PROCEEDINGS

Sports Medicine

International Biobridge Conference

"GENERATION REGENERATION"

CINI FOUNDATION, VENICE-ITALY

2013 & 2014

BIOBRIDGE FOUNDATION

www.biobridge-event.com

regenlab

"This book comprises a collection of clinical reports presented during the 7th and the 8th Biobridge Conferences held in Venice in September 2013 and September 2014 respectively."

SPORTS MEDICINE

LIGAMENTS

Dr. Jen Saunders, Sports & Exercise Medicine, Australia, AUS
"A comparison of the use of PRP and hypertonic glucose injections for the treatment of sacroiliac joint incompetence: a pilot study"

MUSCULOSKELETAL LESIONS

Dr. Alessandro De Rosa, Immunohematology & Transfusion Medicine Department, A.O. S. Camillo Forlanini, Rome, ITA
"Biologic characteristics and therapeutic effectiveness of autologous PRP infiltrations in joints orthopaedic pathologies of the knee"

Dr. Giuseppe Di Pietro, Director of Transfusional Medicine Department ASL 10, San Giovanni di Dio, Florence, ITA
"Use of Regen fibrin polymer device for the production of PRP in the PO San Giovanni di Dio in Florence"

Dr. Patrick Goh, Specialist Sports Physician, Sports Medicine International, Camden Medical Centre, Singapore, SIN
"Optimizing PRP treatment and recovery of injured sportsmen – a five-year medical experience"

Dr. Maria ALBA Stigliano, Director of Immunology & Transfusion Medicine Department, ASL Roma & Santo Spirito Hospital, Rome, ITA
"Autologous PRP in the treatment of inflammatory tendinopathy & degenerative joint disease, the experience of Santo Spirito Hospital in Rome"

Dr. Maksim Strakhov, Orthopaedic Surgeon, Moscow, RUS
"Using of PRP-therapy for athletes with extra-articular pain localization"

Dr. Maria Cristina Tirindelli, Responsible of the Transfusion Center, Campus Biomedico University of Rome, Rome, ITA – Dr. Gianluca Vadalà, Orthopaedic Surgeon, Department of Orthopaedic and Trauma Surgery, Campus Biomedico University of Rome, Rome, ITA
"Clinical efficacy of platelet-rich plasma to treat chronic articular pathologies"

OSTEOARTHRITIS & CARTILAGE

PRP

Dr. Hesham Almolla, Annunziata Hospital of Cosenza, ITA
Dr. Marcello Napolitano, Annunziata Hospital of Cosenza, ITA
Dr. Antonio Crescibene, U.O.C. Orthopaedics and Traumatology P.O. San Francesco – Paola, Cosenza, ITA
"Use of platelet-rich plasma (PRP) in articular and tendon pathology at the Annunziata Hospital of Cosenza"

Dr. Caterina Martini, Orthopaedics Clinic, CTO, AOU Careggi, University of Florence, ITA
Dr. Roberto Civinini, Orthopaedics & Traumatology,
SOD General Complex Orthopaedics, AOU Careggi, Florence, ITA
"Clinical study: treatment of symptomatic coxarthrosis with platelet-rich plasma"

Dr. David Mathers, Rheumatologist, Australia, AUS
Dr. John Van Der Kallen, Rheumatologist, Australia, AUS
"Clinical experience of PRP in knee osteoarthritis in a rheumatology practice"

"This book comprises a collection of clinical reports presented during the 7th and the 8th Biobridge Conferences held in Venice in September 2013 and September 2014 respectively."

Dr. Piero Pasquetti, Director of Rehabilitation Department, CTO Careggi, ITA
"Knee OA – Clinical experience: 100 patients treated with platelet growth factors"

Dr. Vincenzo Pellecchia, Orthopaedic, Varese, ITA
"PRP: a treatment for early osteoarthritis"

CELLULAR MATRIX
Prof. Philippe Adam, Sports Medicine, Medipole Clinic, Toulouse, FRA
"Treatment of degenerative hip osteoarthritis in patients under 50 years old by CT-guided injection of Cellular Matrix"

Dr. Antonio Frizziero, Assistant Professor, Department of Physical & Rehabilitation Medicine School of Medicine university of Padova, Padova, ITA
"Treatment of knee osteoarthritis with Cellular Matrix, a synergistic association of platelet-rich plasma and hyaluronic acid"

Prof. Luca Pierelli, Director of Immunology & Transfusion Medicine Department, San Camillo Forlanini Hospital, Rome, ITA
"Cellular Matrix in osteoarthritis San Camillo protocol"

Dr. Jean-Luc Renevier, Rheumatology, Hospital "Meulan les Mureaux", Paris, FRA
"Preliminary study on the HA + PRP injections in osteoarthritis of the knee after failure of HA alone"

Dr. Jean-Luc Renevier, Rheumatology, Hospital "Meulan les Mureaux", Paris, FRA
"Efficacy and safety of Cellular Matrix in knee osteoarthritis patients after failure of HA"

Prof. Donato Rosa, Associate Professor Musculoskeletal Disease, University Federico II of Naples, Naples, ITA Dr. Agnese D'Apice, Orthopedic & Traumatologist, Napoli, ITA
"Infiltrative therapy combined with PRP-HA in degenerative cartilage pathology: one-step technique"

Dr. Sandra Verna, Hematology & Transfusion Medicine Department, SS Annunziata Hospital, Chieti, ITA
"Effectiveness of a compound consisting of platelet-rich plasma (PRP) and hyaluronic acid (HA) in the treatment of mild-to-moderate knee osteoarthritis: preliminary results"

PRP & BONE MARROW CELLS
Dr. Rosa Leone, Immunohematology & Transfusion Medicine Department, A.O. S. Camillo Forlanini, Rome ITA
"Treatment of chondral lesions of the knee with bone marrow cells and PRP seeded into a hyaluronic acid scaffold. Clinical experience of A.O S. Camillo Forlanini"

TENDINOPATHY

Dr. Jean-Marc Grison, Sports Medicine, Iris Sud Hospital, Bruxelles, BEL
"Study of reathletisation of sportsmen affected by tendinopathy after a treatment with PRP"

Dr. Jacques Le Coz, Sports Doctor & Mesotherapy Practitioner, Paris, FRA
"22 Elbow tendinitis treated with platelet-rich plasma after failure with the usual treatment"

Prof. Antonio Pavan, Full Professor in Clinical Pathology, Transfusion Center Sant'Andrea Hospital University of Rome La Sapienza, Rome, ITA
"Is local injections of PRP in tendinopathy able to effect systemic growth factor concentration?"

Prof. Philippe Peetrons, Iris Sud Hospital, Bruxelles, BEL – Dr. Jean-Marc Grison, Sport Medicine, Iris Sud Hospital, Bruxelles, BEL
"Treatment of tendinopathies using PRP under ultrasonic guidance"

SPORTS MEDICINE

SPORTS MEDICINE
LIGAMENTS

Session: PRP, THE FOUNDATION OF CELL THERAPY – 22nd September 2014

Presentation: **A comparison of the use of PRP and hypertonic glucose injections for the treatment of sacroiliac joint incompetence: a pilot study**

Lecturer: Dr. Jen Saunders, Sports & Exercise Medicine, Australia, AUS

INTRODUCTION

The Sacroiliac joint can become injured through trauma. This most often occurs through falls onto the buttocks, or repetitive micro-trauma. Incompetence can arise form muscle or ligament issues.

Current best practice indicates that sacroiliac joint incompetence can be assisted with highly specialized physiotherapy which cures the problem in 80% of cases. The remaining cases can be successfully treated with prolotherapy (3-6 injections hypertonic glucose injections to the intra-osseous ligament under radiological guidance).

Ultrasound guided Sacroiliac joint (SIJ) injection can be performed also with PRP.

We report our experience using Regen BCT PRP tubes in the treatment of SIJ incompetence. Published data on prolotherapy were used for comparison.

METHODS

A pilot study was undertaken to compare the efficacy of Regen PRP injections vs standard prolotherapy. An initial group of 10 patients was studied.

Prolotherapy data used for comparison where taken from Cusi M, Saunders J, Hungerford B, Wisbey-Roth T, Lucas P, Wilson P. The use of prolotherapy in the sacro-iliac joint. BJSM. 2008.

CLINICAL FINDINGS

Outcome measures were standard pain and function scores.

In figures 1, 2, 3, 4 and 5 below, the results (before-after) with PRP, and for comparison those with prolotherapy (BJSM), are shown.

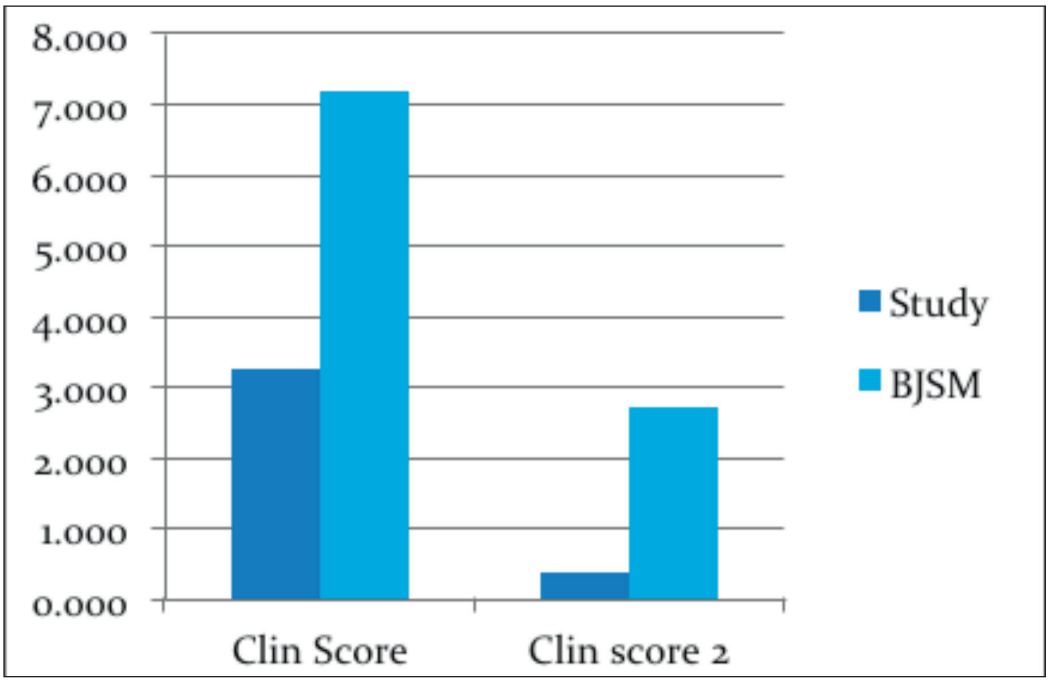


Figure 1: Results Clinical Scores (before-after)

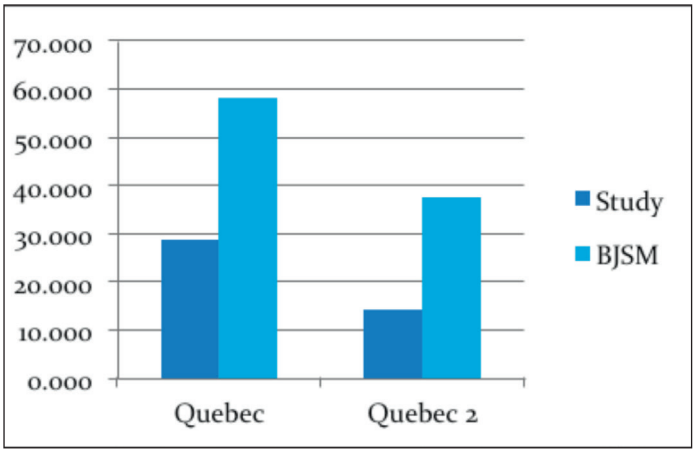


Figure 2: Results Quebec back Pain Inventory (before-after)

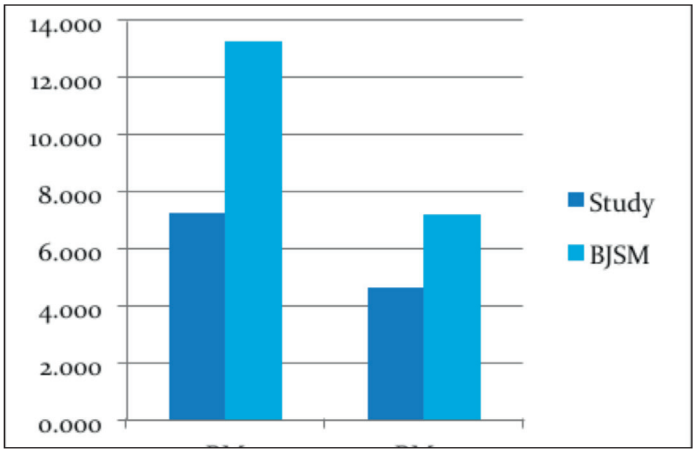


Figure 3: Results Roland Morris Inventory (before-after)

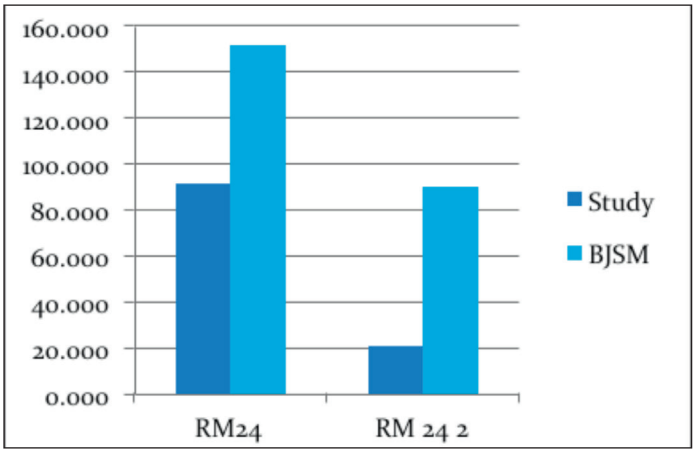


Figure 4: Results RM24 (before-after)

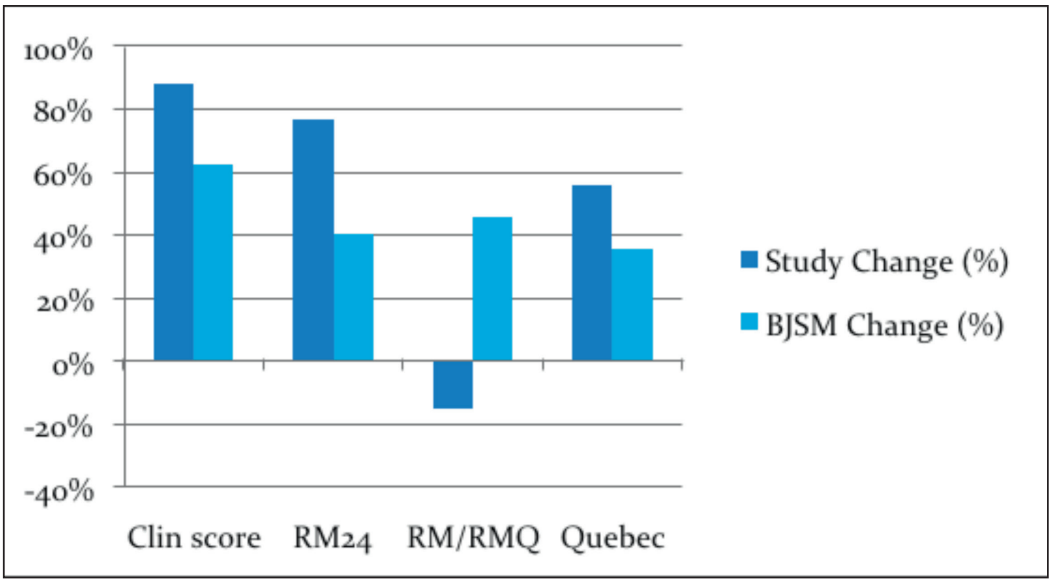


Figure 5: Summary Results (% change)

CONCLUSION

The outcome measures of change in pain scores and improvement in function between the groups were similar with both treatments, with a trend in favour of PRP.

The number of injections required was less for the PRP study group than the prolotherapy controls.

PRP is a valid treatment in SIJ incompetence.

SPORTS MEDICINE

SPORTS MEDICINE
MUSCULOSKELETAL LESIONS

BIOBRIDGE FOUNDATION

regenlab

Session: ORTHOPAEDICS AND CARDIAC SURGERY – 23rd September 2013

Presentation: **Biologic characteristics and therapeutic effectiveness of autologous PRP infiltrations in joints orthopaedic pathologies of the knee**

Lecturer: Dr. Alessandro De Rosa, Immunohematology & Transfusion Medicine Department, A.O. S. Camillo Forlanini, Rome, ITA

INTRODUCTION

Platelet concentrate for non-transfusion use, or platelet-rich plasma (PRP) is an autologous or allogenic blood derived component constituted by concentrated platelets resuspended in the plasma and is especially used when a reparative process is required.

The rational underlying its use is due to the capacity of active platelets to release growth factors or cytokines or to express membrane molecules which are able to accelerate repair and stimulate tissue regeneration through different mechanisms of action.

The department of Immunohematology & Transfusion Medicine (SIMT) of San Camillo Forlanini Hospital in Rome prepares this autologous blood derived product (and its derivates) with two different procedures according to the therapy required and the patient's condition: a multiple bag of 100 ml and a certified medical device from RegenLab.

The most common clinical target in our Hospital is the use of autologous PRP in patients affected by orthopaedics pathologies such as osteoarthritis (OA), meniscus lesions, tendinopathy, muscular and chondral lesions.

Since PRP treatment is able to activate and accelerate repair processes of connective tissue, the objectives of this therapy are: attenuation or elimination of pain, reduction of inflammation, recovery of joint function and reduction/eradication of toxic or aggressive alternative therapies.

METHODS

The therapeutic protocol studied consists of 3 infiltrations of PRP (without activation) into the joint or tissue (tendinous or muscular), given 7-15 days apart.

The volume of PRP injected is standardized but depends on the site to be treated:
- Hip or knee joint (5 ml)
- Shoulder joint (3 ml)
- Tendons, fasciae, muscles (3-5 ml).

At our SIMT facility the clinical evaluation is based on a patient questionnaire (VAS pain scale and Lequesne algo-functional index of the knee if necessary) compiled at the beginning and at the end of the treatment in order to evaluate pain reduction, functional recovery and execution of daily activities.

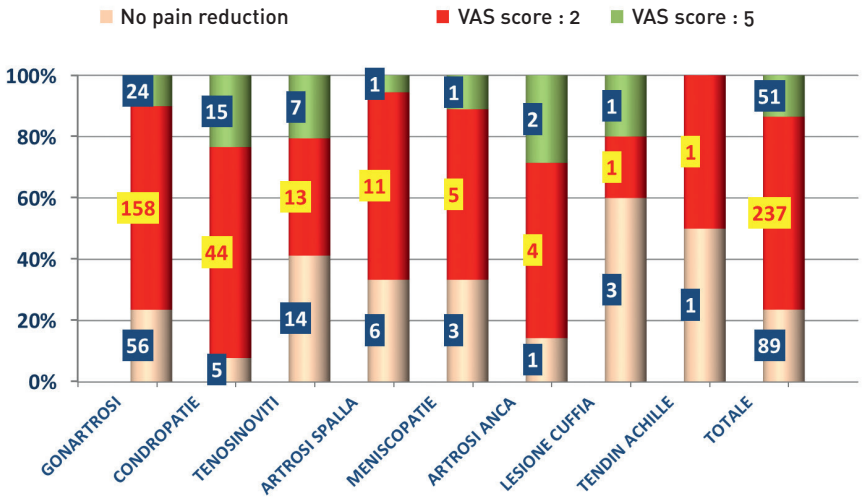
CLINICAL RESULTS

From March 2011 to May 2013, 377 cases were treated, in particular: 238 knee OA, 64 chondropathies, 34 tenosynovites, 18 shoulder OA, 9 meniscus lesions, 7 hip OA, 5 rotator cuff lesions and 2 Achilles tendinitis.

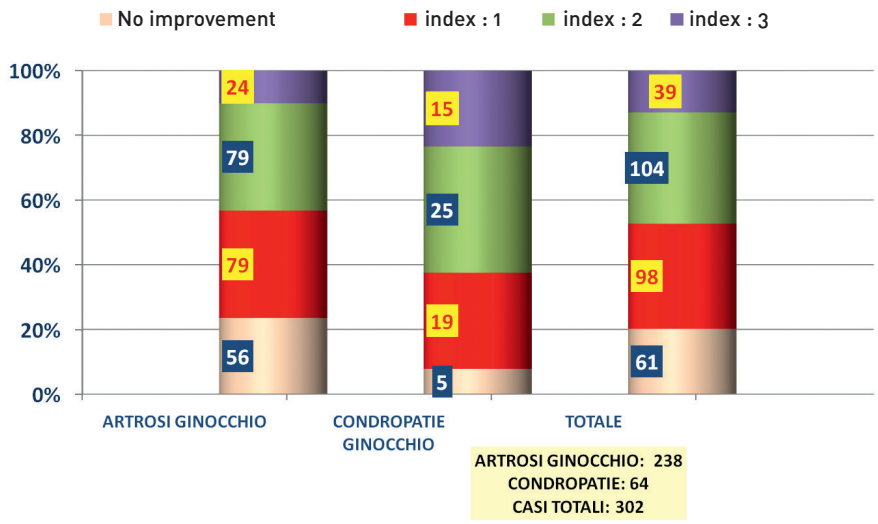
The study population comprised 173 men, of mean age 58.4 (range 15 – 90) and 204 women of mean age 63.9 (range 31 – 87).

1. RESPONSE TO PRP TREATMENT: pain reduction

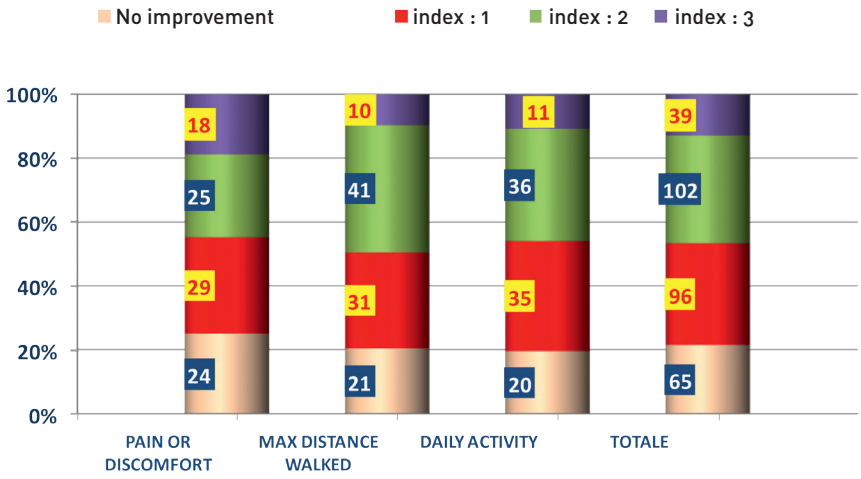
VAS (visual-analogue pain scale)



2. RESPONSE TO PRP TREATMENT: / Lequesne index for knee OA



3. RESPONSE TO PRP TREATMENT: OA and chondropathies of the knee / Lequesne index stratified per sections



CONCLUSION

Autologous PRP treatment was demonstrated to have an effective analgesic action and to provide symptomatic and functional improvements in 80% of cases. The treatment is safe, of limited cost, easy to use and is optimally accepted by patients who, in most cases, reduced or abandoned consumption of oral medication.

Session: PRP, THE FOUNDATION OF CELL THERAPY – 22nd September 2014

Presentation: **Use of Regen fibrin polymer device for the production of PRP in the PO San Giovanni di Dio in Florence**

Lecturer: Dr. Giuseppe Di Pietro, Director of Transfusional Medicine Department ASL 10, San Giovanni di Dio, Florence, ITA

INTRODUCTION

PRP is being increasingly used in modern medicine as a material stimulating regeneration and accelerating tissue healing. Proposed clinical and surgical applications include chondropathy, knee arthropathy, tendinopathy, acute and chronic soft-tissue injuries, enhancement of healing after ligament reconstruction and muscle strains.

PATIENTS AND METHODS

A protocol for the treatment of arthropathy and tendinopathy, radiologically documented and not responsive to other treatments, was established. A total of 123 Patients were evaluated over an observation period of 18 months, from January 2013 to June 2014.

On the basis of the most recent evidence of the literature indicating a probable anti-inflammatory effect of PRP, we also treated 4 patients with inflammatory rather than degenerative arthropathy.

The autologous PRP was produced with the Regen Lab system which yielded 3 mL of PRP following centrifugation of 20 mL of whole blood at 1.500 rpm for 15 minutes (the centrifugation time was empirically increased from 9 to 15 minutes to increase the platelet yield).
The patients were subjected to 3 intra-articular or peritendinous infiltrations, given at monthly intervals. In cases where only a partial improvement of pain and joint range of motion was achieved, patients were subjected to a second cycle of infiltration. For some patients with arthropathy of the knee, infiltrations were performed bilaterally.

RESULTS

Among the 123 patients evaluated, 18 were unsuitable; mainly because of low platelet count or previous malignancies. In the 105 eligible patients, the platelet count in PRP ranged between 0.8 and 2.0 x106/µL.

A total of 451 infiltrations were carried out as detailed in the following table:

	infiltration n°	treated patients n°	second cycle of treatment patients n°
knee	351	82 (9 ongoing treatments)	16
shoulder	55	13	2
elbow	24	6	2
tendinitis of the Achilles tendon	12	3	1
ankle	6	1	-
trochanteric bursitis	3	1	-
total	451	105 (1 patient treated at the elbow and shoulder)	21

The results obtained are in line with findings in the literature: patients treated showed pain reduction and improvement in range of motion. In most patients the therapeutic response was achieved after a single treatment cycle and encouraging results have also been observed in the limited number of patients with inflammatory disease.
There were no adverse effects that required suspension of the treatment.

CONCLUSIONS

Our results confirm that PRP is a valid therapeutic approach, with good compliance by patients, which leads to an improvement in quality of life due to the reduction of pain and improvement in motility. In young patients, these results allowed us to re-evaluate the need of immediate surgical treatment.

BIOBRIDGE FOUNDATION

regenlab

Session: SPORTS MEDICINE & INFILTRATIONS & MUSCULOSKELETAL MEDICINE – 23rd September 2013

Presentation: **Optimizing PRP treatment and recovery of injured sportsmen – a five-year medical experience**

Lecturer: Dr. Patrick Goh, Specialist Sports Physician, Sports Medicine International, Camden Medical Centre, Singapore, SIN

INTRODUCTION

This paper reviews retrospective clinical data from patients treated with PRP over a 5-year period in a Sports Medicine Practice. There is a strong rationale for the use of PRP in sports injuries, as the biomechanical factors involved give rise to tissue damage, which can result in inflammation and pain, all of which can be addressed with PRP.

In our Practice, PRP is used in the non-surgical treatment of tendons (Tennis Elbow, Achilles' Tendinitis, Plantar Fasciitis, Patellar Tendon, Rotator Cuff), Muscle (Calf, Hamstring Tear), Ligaments (Knee MCL, Ankle ATFL) and other joints (cartilage injuries).

Over the past several years, the objective has been the optimization of PRP treatment to achieve maximum effectiveness and minimum downtime in sports injuries. To achieve this, we focused on identifying the most suitable indications, evaluating different types of PRP, optimizing the technique of PRP administration and defining the best post-PRP protocol including immediate care, adjunct care and rehab / exercise. Post-injection pain was initially an issue, lasting for between 1-6 weeks, and this was found to be related to a number of factors, including the site of injection. Post-injection pain was successfully addressed by switching to RBC/WBC-poor PRP, using a peppering technique for injection instead of bolus, the use of Lidocaine and, in the post-PRP protocol, by giving strict instructions to rest, apply ice and elevate and by ensuring early mobilization (especially in the shoulder).

METHODS

A retrospective analysis of the results of PRP treatment of both injured tendons and chondromalacia patellae was conducted based on patient case records.

In the tendon cohort, pain reduction following PRP was evaluated in 101 patients and post-PRP injection soreness was evaluated in 50 patients. The patients suffered from injuries obtained while practicing various sports, but mainly running, soccer and racket sports. A total of 45 patients were included in the chondromalacia patellae cohort.

CLINICAL FINDINGS

Figure 1 shows the number of patients exhibiting a greater than 50% reduction in pain at various time points following PRP injection: 67% of patients achieve pain reduction → 50% within 4 weeks and 88% of patients within 8 weeks.

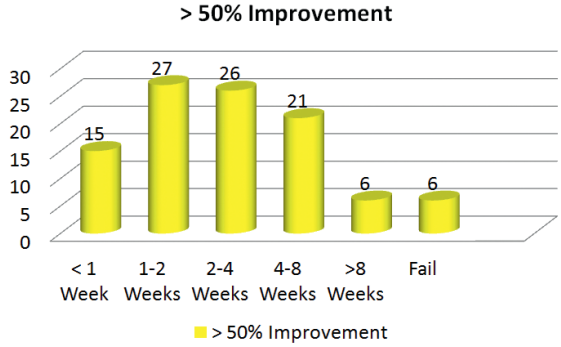


Figure 1: Tendon - Pain Reduction post-PRP

With respect to post-injection pain, of the 50 patients evaluated for this parameter, 78% experienced soreness for 0-3 days and 88% experienced soreness for less than 1 week.

Of the 45 patients suffering from chondromalacia patellae treated with a single PRP injection, 86% had a greater than 50% reduction in pain by 1 month post-injection and 87.5% fully resumed sport activities.

CONCLUSION

Injection of PRP is a promising treatment option for sports injuries. This study showed a significant analgesic effect, even though the patients were received only a single PRP injection.

BIOBRIDGE FOUNDATION

regenlab

Session: PRP, THE FOUNDATION OF CELL THERAPY – 22nd September 2014

Presentation: **Autologous PRP in the treatment of inflammatory tendinopathy & degenerative joint disease, the experience of Santo Spirito Hospital in Rome**

Lecturer: Dr. Maria ALBA Stigliano, Director of Immunology & Transfusion Medicine Department, ASL Roma & Santo Spirito Hospital, Rome, ITA

INTRODUCTION

Platelet growth factors stored in platelet-granules are released though a degranulation process and bind to specific receptors promoting cellular proliferation in fibroblasts, endothelial cells and osteoblasts. The therapeutic use of platelet-rich plasma (PRP) leads to a progressive release of growth factors and induces acceleration in re-ossification and in the reparative processes of ulcers and surgical injuries, improvement in hemostasis and the healing process, pain reduction and reduction in post-operative complications, including infections.

The aim of this study was to evaluate the therapeutic action of PRP in patients affected by degenerative joint diseases, chondropathies and tendinopathies, who were not responsive to previous conventional treatments.

METHODS

From May 2011 to May 2014, we treated 150 patients (64 men and 86 women; mean age 62, range 39 - 89), suffering from joint diseases, chondropathies, tendinopathies, and not responsive to pharmacological and physiotherapeutic treatments; moreover, some patients were potential candidates for the substitution of the joint with a prosthesis.

All patients underwent preliminary orthopaedic examination and radiological exams, pain was evaluated using a VAS scale and joint functionality was evaluated as well.

Patients eligibility criteria included: platelet count → 120000 plt/µl, no assumption of antiplatelet or anticoagulant drugs at least 5 days prior to treatment and absence of infectious diseases, gout, tumors, hepatitis B/C or HIV.

Autologous PRP was obtained with RegenBCT tubes: 8 ml of the patient's own blood were collected in the tube and centrifuged for 5 minutes at 3500 rpm.

Patients with joint diseases underwent 2 to 4 intra-articular infiltrations, each with 4-5 ml of autologous PRP.
For the treatment of tendinopathies, the PRP volume was reduced: 2 ml of platelet-poor plasma (PPP) were removed in order to obtain a higher platelet concentration in the PRP.
PRP infiltrations were given one week apart.

During each visit, patients underwent orthopaedic examination to evaluate the trend of symptomatic pain and eventually improvement in joint functionality.
Patients were followed-up at 3, 6 and 12 months from the end of the therapy.

CLINICAL RESULTS

A quality control performed on the PRP preparations showed a platelet concentration 1.38-1.59 fold higher than patients' natural blood, 30% leukocyte content with respect to baseline and the absence of residual red blood cells.

Treated pathologies are listed below:

Pathology	N° of cases
Rotators cuff lesions	35
Knee OA	69
Osteochondritis	14
Tenosynovitis	13
Other: tibial-tarsal OA 4, shoulder OA 4, glenohumeral OA 4, osteitis pubis 1, hip OA 1, patella fracture 1, epycondilitis 4	19

Following the first PRP infiltration, 78% of patients reported a reduction of pain and an improvement in joint functionality. Inflammatory alterations of tendinous segments rapidly healed with complete recovery of functionality after the second infiltration.

Of the treated patients, 65 % showed recovery in joint mobility of greater than 70% and 75% of patients maintained the beneficial analgesic effect and joint functionality improvement during the entire follow-up period.

Radiological and medical ultrasonography controls evaluated at 6 months from the end of treatment, demonstrated improvement in inflammation, whereas no change in joint degeneration was evident.

No complications or side effects were reported.

CONCLUSION

This study demonstrated the effectiveness of PRP as a treatment for shoulder and knee degenerative joint diseases and for inflammatory tendinopathies, with significant improvement in joint functionality and reduction of pain.

Session: PRP, THE FOUNDATION OF CELL THERAPY – 22nd September 2014

Presentation: **Using of PRP-therapy for athletes with extra-articular pain localization**

Lecturer: Dr. Maksim Strakhov, Orthopaedic Surgeon, Moscow, RUS

INTRODUCTION

Tissue repair in musculoskeletal lesions is often a slow and sometimes incomplete process. In sports patients or professional athletes, the impact of musculoskeletal lesions on life and work is great, and the fast recovery of full efficiency and return to competition is of primary importance. The clinical improvement offered by available treatments is not always sufficient for highly demanding patients to return to their previous level of activity. The search for a minimally invasive solution to improve the status of the chondral surface of the injured joint (but also injuries that affect ligaments and muscles) is therefore highly desirable, especially in these patients.

Platelet-rich plasma (PRP) is a procedure that provides a natural concentrate of autologous growth factors. The attractive possibility to use the patients' own growth factors to enhance the reparative process in tissues with low healing potential, the promising preliminary clinical findings and the safety of these methods, explain the wide application of this biological approach.

METHODS

In this observational study, we evaluated the effectiveness of PRP infiltration therapy in 12 athletes (4 women and 8 men) aged between 14 - 57 years (avg. 27.5 years).

Nosological forms	Number of patients
Impingement syndrome of the shoulder joint. Tenosynovitis rotator cuff.	4
Tennis elbow	2
Plantar fasciitis	1
ARS syndrome. Chronic tenosynovitis of the rectus abdominis	1
Osteoarthritis of the left knee and right ankle	1
Fused fracture of the talus. Osteoarthritis 1-2 tbsp of the right ankle, subtalar joints.	1
Hamstring syndrome	2
Total	12

Evaluation of the clinical results was conducted at 4 observation points: prior to initiating therapy, after 1 injection, after 3 injections and after 6 months. Generally the therapeutic protocol consisted in 3 sessions of RegenPRP infiltrations at a distance of of 1 week.

CONCLUSION

In the described study we observed:

- Significant analgesic effect immediately after the first procedures of administration that increased in a progressive manner until the third administration.

- Improvement in functional status of joints and a 13-fold decrease in the total WOMAC index observed after 3 weeks of treatment (visit 3) and maintained for 6 months.

- Improvement of the end of the observation period after 6 months was observed in 91.6% (11 patients) and no effect-in 1 patient.

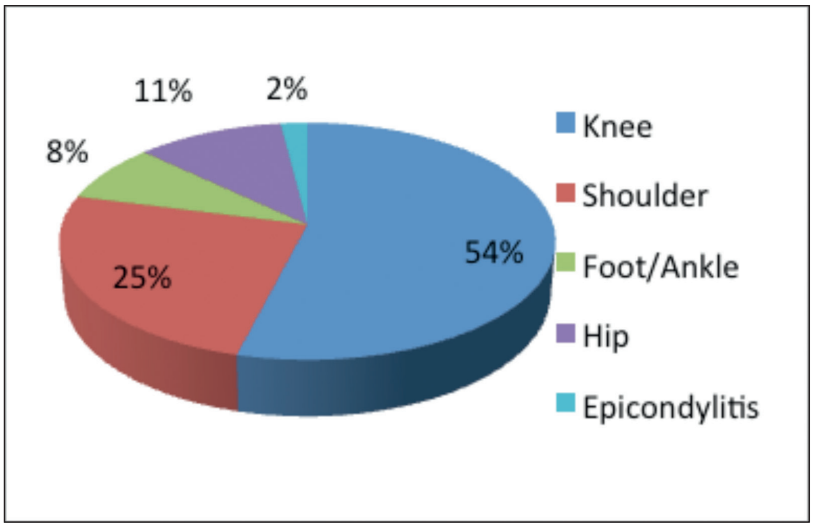
Session: PRP, THE FOUNDATION OF CELL THERAPY – 22nd September 2014

Presentation: **Clinical efficacy of platelet-rich plasma to treat chronic articular pathologies**

Lecturer: Dr. Maria Cristina Tirindelli, Responsible of the Transfusion Center, Campus Biomedico University of Rome, Rome, ITA – Dr. Gianluca Vadalà, Orthopaedic Surgeon, Department of Orthopaedic and Trauma Surgery, Campus Biomedico University of Rome, Rome, ITA

INTRODUCTION

Since 2011 at the Campus Biomedico Hospital (Rome), 800 orthopaedic patients have been treated with RegenKit PRP (10 plantar fascia, 11 epicondylitis, 15 Achilles' tendons, 81 hip, 40 ankle, 201 shoulder, 433 knee). This large case series allowed the carrying out of correlation analysis with several factors.



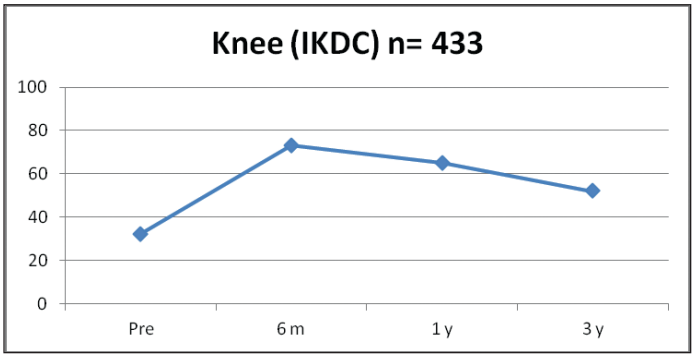
METHODS

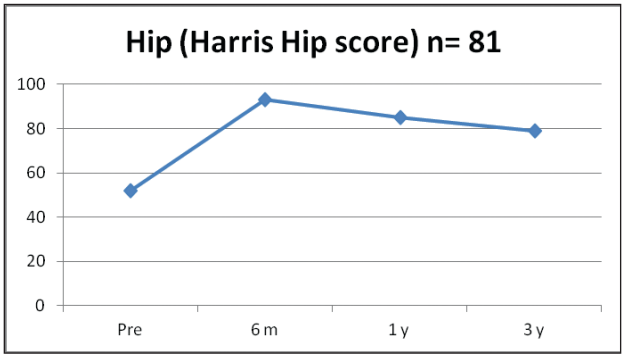
In all clinical cases, 4 ml of autologous PRP was obtained using RegenLab THT tube, in accordance with the manufacturer's protocol.

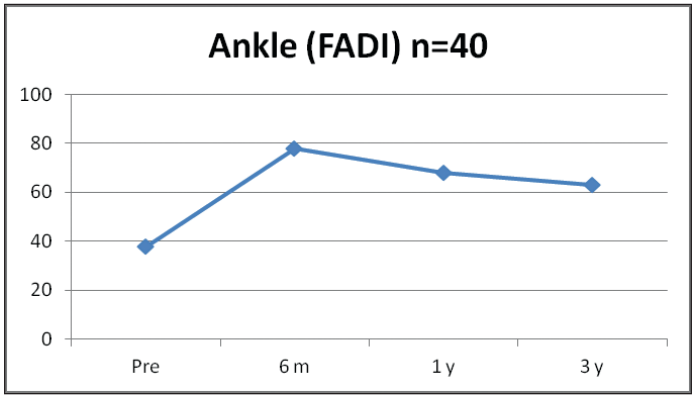
CLINICAL FINDINGS

1- Clinical results in the treatment of CHONDROPATHIES

To evaluate the benefits of PRP in osteoarthritis, specific clinical scores were used for each joint: IKDC for the knee, FADI for the ankle and HHS for the hip. In all treated sites, a trend of improvement compared to the pre-treatment period was observed, with p-values still significant compared to baseline at the final available follow-up at 3 years.



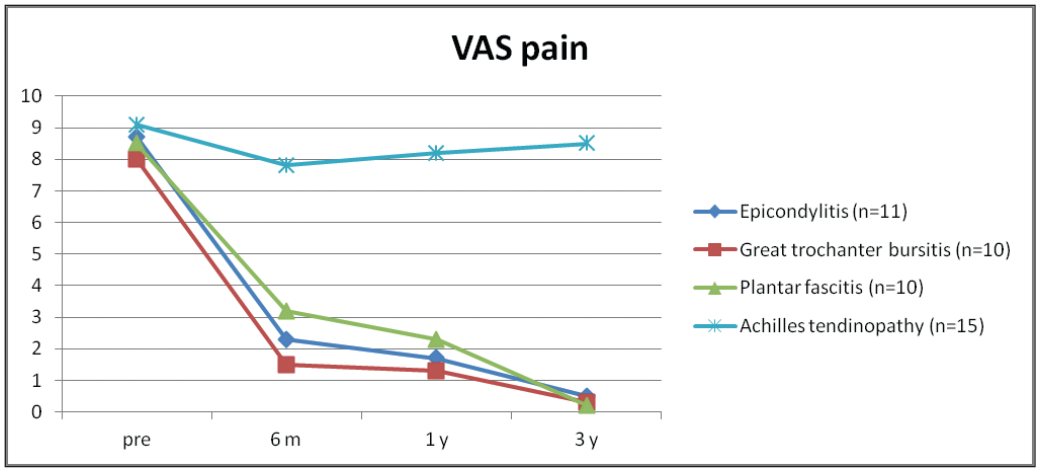




2- Clinical results in the treatment of TENDINOPATHIES

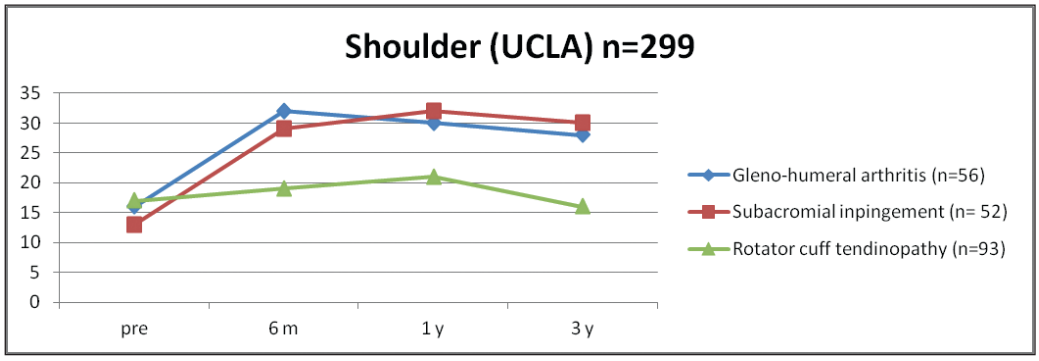
To evaluate the benefits of PRP in tendinopathy, a VAS scale was used. Often, in fact in the absence of the tendon rupture, pain is associated with the functional deficit. Clinical results, which are in agreement with the literature, suggested that PRP is not particularly effective in the treatment of Achilles tendinopathy, while it is a good treatment in other tendon pathologies.
This could be related to the fact that epicondylitis, trocanteritis and fasciteplantare are predominantly insertional tendinopathies, while Achilles tendinopathy has two component: insertional and especially non-insertional.

Therefore, it would seem that PRP is more effective in insertional tendinopathy than in non-insertional tendinopathy. Obviously these empirical data will be verified with further studies comprising histological evaluations.



3- Clinical results in the treatment of SHOULDER

As is shown in the following chart, depending on the shoulder disease treated, the results of treatment varied. In the case of concentric osteoarthritis without defects in the rotator cuff, results were excellent; on the contrary, in diseases involving a tendonitis of the rotator cuff, PRP does not give satisfactory results. Hence, the importance of a correct diagnosis is clear, especially in shoulder pathology.

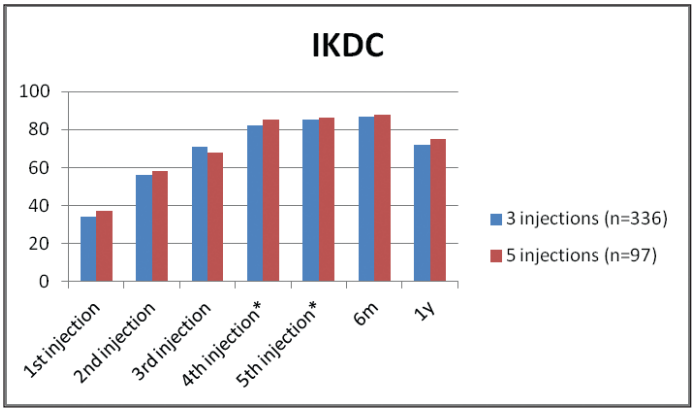


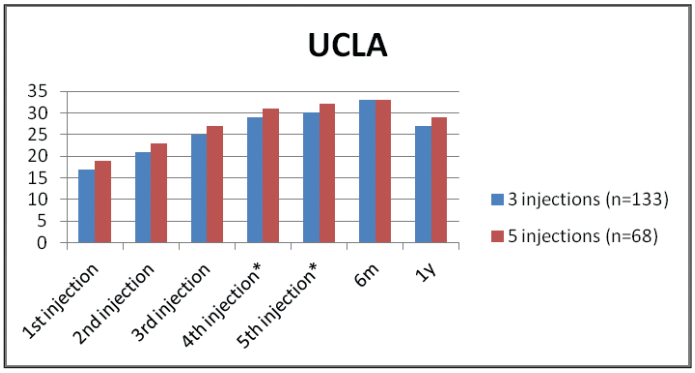
4- Correlation analysis between PRP and various factors

In this correlation analysis, only shoulder and knee pathologies were evaluated as larger samples were available.

• NUMBER of INFILTRATIONS

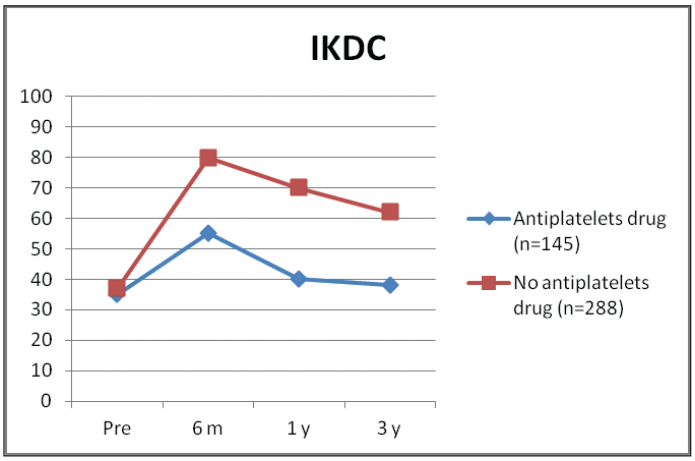
No difference in the effectiveness of PRP were observed between patients who received 3 infiltration compared to those who received more than 3, and up to 5 infiltrations.

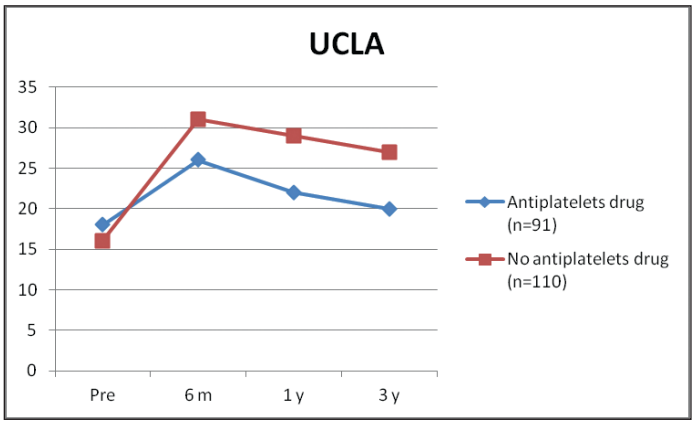




• Concomitant treatment with antiplatelet drugs.

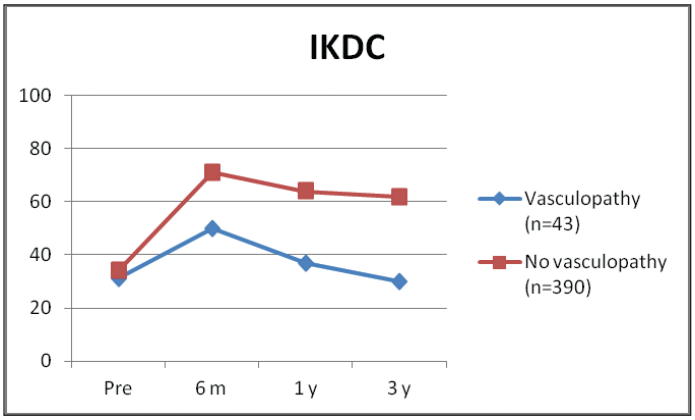
Clinical results suggest that it is best to interrupt treatment with anti-aggregating drugs during the PRP treatment period, with a possible replacement with heparin, in order to ensure better results.

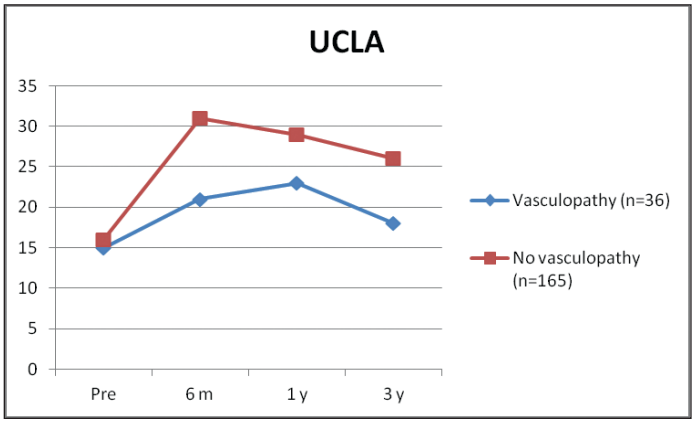




• Use of NSAIDs

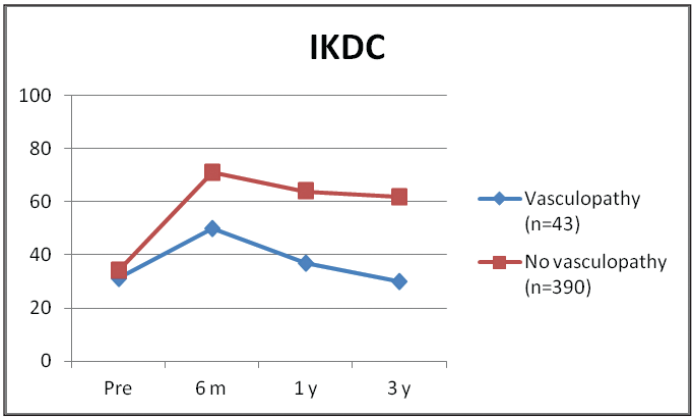
Also in this case it was observed that the use of NSAIDs worsened patient outcomes. This was known from the literature and all patients who were treated with PRP were warned not to take NSAIDs. However, some patients still reported to have taken NSAIDs, because they found that paracetamol was ineffective in controlling their pain or patients had intolerance to the latter treatment.

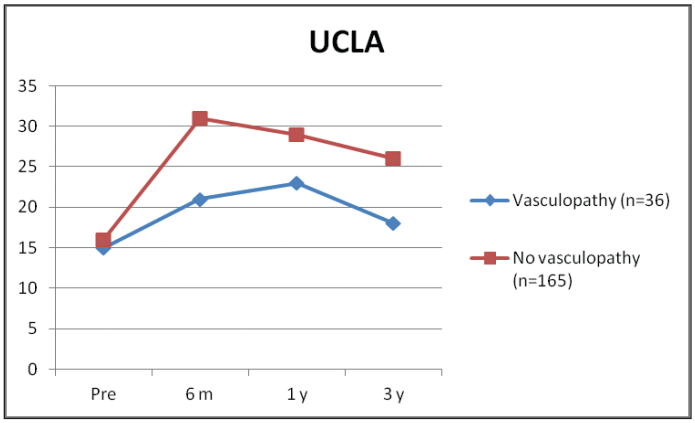




• COMORBIDITIES – VASCULAR DISORDERS

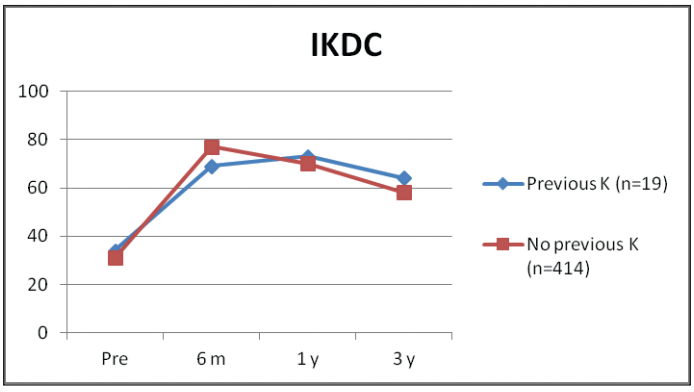
Regarding comorbidities, patients were evaluated for venous insufficiency of the lower limbs. When patients having edematous limbs were treated with PRP, it was found that the effectiveness in these patients was inferior.





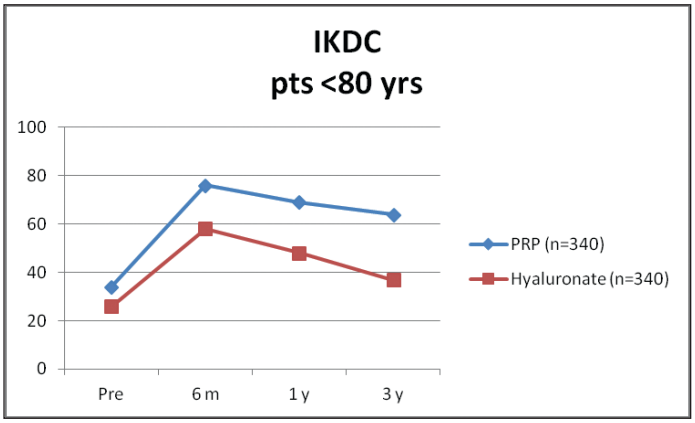
• COMORBIDITIES – TUMORS

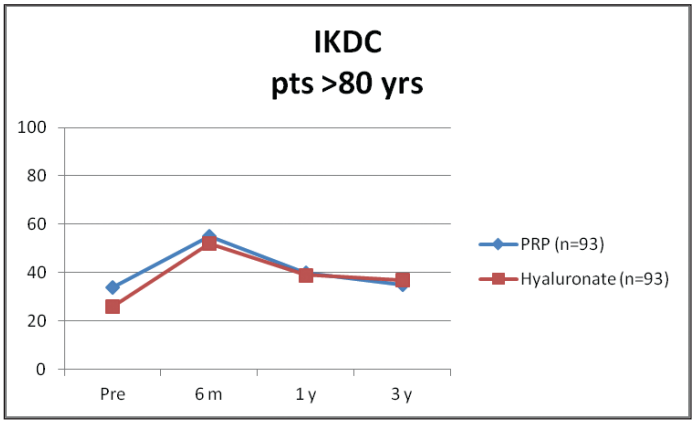
This data is very interesting. In fact, until recently, a tumor was considered an absolute contraindication for PRP treatment. In recent years, however, investigators began to treat patients with previous tumors, who had not received chemotherapy or radiotherapy with negative oncologic follow-up. It was observed that actually there are no differences compared to patients without prior tumor. The sample, however, was very small because it has always been considered an absolute contraindication.

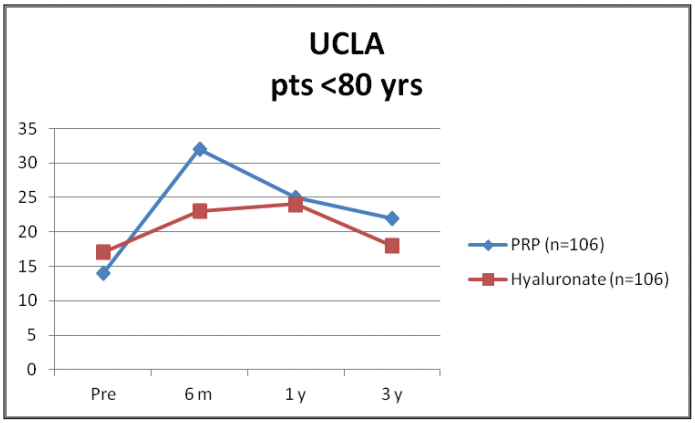


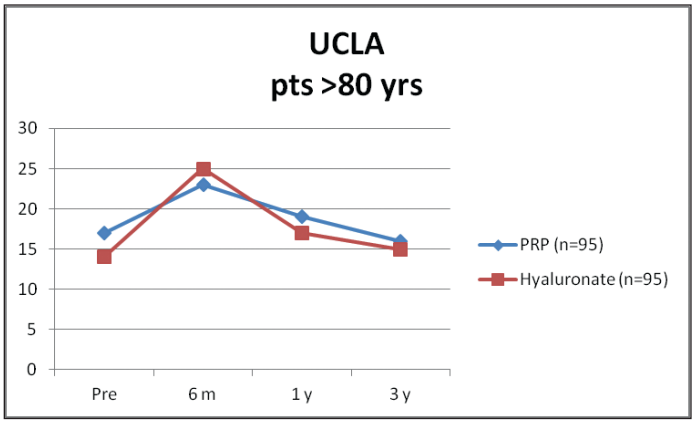
• ELDERLY PATIENTS

To facilitate this analysis, investigators also included a control group: patients undergoing weekly hyaluronic acid (HA) infiltration (3 sessions). Both in the shoulder and in the knee, in patients less than 80 years old, PRP showed greater efficacy than HA, while the difference was not significant in patients over 80 years old.









CONCLUSION

PRP injection in chondropathy of the knee, hip, ankle and shoulder significantly improved the clinical outcomes over time. PRP is effective in insertion tendinopathies such as plantar fasciitis, epicondylitis and greater trochanter bursitis, while the improvement is not significant in Achilles and rotator cuff tendinopathies.

With respect to correlation analysis between PRP and various factors:

- 3 PRP Injections are enough to obtain significant improvements
- Patients taking Aspirin and NSAIDs are poorer responders to PRP injection for chondropathy
- Patients affected by vascular disorders are poorer responders to PRP injection for chondropathy
- Patients with oncological diseases respond to PRP treatment for chondropathy
- Elderly patients (above 80 y) are poorer responders to PRP injection for chondropathy.

SPORTS MEDICINE

OSTEOARTHRITIS & CARTILAGE

-

PRP

BIOBRIDGE FOUNDATION

regenlab

Session: SPORTS MEDICINE & INFILTRATIONS & MUSCULOSKELETAL MEDICINE – 23rd September 2013

Presentation: **Use of platelet-rich plasma (PRP) in articular and tendon pathology at the Annunziata Hospital of Cosenza**

Lecturer: Dr. Hesham Almolla, Annunziata Hospital of Cosenza, ITA – Dr. Marcello Napolitano, Annunziata Hospital of Cosenza, ITA – Dr. Antonio Crescibene U.O.C. Orthopaedics and Traumatology P.O. San Francesco – Paola, Cosenza, ITA

INTRODUCTION

The refinement of the use of platelet-derived growth factors that has occurred over the last decade has led to a broadening of the fields of use, in particular for new treatments in Orthopaedics aimed at improving tissue regeneration. Arthritis is one of the most common chronic diseases in humans and the most frequent cause of disability. It has been calculated that at least 4.000.000 subjects in Italy suffer from symptoms of arthritis, for a total cost of about 6.5 billion Euro; this cost is destined to increase given the ageing of the Italian population.

This document provides a summary of the experience at Cosenza Hospital in the evaluation of the therapeutic potential of activated PRP infiltration in degenerative joint disease.

METHODS

Twenty-seven patients, aged between 18 and 81 years, with a diagnosis of degenerative joint disease lasting for more than 1 year, were treated. The patients were divided into two groups, one with arthritis of the knee, the other with degenerative cartilage disease of the knee. Both groups were treated with a therapeutic protocol consisting of a cycle of three infiltrations of platelet-rich plasma at weekly intervals.

The extemporaneous preparation was made from a sample of about 8 mL of venous whole blood collected into a specific Fibrin Polymer 2 test-tube from RegenLab® and centrifuged before addition of calcium gluconate.

During the initial pre-treatment evaluation, specific questionnaires were administered, the Numerical Rating Scale (NRS) for subjective measurement of pain, and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC); these assessments were repeated 7 days after the end of the cycle of treatment and at 6 months during the follow-up.

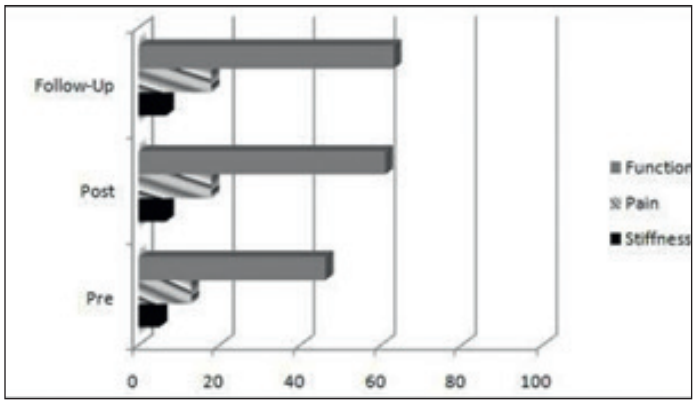
Group 1 was composed of 13 arthritic patients (seven patients had grade 1 disease, four had grade 2 and two had grade 3 disease, according to Kellgren and Lawrence classification). The mean age of patients was 64±11 years; there were seven men and six women. Six patients had bilateral disease so they received the treatment in both joints; in total, nine left-sided joints and ten right-sided joints were treated. The mean body mass index (BMI) of the patients in this group was 29.2 ± 5.9 (range, 23-43).

Group 2 was composed of 14 patients (first or second degree lesion, according to Outerbridge). The mean age of the patients was 26.2±2.0 years; all 14 patients in this group were male; in total, nine right-sided joints and six left sided joints were treated since one patient had bilateral disease. The mean BMI of the patients in this group was 26.2±2.0 (range, 23-29).

CLINICAL FINDINGS

CARTILAGE DISEASE

Cartilage disease			
WOMAC score	**Stiffness**	**Pain**	**Function**
Pre-treatment	5.1±2.2	13.0±4.8	46.2±13.1
Post-treatment	6.8±1.0	18±2.5	61.0±4.7
Follow-up	6.8±1.3	18±2.8	63.1±4.3
NRS score			
Pre-treatment	6.8±1.7		
Post-treatment	2.3±2.1		



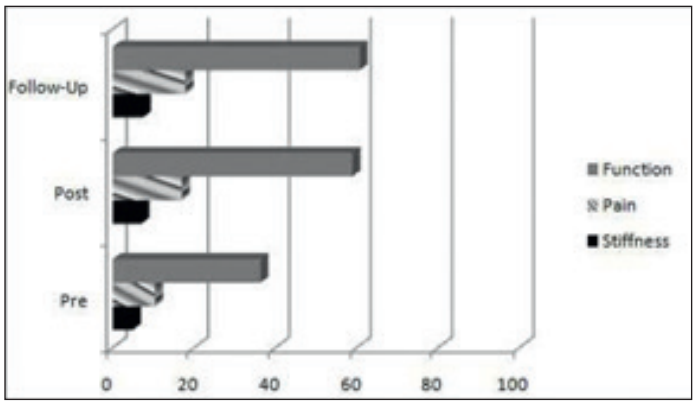
In the group of patients with cartilage disease, the mean NRS score changed from a pre-treatment value of 6.8 ± 1.7 to 2.3 ± 2.1 post-treatment. Improvements in the mean WOMAC score, divided into its three components, were as follows:

- pain, pre-treatment 13.0 ± 4.8, post-treatment 18 ± 2.5 and, for 6 patients, at the 6-month follow-up 18 ± 2.8;
- joint stiffness, pretreatment 5.1 ± 2.2, post-treatment 6.8 ± 1.0 and at the 6-month follow-up 6.8 ± 1.3;
- function, pretreatment 46.2 ± 13.1, post-treatment 61.0 ± 4.7 and at the 6-month follow-up 63.1 ± 4.3.

None of the patients had any adverse effects or allergic reactions.

ARTHRITIS

Arthritis			
WOMAC score	**Stiffness**	**Pain**	**Function**
Pre-treatment	4.9±2.2	10.4±3.9	36.3±11.8
Post-treatment	7±0.9	17±2.5	58.9±9.9
Follow-up	7.4±0.9	17.9±2.8	60.7±7.6
NRS score			
Pre-treatment	8.1±1.7		
Post-treatment	3.4±2.5		



The group of patients with knee arthritis obtained a clear improvement in the NRS score from a mean pretreatment value of 8.1 ± 1.7 to 3.4 ± 2.5 post-treatment. Improvements in the mean WOMAC score, divided into its three components, were as follows:

- pain, pre-treatment 10.4 ± 3.9, post-treatment 17 ± 2.5 and, for 7 patients, at the 6-month follow-up 17.9 ± 2.8;
- joint stiffness, pre-treatment 4.9 ± 2.2, post-treatment 7 ± 0.9 and at the 6-month follow-up 7.4 ± 0.9;
- function, pre-treatment 36.3 ± 11.8, post-treatment 58.9 ± 9.9 and at the 6-month follow-up 60.7 ± 7.6 (Figure 1).

None of the patients had any adverse effects or allergic reactions.

CONCLUSION

In both groups the use of PRP accelerated and improved the healing process, which could be evaluated in terms of:

- Measurable efficacy, intended as an improvement of the psycho-physical state of the patient and his or her quality of life, related to a clear improvement in the range of joint movements and reduction of pain;
- cost-effectiveness and ease of use of the preparation in an out-patient setting;
- lack of side effects.

BIOBRIDGE FOUNDATION

regenlab

Session: ORTHOPAEDICS AND CARDIAC SURGERY – 23rd September 2013

Presentation: **Clinical study: treatment of symptomatic coxarthrosis with platelet-rich plasma**

Lecturer: Dr. Caterina Martini, Orthopaedics Clinic, CTO, AOU Careggi, University of Florence, ITA
Dr. Roberto Civinini, Orthopaedics & Traumatology, SOD General Complex Orthopaedics, AOU Careggi, Florence, ITA

INTRODUCTION

Coxarthrosis, or hip osteoarthritis (OA), is a chronic-degenerative disease which affects the cartilage of the hip due to the wearing of joints, and which progressively impairs regular walking. Two forms of coxarthrosis have been described: primary OA which is principally linked to old age, and secondary OA which is due to congenital joint deformity such as hip dysplasia or to trauma, infection, rheumatic diseases or to aseptic necrosis of the femoral head.

In coxarthrosis, the cartilage layer covering the femoral head and the acetabular cavity becomes progressively thinner until exposure of the underlying bone occurs. Over time, this bone becomes denser and deformed and produces osteophytes that limit movement. Simultaneously, the joint capsule becomes thicker and the muscles retract, leading the patient to adopt a posture typical of an individual suffering from coxarthrosis.

Conventional pharmacological treatment aims to relieve pain through the use of analgesics or anti-inflammatory drugs (NSAIDs). A further therapeutic option is infiltration of hyaluronic acid (HA). However these therapies act only on the symptoms and not on the regeneration of the damaged cartilage tissue, and are not sufficient to avoid surgery for the substitution of the joint.

During the past ten years, numerous scientific publications have emerged (in vitro studies, animals models and humans clinical cases) concerning the use of intra-articular infiltrations of autologous platelet-rich plasma (PRP) for the regeneration and healing of cartilage.

In this study, the clinical experience concerning the effectiveness of PRP treatment for symptomatic coxarthrosis in the Orthopaedic Clinic of the University of Florence is reported (with the collaboration of the Transfusion Medicine Center of Careggi Hospital in Florence).

METHODS

A total of 22 Patients (6 women, 16 men) suffering from symptomatic hip OA classified as grade I, II or III (modified Croft classification) were included in this study (Table 1). Mean age of participants was 53.9 years (range 25-87).

Clinical evaluation: based on Harris Hip score and S-F 12 quality of life.

Preparation method A-PRP: RegenLab technology (Fibrin Polymer 1).

Therapeutic protocol: 3 intra-articular infiltrations (given at monthly intervals) with ultrasound guidance.

GRADE	N° PATIENTS	%
I	7	31,8
II	10	45,4
III	5	22,7
IV	-	-

Table 1:
Hip OA grade repartition of patients included in this study.

CLINICAL FINDINGS

1. RESULTS HARRIS HIP SCORE: mean follow-up 13 months (min. 5 months, max. 18 months)

RESULTS	PRE-OP.	6 MONTHS	FINAL FOLLOW-UP
Excellent	0	12	13
Good	0	7	6
Moderate	9	2	2
Poor	13	1	1

2. RESULTS HARRIS HIP SCORE in function of the n° intra-articular infiltrations (i.a.) of PRP

RESULTS	PRE-OP.	1 INFILT.	2 INFILT.	3 INFILT.
Excellent	0	10	12	13
Good	0	5	7	7
Moderate	9	3	2	2
Poor	13	2	1	1

3. RESPONDERS

GRADE	N° PATIENTS	%
1	6/7	85,7
2	8/10	80,0
3	2/5	40,0
4	-	-

4. RETROSPECTIVE ANALYSIS WITH AN ANALOGOUS SERIES OF PATIENTS (AGE & SEX) TREATED WITH HA

GRADE	N° PATIENTS	%
1	5/7	71,4
2	10/13	76,9
3	7/9	77,0
4	3/4	75,0

CONCLUSION

A strong rational exists to support the use of PRP as a treatment for hip OA.

Short term results deriving from the clinical study reported above showed good outcomes in terms of resolution of pain due to coxarthrosis; the best results were obtained in younger patients with a lower grade of hip OA (I-II). The peak of improvement usually occurred between the 1st and the 2nd infiltration of PRP.

This clinical study showed that PRP treatment gave better clinical results compared to HA treatment, thus providing a specific indication for the use of platelet concentrates as a treatment for coxarthrosis.

BIOBRIDGE FOUNDATION

regenlab

Session: CELLULAR MATRIX, PRP-HA SYNERGY AND INNOVATION IN TISSUE ENGINEERING – 22nd September 2014

Presentation: **Clinical experience of PRP in knee osteoarthritis in a rheumatology practice**

Lecturer: Dr. David Mathers, Rheumatologist, Australia, AUS – Dr. John Van Der Kallen, Rheumatologist, Australia, AUS

INTRODUCTION

Since January 2013 we have been using Platelet rich plasma (PRP) for various rheumatic conditions: Osteoarthritis, Patellofemoral knee pain, Lateral epicondylitis (tennis elbow), Gluteus medius tendonitis (trochanteric bursitis) and Achilles tendonitis.

PRP injections have been shown to be effective in knee osteoarthritis. Here we will present our own experience in knee OA in a clinical setting.

METHODS

We report the results on OA patients who were treated with PRP prepared using RegenKit from RegenLab. Collectively, 39 patients were evaluated (22 female, 17 male, with an average age of 63 years, range 30-94), and KL OA severity of varying grades (KLI-2 knees; KLII-14 knees, KLIII-17 knees, KLIV-18 knees). Of these, 28 patients were taking regular analgesia and 7 patients narcotic analgesia, 11 had been treated with Synvisc (i.a. viscosupplementation), 14 with corticosteroid injections, 4 with oral steroids. A total of 25 patients were performing regular exercise or exercise programmes.

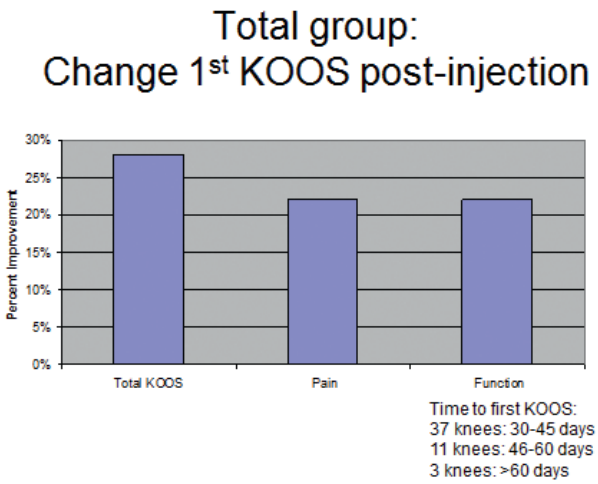
The patients were treated with 1-4 PRP injections (2-4ml). PRP injections were generally administered 4-6 weeks apart.

The KOOS questionnaire (composed of 42 questions related in symptoms, stiffness, pain, function and quality of life, with each question scored from 0 – 4) was administered at each follow-up visit which occurred at between 30-60 days and 90-180 days from baseline.

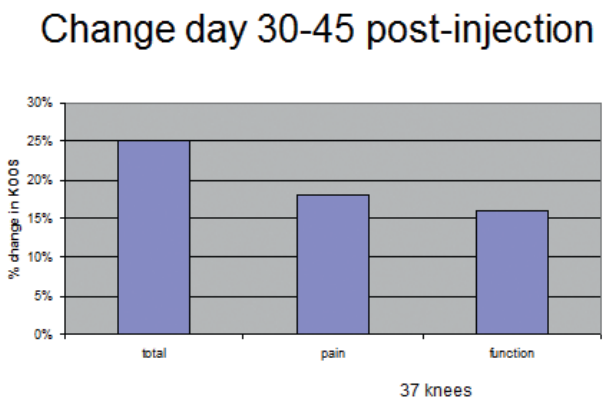
CLINICAL FINDINGS

Clinical responses varied within the study population. Those who had less severe disease and were younger tended to be the best responders. However, even older patients with severe disease responded to the PRP treatment.

Overall the changes were as follows:

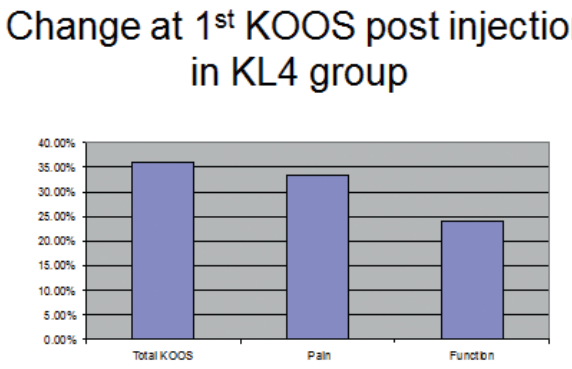


Time to first KOOS:
37 knees: 30-45 days
11 knees: 46-60 days
3 knees: >60 days



37 knees

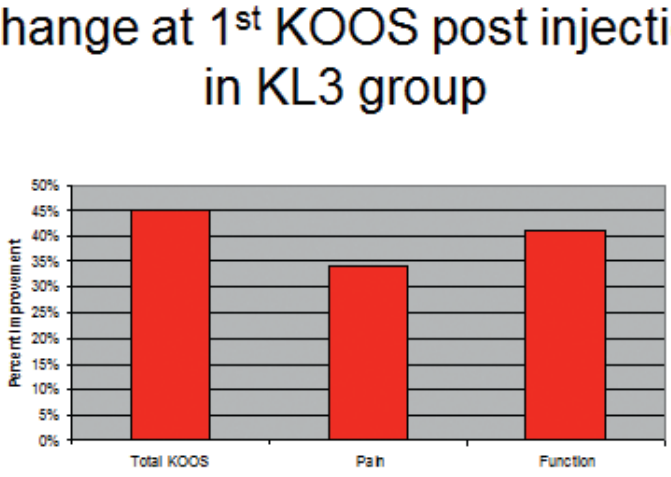
In KL grade IV patients (14 patients, 9 female, 5 male, mean age 63 years, range 44-94; 13/14 patients had previous steroid injections and all were on some form of analgesia) the following results were obtained:



Mean change in total KOOS: 36.1%
Range in total KOOS: -26% to 158%

Time to first KOOS:
10 knees: 30-45 days
6 knees:46-60 days
2 knees: >60 days

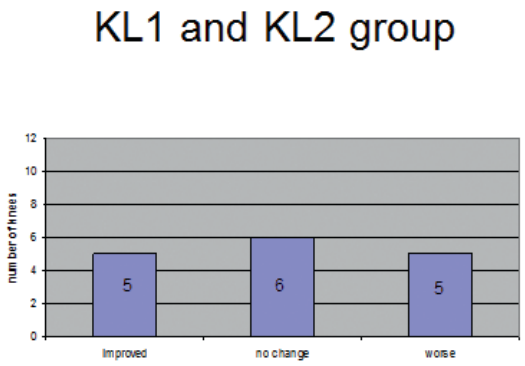
In KL grade III patients (13 patients, 6 female, 7 male, mean age 62.6 yrs, range 55-83), the following results were obtained:



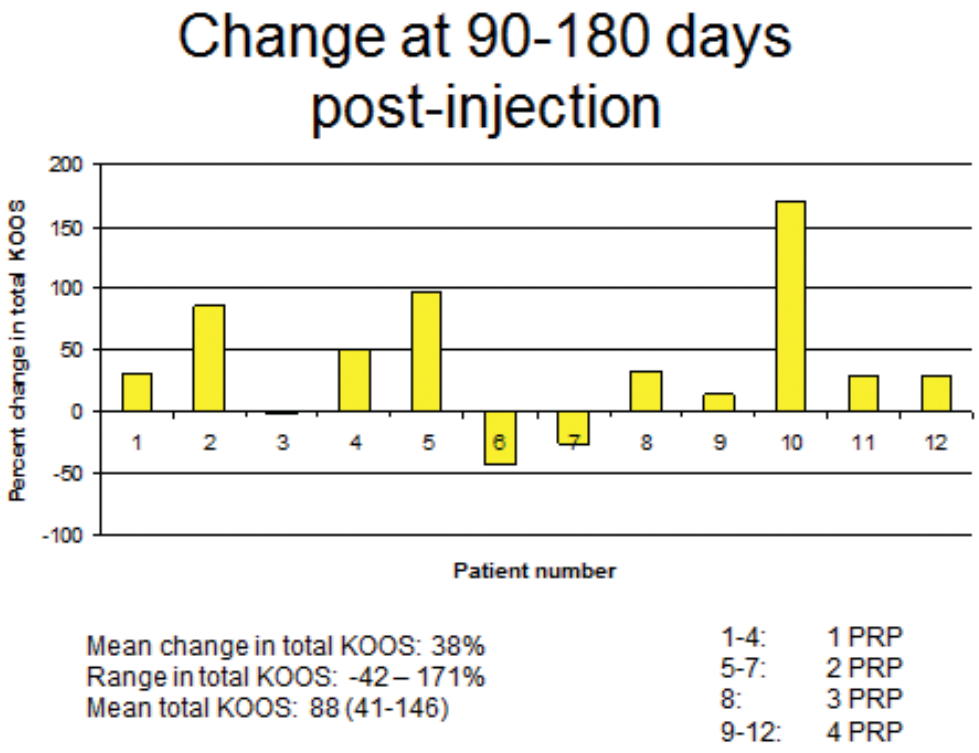
Mean change in KOOS: 45%
Range in total KOOS: -7.5 – 230%

Time to first KOOS:
14 knees: 30-45 days
3 knees: 45-60 days

For KL grade I-II patients (14 patients, 5 female, 9 male, mean age 52.4 years, range 34-77), no significant change in total KOOS, pain or function at 1st KOOS was observed.



Based on the results of this study, it is difficult for us to determine the duration of the benefits of treatment, because if patients had improved, then we didn't perform further PRP injections. We followed 6 patients for 6 months or longer. Of these patients: 2 were worse (2 and 4 PRP injections), 1 was unchanged following 1 PRP injection, but off morphine patches and 3 were significantly improved (3, 1 and 4 PRP injections).



Regarding safety, 1 patient had a significant post injection flare requiring 2 weeks of increased analgesia and rest. No infections or allergic reactions were observedafter i.a. injection.

CONCLUSION

PRP is an effective therapy for the symptomatic treatment of knee OA: 50% of knees respond after 30-45 days, but a better response was seen in more severe disease KL III/ KL IV in comparison with KL I/II.

The response improved with a subsequent injection (70% at day 69) and the effects were long-lasting even after one PRP injection.

Our data has limitations: this was an observational study with no control group, only KOOS was used as an outcome measure, the 1st KOOS assessment was done at variable time point and the follow-up was relatively short. For this reason, further data is needed to better define the groups that respond to treatment and longitudinal data is needed to define the effect of PRP on disease progression.

Session: PRP, THE FOUNDATION OF CELL THERAPY – 22nd September 2014

Presentation: **Knee OA – Clinical experience: 100 patients treated with platelet growth factors**

Lecturer: Dr. Piero Pasquetti, Director of Rehabilitation Department, CTO Careggi, ITA

INTRODUCTION

The earliest changes observed in osteoarthritis affect the articular cartilage, which is in dynamic equilibrium in a microenvironment of cytokines, growth factors and mechanical stress.

PRP - Platelet Rich Plasma - is a source of autologous platelet growth factors, which activate biological mechanisms such as chemotaxis, cell proliferation and cell differentiation which represent key events in the processes of repair and tissue regeneration. Circulating platelets contain a lot of growth factors, stored in alpha-granules. Autologous PRP is obtained from venous blood which is subjected to centrifugation to isolate plasma and platelets from the rest of the blood components.

The aim of our study was to evaluate the effects, in knee OA, of intra-articular injections of autologous PRP, obtained using a dedicated specific kit (RegenLab).

METHODS

From October 2010 to February 2014, we treated 100 patients (55 male and 45 female, mean age 64 years) with knee OA (Kellgren-Lawrence radiological grade II-III). We excluded patients treated with oral anticoagulants or having neoplastic disease, DVT, traumatic cartilage lesions, not controlled systemic diseases, in addition to uncooperative patients.

Patients were treated with three intra-articular injection of PRP, administered every 21 days, and their pain and function evaluated at the beginning of the treatment cycle (T0), and then at 1,3, 6 months and at 1 year (T1, T2, T3, T4) using the WOMAC (Western Ontario and McMaster Universities' Osteoarthritis knee Index) rating scale and VAS (Visual Analogue Scale).

PRP was obtained by collecting 14 cc of peripheral blood that was divided in 2 dedicated tubes and then centrifuged and at 3200 rpm for 12 minutes. After removal of 2 cc of supernatant, platelets were resuspended through careful inversion of the tube. In this way, we obtained from 2 to 2.5 cc of L-PRP with a platelet count 3-5 times higher than that of normal blood. Calcium gluconate was added to a final concentration of 0.5-1%, and the syringe was gently mixed.

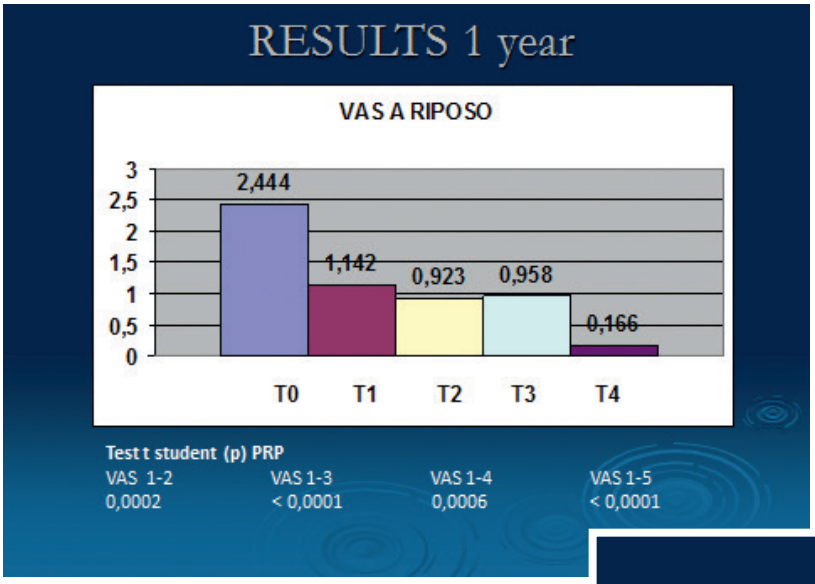
Patients were treated with PRP: one intra-articular injection every 21 days for a total of 3 injections. The injection technique used was: patient supine on the bed, flexed knee, anteromedial or anterolateral access.

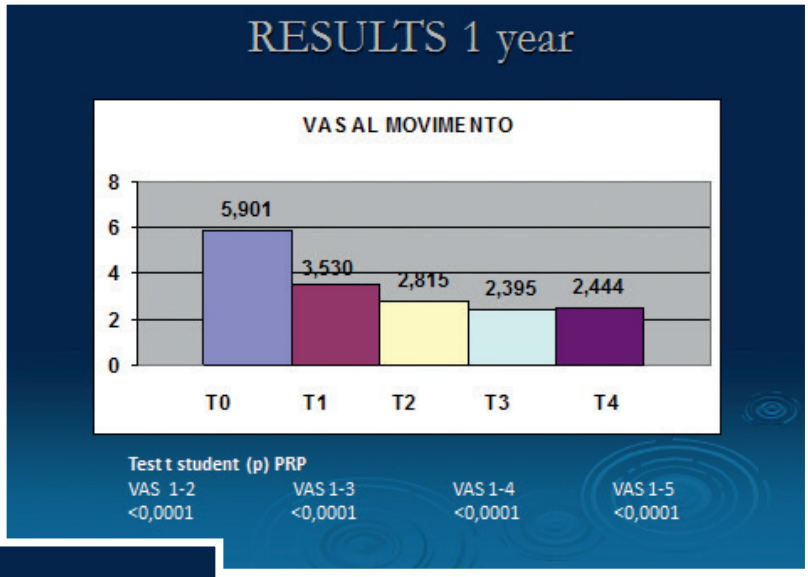
After knee infiltration, patients were invited to rest for two days, not touse NSAIDs or aspirin but, if necessary, to apply ice locally and use 1000mg Paracetamol.

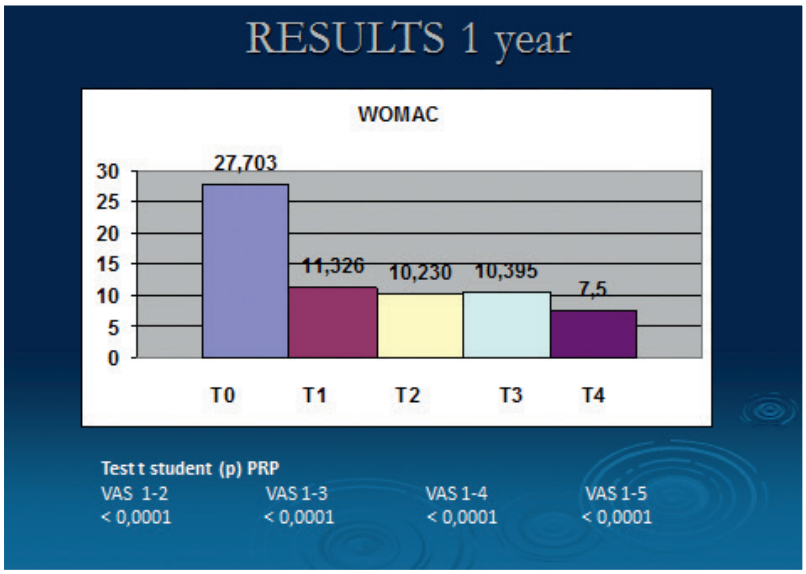
Patients were also instructed to follow a self-managed home program (a dedicated brochure was provided) which consisted in recovery of kinetic chain, exercises for lower limbs, body weight reduction.

CLINICAL FINDINGS

A highly statistically significant improvement was observed for VAS pain at rest ($p \leftarrow 0.0002$), VAS pain on movement ($p \leftarrow 0.0001$), WOMAC ($p \leftarrow 0.0001$) starting from the 1st month in comparison with basal values. The improvement increased in the subsequent months, remaining significant up to 1 year for all evaluated parameters ($p \leftarrow 0.0001$).







CONCLUSION

PRP injected in the knee joint represents a valid therapy for controlling OA pain, stiffness and joint dysfunction.

All patients reported a statistically significant, long-lasting improvement in both functional and pain parameters and a high level of satisfaction was reported by the majority of patients, many of whom requested the same treatment in the contralateral knee.

BIOBRIDGE FOUNDATION

regenlab

Session: ORTHOPAEDICS AND CARDIAC SURGERY – 23rd September 2013

Presentation: **PRP: a treatment for early osteoarthritis**

Lecturer: Dr. Vincenzo Pellecchia, Orthopaedic, Varese, ITA

INTRODUCTION

Hyaline cartilage, known for its unique properties, enables almost frictionless joint movement and protects the underlying bone from excessive load and trauma by dissipating the forces produced during movement. However, cartilage has limited intrinsic healing potential because it is avascular and has few specialized cells with a low mitotic activity. Once cartilage is injured, it gradually degenerates, leading to osteoarthritis (OA). The prevalence of chondral defects is frequent in sport injuries (especially in patients older than 40 years), and these often cause persistent pain. The incidence of OA increases steadily with age, affecting 12.1% of the population from 25 to 74 years old, and it is the leading cause of physical disability in people older than 65 years. Community-based studies have shown that 10% of the population older than 55 years has troublesome knee pain, and among this population, 25% are severely disabled. Many conservative treatment options—such as oral and topical nonsteroidal anti-inflammatory drugs, diacerhein, intra-articular corticosteroids, and visco-supplementation — have been used for the treatment of OA and have yielded short-term efficacy with local or systemic side effects. The high social costs of bone and cartilage pathologies have influenced the trend towards preventive interventions and therapeutic options that regenerate tissue homeostasis and retard progression to OA. Intra-articular injection of platelet-rich plasma (PRP) is one therapeutic option with promising preliminary clinical results.

The aim of this study was to investigate the efficacy of intra-articular injections of PRP in active patients with symptomatic knee osteoarthritis, and to determine whether PRP was equally as effective in patients who had undergone or not a previous surgical intervention for cartilage lesions.

STUDY DESIGN

A cohort of 50 patients, with symptomatic knee OA of grade I-III per Kellgren-Lawrence classification, were prospectively followed. All patients (31 men and 19 women) were treated with 2 intra-articular injections (once monthly) with autologous PRP (Regen ACR-C, Regen Lab, Switzerland) and followed up for a minimum period of 1 year (range, 12-26 months). The mean age of patients was 47.7 years, ranging from 32 to 60 years, and body mass index was 26.7 +/- 2.4. All patients were involved in various sports activities, such as soccer (14%), skiing (14%), motocross (12%), basketball or volleyball (12%), jogging (10%), and others (tennis, cycling, walking, trecking, etc) but not at a professional level. Twenty-five patients (50%) had undergone a previous surgical intervention for cartilage lesions of grade III and IV per International Cartilage Repair Society classification repair on the ipsilateral knee, at least 1 year before PRP treatment (S1 group), while 25 patients did not undergo any previous surgery for the knee (S2 group). Average time from previous surgery to treatment was 22.4 +/- 17.2 months, ranging from 1 to 3 years. Previous surgery for cartilage included cartilage shaving (S1a) and microfracture (S1b), for grade 3 and 4 cartilage lesions (International Cartilage Repair Society classification).

The standard radiographic evaluation included a standing anteroposterior long-leg radiograph (including hips and ankles), standing anteroposterior/lateral views of the knees, skyline patellofemoral and standing 45° flexion knee views, and magnetic resonance imaging. Standard blood investigations were done before treatment, including complete blood count.

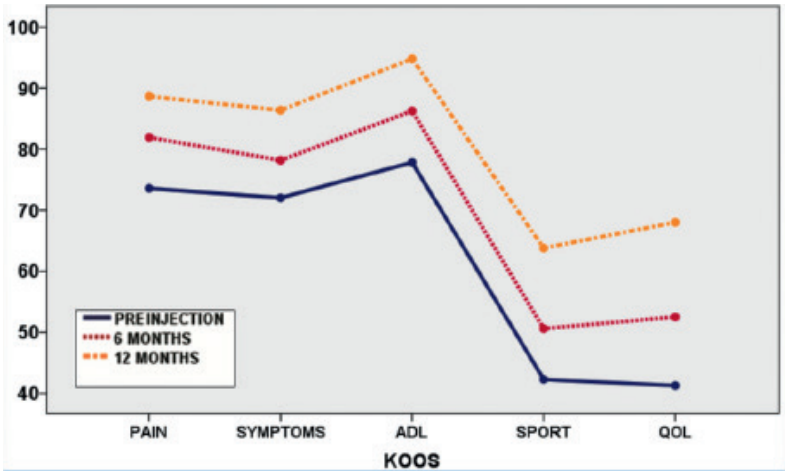
Patients	No.	Age, y	Male / Female, No.	Right / Left Knee, No.	Kellgren-Lawrence Grade, No.			Intl Cartilage Repair Society Grade,[a] No.	
					1	2	3	3	4
All	50	47.7 ± 2.52	31 / 19	20 / 30	11	19	20	—	—
S1: previous surgery	25	44.7 ± 2.01	14 / 11	7 / 18	3	11	11	14	11
S1a: cartilage shaving	12	44.4 ± 2.39	4 / 8	2 / 10	3	6	3	9	3
S1b: microfracture	13	45.0 ± 1.68	5 / 8	5 / 8	0	5	8	5	8
S2: no previous surgery	25	50.4 ± 2.77	17 / 8	13 / 12	8	8	9	—	—

Therapeutic protocol:

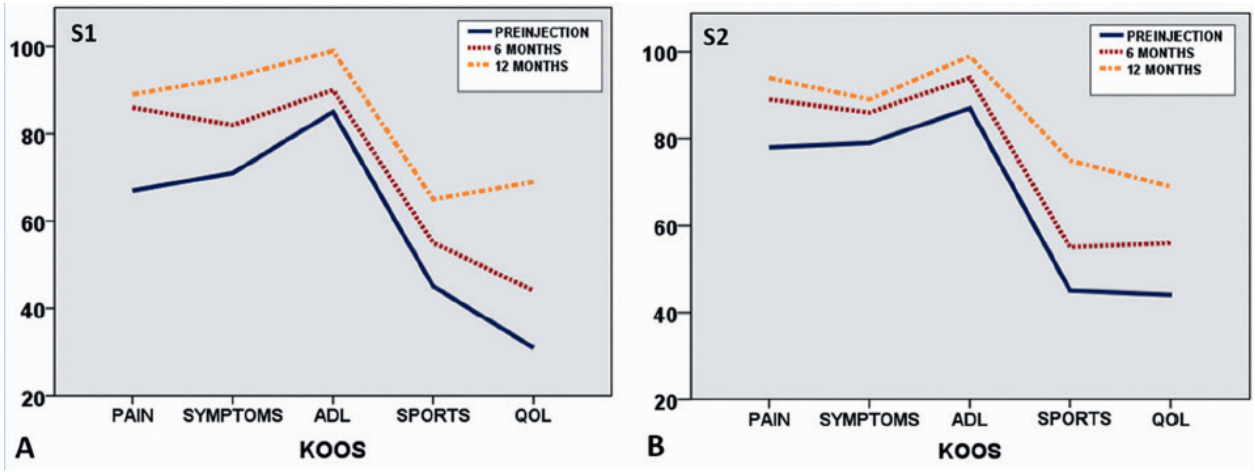
All patients were treated with 2 intra-articular injections of autologous PRP (1-month interval between injections). After extraction of 8 mL of peripheral blood, the sample was centrifuged for 9 minutes at 3500 revolutions per minute according to RegenLab recommendations. Thereby, 4 mL of PRP were obtained and were immediately available for intra-articular infiltration by a suprapatellar approach under sterile aseptic conditions.
The PRP was not activated before injection.

CLINICAL FINDINGS

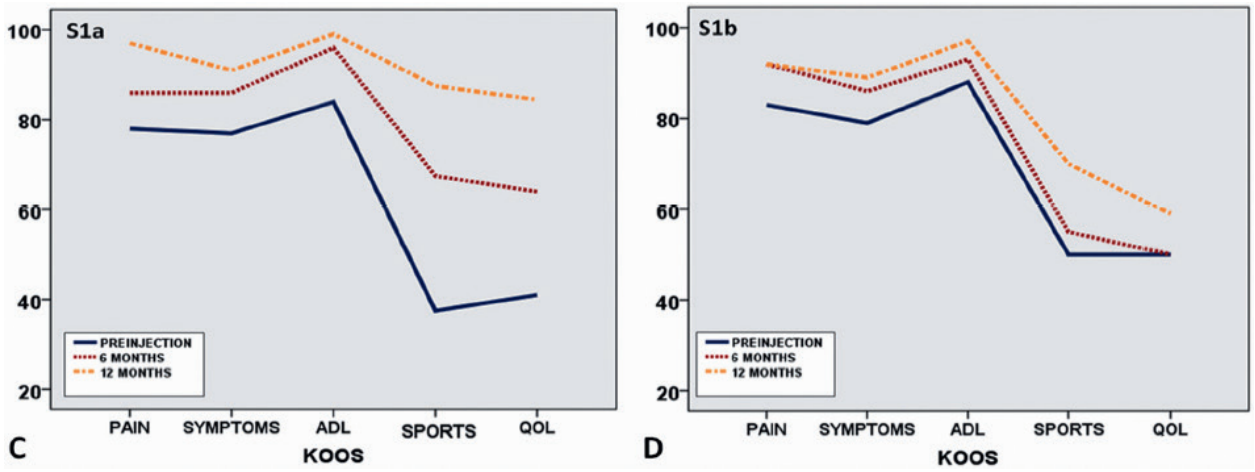
1) All patients showed a significant improvement in all scores at 6 and 12 months ($P \leftarrow 0.01$), demonstrating that PRP injections can represent a valuable treatment in patients with knee OA, as can be seen from the following diagram:



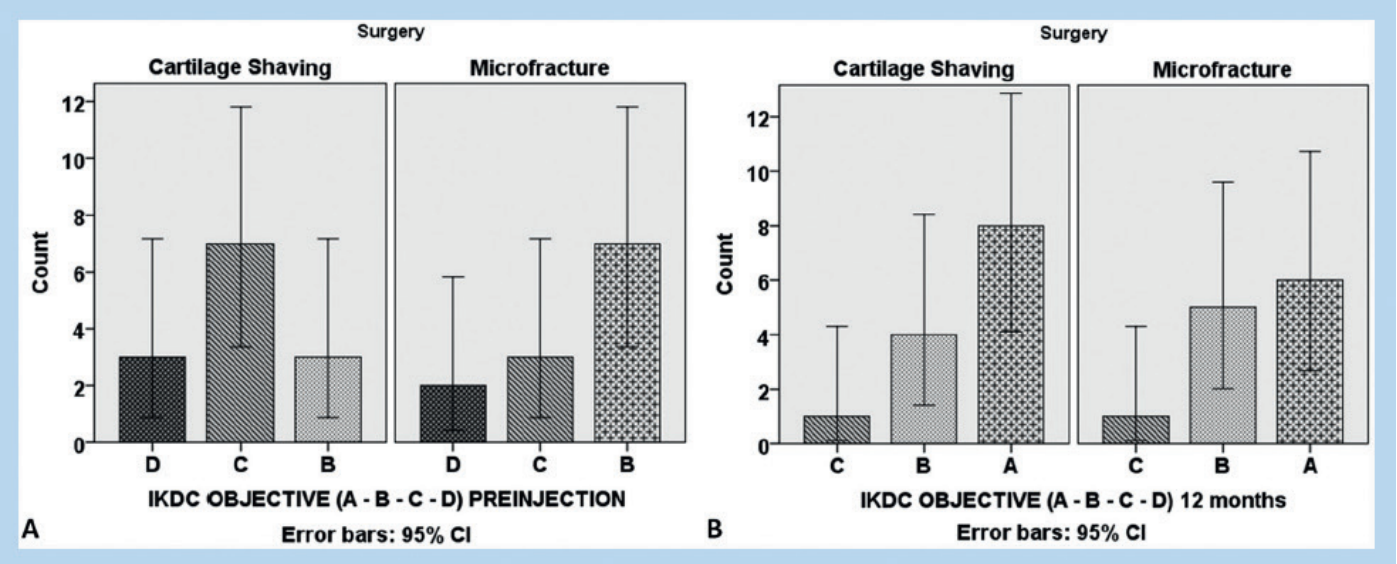
2) No significant differences in improvement (Mann-Whitney U test) were observed between pre-operated group (S1) versus the non-operated group (S2)



3) There was no significant difference in improvement between patients with previous cartilage shaving (S1a) or previous microfracture (S1b) in all evaluated scores



4) No significant differences were observed between patients who had undergone cartilage shaving or microfracture in improvement in the IKDC score (Mann-Whitney U test).



CONCLUSION

A number of viable biological approaches have been made available to prevent progression to OA. PRP represents a user friendly therapeutic option that is well tolerated and shows encouraging preliminary clinical results in active patients with knee OA. Patients who underwent previous cartilage shaving and/or microfractures, also showed favorable results, indicating that PRP could be an additional therapy for these patients. This study did not show significant differences between male and female patients.

Standardization of PRP protocols, long-term follow-up, and prospective blinded randomized studies should clarify questions regarding the effectiveness of PRP and the durability of clinical improvement.

SPORTS MEDICINE

OSTEOARTHRITIS & CARTILAGE

-

CELLULAR MATRIX

Session: CELLULAR MATRIX, PRP-HA SYNERGY AND INNOVATION IN TISSUE ENGINEERING – 22nd September 2014

Presentation: **Treatment of degenerative hip osteoarthritis in patients under 50 years old by CT-guided injection of Cellular Matrix**

Lecturer: Prof. Philippe Adam, Sports Medicine, Medipole Clinic, Toulouse, FR

INTRODUCTION

The impingement of the hip is a syndrome where a premature contact between the femoral neck and the cotyle occurs, with the result that the articular cartilage and fibro-cartilage (labrum) are crushed between these two bony parts. These conflicts are responsible for pre-arthritic lesions, especially in young, sportive patients over 18-20 years.

There are three types of FAI: pincer, cam, and combined impingement:
• Pincer. This type of impingement occurs because extra bone extends out over the normal rim of the acetabulum. The labrum can be crushed under the prominent rim of the acetabulum.

• Cam. In cam impingement the femoral head is not round and cannot rotate smoothly inside the acetabulum. A bump forms on the edge of the femoral head that grinds the cartilage inside the acetabulum.

• Combined. Combined impingement just means that both the pincer and cam types are present.

The treatment of hip impingement usually starts with physical therapy in order to improve the range of motion of the hip and strengthen the muscles that support the joint. This can relieve some stress on the injured labrum or cartilage. If symptoms (pain) are present, non-steroidal anti-inflammatory medications can help reduce pain and inflammation.

Surgical treatment by arthroscopy is reserved for cases where pain is not relieved by nonsurgical treatment. The surgeon can correct the impingement by trimming the bony rim of the acetabulum and also by shaving down the bump on the femoral head. Some severe cases may require an open operation with a larger incision to undertake these procedures.

In this study, we evaluated the effect of PRP+HA (Cellular Matrix, RegenLab) in patients with hip dysplasia and/or impingement.

METHODS

A total of 13 patients (6 men and 7 women), with unilateral hip osteoarthritis (23 to 60 years old, mean age 42,8) were treated with 2 CT guided intra-articular injections of HA + PRP (Cellular Matrix, RegenLab) with an interval of two months between injections. CT injections were performed under analgesia (oxygen/nitrogen mix).

Inclusion criteria were: patients practicing sport; presence of dysplasia and /or impingement; if impingement was present: cam effect or pincer effect or combined; presence of cartilaginous lesions with/without fibro-cartilaginous lesions; failure of NSAIDs and classic visco-supplementation.

Patients were divided into two groups:
• Group 1: 7 patients with femur-acetabular impingement syndrome with labral lesions (3 cam, 2 pincer, 2 combined; 5 patients were injected after surgery and 2 did not have prior surgery.

• Group 2: 6 patients without impingement (dysplasia, degenerative).

X ray changes were graded using Tönnis' classification of osteoarthritis: in 6/13 were classified as Grade 1 (mild: increased sclerosis, slight joint space narrowing or slight loss of head sphericity); the remaining 7 patients were classified as Grade 2 (moderate: small cysts and moderate joint space narrowing, moderate loss of head sphericity).

The Oxford Hip Score was administered at three timepoints during the study to evaluate pain and function: before and after the first injection, then at a follow up of one month.

RESULTS

The efficacy of treatment was estimated by changes in the Oxford Hip Score: good meant progress, especially for patients with impingement. Individual patient and cumulative efficacy results are reported below.
No side effects were observed after injection of PRP-HA.

Table 1: Individual results (the most successful cases are highlighted in red).

Cases	Clinical framework	AGE	SEX	LOCATION	TÖNNIS Grade (X ray)	OXFORD Score
1	No impingement (soccer)	43	M	Right Hip	2	31/34/41
2	Mixt IS : Cam + Pincer (surgery)	31	M	Right Hip	1	28/39/43
3	IS : Pincer (no surgery)	46	W	Left Hip	1	29/32/35
4	IS : Cam (surgery, rugby XIII)	22	M	Left Hip	1	36/44/48
5	No impigement	51	W	Right Hip	2	38/44/47
6	IS : Pincer (no surgery)	59	W	Left Hip	1	18/22/22
7	No impingement	52	W	Left Hip	2	30/34/33
8	Mixt IS : Cam + Pincer (surgery, fitness)	44	W	Left Hip	1	29/34/36
9	No impingement (ski, tennis)	53	M	Left Hip	2	36/44/44
10	Dysplasia + Cam (surgery)	25	W	Right Hip	1	20/20/27
11	No impingement	60	M	Right Hip	2	26/26/27
12	No impingement	47	W	Left Hip	2	36/37/39
13	IS : Cam (surgery, rugby XV)	23	M	Right Hip	2	33/44/46
14	IS : Cam (no surgery, aerofight)	18	W	Right Hip	0	16/37

The following 4 cases were considered particularly significant:

Case 1: soccer player, male 43 years, no impingement, Tönnis 2, Oxford improvement from 31 to 34 after the 1st injection, to 41 after the 2nd injection.

Case 3: pincer, no surgery, female 46 years, Tönnis 1, Oxford improvement from 29 to 32 after the 1st Injection, to 35 after the 2nd injection.

Case 4: rugby player, male 22 year, com surgery, Tönnis 1, labral cavitation, Oxford improved from 36 to 44 after the 1st injection, to 48 after the 2nd injetion.

Case 5: female 51 years, no impingement, Tönnis 2, Oxford improved (from 38 to 44 after the 1st injection, to 47 after the 2nd injection), clear chondropathy but good function.

Table 2: Cumulative results

Oxford Score : Synthesis

* **Mean score before** injection is **30** (***moderate***)
* **Mean score after** two injections is **37,6 (*mild*) : 25% increase**
* **6/13 have satisfactory joint function (46%)** after 2 injections
* **No side effects** after CM injection
* Good progress and improvement specially for **patients with impigement** (**37%** versus 17% for other group)
* Separated case 14 (cam) : before 16 (severe), and after one CM injection **37** (mild, **over 50%**)

CONCLUSION

PRP+HA (Cellular Matrix) is an effective and safe alternative for the treatment of mild to moderate (Tönnis 1 and 2) degenerative arthritis of the hip, especially in young sportive patients with impingement syndrome.

PRP+HA is highly complementary to surgery for healing and reducing pain.

PRP+HA treatment alone is very effective for labral lesions. In this condition, as in the case of knee menisco-arthritis, it is important to save fibro-cartilage to avoid arthritis.

Session: PRP, THE FOUNDATION OF CELL THERAPY – 22nd September 2014

Presentation: **Treatment of knee osteoarthritis with Cellular Matrix, a synergistic association of platelet-rich plasma and hyaluronic acid**

Lecturer: Dr. Antonio Frizziero, Assistant Professor, Department of Physical & Rehabilitation Medicine School of Medicine university of Padova, Padova, ITA

INTRODUCTION

Osteoarthritis (OA) is the most common joint disease and guidelines recommend both pharmacologic and non-pharmacologic measures, in addition to combined approaches. Joint injection is used in patients unresponsive to standard therapies and commonly used agents include corticosteroids and hyaluronic acid (HA). Recently, Platelet-Rich Plasma (PRP) has found widespread use with good results. The association of PRP and HA has the potential to be an even more effective treatment as compared to the individual components, because both PRP and HA can influence the disease process through differing mechanisms.

We initiated a study aimed to evaluate the clinical efficacy of a PRP combined with HA (Cellular Matrix, RegenLab) in patients with mild-moderate knee OA and to compare the results with those obtained in a cohort of patients treated with HA alone (SINOVIAL or SINOVIAL FORTE, IBSA). The study is still ongoing and preliminary data are reported here.

METHODS

A total of 25 patients (7 male, 18 female; age 44-80) with knee OA from 3 different treatment cohorts were included: Cellular Matrix (n=5), SINOVIAL (n=10), SINOVIAL Forte (n=10).

All patients were suffering from mild-moderate knee OA (Kellgren Lawrence II to III) and were treated in the affected joint once a week for 3 weeks with Cellular Matrix, Sinovial or Sinovial Forte.

OA symptoms were evaluated by the Lequesne Index and the WOMAC Index (sections pain, stiffness and function) at baseline, 5 weeks, 3 and 6 months.

The treatment effect was analyzed based on the percent improvement from baseline, by analysis of variance (ANOVA). The same model was used to compare the effects of Cellular Matrix with Sinovial and Sinovial Forte. Given that the study is still ongoing, the treatment effect was tested only at 5 weeks (last available observation for patients treated with Cellular Matrix) using descriptive statistics and graphical analysis to show data and results.

CLINICAL FINDINGS

Figures 1.A and 1.B describe, respectively, the mean Lequesne Index and mean percent improvement, by treatment and visit. There were no statistically significant difference in percent improvement between treatments although Cellular Matrix appeared better at 5 weeks (63.27% improvement vs 44.29% for Sinovial Forte and 37.8% for Sinovial).

FIGURE 1.A

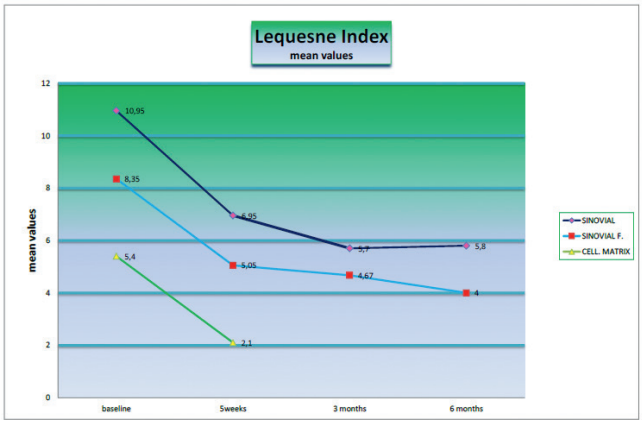
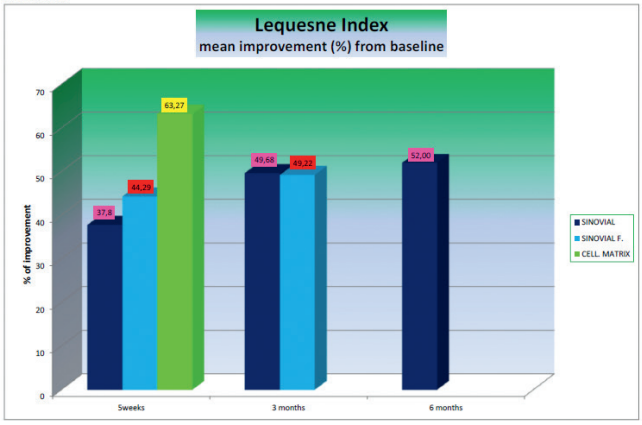


FIGURE 1.B



Figures 2.A and 2.B describe respectively mean WOMAC pain and mean percent improvement, by treatment and visit. As can be seen, there were no statistically significant difference in percent improvement among treatments, but Cellular Matrix appears more efficacious in pain amelioration (64.4 % improvement vs 58.27% for Sinovial and 44.01% for Sinovial Forte).

FIGURE 2.A

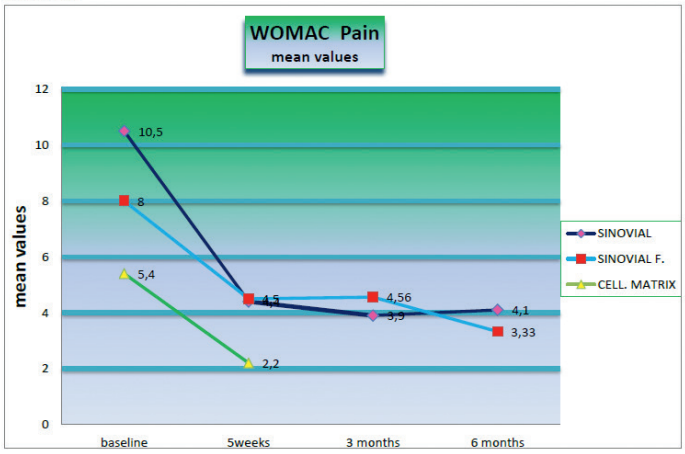
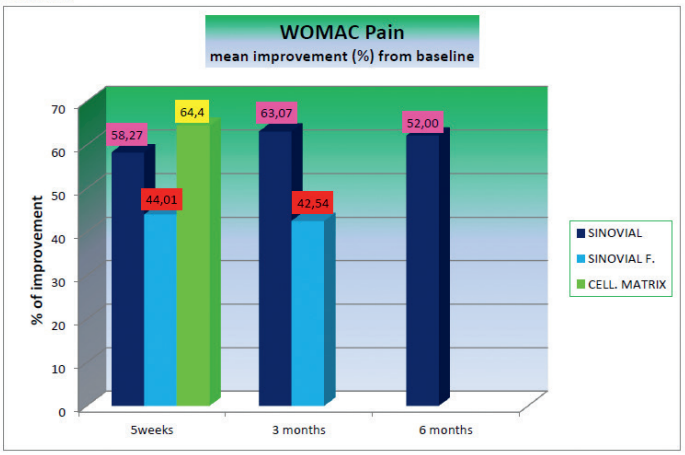


FIGURE 2.B



Figures 4.A and 4.B describe respectively mean WOMAC function and mean percentage improvement, by treatment and visit. There are not statistically significant difference in percentage improvement among treatments. Cellular Matrix improves function better of Sinovial forte (respectively of 46.67% vs 31.48%).

FIGURE 4.A

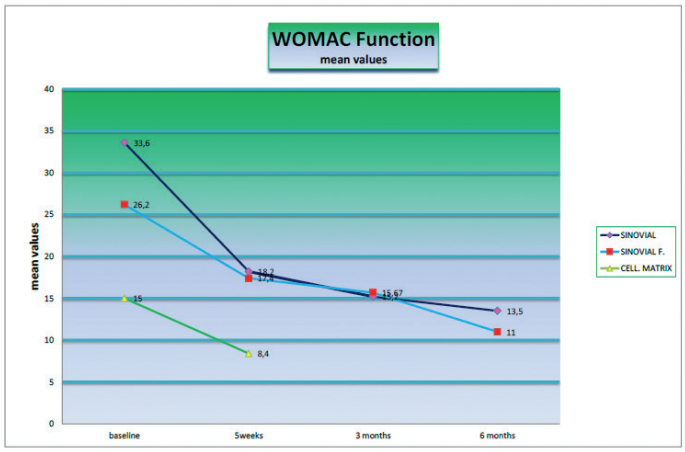
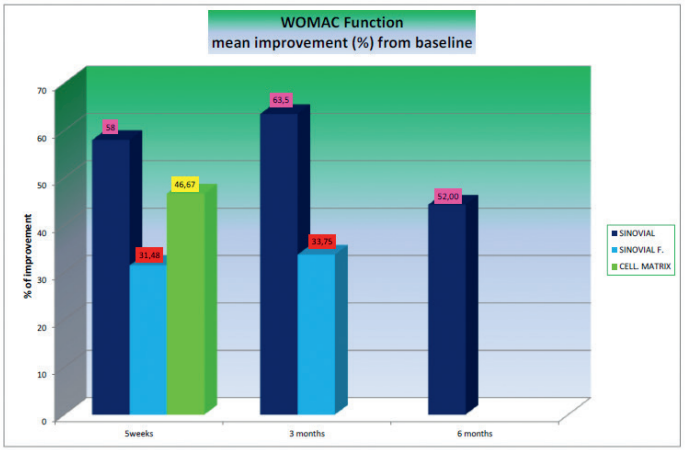


FIGURE 4.B



CONCLUSION

These preliminary data, from this ongoing study, showed an interesting efficacy profile for Cellular Matrix in reducing pain and improving function staring from the first weeks post-treatment. The effect of Cellular Matrix was in some instances better than that achieved with the HA treatments (Sinovial, Sinovial forte), even though no statistically significant differences were observed between treatments. These data support the hypothesis that PRP and HA components of Cellular Matrix exhibit synergistic activity when combined, which may be related to their different mechanisms of action in reducing inflammation and modifying the articular microenvironment.

Session: CELLULAR MATRIX, PRP-HA SYNERGY AND INNOVATION IN TISSUE ENGINEERING – 23rd September 2014

Presentation: **Cellular Matrix in osteoarthritis San Camillo protocol**

Lecturer: Prof. Luca Pierelli, Director of Immunology & Transfusion Medicine Department, San Camillo Forlanini Hospital, Rome, ITA

INTRODUCTION

Osteoarthritis (OA) is the most common rheumatic disease, with localization to the knee in 30% of cases. In the treatment of knee OA the infiltrative "route" is widely used as follows: Hyaluronic acid (HA) for the correction of the biomechanical deficit or platelet-rich plasma (PRP) for the regenerative stimulus induced by growth factors (GF). Basic research has suggested that HA and PRP can be used in combination without impairment of their characteristics, but with synergistic action on the treated diseases, through the formation of a three-dimensional scaffold able to release high concentrations of GF.

METHODS

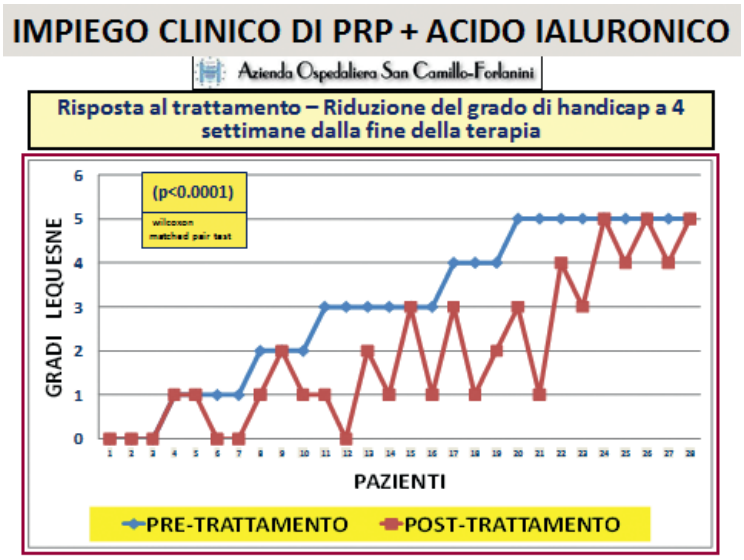
From December 2013 to March 2014, we treated 28 patients (13 females and 15 males, aged between 19 and 76 years old, median age 61 years old), suffering from varying grades of knee OA (Kellgren Lawrence I to III) with involvement of the articular cartilage.

Once a week, for three consecutive weeks, patients were subjected to sampling of 4 ml blood which was collected in the Regen BCT-HA Cellular Matrix cell-separation tube.

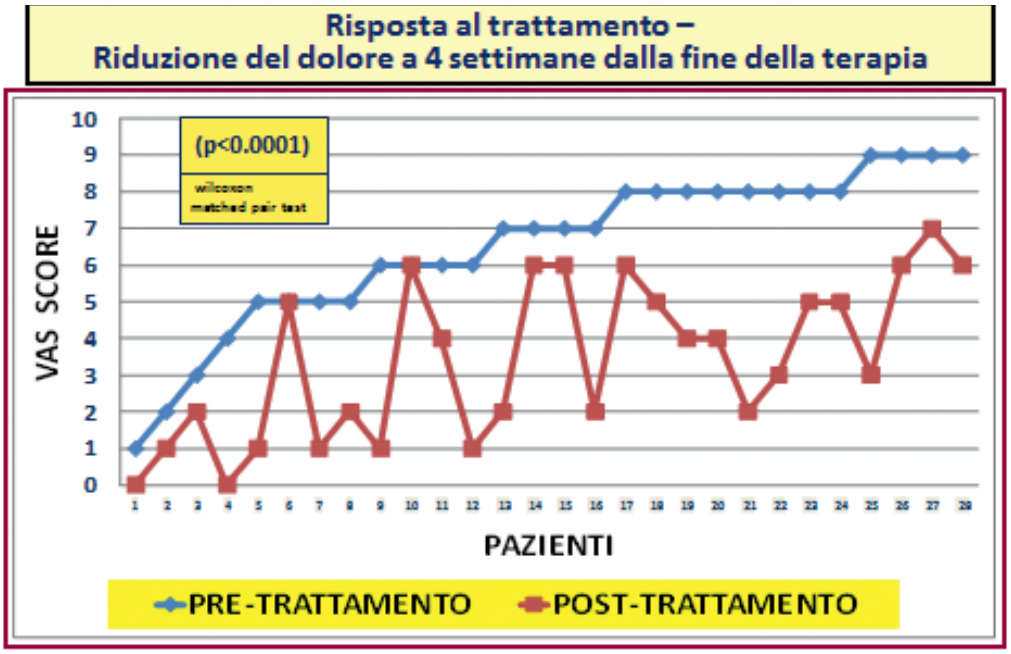
The PRP (2-3 ml) obtained after centrifugation was mixed, by inversion, with the HA (1.550 Kda (2 ml – 40 mg)) present in the tube; this mixture was then injected in the joint using the supero-lateral approach. The patients were subjected to clinical examination and assessment of pain and function respectively by means of the VAS (Visual Analogue Scale) and the Lequesne algo-functional Index at different time points: before treatment, at the end of the treatment and 1 month after.

CLINICAL FINDINGS

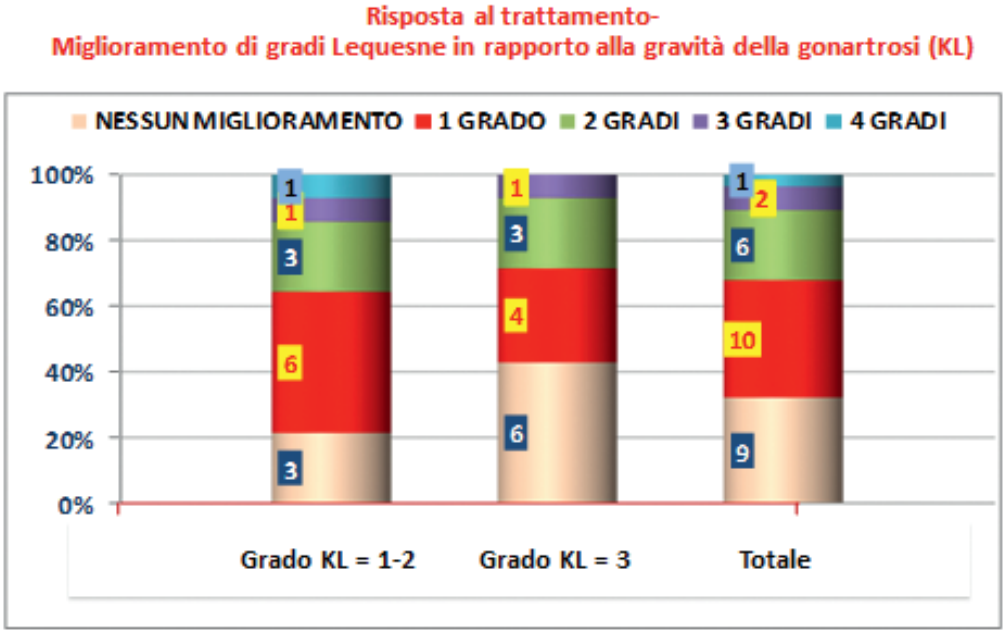
No patient showed adverse effects or worsening of symptoms at the injected site. In the group of patients treated, pain and degree of disability were significantly reduced after treatment ($p \leftarrow 0.0001$, Wilcoxon mixed-pair test). Of the 28 patients treated, 68% presented an improvement of the disability, and 93% an improvement in pain symptoms, 4 weeks after the end of therapy. Treatment with PRP-HA seems to be more effective (not statistically significant), in the milder grades of osteoarthritis (Kellgren-Lawrence 1-II), compared to a historical control cohort treated with PRP alone.



PRP+HA Response - Reduction of the disability degree (Lequesne Index) at 4 weeks after the end of therapy. Data pre and post treatment



PRP+HA Response - Reduction of Pain (VAS score) at
4 weeks after the end of therapy.
Data pre and post treatment



PRP+HA Response –Improvement in the Lequesne
Index scores in relation to the initial K-L OA severity.

CONCLUSION

The administration of PRP-HA was shown to be effective in pain reduction with improvement in symptoms and functional handicaps. This treatment modality was safe, easy to use and well accepted by patients.

The main objective of the combined PRP+HA treatment is the modification of the articular microenvironment through the modulation of inflammatory response and cellular growth obtained with products acting with different, albeit complementary, mechanism of action, thus allowing an efficacious treatment at affordable costs.

Session: SPORTS MEDICINE & INFILTRATIONS & MUSCULOSKELETAL MEDICINE – 23rd September 2013

Presentation: **Preliminary study on the HA + PRP injections in osteoarthritis of the knee after failure of HA alone**

Lecturer: Dr. Jean-Luc Renevier, Rheumatology, Hospital "Meulan les Mureaux", Paris, FRA

INTRODUCTION

For patients with knee osteoarthritis (OA) who have experienced failure of hyaluronic acid (HA) injection, to date the only available option has been total knee arthroplasty. Despite the fact that significant progress has been made in recent years, total knee prosthesis remains a restrictive surgery at 65 years of age.

Intra-articular injection of platelet rich plasma (PRP) has been gaining usage as a treatment for OA and the body of clinical literature supporting this therapy has grown steadily over the past several years.

The objective of this study was to compare the clinical benefits of the combination of HA and PRP to PRP alone and to try to determine the best criteria for patient selection and the appropriate number of injections.

METHODS

The design of this pilot study foresaw the enrollment of 20 patients ranging in age from 45 to 74 with OA of Grade II/II on the Kellgren Lawrence Scale. Patients should have been taking NSAIDs and analgesics for less than 3 months but were allowed to enter the study if they had been taking symptomatic slow-acting drugs for OA for more than 3 months. Patients had to have failed HA therapy.

PRP alone (RegenKit) or PRP+HA (Regen Lab Cellular Matrix) were injected in the target knee using the external supra-patellar technique. Effusion, where present, was removed prior to the injection.

Immediate side-effects were monitored and patients were instructed not to walk and to remain at rest for a half-day.

PRP+HA was administered to 10 patients, 5 women (average age= 62.2 years, average weight = 74.4 kg) and 5 men (average age = 65.2, average weight = 90.4 kg). The first injection was given on 11 June 2012.

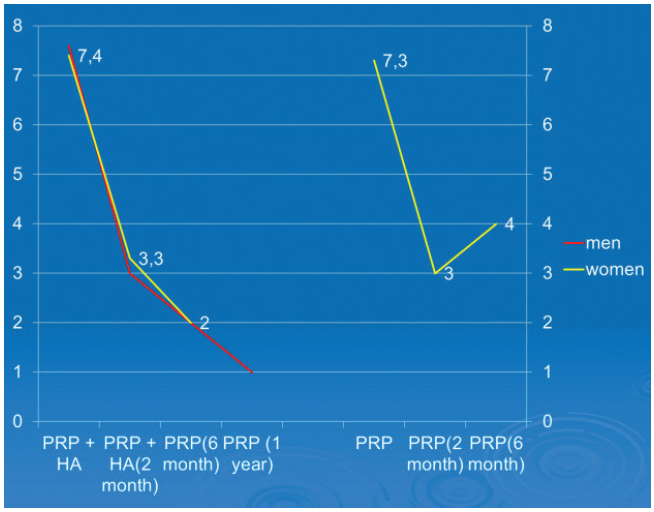
PRP alone was administered to 10 patients, 9 women (average age= 62.2 years, average weight = 91 kg) and 1 man (age = 59, weight = 100 kgs). The first injection was given on 25 January 2013.

CLINICAL FINDINGS

The group of 5 women treated with PRP+HA had an average WOMAC A1 score at Day 0 of 7.4 prior to injection. One patient experienced swelling of the knee immediately following injection and underwent knee arthroscopy. Three of the patients had a second injection of PRP+HA at between 6-8 weeks following the first injection. The remaining patient had a second injection of PRP alone at 6-8 weeks but was judged to be a failure at 3 months due to swelling of the knee. All patients had an injection of PRP alone at 6 months.

The group of 5 men treated with PRP+HA had an average WOMAC A1 score of 7.6 prior at Day 0 to injection. One patient had a second injection of PRP+HA after 6-8 weeks. The 4 remaining patients had a second injection of PRP alone after 6-8 weeks. All patients had an injection of PRP alone at 6 months.

The group of 10 patients treated with PRP alone had an average WOMAC A1 score of 7.3 prior to injection. All patients had a second injection of PRP at 8 weeks. Two patients had a third injection at 6 months. No side-effects were observed in patients treated with PRP alone.



CONCLUSION

The objective of this pilot study was to evaluate the effect of PRP+HA combination in knee OA patients who had not responded to treatment with HA alone. The results suggest that the PRP+HA combination was effective in this patient group g. While the results appear to be encouraging, further studies are required.

Session: CELLULAR MATRIX, PRP-HA SYNERGY AND INNOVATION IN TISSUE ENGINEERING – 22nd September 2014

Presentation: **Efficacy and safety of Cellular Matrix in knee osteoarthritis patients after failure of HA**

Lecturer: Dr. Jean-Luc Renevier, Rheumatology, Hospital "Meulan les Mureaux", Paris, FRA

INTRODUCTION

After failure of HA injection in patients with knee osteoarthritis, surgery was the only alternative. Despite progress, the total knee prosthesis is a restrictive surgery at 65 years old.

The main objective of our study was to test the combination of HA and PRP (Cellular Matrix) in patients with knee osteoarthritis knee who had failed treatment with HA alone. In a previous study on 10 patients, we observed that the best treatment regimen for Cellular Matrix appeared to be a total of three injections: one injection at day 0, one injection at month 2 and one injection at month 6.

To confirm the above observation, a multicenter study was undertaken in 5 sites in France. Preliminary data are reported here.

METHODS

From September 2013 to April 2014, 71 patients (34 females and 37 males, aged between 40 and 84 years old, mean age 63 years old, mean BMI 26.83), suffering from knee OA of Kellgren Lawrence grade II (33) and III (38), not responsive to HA treatment in the previous 3 months, and not taking analgesics or NSAIDs or anti-OA in the previous 3 months, were enrolled.

Patients were treated with Cellular Matrix at day 0, month 2 and month 6 and were evaluated at these time-points and at a final follow up at month 9. If effusion was present, an arthrocentesis was done before injecting the product into the joint.

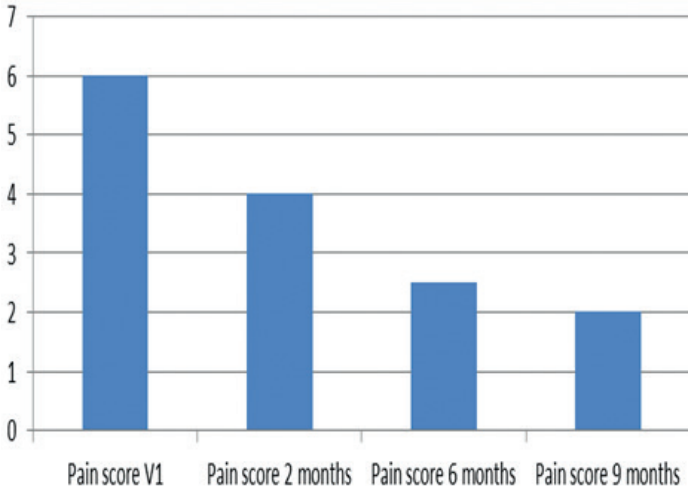
Pain was evaluated at the above time-points using the WOMAC scale (where the severity of symptoms was assessed on a 0-10 mm VAS).

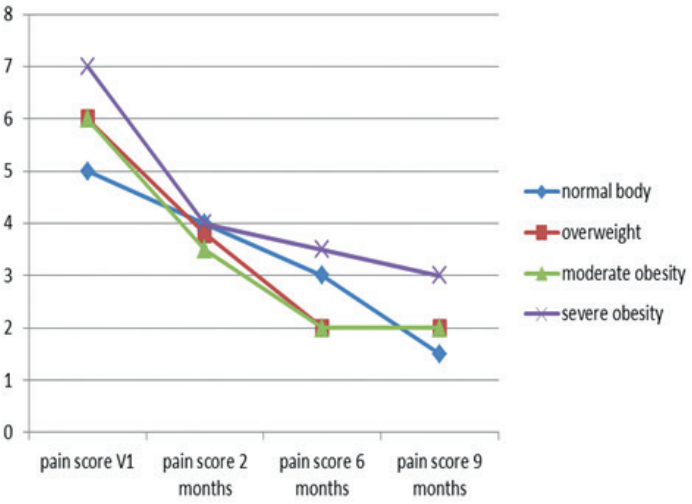
CLINICAL FINDINGS

Of the treated patients, 87.3% improved. There was a significant difference in the WOMAC pain scale at month 9 compared with day 0 (mean values 2.03 vs 5.93, respectively). The difference in the WOMAC pain scale was also significant between the first and the second injections and between the second and third injections.

There was no significant difference in pain scores between radiological grade II and III. The product was efficacious also in obese patients.

No significant side effects were reported.





CONCLUSION

This French multicentre, prospective, 9 month study in patients with knee OA, demonstrated that 3 injections PRP+HA (2 ml of PRP + 2 ml of non-cross-linked HA, Cellular Matrix) represent a new medical alternative to knee surgery in patients who do not respond to treatment with HA alone.

These results appear to be encouraging and require further studies to better confirm the best treatment regimen.

Session: CELLULAR MATRIX, PRP-HA SYNERGY AND INNOVATION IN TISSUE ENGINEERING – 23rd September 2014

Presentation: **Infiltrative therapy combined with PRP-HA in degenerative cartilage pathology: one-step technique**

Lecturer: Prof. Donato Rosa, Associate Professor Musculoskeletal Disease, University Federico II of Naples, Naples, ITA – Dr. Agnese D'Apice, Orthopaedic & Traumatologist, Napoli, ITA

INTRODUCTION

OA is a joint disease with chronic evolution characterized by degenerative lesions of articular cartilage. In the treatment of knee OA, the infiltrative "route" with Hyaluronic acid (HA) is widely used. HA is a natural polymer belonging to the family of glycosaminoglycans (GAGs), its viscoelasticity is crucial for the lubricating and shock absorber capacity of the synovial fluid. HA also exerts biological functions due to its interaction with CD44 receptors.

Autologous Platelet Rich Plasma (PRP) is derived from the patient's own blood blood and is characterized by high content of growth factors stored in the α-granules of the platelets and released after activation. Due to the presence of numerous growth factors (like IGF1, BMP7, TGF-ß, PDGF, FGF2, HGF), PRP guarantees a specific pro-regenerative stimulus and a modulation of the inflammatory processes. It has been shown that PRP is also able to stimulate endogenous HA production.

The aim of our study was to evaluate the efficacy of a new therapeutic procedure where PRP and HA are combined in a single step (Cellular Matrix- Regen Lab) thus permitting the injection of both at the same time.

METHODS

For this study, we recruited 11 patients with chronic degenerative cartilage disease (OA) of the knee. The inclusion criteria were as follows: presence of pain or swelling at the knee for at least 4 months, cartilage degeneration assessed by imaging (X-ray and / or MRI). Exclusion criteria were: presence of systemic disorders such as diabetes, rheumatoid arthritis, blood diseases (coagulopathy), severe cardiovascular disorders, infection, immunosuppression, patients receiving anticoagulant drugs, use of NSAIDs 5 days before blood collection, Hb ← 11, platelet counts ←150,000/mmc.

From each patient included in the study, 4 ml of peripheral blood was collected. PRP was obtained by centrifugation (5 min, 1500g RCF), using a special cell-separator tube, A-CP HA (Regen Lab). Then PRP was mixed with the HA (40mg; 1550KDa) by inverting the tube several times. The PRP-HA combination thus obtained was injected into the affected knee joint.

The patients received one intra-articular injection every 15 days for a total of 3 injections and were clinically assessed before treatment, at the end of the treatment cycle and after 3 and 6 months following the last infiltration.

For the clinical assessment, the WOMAC and KSS (Knee Society Score) scales were used.

CLINICAL FINDINGS

The results of our study showed that treatment with PRP-HA led to a significant improvement in the clinical and functional parameters of the knee joint and improved the quality of life of the patients. These benefits started at the end of treatment and persisted during follow-up at 3 and 6 months.

Patient Demographic Characteristics

Patient Characteristics	N = 11
Age, y	
Mean +/- SD	57.8 ± 10.9
Range	31-72
Gender	
Male *n (%)*	4 (36.3%)
Female *n (%)*	7 (63.6%)
Kellgren-Lawrence	
I *n (%)*	3 (27.3%)
II *n (%)*	3 (27.3%)
III *n (%)*	4 (36.3%)
IV *n (%)*	1 (9.1%)
Previous procedures	
HA n (%)	8 (72.7%)
Surgical procedures n (%)	2 (18.2%)

SD, standard deviation

Scale (normal range)	T0 (Normal range)	T1 (3 months)	T2 (6 months)
WOMAC (0-9)	47.5	14.9	22.5
SYMTOMS* (0-25)	7.6	19.9	12.3
PATIENT SATISFACTION (KSS)* (0-40)	16.2	27.55	20.3
PATIENT EXPECTATIONS (KSS)* (0-15)	12.2	14,44	13.2
FUNCTIONAL ACTIVITIES (KSS)* (0-100)	38.9	74	64.7

*KSS: Knee Society Score

CONCLUSION

Based on these initial data, we consider Cellular Matrix to be a viable treatment option for degenerative joint diseases. Further studies are needed to confirm these results.

Session: CELLULAR MATRIX, PRP-HA SYNERGY AND INNOVATION IN TISSUE ENGINEERING – 23rd September 2014

Presentation: **Effectiveness of a compound consisting of platelet-rich plasma (PRP) and hyaluronic acid (HA) in the treatment of mild-to-moderate knee osteoarthritis: preliminary results**

Lecturer: Dr. Sandra Verna, Hematology & Transfusion Medicine Department, SS Annunziata Hospital, Chieti, ITA

INTRODUCTION

The knowledge of the pathophysiological mechanisms involved in articular healing processes has recently allowed the development of new bio-active treatments able to improve symptoms and function in patients suffering from knee osteoarthritis. In particular, intra-articular injections of either PRP or HA have demonstrated significant clinical effectiveness in many published studies, with a very good safety profile.

Basic research supports the hypothesis that PRP and HA may be used advantageously in combination. From the biological point of view, PRP and HA can elicit a synergistic therapeutic effect. However, no study has investigated the therapeutic efficacy of such an association.

The aim of our study was to compare the results of the treatment of knee OA with an association of PRP and HA (Cellular Matrix), in comparison with PRP alone and HA alone.

METHODS

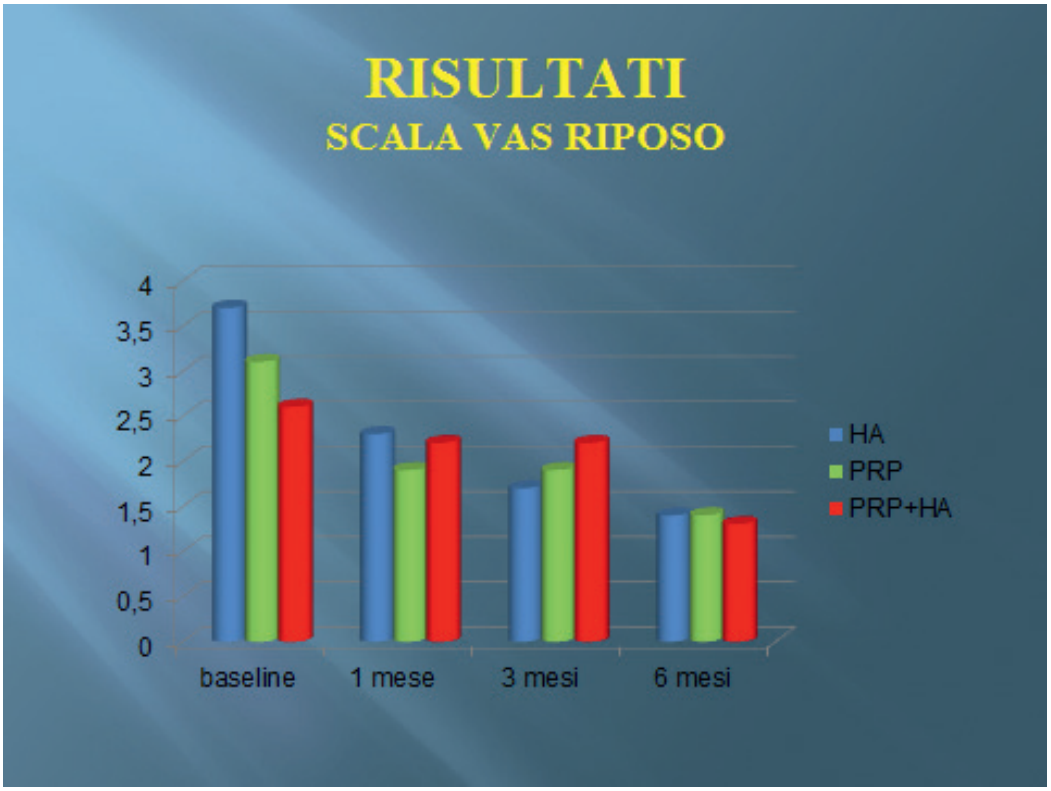
In this study, we evaluated 120 patients (37 males, 83 females, mean age 58.3) with mild-moderate knee OA (KL grade I-III). Of these, 40 were treated with PRP (4 ml), 40 with HA (LMW 50 mg / 2 ml), and 40 with HA+ PRP (Cellular Matrix BCT-Ha or ACP-HA, Regn Lab). All patients underwent a cycle of 3 intra-articular injections, once a week for 3 weeks and were invited to follow a specific rehabilitation program.

Clinical and functional assessments (VAS pain, KOOS) were performed at baseline and at the follow up visits at 1, 3, 6 month after the end of the treatment. Safety was also evaluated.

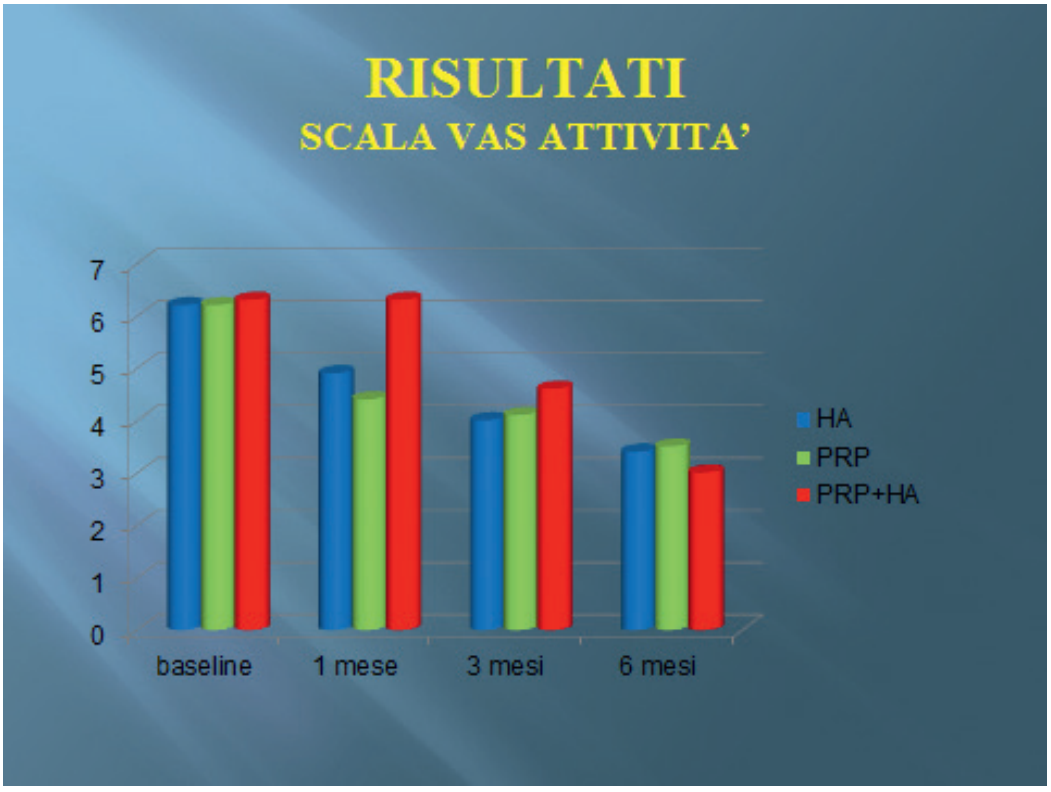
CLINICAL FINDINGS

After 1, 3 and 6 months, all patients reported a significant improvement in symptoms and function. In particular, a reduction of pain (VAS) and a decrease in analgesic consumption was observed already after 1 month in all treated patients. No statistically significant difference between groups were observed, although a greater improvement in KOOS scale was observed for the association PRP + HA at 1, 3 and 6 months.

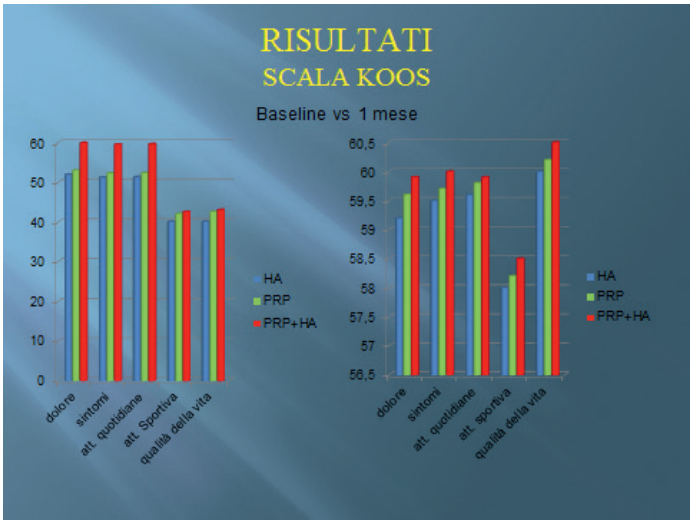
With respect to safety, a limited number of local side effects occurred: 2/3 events in both the PRP and PRP+HA groups.



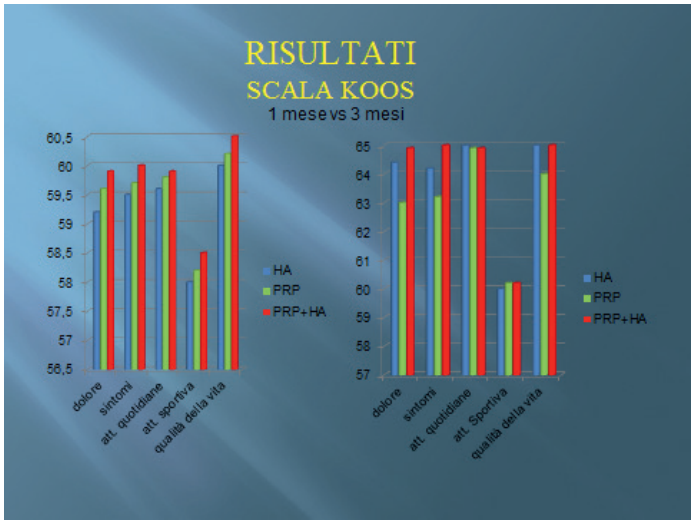
VAS pain at rest
Data of all treated groups: HA, PRP, PRP+HA
at baseline and at 1, 3, 6 months



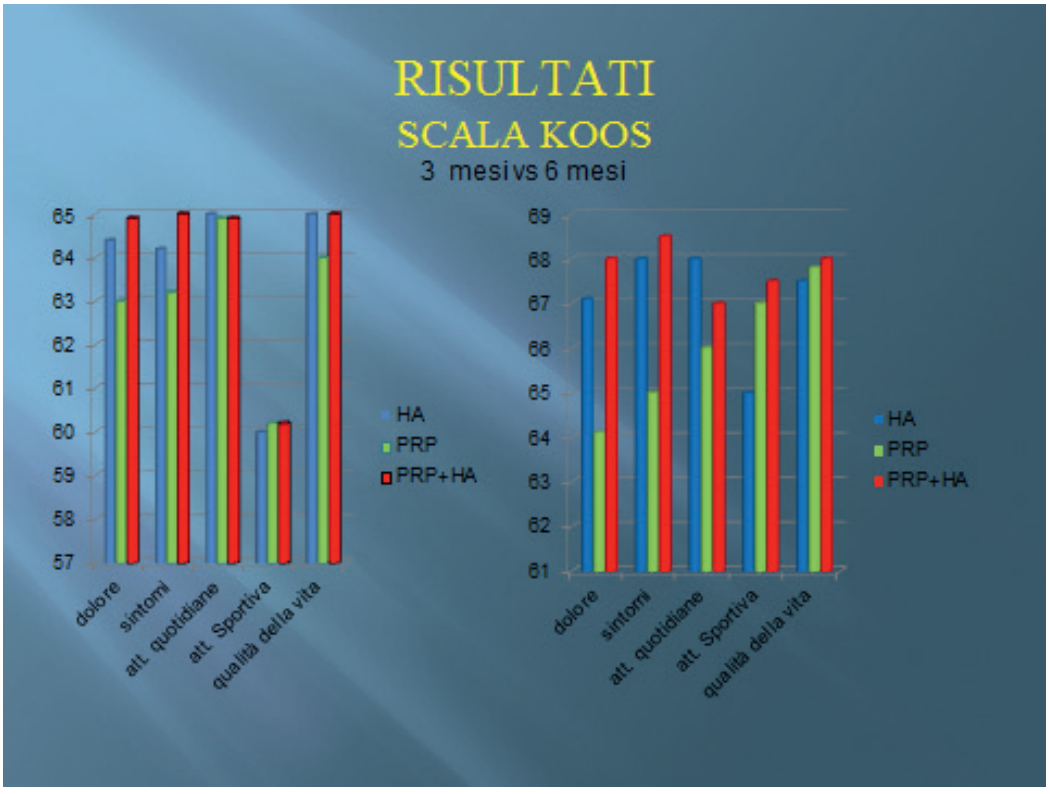
VAS pain on movement
Data of all treated groups: HA, PRP, PRP+HA
at baseline and at 1, 3, 6 months



KOOS scale
Data of all treated groups: HA, PRP, PRP+HA
at baseline and at 1 months



KOOS scale
Data of all treated groups: HA, PRP, PRP+HA
at 1 months vs 3 months



KOOS scale
Data of all treated groups: HA, PRP, PRP+HA
at 3 months vs 6 months

CONCLUSION

The association PRP+HA (Cellular Matrix) was shown to be an efficacious treatment in knee OA.

The positive results are due to the ability of the product to act in a combined manner on both the biomechanical and biological aspects of the healing process.

SPORTS MEDI-CINE

SPORTS MEDICINE
OSTEOARTHRITIS & CARTILAGE
-
PRP & BONE MARROW CELLS

Session: ORTHOPAEDICS AND CARDIAC SURGERY – 23rd September 2013

Presentation: **Treatment of chondral lesions of the knee with bone marrow cells and PRP seeded into a hyaluronic acid scaffold. Clinical experience of A.O S. Camillo Forlanini**

Lecturer: Dr. Rosa Leone, Immunohematology & Transfusion Medicine Department, A.O. S. Camillo Forlanini, Rome ITA

INTRODUCTION

Articular cartilage, or hyaline cartilage, has a limited regenerative capacity. Cartilaginous reparative processes, mostly mesenchymal stem cell (MSC) migration from the underlying bone marrow, often result in new fibrocartilage which is structurally less resistant than native cartilage. As a consequence, cartilage lesions tend to become larger, more symptomatic and involve the whole joint and eventually to lead to osteoarthritis. Up to now, surgical options have comprised symptomatic approaches (arthroscopic lavage and debridement), reparative approaches (microfractures and osteo-chondral grafts) and regenerative approaches (autologous chondrocytes transplantation (ACT)). This latter approach, despite good clinical outcomes, is not viable in clinical practice because of high costs, extended timeframe for laboratory cell culture and the need for two surgical interventions.

Recent advances in tissue engineering allow orthopaedic surgeons to take advantage of an innovative and minimally invasive regenerative approach in ONE STEP. This consists of the extemporaneous implantation of medullary concentrate and PRP, both autologously derived and prepared during a single operatory session, seeded onto three-dimensional scaffolds. The final aim is to generate a reparative tissue which has the same functional and mechanical properties as native hyaline cartilage, thereby avoiding progression to osteoarthritis.

We report here the clinical experience on 8 patients with the above ONE STEP regenerative approach at San Camillo Forlanini Hospital (Rome).

METHODS

Eight patients (3 women, 5 men, mean age 31.9 years – range 15-50 years), suffering from knee chondral lesions of III and IV grade (Outerbridge), were enrolled in this study. These patients underwent ONE STEP surgery (medullary concentrate + PRP + scaffold).

Location of lesions: medial condyle (4 patients), lateral condyle (1 patient), trochlea (2 patients) and patella (1 patient).

Dimension of lesions: 3 patients = 1-2 cm2, 3 patients = 2-3 cm2, 2 patients → 3 cm2.

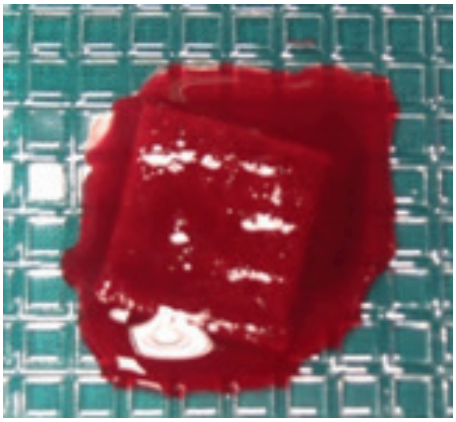
Exclusion criteria: osteoarthritis, malignant bone tumors, ACL-PCL lesions, patellar instability, kissing lesions and oncohematologic pathologies.

Preparations of autologous products:

MEDULLARY CONCENTRATE: 7 ml of medullary concentrate were obtained from 60 ml of medullary blood harvested from the posterior iliac crest through centrifugation.

PRP and THROMBIN: 2 ml of autologous hyper-concentrated PRP and 2 ml of autologous thrombin (respectively RegenLab BCT and RegenLab ATS technology) were obtained from 16 ml of peripheral blood through centrifugation.

Once the autologous cell-concentrates were prepared, they were mixed and loaded on a hyaluronic acid membrane (2 cm x 2 cm) as scaffold:

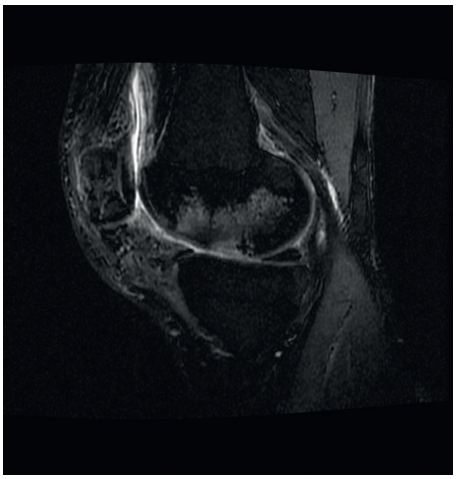


- 5 ml of autologous medullary concentrate
- 1 ml of autologous hyper-concentrated PRP
- 1 ml of autologous thrombin
- 1 ml of Calcium Gluconate

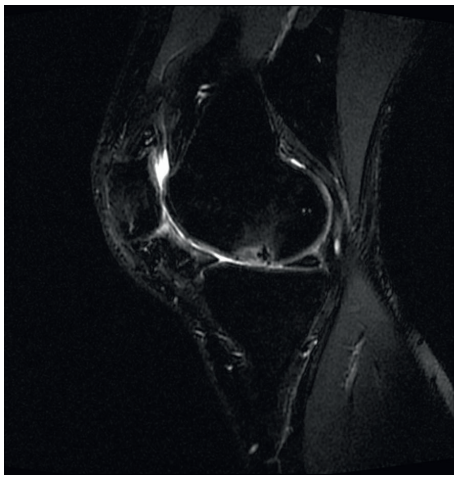
The membrane was implanted arthroscopically in order to completely cover the area of the cartilage lesion. Each patient was followed-up at 3, 6 and 12 months. Post-surgery clinical evaluations were carried out with NMR and subjective clinical evaluation of the patient (IKDC index 2000).

CLINICAL RESULTS

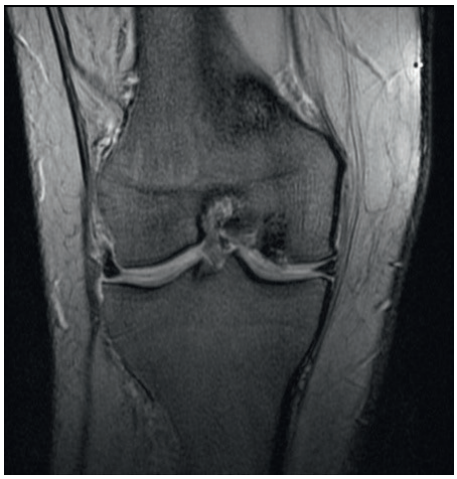
1. NMR ANALYSIS



3 months

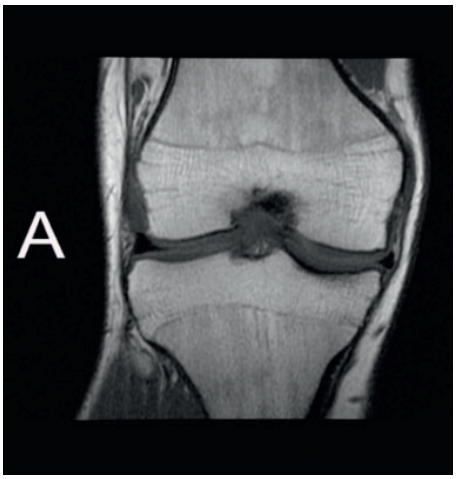


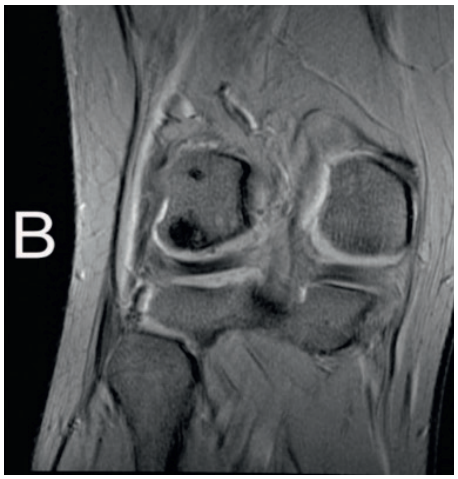
6 months

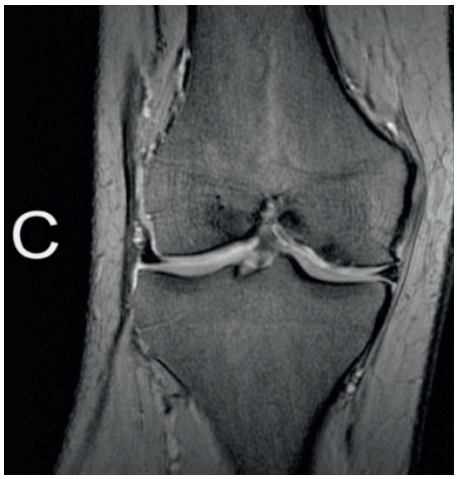


12 months

T = 3 months → considerable edema at subchondral bone
T = 6 months → substantial edema reduction at subchondral bone
T = 12 months → edema disappearance, integral covering of chondral lesion and reestablishment of articular surface.







24 months

T = 24 months → appreciable slight remodeling of subchondral bone, which likely indicates cartilage is still in remodeling phase.

2. SUBJECTIVE CLINICAL EVALUATION: IKDC

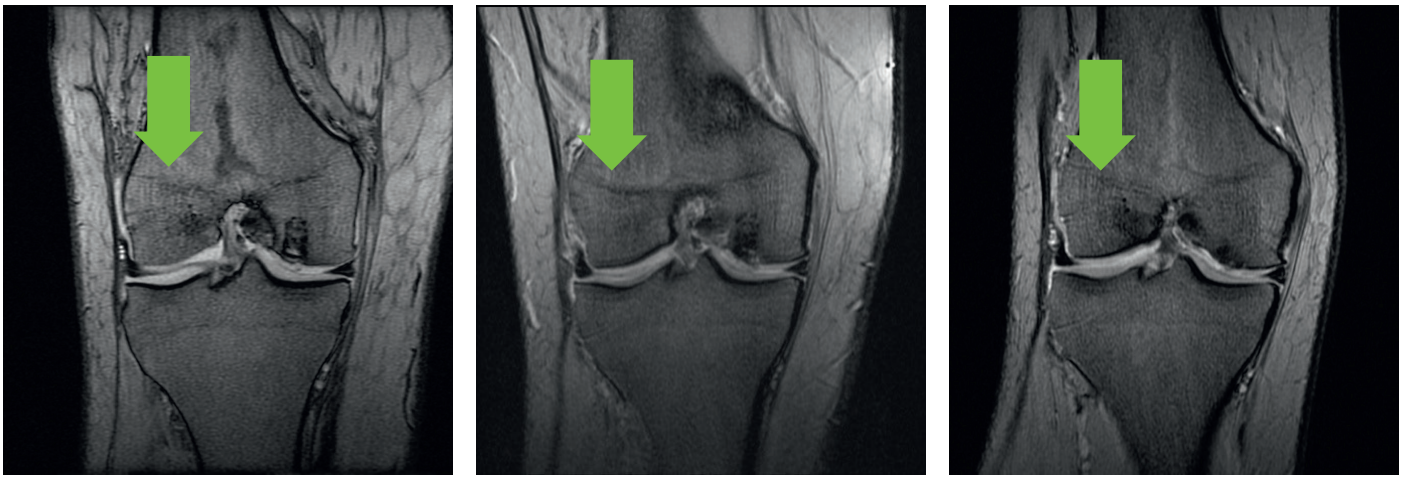
(EXCELLENT: 75 – 100 pt; GOOD 55 – 75 pt; MODERATE: 35 – 55 pt; POOR: 18 – 35 pt)

IKDC PRE-SURGERY:	mean 32.5 pt (POOR)
IKDC 6 MONTHS POST-SURGERY:	mean 78.5 pt (EXCELLENT)
IKDC 12 MONTHS POST-SURGERY:	mean 81.6 pt (EXCELLENT)

3. COMPARATIVE EVALUATION: RESULTS OF THIS STUDY vs. RESULTS OBTAINED WITH ACT

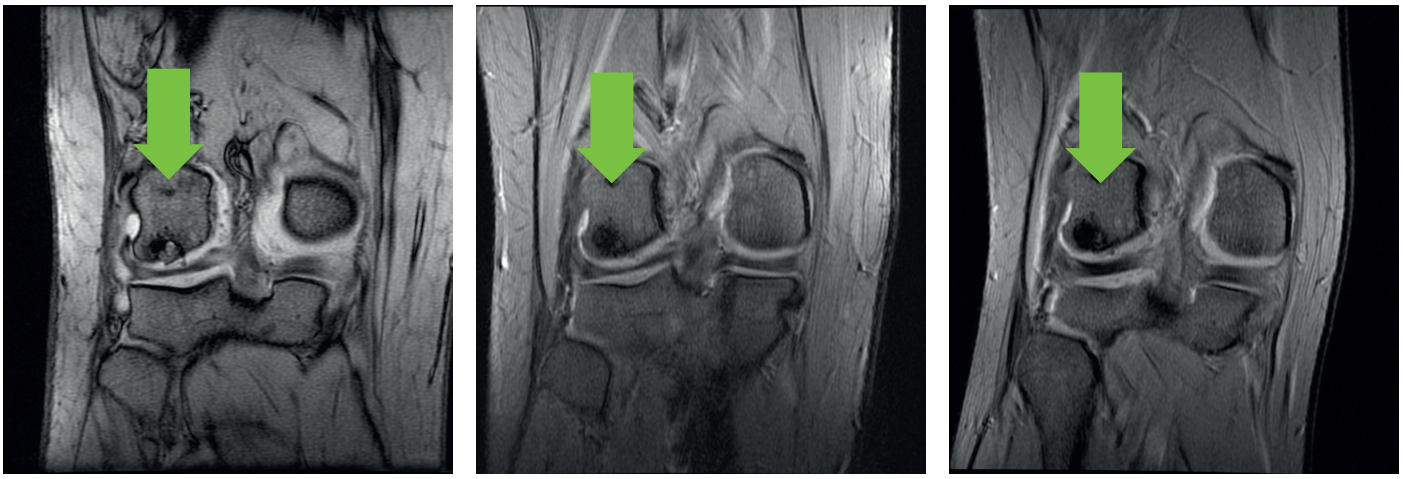
(autologous chondrocytes transplantation, retrospective evaluation of ACT data)

3.1 NMR EVALUATION



3 months 12 months 24 months

(Patient treated with bone marrow + PRP + scaffold)



3 months 12 months 24 months

(Patient treated with autologous chondrocytes transplantation)

3.2 IKDC EVALUATION

IKDC for patients treated with bone marrow + PRP + scaffold

IKDC PRE-SURGERY:	mean 32.5 pt (POOR)
IKDC 6 MONTHS POST-SURGERY:	mean 78.5 pt (EXCELLENT)
IKDC 12 MONTHS POST-SURGERY:	mean 81.6 pt (EXCELLENT)

IKDC for patients treated with autologous chondrocytes transplantation

IKDC PRE-SURGERY:	mean 32.1 pt (POOR)
IKDC 6 MONTHS POST-SURGERY:	mean 80.2 pt (EXCELLENT)
IKDC 12 MONTHS POST-SURGERY:	mean 80.1 pt (EXCELLENT)

CONCLUSIONS

For all patients in this study clinical observations showed a recovery of the chondral lining (NMR) and improvement of joint functionality (IKDC index).

Comparative effectiveness analysis between the two different regenerative approaches described above (bone marrow vs. ACT), showed comparable scores with the IKDC index, whereas NMR images at T = 24 months showed better results for the bone marrow approach, supporting this new ONE STEP regenerative procedure.

TENDINOPATHY

TEN-
DINO-
PATHY

Session: SPORTS MEDICINE & INFILTRATIONS & MUSCULOSKELETAL MEDICINE – 23rd September 2014

Presentation: **Study of reathletisation of sportsmen affected by tendinopathy after a treatment with PRP**

Lecturer: Dr. Jean-Marc Grison, Sports Medicine, Iris Sud Hospital, Bruxelles, BEL

INTRODUCTION

Treatment of musculoskeletal pathologies and, in particular, tendon injuries with PRP is increasing.

We performed a study aimed aimed at evaluating the effects of PRP in the treatment of Achilles tendinopathy and epicondylagias.

METHODS

We evaluated a group of 33 athletes practicing regular physical activity, affected by unilateral Achilles tendinopathy (12) or unilateral epicondylagias (21).

These patients were treated with PRP obtained using REGENLAB Classic PRP kit. All patients received 1 injection, followed by a second injection if deemed necessary and were followed-up for an average of 13 months.

Patients were interviewed regarding pain and limitation using a standardized questionnaire and underwent clinical testing to evalate the following parameters in the injured arm/leg: isometric force (amplitude and time of maintenance), flexion and extension of the wrist for epicondylagias or dorsiflexion of the ankle for tendinopathies. Clinical tests were also performed on the patients' healthy limbs

The results of clinical tests of the injured limb were compared to those of the healthy one by STUDENT t TEST. Pain and mobility were evaluated by Spearman's rank correlation coefficient. VAS (Visual analogue scale) and Blazin Classification were used to assess pain before and after PRP injection. Time to return to sport was evaluated by analysis of variance (ANOVA). Time to return to training with or without eccentric exercise was analysed by Student's t test.

A total of 33 patients were submitted to eccentric exercises before PRP treatment, and 20/33 underwent the same test following PRP treatment.

After PRP injection, patients were instructed to rest, use Paracetamol where necessary, not to play sports for four weeks and to then gradually return to physical activity.

RESULTS

Pain frequency in activities of daily life before and after PRP injection

Tableau 6 : fréquence de la douleur dans la vie de tous les jours (annexe, questionnaire, p.83)

Avant l'injection (N=33)					
Pér. uniq. doul. lim. ds tps[1]	d. ct, int. égale[2]	d. ct, int. variable[3]	Ep. doul. r. r.[4]	Ep. doul. r. ir.[5]	Acc. de doul. soud. et brefs[6]
0	4	11	9	6	3
Après l'injection (N=33)					
Pér. uniq. doul. lim. ds tps	d. ct, int. égale	d. ct, int. variable	Ep. doul. r. r.	Ep. doul. r. ir.	Acc. de doul. soud. et brefs	Plus de douleur
8	2	2	3	2	1	15

A significative pain reduction during daily activities and exercise was seen after PRP injection

Pain during exercise before and after PRP injection (Blazin classification)

Tableau 7 : classification de Blazin (Paclet et coll., 2001) avant et après l'injection (annexe, questionnaire, p.83)

Avant l'injection (N=33)				
Stade 1	Stade 2	Stade 3a)	Stade 3b)	
1	5	7	19	
Après l'injection (N=32)				
Stade 1	Stade 2	Stade 3a)	Stade 3b)	Aucun stade
5	3	5	0	19

Le tableau ci-dessous compare la douleur lors de l'effort avant et après l'injection de PRP (tableau 7).

Pain during sleep and in other situations, before and after PRP injection

Tableau 23 : comparaison de la douleur dans diverses situations avant l'injection de PRP et après

A. Epicondylalgies		
Test de Wilcoxon échantillons appariés	**N**	**p-valeur**
EVA*[9] : dans la vie de tous les jours	19	**0,0002*** **
EVA : dans la vie professionnelle	18	**0,0003*** **
EVA : pendant le sommeil	19	**0,0039** **
EVA : pendant l'échauffement préalable à l'activité physique	19	**0,0005*** **
EVA : pendant l'activité physique	19	**0,0003*** **
EVA : pendant après l'activité physique	19	**0,0005*** **

B. Tendinopathies achiléennes		
Test de Wilcoxon échantillons appariés	**N**	**p-valeur**
EVA*[10] : dans la vie de tous les jours	12	**0,002** **
EVA : dans la vie professionnelle	11	**0,003** **
EVA : pendant le sommeil	12	**0,005** **
EVA : pendant l'échauffement préalable à l'activité physique	11	**0,003** **
EVA : pendant l'activité physique	11	**0,005** **
EVA : pendant après l'activité physique	11	**0,005** **

A significant pain reduction during sleep and in the other daily activities was observed after PRP injection

Tableau 24 : incidence de la douleur sur la mobilité et l'endurance musculaire à deux moments différents

A. Epicondylalgies				
Test Anova		**Flexion active**	**Flexion passive**	**Maintien en isométrique**
p-valeur	**Au moment du rendez-vous**	0.06	0.33	0.20
	Lors du dernier contact avec les patients	0.13	0.49	0.10

B. Tendinopathies achilléennes					
Test Anova		**Flexion dorsale c/mur**	**Flexion dorsale active**	**Flexion dorsale passive**	**Maintien unipodal**
p-valeur	**Au moment du rendez-vous**	0.96	0.77	0.77	0.50
	Lors du dernier contact avec les patients	0.70	0.08	**0.02***	0.65

Regarding pain during exercize, (Blazin's test) we observed a highly significant reduction in patients with epicondylagias (improvement in 18/21 (85.7%) patients, with no change in the remaining 3/21 (14.3%). For patients with Achilles Tendinopathy, we observed an improvements in 9/11 (81.5%) patients and no change in 2/21 (9.5%).

Effect of eccentric exercises before PRP injection on mobility and isometric force

Tableau 28 : effet de la pratique d'exercices excentriques pré-injection sur différentes variables

A. Epicondylalgies	
Test de Student	**P-valeur**
Délai de reprise de l'entraînement	0,06
Flexion active, côté sain	0,59
Flexion active, côté lésé	0,13
Flexion passive, côté sain	0,76
Flexion passive, côté lésé	0,48
Maintien isométrique, côté sain	0,21
Maintien isométrique, côté lésé	0,90
B. Tendinopathies achilléennes	**P-valeur**
Délai de reprise de l'entraînement	0,96
Flexion dorsale contre un mur, côté sain	0,62
Flexion dorsale contre un mur, côté lésé	0,20
Flexion dorsale active, côté sain	0,61
Flexion dorsale active, côté lésé	1,00
Flexion dorsale passive, côté sain	0,32
Flexion dorsale passive, côté lésé	0,57
Temps du maintien sur pointe de pied, côté sain	0,42
Temps du maintien sur pointe de pied, côté sain	0,25

Effect of eccentric exercises after PRP injection on mobility and isometric force

Tableau 29 : effet de la pratique d'exercices excentriques post-injection sur différentes variables

A. Epicondylalgies	
Test de Student	**P-valeur**
Délai de reprise de l'entraînement	0,07
Flexion active, côté sain	0,53
Flexion active, côté lésé	0,81
Flexion passive, côté sain	0,75
Flexion passive, côté lésé	**0,047***
Maintien isométrique, côté sain	0,87
Maintien isométrique, côté lésé	0,43
B. Tendinopathies achilléennes	**P-valeur**
Délai de reprise de l'entraînement	0,51
Flexion dorsale contre un mur, côté sain	0,07
Flexion dorsale contre un mur, côté lésé	0,72
Flexion dorsale active, côté sain	0,16
Flexion dorsale active, côté lésé	0,54
Flexion dorsale passive, côté sain	**0,04***
Flexion dorsale passive, côté lésé	0,13
Temps du maintien sur pointe de pied, côté sain	0,91
Temps du maintien sur pointe de pied, côté sain	0,75

CONCLUSION

In this group of athletes, the average time to return to sport activities after PRP injection was 17 weeks, with a significant reduction in pain and a marked functional improvement in most patients.

We also observed that pretreatment with eccentric exercises influences pain perception and that an eccentric rehabilitation program post-PRP injection tended to delay the return to training in case of epicondylagias.

The peak of response to PRP treatment was observed 3 months after treatment.

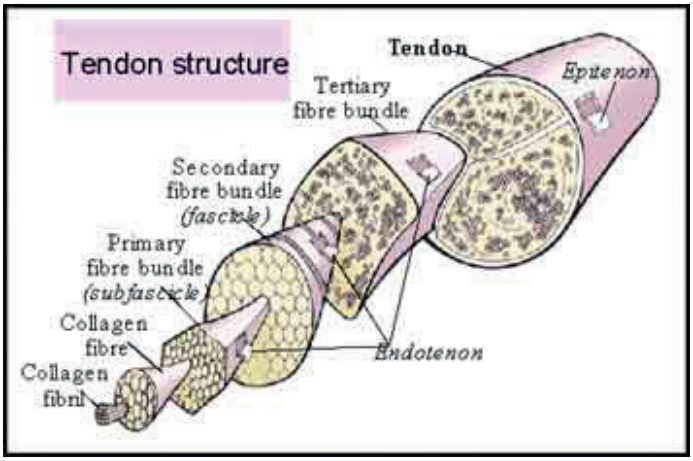
Session: SPORTS MEDICINE & INFILTRATIONS & MUSCULOSKELETAL MEDICINE – 23rd September 2013

Presentation: **22 Elbow tendinitis treated with platelet-rich plasma after failure with the usual treatment**

Lecturer: Dr. Jacques Le Coz, Sports Doctor & Mesotherapy Practitioner, Paris, FRA

INTRODUCTION

Tendon is defined as a formation of connective fibrous nature, which permits the attachment of muscles to the ends of bone or to the dermis, allowing the contractile apparatus to carry out its functions. In the case of severe tendon injury, involving a total or partial tendon rupture, there is loss of the movement generated by the affected muscle. Collagen (predominantly type I) and elastin are the major components of tendons. Collagen and elastin are embedded in a matrix of proteoglycans and water, where the collagen is 65-75% of the dry mass of the tendon, while the elastin accounts for only 2%. The collagen fibers have a different spatial arrangement in the various structures that compose a tendon: in the epitenon they have a mainly longitudinal arrangement, while in the peritenon they become oblique and transverse and finally in the endotenon they have a complex three-dimensional structure. The complexity of the structure of a tendon is very important because its basic function is to transmit the force created by the muscle to the bone to make possible joint movement. This is determined by complex macro-and microstructure of tendons and tendon fibers.



The tendon, like many other tissues of our body, can undergo inflammatory processes of various natures. This inflammation can be the result of exposure for long periods to loads and stresses which the tendon isn't able to withstand. Tendonitis is an inflammatory process involving one or more tendons present in the human body. This inflammation is commonly caused by the repetition of chronic stresses that, in the long run, alter the normal structure of the fibrils. Epicondylitis is an inflammation of the tendons that affects the elbow, in particular the lateral epicondyle. The aim of the clinical investigation described here was to assess the effectiveness of the use of injections of autologous PRP (Platelet Rich Plasma) in the treatment of tendonitis and epicondylitis.

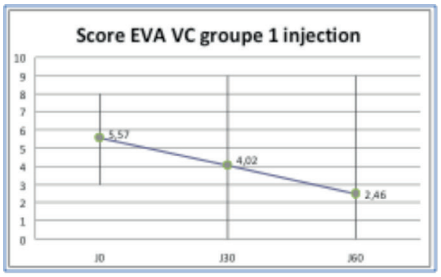
METHODS

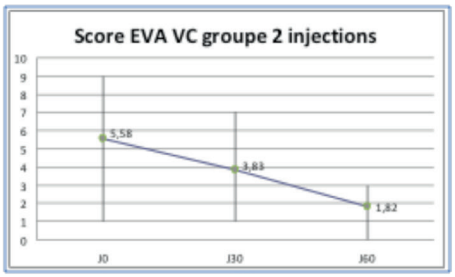
During this study (April 2009/ February 2011), the efficacy of PRP was investigated in 22 patients (19 epicondylitis and 3 tendonitis with an average duration of 7 months). Six of the patients practiced professional sport, fourteen of them played sport at amateur level and the remaining two were also considered active. The median age of the patients was 48 years and each of them had failed two or more conventional treatments.

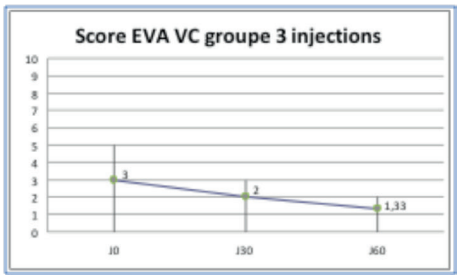
All patients received at least one injection of PRP (2 ml in the tendon with a 6 mm/27g needle using the point-for-point technique). Twelve patients received a second injection of PRP and 3 patients received a third injection of PRP. The PRP was prepared using a RegenLab®Medical Device.

CLINICAL RESULTS

The results of the treatment were evaluated by a VAS pain scale ("EVA" in graphs below), in which 0 is absence of pain and 10 is maximum pain, at day 0, day, 30 and day 60.

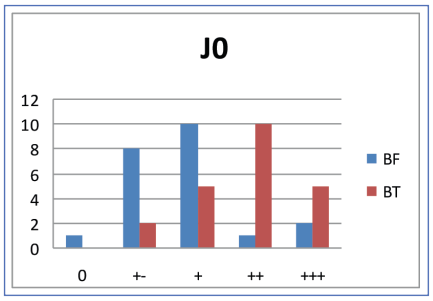


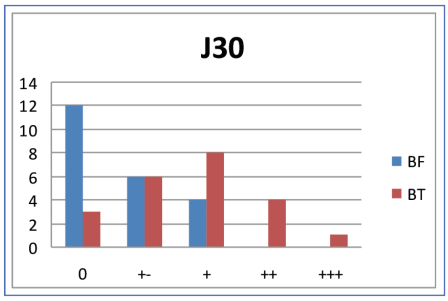


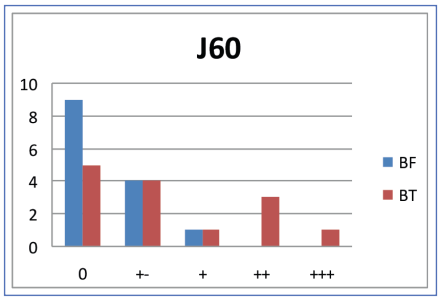


In patients with epicondylitis radial tests, BF (flexed arm) and BT (tense arm), were also performed at the same time-points.

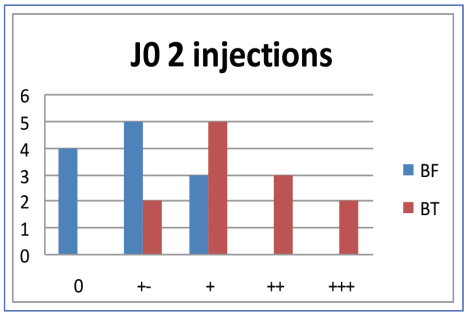
BF and BT after first injection

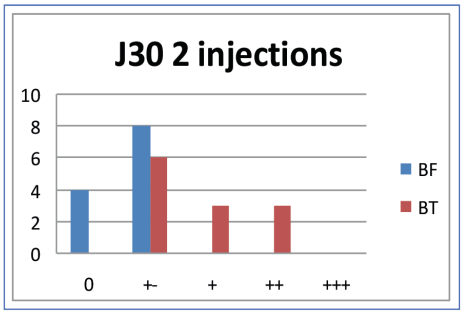


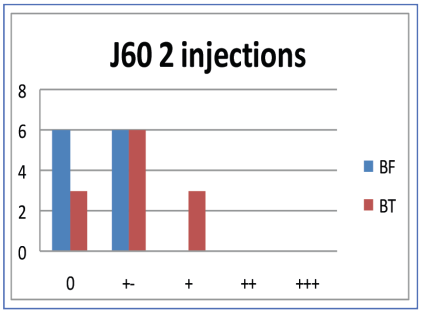




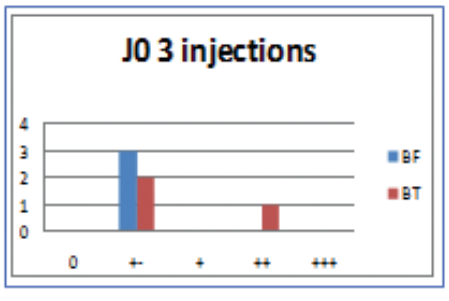
BF and BT after second injection

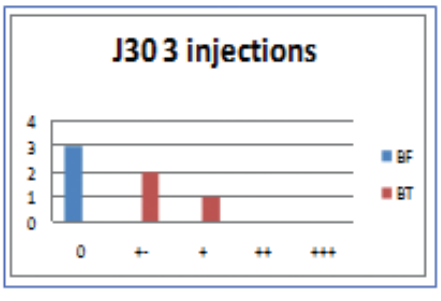


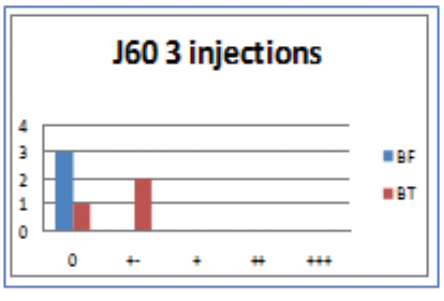




BF and BT after third injection







The graphs above show a decrease of pain following treatment for the BF and BT tests.

CONCLUSION

The injection of PRP to treat epicondylitis and tendonitis does not require surgical access. The technique developed isn't invasive and is easy to perform. In this study, 86% of the treated patients obtained good results in terms of pain relief and functional recovery. The results persisted over time. The only adverse effect, pain following injection, was correlated to the injection and it disappeared in a short time.

Session: PRP, THE FOUNDATION OF CELL THERAPY – 22nd September 2014

Presentation: **Is local injections of PRP in tendinopathy able to effect systemic growth factor concentration?**

Lecturer: Prof. Antonio Pavan, Full Professor in Clinical Pathology, Transfusion Center Sant'Andrea Hospital University of Rome La Sapienza, Rome, ITA

INTRODUCTION

Platelet-rich plasma (PRP) therapy has the potential to accelerate muscle and tendon healing, allowing injured athletes to return to sport earlier. However, PRP and many of the growth factors it contains were added to the World Anti - Doping Agency (WADA) Prohibited List in 2010 due to concerns that it may increase levels of ergogenic growth factors. On subsequent review, in view of the lack of evidence to support this decision, PRP was removed from the Prohibited List in 2011.
Although the contents of the PRP preparations themselves have been studied, the systemic effects and potential doping implications of PRP therapy are largely unexplored.

To understand the short/medium term systemic effects of local PRP injections, we measured the plasma concentrations of IGF-I, IGF binding protein type 3 (IGFBP-3), FGF, VEGF, and PDGF before and after PRP injection in tendons.

METHODS

From January to April 2014, 20 patients (17 male, 3 female) with chronic tendon injuries were enrolled at the Physical Medicine and Rehabilitation Unit in Sant'Andrea Hospital, Roma. Chronic tendon injuries in the twenty enrolled patients were as follows: 9 Achilles tendon injury, 5 epicondylitis, 2 epitroclea injury, 2 patellas tendinopathy, 1 trochanter tendon injury and 1 Plantar fasciitis.

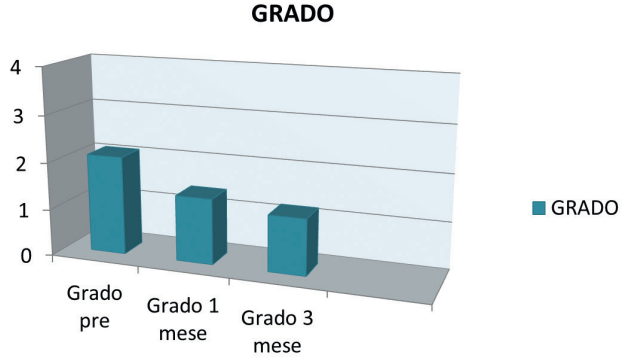
The primary purpose of the study was to analyze the systemic effects of PRP injection on serum PDGF, VEGF, FGF, IGFBP-3, IGF-1. The second was to compare effectiveness with the systemic leels of one or more of these bioactive molecules (GFs) and identify possible correlations.

The treatment protocol consisted of 2 injections of autologous PRP (prepared with RegenKit) over 2 weeks. The designated injection location was recorded before injection. The injection technique involved a single skin portal using a 22-g needle and then injection of multiple small aliquots into the tendinous lesion with Color Doppler guidance. No local anesthesia was applied.

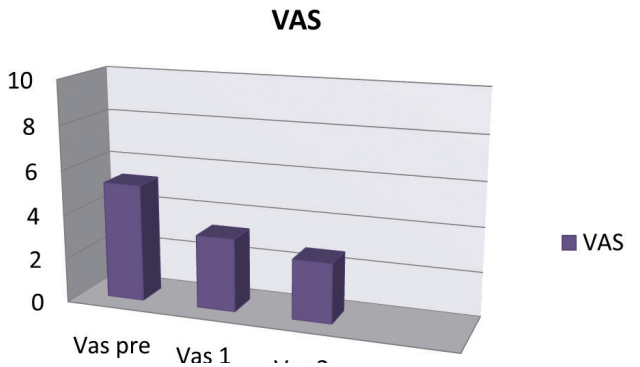
Systemic growth factor evaluation was performed at four observation times: before treatment (T0), 24 hrs after the first infiltration (T1), 6 days after the first infiltration (T2), 24 hour after the second infiltration (T3) and 6 days after the second infiltration (T4). Clinical improvements were evaluated using clinical grade status and response to treatment (range 0-4) plus VAS and VISA scale.

CLINICAL FINDINGS

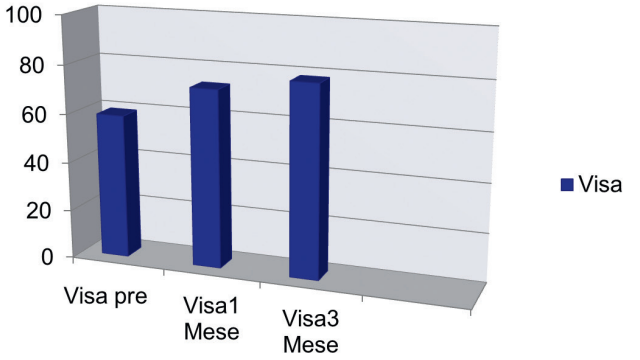
CLINICAL OUTCOME ASSESSMENTS:



Grado PRE	Grado 1 month	Grado 3 months
2,1 ± 0,39	1,4 ± 0,76 P<0,008	1,2 ± 0,77

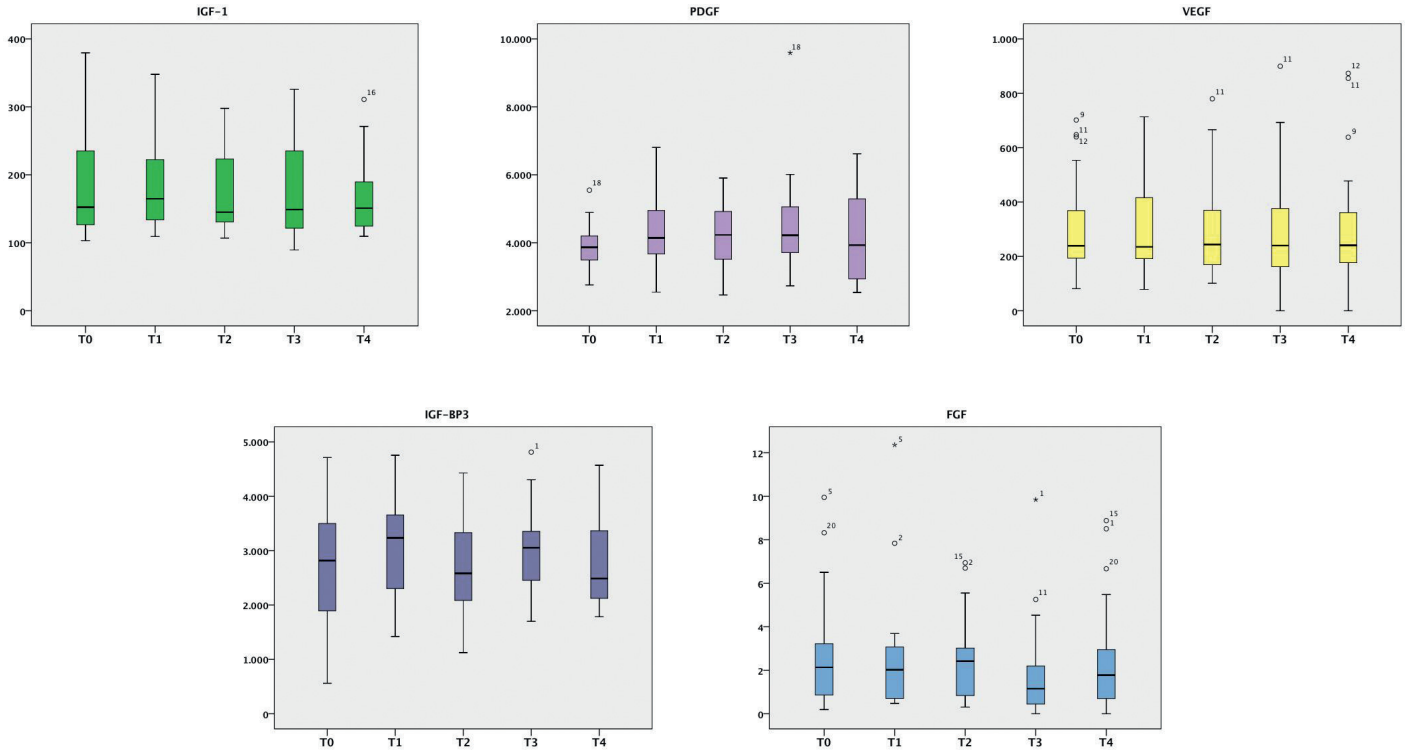


VAS PRE T0	VAS 1 month T1	VAS 3 months T2
5,3 ± 1,85	3,3 ± 1,63 P<0,001	2,7 ± 1,88



Visa PRE	Visa 1 month	Visa 3 months
59,2 ± 18,52	72,9 ± 16,54 P<0,005	78,3 ± 17,39 P<0,001

GROWTH FACTORs EVALUATION:



CONCLUSION

The results of this study show a wide variation in systemic growth factor concentrations and no significant correlation between PRP injection and changes in systemic growth factor concentration. However, 4 patients showed a clear increase in systemic FGF levels after PRP injection. These preliminary observations, in particular the variations in systemic FGF levels, are partially in agreement with the report of Wasterlain et al. 2013. Further clinical studies should include a control group, considering age, gender, type of tendon injury, etc. It would also be useful to measure additional bioactive molecules, such as TGF-β, IL-1 and IL-6.

BIOBRIDGE FOUNDATION

regenlab

Session: SPORTS MEDICINE & INFILTRATIONS & MUSCULOSKELETAL MEDICINE – 23rd September 2013

Presentation: **Treatment of tendinopathies using PRP under ultrasonic guidance**

Lecturer: Prof. Philippe Peetrons, Iris Sud Hospital, Bruxelles, BEL – Dr. Jean-Marc Grison, Sports Medicine, Iris Sud Hospital, Bruxelles, BEL

INTRODUCTION

Tendinopathy is a degenerative disease of the tendon with fibroangioblastic replacement of the tendinous fibres and is not an inflammatory disease, although it is often erroneously referred to as tendinitis.

A number of preparations have been used in the treatment of tendinopathies by intratendinous and peritendinous injection. These include steroids, autologous blood, hyerosmotic dextrose, vascular sclerotizing agent, botulinic toxin, mesotherapy and PRP. Steroid injection is still widely used and is administered preferably peritendinously as it may alter the tendon and lead to a tendon tear. For this reason, we consider the use of steroids in sports medicine as a contra-indication. Steroids can provide good results in the short term (3 months) but not in the intermediate or long term.

Prolotherapy, sclerosing agents, autologous blood and PRP all show good results for lateral epicondylitis, compared with no intervention or placebo. Prolotherapy and sclerosing agent show good effects on pain but do not treat the cause of tendinopathy and, in fact, they tend to reduce vascularization. On the other hand, tendon needling and PRP injections tend to enhance vascularization and, therefore, positively impact on tendon healing. PRP appears particularly suited to treating tendinopathy due to the degenerative nature of the disease.

Tendon healing occurs in three continuous phases: the inflammatory peritendinous phase with hypervascularization and pain which lasts around 3-7 days and during which steroid can have short-term activity. This is followed by cellular and collagen reconstruction which needs vascularization and growth factors and lasts around 1- 12 weeks and during which PRP has the potential to act. The final phase is tendon reformation and total healing which can take from 6 – 18 months. The objective of using regenerative treatment, such as PRP, is to reduce the total healing time.

Vascularization plays a key role in tendon healing as without vascularization, there will be no reformation of tendon fibers. There is some evidence for a link between vascularization and pain but this has yet to be conclusively demonstrated. There exists, therefore, a strong rationale for the use of PRP in the treatment of tendinopathies and in particular those cases without response to rehabilitation treatment, in partial ruptures and in insertion tendinopathies (CET, CFT in the elbow, jumper's knee). PRP is also indicated for ligamentous lesions such as MCL in the knee and for muscle injection where it can potentially replace steroid injections, provide an alternative to surgery and replaces oral NSAIDs which are not effective because of the degenerative nature of the lesions in the tendons.

To achieve best results, we believe that PRP should be administered by intratendinous injection, near vessels, with continuous ultrasound guidance.

METHODS

In this paper we describe a clinical study on the treatment of tendinopathy using a single injection of PRP, prepared with Regen Kit, with ultrasound guidance. This was a prospective, non-randomized study which ran from March 2010 – March 2012 and involved 68 patients. Patients were followed-up at 3 months (18 patients) and 6 months (50 patients) following PRP injection. Response to treatment was evaluated using a Visual Analogic Scales, with grading from 0 (no pain) to 10 (unbearable pain), in four differing settings including daily life, professional life, sports and night pain.

Patients with the following tendinopathies at the following sites were enrolled: 31 lateral epicondyles, 17 Achilles' tendons, 10 patellar tendons, 4 medial epicondyles, 3 rotator cuffs, 2 proximal hamstrings and 1 Gluteus Medius (peritrochanteric).

CLINICAL FINDINGS

In the group of 50 patients who were followed-up at 6 months, the effect of PRP injection was evaluated in 80% as very good (Decrease of all VAS → 3 points when applicable) to

excellent (Decrease of all VAS → 4 points when applicable) or complete healing (all VAS = 0 or 3 VAS =0 and 1VAS =1)

No effect of treatment was noted in the remaining patients (10/50) with tendinopathies in the following locations: 2/3 rotator cuff, 1/2 hamstrings, 1/1 gluteus medius, 5/31 common extensor tendon, 1/17 Achilles.

In the second group of 18 patients who were followed-up at three months, 72.2% improved: 3 patients showed complete healing with another 10 patients showing improvement. Tendinopathy location was as follows: 9 common extensor tendon, 3 Achilles, 1 Patellar. The results were less positive than in the group of patients followed to six months which has led us to the conclusion that the mean time of healing may be in the range of 4 months. The remaining 5 patients did not show improvement and were stationary and tendinopathy locations were: 2 common extensor tendon, 2 Achilles, 1 Patellar.

CONCLUSION

In this clinical study, a single injection of Regen Lab PRP in tendinopathy was found to be a well-accepted treatment. No tendon ruptures were observed during follow-up and this is a very positive result for PRP. Patients were prescribed a maximum of 3 days complete rest, with the exception of manual workers with elbow pathology who were given 3-week rest periods. No casts, crutches or ortheses were used. Light sports, physiotherapy or training activity were allowed after 3 weeks with return to normal sports activities at 3 months. Improvement in tendon imaging was observed after 3-6 months. There was little difference in intratendinous Doppler (little reduction of Doppler signal in the majority of patients) before 6 months indicating that vascularization, which is key to regeneration, remains present. The maximal effect of PRP injection appears to start at around 2-4 months from treatment

The results of this clinical study indicate that "non-classical" indications are the least responsive to PRP injection (gluteus medius, Hamstrings, rotator cuff). In the shoulder, rotator cuff partial intrasubstance tears are the only good indication as they are covered by tendon on each side and these lesions are often underestimated with ultrasound. Some of the patients described above who had not improved after 6 months were contacted after 9 months and were improving. It seems, therefore, that PRP could be a real long term treatment.

The only adverse event observed was pain following injection especially in the elbow during the inflammatory phase which lasted 2-3 days. It should be noted that no NSAIDs were allowed but Paracetamol was acceptable.

CINI FOUNDATION, VENICE-ITALY 2013-2014

www.biobridge-event.com

BIOBRIDGE FOUNDATION

regenlab