



Platelet-Rich Plasma in the Lower Extremity




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Objectives

- To discuss the history and definition of platelet-rich plasma as it pertains to orthopedic sports medicine
- Define PRP
- How it works?
- Indications
- Applications

Introduction

- In Orthopedics we continue the quest to find ways to enhance healing.
- Accelerated healing means quicker return to play



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Introduction

- PRP is defined as autologous blood with a concentration of platelets above baseline values

Normals:

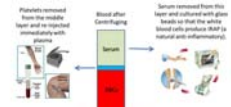
- 150,000 and 450,000 platelets per microliter (mcL)
- Males average: 237,000 per mcL
- Females average: 266,000 per mcL

- In vitro studies suggest that growth factors released by platelets recruit reparative cells and may augment soft tissue repair.

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Various Options Available



- There are numerous investigational options available which can enhance and accelerate healing:
 - Amniofix (Primitive cells)
 - ACP (Autologous Conditioned Plasma w/ 2-3x platelets)
 - Stem Cells (Similar to PRP from bone marrow aspirate)
 - Orthokine Therapy (only available in Europe)
 - Kobe Bryant, Alex Rodriguez
 - PRP (Platelet Rich plasma w/ 4-8x platelets)



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Why PRP?




History of PRP



- Utilized and studied since the 1970s
- Used primarily in maxillofacial and plastic surgery up until recently
- First used in orthopaedics for an adjunct to spinal fusion surgery as bone graft (questionable efficacy for fusions)
- Role in muscle and tendon healing has become popular in the last few years in orthopedics
- Numerous animal studies, basic science studies, and case reports/level IV studies in literature; few controlled trials

Basic Science

- Normal Plasma: 150,000-350,000 platelets/ μ L in 5 mL
- Definition of PRP: platelet rich = $>1,000,000$ platelets/ μ L in 5 mL of plasma
- Platelets:
 - proteins, cytokines, bioactive factors
 - initiate and regulate basic aspects of wound healing
- Plasma: fluid portion of blood that contains clotting factors and other proteins



Basic Science

- PRP: 3 to 5 fold increase in growth factor concentrations contained within α -granules
 - TGF- β , PDGF, IGF-I and II, FGF, VEGF, and endothelial cell growth factor
 - These cytokines play a role in cell proliferation, chemotaxis, cell differentiation and angiogenesis
 - These cytokines are present in normal biologic ratios in PRP vs. BMP
- PRP is not: “platelet gel”, “fibrin glue”, or “platelet concentrate”

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Stages of Healing

Tissue Repair Phases and Timescale

Hours Days Weeks Months

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Basic Science

- Other Bioactive factors in granules (non-growth factors)
 - serotonin, histamine, dopamine, calcium, and adenosine
- Fundamental effects on healing, particularly inflammation stage
- Platelets in PRP are delivered in a clot
 - contains several adhesion molecules that play a role in cell migration
 - clot itself acts as a scaffold

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Major Indications for PRP

- Chronic (Tendinopathies)
 - Adjuvant to Non-Healing tissue
 - Introduce Growth Factors to increase rate of healing
 - Stimulate healing in chronic tendinopathy
- Acute (Ligamentous/muscle injuries)
 - Reduce return to play time
 - Accelerate ligament and muscle healing
- Intraoperative Augmentation

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Preparing PRP

- Made from anti-coagulated blood; whole blood clots incorporate all the platelets
- First centrifuge: separates red blood cells from white blood cells, plasma, and platelets
- Second centrifuge: further concentrates platelets, producing the PRP separate from platelet-poor plasma

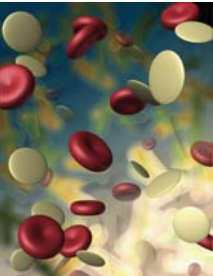


Platelet-poor plasma
Buffy coat (platelets and white blood cells)
Red blood cells

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Preparing PRP

- PRP may/may not be clotted to allow for delivery
 - degranulation begins
 - 70% of stored growth factors are released within 10 minutes
 - 100% within 1 hour
 - Calcium chloride/thrombin to activate
- Lifespan of platelet is 8-10 days



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Effects of PRP

- Essentially, PRP is adding multiple numbers of the same growth factors/cytokines that are needed in each phase of healing...theoretically speeding up the process
- Specifically aimed at soft tissue: tendon, ligament, muscle and skin
- Effect on tendon: increased cell proliferation and total collagen production; rats are getting back into the maze faster
- Effect on muscle: basic FGF and IGF-I are known cytokines that improve muscle healing

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Clinical Applications


- Historically, PRP used for chronic tendinopathies
- Newest literature uses PRP for acute ligamentous and muscle injuries to expedite return to play
- Indications for use have outpaced the basic science and clinical trials validating the efficacy



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Clinical Applications



- Chronic tendinopathy
 - Epicondylitis
 - Achilles
 - Patellar tendon
 - Plantar fascia
 - Osteoarthritis
- Intra-operative (bone healing)
 - TKA
 - ACL reconstruction
 - Acute Achilles repair
 - Rotator cuff repair
 - Acute articular cartilage repair
- Acute Muscle Injuries (sprains)



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Contraindications

- Septicemia, Thrombocytopenia, or Anemia
- Pregnancy
- Platelet dysfunction syndrome
- Hypofibrinogenemia
- History of corticosteroid injection at the treatment site or systemic with in 2 wks
- NSAIDS with in 48 hours
- Recent fever or illness/active infection
- History of cancer/active tumor






Achilles tendinopathy

- Tendonitis vs Tendinopathy:
- Inflammation vs Microtears (mucinoid degeneration)
- PRP is not indicated for paratendinitis alone (if that exists)
- Refractory Achilles tendinopathy pts who have failed multiple PT rounds and other conservative modalities
- Protection with brace advocated after injection, as is cessation of athletic activity
- Gradual return to activities/sport in 10-12 weeks




Results



- Use in Achilles tendinopathy
- de Jonge et al., 2011, AJSM
- Double-blind randomized placebo-controlled study
- 27 in PRP group and 27 in control group
- No statistically significant difference pain score and activity level



Plantar fasciitis

- Chronic refractory plantar fasciitis pts who have failed PT and multiple conservative modalities such as orthoses, NSAIDs, and cortisone shots
- No data on whether PRP is beneficial for pts with tears of plantar fascia
- Immediate WB and PT protocol after injection
- Gradual return to activities over 6-8 weeks, longer for running athletes



Results

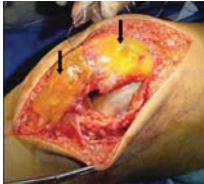
- Barrett and Erredge, 2004
- Retrospective, cohort
- 9 patients
- 7/9 with complete pain relief at one year





Patellar tendinopathy


- Demonstrated intra-substance changes on MRI or US; most commonly found at the proximal bone-tendon junction
- Severe symptoms present for more than three months
- Treatment of chronic patellar tendinopathy as an adjunct to rest and PT
- May be used as an alternative to surgical treatment after failed conservative therapy
- “Washout period” recommended for a week at least (no NSAIDs)



Results


- Kon et al., 2009
- Prospective, cohort
- 20 patients
- 70% with marked or complete improvement
- 80% satisfied



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Acute Ligamentous Injury

- MCL sprains



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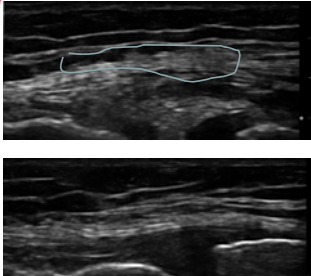
Results

- Mandelbaum and Gerhardt, AJSM Nov 2009
- Retrospective
- 22 professional soccer players with Grade II MCL
- PRP in <72 hours from injury
- RTP shortened by 27% compared to control group



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MCL injury



- MCL, see disruption of MCL fibers, not a complete tear
- Post PRP

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Acute Muscle Injury


- Acute grade 2-3 muscle strains
- Acute severe muscle contusion
- Muscle healing follows same stages as wounds
- May decrease return to play times
- Concerns regarding potential fibrotic healing response



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Results

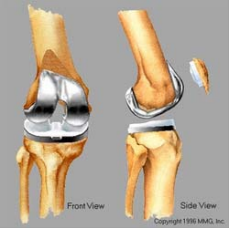
- Sanchez et al., 2009
- Prospective, cohort
- 22 muscle injuries in 20 high level professional athletes
- Full recovery in half the time in all patients



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Intra-operative Uses

- TKA: Earliest uses of PRP in Orthopedics were in pts who had undergone TKA
- Primary indication is to promote wound healing and decrease blood loss




Front View Side View
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Results

- Berghoff et al., 2006
 - 66 TKR pts in control group, 71 in intervention group
 - Autologous PRP fibrin sealant sprayed in knee prior to closure
 - Results:
 - higher postoperative hgb
 - shorter hospital stays
 - less incidence of transfusion
 - fewer narcotics taken
 - better knee ROM at 6 week follow-ups



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Intraoperative use in ACL

- Various preparations and uses have been attempted



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Results

- Orrego et al., 2008
 - Randomized controlled trial
 - 108 ACL reconstruction patients
 - PRP injected grafts versus non-PRP grafts
 - Enhanced graft maturation process evaluated by MRI
 - No difference in tunnel widening or bone-tendon interface
- Silva and Sampio, 2009
 - Prospective, cohort
 - No difference in MRI signal intensity at 3 mos

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Intra-operative Uses

- Acute achilles tendon repair: augmenting primary repair in athletes



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Results

- Sanchez et al (AJSM 2007)
- Case-control
- 12 patients with Achilles repair
- compared this group with age-matched controls having primary repair and no PRP
- Faster return of ROM, jumping and jogging than control group

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Use in Osteoarthritis

- Acute articular cartilage repair/treatment of degenerative joint disease



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Results

- Bennett and Schultz (American Journal of Surgery, 1993)
 - first described good results using PRP for articular cartilage lesions; type II collagen synthesis and induction of chondrogenesis from mesenchymal stem cells were reported
- Wu et al (Med Hypotheses, 2009)
 - suggested that PRP can be used as a chondrocyte carrier for treatment of acute cartilage lesions of the knee (no data regarding outcomes as of yet)

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Results


- Cugat, 2011
 - 312 with osteoarthritis
 - 3 intra articular injections
 - Quality of life questionnaires at 6 months
 - Improvements in function and quality of life by OA specific clinical assessment instruments

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Regulation of PRP in Sports

WADA: World Anti-Doping Agency


- Official Stance:
 - PRP does not demonstrate potential for performance enhancement beyond a potential therapeutic effect
 - Restricted to use in tendons or musculotendinous junction
 - NOT APPROVED in the muscle itself



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Regulation of PRP in Sports

- Truth? PRP is unlikely to provide a athletic advantage because unbound IGF-I has too short of a half-life (10 minutes to 16 hrs) to provide a performance advantage
- Also isoform IGF-Iea (found in PRP) is not the isoform responsible for muscle hypertrophy (IGF-Iec/MGF)
- Finally, the dose of IGF-I is sub-therapeutic (300 µg) to produce a systemic anabolic effect (160 mg)



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Regulation of PRP in Sports

- Olympic-affiliated and international anti-doping governing bodies have no jurisdiction over professional sports leagues in the US (NBA, MLB, NFL, NHL)
- PRP is not specifically addressed in any of the lists of banned substances to date
- Throughout the literature, there is no suggestion that PRP has a systemic effect or provides a sports advantage; only anecdotal reports exist suggesting that PRP accelerates the repair of an (acutely) injured area

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Potential Advantages

- Low chance of rejection (pts own blood)
- PRP can be prepared at the time of care in a simple and relatively inexpensive manner (vs stem cells)



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Potential Limitations

- Optimal dose range of PRP has yet to be defined
- Theoretical cancer-like effect of uncontrolled differentiation of cells
- Review of literature shows a clear lack of standardization in the preparation of PRP
- Uniform protocols and quantification of standard platelet yields are necessary
- ACP (autologous conditioned plasma) vs. PRP: is it Arthrex or less WBC's that make it better?
- Timing and number of treatments

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Conclusion

- PRP and PRP-related products have been applied to a diversity of tissues in a variety of surgical fields
- Goal of PRP is to deliver a high concentration of platelet-growth factors to enhance healing response
- PRP may be advantageous in sports medicine, but little evidence other than case series and reports exist to support PRP's effectiveness
- A significant amount of basic science and clinical research needs to be done to define PRP's role

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Thank You!