of blood vessels that will supply oxygen and nutrients to the damaged tissue.

After an injury or tissue damage, they are activated and coordinate a large number of intercellular or intracellular paths with the aim of restoring the integrity of the tissue and its hemostasis.

PRGF-Endoret contains a cocktail of autologous growth factors that proceed from both the plasma and the platelets. In fact, the platelets have a complex storage system in the form of intracellular granules that allow them to transport a large number of biologically active molecules. According to some authors, this list of proteins and peptides can come close to 500 molecules. Alpha ( $\alpha$ ) granules are the most abundant as there are around 40 to 80 alpha granules per platelet, but they are also the ones with the greatest retention capacity. In addition, they contain a series of antibacterial proteins that are generically called thrombocidines and which are lethal for a large variety of bacterial species.

However, it is important to remember that the plasma contains important growth factors and that the combination of the plasma and platelet factors is a key element in the biological action of PRGF-Endoret.

PRGF-Endoret technology is based on the preparation of platelet-rich 100% autologous plasma. The application of this plasma to damaged tissue areas speeds up the regeneration of a large number of tissues without any adverse effects.

Plasma rich in growth factors is a personalised technology that has revolutionised the field of regenerative medicine.

This article is being published to highlight the clinical cases which have been observed in patients with injuries or damages of the soft tissues in the maxillofacial areas while applying PRGF-Endoret. Its application over the last decade has extended to many fields of medicine from oral and maxillofacial surgery to dermatology, cosmetics, orthopaedic surgery and sports medicine, and more recently to ophthalmology.

The set of therapeutic formulations of PRGF-Endoret are obtained by means of a simple protocol based on a tiny volume of the patient's blood. The blood is centrifuged (580g) in 9 ml citrated tubes during 8 minutes allowing the separation of red and white blood cells from the platelet-rich plasma. The two fractions of PRGF-Endoret are separated from the rest of the blood components by means of the plasma transfer device (PTD). Later, and prior to its therapeutic application, the fractions of PRGF-Endoret are activated with calcium chloride, leading to a series of therapeutic formulations.

In a couple of revision articles, the research team along with the Nurden Doctors from the Reference Centre in France, have characterised the protein content of platelets in order to learn about the set of molecules present in PRGF-Endoret formulations.

Platelets release substances that promote tissue regeneration and which modulate both angiogenesis and inflammation. Important among other factors we have PDGF: platelet-derived growth factor, TGF- $\beta$ : transforming growth factor  $\beta$ , bFGF: basic fibroblast growth factor, VEGF: vascular endothelial growth factor, EGF: epidermal growth factor or angiopoietin-1 among others.

Calcium acts as a cofactor in the activation process of PRGF-Endoret, which allows the conversion of the fibrinogen of the plasma into fibrin, generating a gel or clot with important biological functions. Fibrin is an excellent matrix to maintain and house the cells.

The use of growth factors and fibrin for regenerative purposes

represents a new approach to personalised medicine that a large number of patients could benefit from.

The stimulation of cell proliferation and migration along with the call to circulating cells to come to the location of the injury are basic aspects of the action of PRGF-Endoret.

The biological mediators of PRGF-Endoret stimulate and encourage such important processes for tissue regeneration as cellular proliferation and migration, chemotaxis, inflammation and the auto/paracrine synthesis of new molecules with biological activity.

The growing interest in the range of biological options that PRGF-Endoret offers has even reached the field of stem cells. Stem or progenitor cells are characterised on the one hand by their unlimited capacity for proliferation, and on the other by the possibility of undergoing asymmetrical division or self-renewal maintaining their stemness while at the same time they can differentiate to diverse types of cells. There are different types of stem cells depending on their origin and their anatomical location. There is evidence that the content of biologically active agents in PRGF-Endoret affects the mobilisation, adhesion, proliferation, survival, activation and differentiation of mesenchymal stem cells and other subtypes of precursor cells. In addition, the cocktail of growth factors of PRGF-Endoret is an ideal resource for the cultivation and expansion of stem cells in the laboratory.

Our research team has proven that PRGF-Endoret presents bacteriostatic activity with a large number of bacterial and fungal strains. The platelets contain a series of antibacterial proteins called thrombocidines. In addition to thrombocidines, platelets transport and release other antimicrobial peptides among which we should mention platelet factor 4, RANTES, tissue activating peptide 3, the basic protein of platelets, thymosin  $\beta$ -4, and fibrinopeptides A and B.

In fact, the bacteriostatic effect of PRGF-Endoret is identical to that of a platelet and leukocyte-rich plasma.

The versatility of PRGF-Endoret has allowed its use in the treatment of a wide range of clinical problems within the field of oral and maxillofacial surgery. An example of this is the following series of applications developed by our research team over the last two decades and summarised in the scientific dossier. From the treatment of the alveolus post-extraction to the use of this technology in gingival recessions or in the humectation of dental implants to encourage their osseointegration, the range of therapeutic possibilities is enormous. PRGF-Endoret offers the possibility of working with a liquid formulation, with a three-dimensional matrix or with a retracted fibrin membrane. Such a possibility drastically increases the number of therapeutic options and applications.

PRGF-Endoret is the first 100% autologous platelet-rich plasma to be described in the literature worldwide. It is, likewise, a pioneering technology in translational regenerative medicine. Over 10 years of research, added to its exclusive properties, make PRGF-Endoret a unique technique. PRGF-Endoret is prepared with small volumes of patient's blood and does not require the use of thrombin or chemical agents for its activation. Unlike other products, it does not include white blood cells (leukocytes) in its composition, which gives it more effective anti-inflammatory properties. It is the most versatile technology, as its multiple formulations offer a large number of therapeutic applications.

Thus, PRGF-Endoret has a lot of advantages over other systems and technologies in regenerative medicine. They are:

- 100% biocompatible, versatile and safe;
- It is the market's first 100% autologous technology;
- Control over its activation and use;
- A simple protocol: just one centrifugation;
- A fast protocol: just 8 minutes of centrifugation and 20 minutes of preparation;
- Its clinical efficiency in the stimulation of tissue healing and regeneration has been described in a large number of

international articles;

- It does not contain leucocytes, avoiding their proinflammatory activity;
- Powerful bacteriostatic properties;
- Excellent therapeutic potential in different clinical applications;
- In none of the treatments carried out over the years have any undesired effects been observed.

PRGF-Endoret is also crucial to the future of regenerative medicine because of its versatility and special features which set apart from other systems and technologies?

- It is a pioneer in the development of specific protocols for tissue regeneration;
- It is backed by a large number of international scientific studies and publications;
- It is the only technique that holds the obligatory health certifications required for each one of the following applications: healing of venous ulcers, consolidation of bone fractures and grafts, treatment and healing of injuries or damages to soft tissue in the maxillofacial area, fixation of prostheses in the hip, knee, etc., oral implantology, injuries and breakages of ligaments, muscles and tendons, treatment of skin burns, injuries and lesions, regeneration of aged skin;
- It is a versatile system that makes it possible to create different formulations that adapt to the characteristics of each application;
- Excellent efficiency of the volume of blood extracted with this system.

In short, as shown by the series of letters to the editor published during recent years, we can define PRGF-Endoret as a platelet-rich autologous plasma whose effectiveness and safety have been widely proven. However, it is important to remember that not all platelet-rich plasmas are PRGF-Endoret.

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*Павленко О.В., Біда Р.Ю.*

**Застосування методики PRGF-Endoret для регенерації дефектів м'яких тканин, що застосовується у відновній медицині**

Інститут Стоматології Національної медичної академії післядипломної освіти ім. П.Л.Шупика  
rosya.bida@gmail.com

**Резюме:** Проблема діагностики і лікування хворих з гострими гнійними запальними захворюваннями щелепно-лицевої ділянки залишається актуальною в даний час. Незважаючи на підвищення якості рівня надання стоматологічної допомоги, удосконалення відомих і застосування сучасних методів діагностики і лікування даної патології, кількість хворих з одонтогенними запальними процесами щелепно-лицевої ділянки продовжує збільшуватись. Робота присвячена вивченню методики лікування гнійно-запальних процесів м'яких тканин щелепно-лицевої ділянки з використанням плазми збагаченої тромбоцитами. Використання збагаченої тромбоцитами плазми у комплексному лікуванні гнійно-запальних процесів позитивно впливає на процеси регенерації м'яких тканин щелепно-лицевої ділянки, особливо у пацієнтів молодого та середнього віку.

**Ключові слова:** плазма збагачена тромбоцитами, запальні процеси, м'які тканини, щелепно-лицева ділянка.

*Павленко А.А., Біда Р.Ю.*

**Применение методики PRGF-Endoret для регенерации дефектов мягких тканей, применяемая в восстановительной медицине**

Институт Стоматологии Национальной медицинской академии последипломного образования им. П.Л.Шупика  
rosya.bida@gmail.com

**Резюме:** Проблема диагностики и лечения больных с острыми гнойными воспалительными заболеваниями челюстно-лицевой области остается актуальной в настоящее время. Несмотря на повышение качества уровня оказания стоматологической помощи, совершенствование известных и применения современных методов диагностики и лечения данной патологии, количество больных с одонтогенными воспалительными процессами челюстно-лицевой области продолжает увеличиваться. Работа посвящена изучению методики лечения гнойно-воспалительных процессов мягких тканей челюстно-лицевой области с использованием плазмы обогащенной тромбоцитами. Использование обогащенной тромбоцитами плазмы в комплексном лечении гнойно-воспалительных процессов, положительно влияет на процессы регенерации мягких тканей челюстно-лицевой области, особенно у пациентов молодого и среднего возраста.

**Ключевые слова:** плазма обогащенная тромбоцитами, воспалительные процессы, мягкие ткани, челюстно-лицевая участок.

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