Platelet Rich Plasma (PRP)

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What is PRP?

• In medicine since 1970s
  – First uses in bone healing began in late 1990s
  – Gained popularity for tissue healing in early 2000s

• Blood derived, autologous substance with high plasma concentration
  – Normal blood sample: 93% RBC, 6% platelets, 1% WBC
  – PRP blood sample: 6% RBC, 93% platelets, 1% WBC
PRP Applications

• Commercial preparation of PRP result in various versions
  – Leukocyte rich vs. leukocyte poor
  – Ideal makeup not yet determined
• Direct application
• Single or multiple injections
• Gel
• Collagen sponge
Creating PRP

• Can only be made from anticoagulated blood
• Citrate is added to whole blood
• 2 centrifugation steps:
  1. Separation of RBC & WBC from plasma & platelets
  2. Further concentration of platelets
• Substance added to activate clotting mechanism once injected*
  – Thrombin
  – CaCl$_2$
  – Type 1 collagen
Clotting Mechanism Substances

• Thrombin
  – Allows approx. 70% growth factors released within 10 minutes
    • 100% within 1 hour
  – Platelets may produce additional small amounts of growth factors during the rest of lifespan
  – Can cause complications → formation of antibodies
Clotting Mechanism Substances

- **CaCl$_2$** – platelet rich fibrin matrix (PRFM)
  - Added during 2$^{nd}$ centrifugation step
  - Prothrombin $\rightarrow$ CaCl$_2$ $\rightarrow$ autologous thrombin
  - Results in a dense fibrin matrix = slower platelet activation
  - $\sim$ 7 days
Clotting Mechanism Substances

• Type I collagen
  – Allows injection of PRP not yet activated
    • Followed by collagen injection
  – Equally effective as thrombin in stimulating growth factors
  – Decreased risk of clot formation compared to thrombin
How PRP works

• 3 stages:
  1. Activation
     • Thrombin
     • CaCl$_2$
     • type 1 collagen
  2. Secretion
     • Alpha and dense granules $\rightarrow$ stimulate 3 stages of healing
  3. Aggregation of WBC

- **Elbow Tendinopathy/Lateral Epicondylitis**
  - Failed with conservative treatment
  - 20 patients:
    - 15 received PRP
    - 5 received local anesthetic – control
  - Of those who received PRP:
    - 60% showed improvement at 8 weeks
    - 81% at 6 months
    - 93% at follow up (12-38 months)
    - 99% were able to return to ADLs
  - Control group:
    - 3/5 sought treatment outside of study after 8 weeks
• **Strengths**
  – No adverse effects or complications reported
  – One of few studies to have a control group
  – Used human subjects

• **Critiques**
  – Small sample size (n=20)
  – 60% attrition rate
  – Not randomized
  – Not blinded

• **Rehab protocol:**
  – Standard eccentric strengthening and functional progressions
  – Return to activities over 6-8 week when full ROM is achieved and localized pain or tenderness has diminished
  – Not necessary to immobilize elbow post injection

- **Acute Achilles tendinopathy in athletes**
  - n=12 – 6 received PRP treatment, 6 control
  - PRP was applied in 2 ways per subject:
    - CaCl$_2$ added to PRP and sat externally for 30 mins allowing matrix to form
      - Matrix directly incorporated into Achilles repair
    - CaCl$_2$ added to PRP then immediately sprayed onto repair just prior to closure
  - PRP treatment group showed a larger ROM and earlier return to activity (± 4-7 wks) then control
• Strengths
  – No adverse effects or complications reported
  – One of few studies to have a control group
  – Used human subjects

• Critiques:
  – Small sample size
  – Not randomized

• Rehab Protocol:
  – Braced
  – No athletic activity
  – AROM and AAROM solely in plantar/dorsiflexion plane initiated immediately
  – Gradual standard progression of strengthening
  – Gradual return to activities over 6-8 weeks – depending on size/severity of lesion
Barrett S, Erredge S. Growth factors for chronic plantar fasciitis. 
*Podiatry Today.* 2004;17:37-42.

- **Chronic refractory plantar fasciitis**
  - n=9
  - Participants underwent “washout” 90-day period prior to PRP injection:
    - No brace
    - No NSAIDS
    - No corticosteroids
  - 6 of 9 patients were asymptomatic after 2 months
    - The other 3 achieved this same status after a second PRP injection
  - At 1 year: 77.9% were still asymptomatic
• **Strengths**
  – No adverse effects or complications reported
  – Used human subjects

• **Critiques**
  – No control group
  – Small sample size

• **Rehab protocol:**
  – Immediate WB
  – Standard rehab program for strengthening
  – Gradual return to activities over 6-8 weeks
  – More of a gradual training schedule for running athletes

- **Patellar Tendinopathy AKA Jumper’s knee**
  - Histologically the tendon attained increased levels of types I and III collagen and macrophages

- **Strengths:**
  - No adverse effects

- **Critiques:**
  - Not performed on human subjects
  - Small sample size (n=3)
  - No control group
• Postinjection protocol:
  – Standard rehab for strength
  – Gradual return to activities over 6-8 weeks
  – Consistent use of ice, especially in early stages
  – Criteria to return to sport:
    • Painless full ROM
    • Ability to tolerate ascending and descending stairs

- Total Knee Arthroplasty
  - N=137
    - 71 received PRP
    - 66 were control
  - PRP mixed with thrombin and Cacl$_2$ sprayed into knee just prior to closure
  - Intervention group demonstrated:
    - Higher post-op hemoglobin levels
    - Shorter hospital stays
    - At 6-week follow up had significantly greater knee ROM
• **Strengths**
  – Used human subjects
  – Control group
  – Large sample size

• **Critiques**
  – Unconventional PRP preparation

- **ACL Reconstruction**
  - Treated with collagen-PRP hydrogel at ACL transection site
  - Showed improvement in:
    - Load at yield
    - Maximum load
    - Stiffness at 4 weeks post-op
• **Strengths**
  – No adverse effects

• **Critiques**
  – No human subjects
  – Small sample size

- **Osteoarthritis**
  - n=40
  - Treated with 3 separate intra-articular PRP injection
  - Outcome measures showed significant improvement in visual analog pain scale and subjective functional scales at 6-month follow up
    - Patients under 60 years showed 85% satisfaction
    - Patients over 60 years showed 33% satisfaction
• **Strengths**  
  – Human subjects

• **Critiques**  
  – Small sample size  
  – Not randomized
Bottom Line

• PRP is a promising, but not yet proven treatment for joint, tendon, ligament, and muscle repair
• PRP is autologous – simple administration
• Current studies suggest an excellent safety profile
• No standardized method of producing PRP in place → conflicting results in studies
Bottom Line

- Local anesthetics may change pH environment which could change effects of PRP
- Multiplaner injection technique recommended to accommodate larger surface area
- 24-48 hours post injection patients are encouraged to ice and elevate limb for pain and inflammation control
- No NSAIDS within first 2 weeks after injection – may inhibit prostaglandin pathway
References


References


