PRP and tendinopathy, from *in vitro* to clinical trials

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What’s PRP?

• = Platelet-Rich Plasma
• Centrifugation of autologous blood
• High concentration of platelets \((3-10x)\)
• Platelets \(\rightarrow\) roles in coagulation, inflammation, immunity modulation, « restorative » properties
• Liberation of cytokines and growth factors \((\text{VEGF, PDGF, TGF-} \beta, \text{IGF-1, HGF})\)
• Activation by thrombine, \(\text{CaCl}_2\) or collagen in situ
  \(\rightarrow\) degranulation \(\rightarrow\) liberation of GF
What’s PRP?

- No consensus
- No local anesthetic
- Avoid NSAIDs
- Controversed in literature
- Very popular in sport
- Removed from the doping list of the WADA
Many varied techniques ➔ different PRP
- variation of *platelet concentration*
- presence or not of *erythrocytes* and *leucocytes*
Leucocytes or not?

![Graphs showing data on platelets, WBC, IL-1β, COL1A1, and TNF-α levels across different conditions (Control, sPRP, hcPRP, IrPRP, cPRP).](image)
Animal studies

- Tendons = *small metabolic index*

- GF ➔ tenocyte proliferation, *collagen synthesis*, stimulation of angiogenesis, analgesic properties (Anitua 2009; Bosch 2011)

- **Stimulation and acceleration of tissue regeneration** (Virchenko 2006; Bosch 2011; Kaux 2012)

- The application of *mechanical loads* is required to obtain an optimal tissue quality (Virchenko 2006; Kaux 2012)
Animal studies

• Each GF has a specific action during the healing process (Molloy 2003; Anitua 2007)

• Improve cicatricial process and decrease time of cicatrization:
  - differenciation of cells from circulation (Anitua 2006 & 2007; Kajikawa 2008)
  - improve MMPs-3 expression → remodeling ECM (de Mos 2008)
  - improve initial stages of healing (Anitua 2006 & 2007; Kajikawa 2008; Kaux 2012)
  - improve type I collagen fiber synthesis and organisation, neovascularisation (Lyra 2009; Kajikawa 2008; Mishra 2009; Kaux 2012)
  - better maturation of the tendinous cal (Aspenberg 2004; Virchenko 2006; Kaux 2012)
Clinical studies

- **Chronic tendinopathies**
- Initiate an *acute inflammatory reaction* that quickly moves on to the *proliferative phase*
- ***NOT*** to be used for acute tendinitis nor tenosynovitis

*Acta Orthop. Belg., 2013, 79, 10-15*

*Platelet-rich plasma application in the management of chronic tendinopathies*

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*From the University and University Hospital of Liège, Belgium*
Lateral epicondylitis

Treatment of Lateral Epicondylitis With Platelet-Rich Plasma, Glucocorticoid, or Saline

A Randomized, Double-Blind, Placebo-Controlled Trial

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Investigation performed at the Diagnostic Centre, Region Hospital Silkeborg, Silkeborg, Denmark
Comparison of the therapeutic effects of ultrasound-guided platelet-rich plasma injection and dry needling in rotator cuff disease: a randomized controlled trial

Dong-wook Rha, Gi-Young Park, Yong-Kyun Kim, Min Tae Kim and Sang Chul Lee
Patellar tendinopathies

Platelet-Rich Plasma Versus Focused Shock Waves in the Treatment of Jumper’s Knee in Athletes

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Investigation performed at the Sant’Andrea Hospital, Sapienza University of Rome, Rome, Italy

Background: Tendinopathies represent a serious challenge for orthopaedic surgeons involved in treatment of athletes.

Purpose: To compare the effectiveness and safety of platelet-rich plasma (PRP) injections and focused extracorporeal shock wave therapy (ESWT) in athletes with jumper’s knee.

Study Design: Randomized controlled trial; Level of evidence, 1.

Methods: Forty-six consecutive athletes with jumper’s knee were selected for this study and randomized into 2 treatment groups: 2 autologous PRP injections over 2 weeks under ultrasound guidance (PRP group; n = 23), and 3 sessions of focused extracorporeal shock wave therapy (2.400 impulses at 0.17-0.25 mJ/mm² per session) (ESWT group; n = 23). The outcome measures were Victorian Institute of Sports Assessment–Patella (VISA-P) questionnaire, pain visual analog scale (VAS), and modified Blazina scale. A reviewer who was blinded as to the group allocation of participants performed outcome assessments before treatment and at 2, 6, and 12 months after treatment. Nonparametric tests were used for within-group (Friedman/Wilcoxon test) and between-group (Kruskal-Wallis/Fisher test) testing, and the significance level was set at .05.

Results: The 2 groups were homogeneous in terms of age, sex, level of sports participation, and pretreatment clinical status. Patients in both groups showed statistically significant improvement of symptoms at all follow-up assessments. The VISA-P, VAS, and modified Blazina scale scores showed no significant differences between groups at 2-month follow-up (P = .635, .360, and .339, respectively). The PRP group showed significantly better improvement than the ESWT group in VISA-P, VAS scores at 6- and 12-month follow-up, and modified Blazina scale score at 12-month follow-up (P < .05 for all).

Conclusion: Therapeutic injections of PRP lead to better midterm clinical results compared with focused ESWT in the treatment of jumper’s knee in athletes.

Keywords: jumper’s knee; platelet-rich plasma; extracorporeal shock wave therapy; tendinopathy/therapy
Patellar tendinopathies

Kaux et al, Journal of Sports Medicine & Physical Fitness, in press
Patellar tendinopathies

- Patients with best improvement → younger (24.7 vs 32.2 y.o.)
  - VAS ≤ 1
  - Significant increase of IKDC score
  - Significant improvement of pain during isokinetic evaluation and optojump
  - 70% return to sport (50% same level)

Kaux et al, Journal of Sports Medicine & Physical Fitness, in press
Achilles tendinopathies

- **RCT** PRP vs isotonic saline \((n = 54)\) + eccentric activities for 3 months ➔ after 24 weeks algo-functional scores, patient satisfaction, and return to sports activities significantly *improved in both groups* ➔ idem after 1 year + *no US differences* (de Vos 2010 & 2011; de Jonge 2010)

- **Critics:**
  - no eccentric treatment before study
  - injection could cause local bleeding
  - change in pressure-volume related to the presence of saline solution
  - relatively invasive for control groups
  - PRP quality may not have been optimal

  (Creaney 2010; McCormack 2010; Rabago 2010)
No efficacy of PRP?

Platelet-Rich Plasma as a Treatment for Patellar Tendinopathy

A Double-Blind, Randomized Controlled Trial

Jason L. Dragoo,†,‡ MD, Amy S. Wasterlain,†,‡ MD, Hillary J. Braun,† BA, and Kevin T. Nead,† MPhil
Investigation performed at Stanford University, Redwood City, California, USA

Platelet-rich therapies for musculoskeletal soft tissue injuries (Review)

Moraes VY, Lenza M, Tamaoki MJ, Faloppa F, Belloti JC

Strong evidence against platelet-rich plasma injections for chronic lateral epicondylar tendinopathy: a systematic review

Robert-Jan de Vos, ¹,²,³ Johann Windt, ⁴ Adam Weir ¹
US guidance or not?

Retrospective Analysis of Postinjection Ultrasound Imaging After Platelet-Rich Plasma or Autologous Blood: Observational Review of Anatomic Distribution of Injected Material

Michael L. Loftus
Yoshimi Endo
Ronald S. Adler

AJR American Journal of Roentgenology
Diagnostic Imaging and Related Sciences
Second infiltration?
Potential side effect: exuberant inflammatory reaction (Kaux 2014)
Conclusion

- **PRP** seems to be efficient in *chronic tendinopathies*
- PRP remains *controversial*
- Ideal PRP treatment
  - *reproducible* for all patients
  - *poor* in leukocytes and erythrocytes (?)
  - platelet *activation* (?)
  - *no* local anesthetics nor NSAIDs
  - infiltration *US*-guided (?)
  - *rehabilitation* protocol post-infiltration
Dank u voor uw aandacht!

http://hdl.handle.net/2268/163372