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Platelet-Rich Plasma and Air Cryotherapy Treatment: Principles, Method and Benefits

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ABSTRACT

Between 16 September 2018 and 15 September 2023, within the Polimed Dacia Medical Center, the project "Innovative method of medical recovery through platelet-rich plasma and air cryotherapy treatment" was implemented, funded by the Competitiveness Operational Program, priority axis 1. By using this service, patients were able to recover the normal functionality of the joint faster.

Platelet-Rich Plasma (PRP) is a blood-derived product with a higher concentration of platelets in plasma, which is used to provide supraphysiological amounts of growth factors.

Due to their analgesic and anti-inflammatory properties, cryotherapies are widely used to improve the rehabilitation of patients with various joint diseases.

We observed that PRP treatment combined with cryotherapy in joint injuries and tendon inflammations have a beneficial effect on the recovery of affected tissues. In the case of joint immobilization over a long period of time, the occurrence of inflammatory processes decreases considerably after the use of the aero cryotherapy.

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Introduction and Objective of the Study

Between 16 September 2018 and 15 September 2023 within the Polimed Dacia Medical Center, the project "Innovative method of medical recovery through Platelet-Rich Plasma (PRP) and air Cryotherapy Treatment" was implemented, funded by the Competitiveness Operational Program, priority axis 1. action 1.2.1: Stimulating the demand of enterprises for innovation through CDI projects carried out by enterprises individually or in partnership with research institutes and universities, in order to innovate processes and products in economic sectors with growth potential By using this treatment, patients will be able to recover faster the normal functionality of the joint. The introduction of the innovative treatment based on the "method of diagnosis and recovery through PRP treatment and aerocryotherapy" was carried out within the activity 4.D. Activities for putting into production the results of research and development and 4.3 Sub-activity - activities for the realization of the service.

Platelet-Rich Plasma is a revolutionary natural method that uses one's own blood to accelerate the healing of soft tissues.

Infiltrations with platelet-rich plasma, or autologous preparation with conditioned plasma, represent one of the modern treatment options for certain joint problems. Although platelets- small blood cells that intervene in the coagulation process- are known mainly for their role in stopping bleeding, through their rich content in growth factors, they have regenerative properties and an important role in restoring injuries, which led to the use of plasma enriched with platelets in the field of orthopedic conditions [1,2].

Treatment with platelet-rich plasma increases the body's natural ability to heal, reduces tendon and joint inflammation and accelerates the repair process of damaged tendons and ligaments. Platelet-enriched plasma is an autologous preparation (obtained from one's own plasma), thus there are no risks related to the transmission of certain diseases or immunogenic reactions, and in addition, it is devoid of systemic adverse effects [3,4].

Platelet-enriched plasma is produced from a person's own blood, in which there is an increased concentration of platelets; platelets and blood plasma contain multiple essential factors for the recruitment, multiplication and specialization of cells that are necessary for the healing of damaged structures (cartilaginous tissue, bone tissue, ligaments, tendons, muscles).

Although blood is mainly a liquid (called plasma), it also contains small solid components (red cells, white cells, and platelets). The platelets are best known for their importance in clotting blood. However, platelets also contain hundreds of proteins called growth factors that are very important in the healing of injuries [5-7].

Materials and Methods

Platelet-rich plasma is plasma with many more platelets than what is typically found in blood. The concentration of platelets — and, thereby, the concentration of growth factors — can be 5 to 10 times greater than usual. To develop the platelet-rich plasma preparation, blood was first drawn from the patient. The platelets were separated from other blood cells and their concentration was increased during a process called centrifugation. These platelets were then injected into the injured site.

Platelet-enriched plasma technique: a venous blood sample was obtained from the patient, the blood was centrifuged, in order to separate the plasma and platelets from the network of blood components. Platelet-rich plasma was later collected and injected into the injured area.

Venous blood (from the veins of the forearm) was collected from the patient, the amount differed from case to case, it varied between 8 ml, 5 - 15 ml, 15 - 20 ml. The collection was done in a tube with anticoagulant, at a temperature of 21°C–24°C to prevent platelet activation during centrifugation of the blood.

Afterwards, the blood was centrifuged at 1,200 rpm and enriched with various compounds to enhance the therapeutic effect. PRP preparations may differ depending on the patient's condition. PRP administration was performed under local anesthesia in the targeted area.

The procedure was simple and it was performed in an outpatient setting, without hospitalization. Minor local adverse effects were registered, but they were short-lived. The number of sessions for the administration of PRP and the time interval at which it was carried out were established by the specialist doctor.

PRP was obtained through a simple method that tooked around 12 minutes following a few steps:

- Collect 10 ml of the patient's venous blood (similar to any blood collection for routine tests)
- Collected blood was placed in a tube with artificial plasma and activation factors
- The test tube was inserted into a centrifuge for 5-10 minutes
- The obtained product was injected into the joint using a minimally painful sterile method.

A total of 118 cases with a diagnosis of chondropathy in the knee joint were included in the study. Platelet-rich plasma treatments, air cryotherapy and injectable treatments with visco-elastic solutions were applied in case of bilateral damage.

Platelet-rich plasma is a blood-derived product with a higher plasma platelet concentration that is used to deliver supraphysiological amounts of growth factors. Due to their analgesic and anti-inflammatory properties, cryotherapy is widely used to improve the rehabilitation of patients with various joint conditions.

Injections of platelet-rich plasma are a novel treatment for managing pain related to osteoarthritis (OA) of the knee. Researchers are still investigating this option. [8,9].

Inclusion Criteria:

- Patients with Arthrosis or Chondropathies in Early or Moderate Stages of the Disease;
- Patients with joint pain in evolution for 3 months, without improvement under conservative treatment (NSAIDs, physio- and physical therapy), with arthose changes in imaging investigations
- Patients with incomplete injuries of intra-articular ligaments
- Patients over 18 years of age;
- Patients who were able to express their agreement to the intervention through written Informed Consent;

Exclusion Criteria:

- Patients with Comorbidities Such as Diabetes, Coagulopathy, InTreatment with Anticoagulants or Antiaggregants, Immunosuppression;
- Patients older than 80 years and younger than 18 years;
- Serious General Condition of the Patient
- Patients with NSAID treatment in the last 5 days before the procedure;
- Patients with Hb lower than 11 g/dl, platelets lower than 150,000mm3-1;
- Patients with Joint Infections at least 12 months ago;
- Patients with meniscectomy greater than 50%;
- Patients with axis deviations greater than 5 degrees.
- Chronic Decompensated Cardiovascular Diseases, Rhythm Disorders
- Raynaud's Syndrome, Acrocyanosis, Systemic Vasculitis, Cryoglobulinemia, Agammaglobulinemia, Cryofibrinogenemia
- Recent Stroke
- Fever
- Tuberculosis
- Malignant Tumors
- Hypothyroidism
- Hysterical Neurosis
- Cold Intolerance
- Pregnancy

Paraclinical Investigations (Laboratory and Imaging):

- Blood count - Collection of Venous Blood in a Vacutainer with EDTA
- ESR measurement - Red Blood Cell Sedimentation Rate - Collection in Vacutainer with Sodium Citrate
- CRP dosing - C-Reactive Protein for Patients with Chronic Inflammatory Conditions in Acute cases - Collection in Vacutainer with Coagulation Activator and Serum Separator
- Ultrasound of Soft Parts, Periarticular in the Case of Patients with Volume Changes of the Joint

Treatment with PRP:

- Preparation of materials for treatment: PRP collection kit from LIAMED.
- Collection of Biological samples for the Separation of Plasma Rich in Platelets. Collection of Venous Blood, Separation of Plasma Rich in Platelets by centrifugation at 2700 rpm, for 10 min
- Intra-Articular Injection of Plasma Rich in Platelets After Disinfecting the Skin with Betadine solution and following the rules of asepsis and antisepsis.
- After performing the PRP injection, the punctured in tegumentary area will be protected with sterile self-adhesive dressing and iodine tincture.
- Aero cryotherapy treatment at patients with PRP post-procedure pain and joint volume changes:
- Preparing Patients for Aero Cryotherapy
- Local treatment with the help of CRYOMED equipment
- Preparation of the equipment for local Cryotherapy
- Completing the informed consent form for aero Cryotherapy
- Completing the Treatment form for aero Cryotherapy
- Measuring the Temperature of the area where the application

will be made, before the treatment
- Applying the Treatment with temperature measurement at close intervals, so that the local temperature is between 4 and 16º C
- Checking the temperature at the end of the treatment and completing it in the patient's treatment form.

Results

We observed that the platelet-rich plasma treatment combined with cryotherapy in joint injuries and tendon inflations it had a beneficial effect on the recovery of affected tissues.

In the case of joint immobilization over a long period of time, the occurrence of inflammatory processes decreased considerably in the use of air cryotherapy.

The introduction of the innovative treatment aimed to apply the method of diagnosis and recovery through treatment based on platelet-rich plasma and aero cryotherapy to patients who complied with the criteria for inclusion in the treatment, as established in activity 2.3 of the project.

By using this service, patients were able to recover more quickly the normal functionality of the joint after various traumatic injuries or degenerative processes of the articular surface or articular ligaments, both through the reparative effect of plasma rich in platelets and through the reduction of local pain as a result of volume restoration from the intra-articular space.

Within the project entitled "INNOVATIVE METHOD OF MEDICAL RECOVERY THROUGH TREATMENT WITH PLATELET-RICH PLASMA AND AEROCRYOTHERAPY" in the initial stage of the project, the functionality of the knee joint was evaluated, by carrying out a joint motility test with a cycle ergometer.

For testing the effort and the mobilization capacity under the load of the joint, the force was used at which joint movement was possible in normal activity mode.

In the same group of patients, the Oxford score was performed to evaluate the functionality of the knee joint in conditions of normal use of the joint. Following the analysis of the questionnaire, a correlation of almost 80% was obtained for the consulted patients, between the low values of the effort capacity, a force of 50-75 W, a score between 6-8 in the self-assessment of the personal status and the values resulting from the calculation of the score, with classified as severe or moderate arthritis, but at the same time there were patients with low Oxford score values but with an increase in joint mobilization force over 85 W, but with a low level of pain intensity.

Scheme for Realization of the Recovery Service Through Platelet-Rich Plasma Treatment and Aero Cryotherapy:
- Specialized Medical Consultation: Orthopedics-Traumatology, Medical Recovery, Sports Medicine.
- Completing the form to Determine the Value of the Oxford Score
- Informing patients about the treatment method and completing the informed consent form
- Completing the self-assessment questionnaire regarding the patient's state of health
- Verification of the applicability criteria of the innovative treatment

Discussions

To Speed Healing, The Injury Site is Treated with the PRP Preparation. This can be done in One of Two Ways:

Platelet-rich plasma can be carefully injected into the injured area. For example, in Achilles tendinitis, a condition commonly seen in runners and tennis players, the heel cord can become swollen, inflamed, and painful. A mixture of PRP and local anesthetic can be injected directly into this inflamed tissue. Afterwards, the pain at the area of injection may actually increase for the first week or two, and it may be several weeks before the patient feels a beneficial effect [10].

Platelet-Rich Plasma (PRP) may also be used to improve healing after surgery for some injuries. For example, an athlete with a completely torn heel cord may require surgery to repair the tendon. Healing of the torn tendon can possibly be improved by treating the injured area with PRP during surgery. This is done by preparing the PRP in a special way that allows it to actually be stitched into torn tissues [11].

During the past several years, much has been written about a preparation called platelet-rich plasma and its potential effectiveness in the treatment of injuries. Many famous athletes — golfer Tiger Woods, tennis star Rafael Nadal, and several others — have received PRP for various problems, such as sprained knees and chronic tendon injuries. These types of conditions have typically been treated with medications, physical therapy, or even surgery. Some athletes have credited PRP with their being able to return more quickly to competitions [12-15].

A review that analyzed 14 randomized controlled trials with a total of 1,423 participants concluded that PRP may help manage pain associated with knee osteoarthritis. The authors noted the following at 3-, 6-, and 12-month follow-ups.

Chronic complex musculoskeletal injuries, with a slow healing process, represent challenges for both doctors and researchers [16].

Ortho biology is a relatively new science, which involves the introduction of biological sources (cell-based therapies, plasma enriched in platelets, bone marrow concentrate, adipose tissue grafts). The techniques used in Ortho biology offer the chance to accelerate the healing of bone structures and soft tissues. Platelet-rich plasma is an Ortho biological technique that has recently gained popularity as an adjunctive treatment for musculoskeletal injuries. PRP represents a volume of fractionated plasma from the patient's blood that contains platelet concentrate. Platelets contain alpha granules that are rich in growth factors: platelet-derived growth factor, TGF-beta, insulin-like growth factor, vascular endothelial growth factor, and epidermal growth factor, all of which play a key role in repair mechanisms of tissues.

Plasma enriched with platelets is a treatment option increasingly used for a wide spectrum of medical conditions and for aesthetic procedures. PRP therapy was initially used successfully in sports medicine and by orthopedic doctors to relieve joint pain. Knee infiltrations with PRP are among the most popular among patients.

Plasma rich in platelets and growth factors (VEGF, PDGF, TGF B, EGF, IGF) has the role of intensifying the natural tissue regeneration process by mitigating inflammatory processes and by stimulating the angiogenesis process.

The formation of a new vascularization, starting from the existing vascularization, is called angiogenesis. Normally, angiogenesis is determined by physiological processes such as pregnancy, menstruation, or pathological processes, such as the occurrence of inflammation [16,17].

By supporting the natural reparative processes, the goal of PRP therapy is to restore normal functioning of the affected tissues.

Pain Levels: Compared with placebos, PRP injections significantly reduced pain scores at each follow-up appointment.

Physical Function: Compared with controls, PRP significantly improved physical function at these follow ups.

Adverse Effects: Some people experienced adverse effects, but these were no more significant than those produced by other types of injection. While the results appear promising, 10 of the 14 studies reviewed had a high risk of bias, and four had a moderate risk of bias [18].

More studies are needed to determine whether PRP could offer a suitable option to manage pain from osteoarthritis of the knee.

It has been observed that PRP treatment combined with cryotherapy in joint injuries and tendon inflammations have a beneficial effect on the recovery of affected tissues. In the case of joint immobilization over a long period of time, the occurrence of inflammatory processes decreases considerably after the use of aero cryotherapy [18].

Carrying out Tests to Establish the Functional Parameters after the PRP Treatment: Testing the effort and the patient's ability to mobilize the joint by using the cycle ergometer: the patient, under the supervision of the specialist doctor or the medical assistant, was asked to mobilize the mechanism of the cycle ergometer at the maximum level of resistance, possible, indicated by the patient. - Completion of the cycle ergometer monitoring sheet with the value in Watts of the resistance to the mobilization of the cycle ergometer rotation mechanism. In the case of the impossibility of mobilizing the joint, the reason for not performing the test was noted.

Testing patients regarding joint mobilization, balance and symmetry while walking with the help of the computerized neuromotor recovery system - REO AMBULATOR.

The patient, under the supervision of the specialist doctor or physiotherapist/physiotherapist, was asked to perform the test to check balance, cadence, bearing, symmetry and accuracy of limb and body movements while walking.

Completing the computerized neuromotor recovery equipment monitoring sheet. In the case of the impossibility of mobilizing the joint, the reason for not performing the test was noted. Evaluation at the control visit between 2 and 6 months after the treatment:

Stress testing and the patient's ability to mobilize the joint by using the cycle ergometer - stress test -Testing Regarding Joint Mobilization, Balance and Symmetry While Walking with the Help of the Computerized Neuromotor Recovery System - REO AMBULATOR.

Completing the form to determine the value of the post-therapy Oxford score.

Treatment with platelet-rich plasma could hold promise, however, current research studies to back up the claims in the media are lacking [19].

Although PRP does appear to be effective in the treatment of certain chronic tendon injuries and low- to moderate-grade knee osteoarthritis, the medical community needs more scientific evidence before it can determine whether PRP therapy is truly effective in other conditions.

Some of the key advantages of PRP injections are that they can reduce the need for anti-inflammatories or stronger medications like opioids. In addition, the side effects of PRP injections are very limited because, since the injections are created from your own blood, your body will not reject or react negatively to them. Even though the success of PRP therapy is still questionable, the risks associated with it are minimal. There may be increased pain at the injection site, but the incidence of other problems — infection, tissue damage, nerve injuries — appears to be no different from that associated with cortisone injections.

The good results obtained after PRP treatments have expanded the medical specialties that use platelet-enriched plasma therapy. Today, PRP therapy is used in orthopedics, sports medicine, regenerative gynecology, dermatology, urology and dentistry.

The administration of autologous products (obtained from one's own blood) prevents surgical intervention by restoring the function of the damaged tissue, accelerating the healing processes and determining the appearance of new healthy cells.

The effectiveness of the use of platelet-rich plasma (PRP) increases when the technique is used together with physio-kinetotherapeutic treatments.

Diseases in which the Treatment with Platelet-Rich Plasma (PRP) is Effective:

- Articular Cartilage Repair (Knee, Hip, Shoulder)
- Restoration of the Achilles Tendon
- Lesions Or Cracks of the Rotator Cuff
- Osteoarthritis
- Injuries of the Anterior Cruciate Ligament
- Pelvic Pain and Instability
- Injuries Or Pain in the Dorsal, Lumbar or Cervical Spine
- Tendinosis (Lateral Epicondylitis)
- Tendinitis and Ligament Injuries
- Chronic Pain in the Knee Joint
- Muscle Injuries [19].

Platelet-enriched plasma and hyaluronic acid stimulate the anti-inflammatory and restructuring mechanisms of the extracellular matrix in osteoarthritic processes.

In the treatment of osteoarthritis, both Platelet-enriched Plasma and Hyaluronic Acid treatments lead to a decrease in catabolism (joint destruction), but PRP treatment caused a significant reduction in MMP-13, an increase in HAS-2 expression in synoviocytes and an increase in cartilage synthesis activity compared to hyaluronic acid.

PRP acts by stimulating the endogenous production of hyaluronate and reduces cartilage catabolism.

Platelet-rich plasma has similar effects to hyaluronic acid: it suppresses the concentration of inflammatory mediators and the

expression of inflammatory genes in synoviocytes and cartilage [20].

The antinociceptive and anti-inflammatory activities of PRP support its use in osteoarthritis to reduce pain and modulate the disease process.

The procedure is performed on an outpatient basis (in the consulting room), it does not require hospitalization. The approximate duration of the procedure is 30 minutes.

Depending on the severity of the condition, 1-3 infiltrations can be done, and the platelet concentration is variable, between 4 and 20 times (4-20X) [21].

If it is recommended to perform more than one procedure, for example, if 2-3 infiltrations are necessary, then the injection interval is between 7-14 days (the time period required between the moments of performing the procedures).

In most cases, a "standard" platelet concentration of 4X is used, a volume of 15 ml of venous blood is taken in a test tube, it is prepared for 10 minutes in a centrifuge and a volume of approximately 4 ml of plasma. The resulting volume of concentrated plasma is injected at the site of the disease (at the level of the affected joint or tendon).

In certain situations, when we want to increase the healing potential, we can increase the concentration of growth factors up to 20 X, which is why we collect a larger volume of blood (approximately 60 ml) [22].

The procedure is not painful; the patient moves without means of support or immobilization (no need for crutches or orthosis).

Since it is an autologous treatment (we use the patient's own blood), there are no allergic reactions to the injected product. The risks are those associated with the injection: the occurrence of infection at the injection site, which is why we only use sterile single-use kits, and the injection technique complies with all antisepsis protocols. [23-25].

We recommended that before and in the morning of the injection, the patient must hydrate enough (drink 2-3 liters of water), reduce coffee consumption (can have a coffee in the morning), so as to improve the quality of the collected blood. If, during the period in which the treatment is to be performed, he has an active infection in the body (dental abscess, urinary tract infection, digestive tract infection, viral infection) or follows a prolonged treatment with anti-inflammatory medication, the procedure will be delayed, until the biological condition will allow.

After the infiltration, ice will be applied to the injection site for 2-3 days to prevent inflammation or a possible hematoma, and sports rest or avoiding sustained effort is recommended.

After performing the procedure (post-infiltration), we recommended to apply an ice pack to the injection site 2-3 times a day and reduce physical efforts.

After completing the treatment, patients are advised to follow a physiotherapy and kinesitherapy program in the medical recovery center to improve muscle tone and function.

After the infiltration with PRP is performed (the procedure lasts around 15 minutes), the patient remains in the office for another 5-10 minutes, during which he practices flexion-extension exercises that help integrate the injected substance into the joint cavity.

An anti-algesic treatment for 3 days post-infiltration (no anti-inflammatory treatment) is recommended, together with some recovery exercises determined according to the pathology of each one.

Conclusions

Treatment with platelet-rich plasma in joint lesions, inflammatory processes of the tendons in combination with cryotherapy led to a reduction in the recovery time and a more effective restoration of the affected tissues.

The application of air cryotherapy with antialgic and anti-inflammatory effect decreases the risk of developing inflammatory processes and joint pain.

The regeneration process was initiated in the interval of 2-3 weeks and continued up to 6-9 months after the completion of the treatment. The clinical evolution of the patient was tested, we observed the evolution, but also paraclinically - sometimes it was necessary to repeat the imaging investigations (ultrasound or MRI) to compare the images of the affected area before and after therapy.

The ideal candidate for PRP therapy was the young patient (approximately 16- 45 years old), physically active, with an early or moderate mechanical or traumatic joint disease, and who has not been diagnosed with any disease autoimmune diseases that generally affect the joints (rheumatoid arthritis, ankylosing spondylitis, lupus, etc.).

After the age of 45, the potential for biological healing through infiltrations decreased, but there are some conditions in which studies show good results and this form of treatment can be recommended after medical consultation. Over the age of 55, the effectiveness is much reduced or absent and the indications are limited. Healing after PRP infiltrations was done through several stages:

- The Inflammation Stage, which occurred in the first 2-3 days after infiltration;
- Cell proliferation stage (release of growth factors that played a remodeling role in the next stage);
- Tissue Remodeling Stage – it was done by Replacing the Destroyed cells with new healthy ones.

The number of infiltrations varied from one case to another considering the wide spectrum covered by PRP infiltrations, between 1-3 infiltrations, depending on the diagnosis and the evolutionary stage of the condition.

The final result of the infiltration was observed after a period of 6-12 months, but the reduction of symptoms appeared after the first 2 weeks.

In patients with advanced arthrosis, for optimal results, the administration of PRP should be correlated with hyaluronic acid

The Obtained Effects:

- The application of PRP treatment in joint injuries, inflammatory processes of the tendons in combination with cryotherapy led to a reduction in recovery time and a better repair of the affected tissues
- The application of aero cryotherapy with anti-algesic and anti-inflammatory effect reduced the risk of inflammatory processes and joint and peri-articular pain in the case of long-term immobilization
- The application of cryotherapy from the beginning of the recovery treatment increased the comfort and the degree of involvement of the patients during the recovery.
- Applying local cryotherapy reduced the side effects of a systemic medication used to reduce the inflammatory syndrome and pain.

Conflict of interests

The Authors Declare that they Have No Conflict of Interests.

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