Tendinopathy: Role for Biologics?

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What the community is told

**What are the potential benefits of Stem Cell Therapy?**
There are endless orthopedic benefits of Stem Cell therapy for joints. Increased tissue healing, decreased inflammation, reproduction of cartilaginous tissue, restored range of motion, decreased pain and much more.

**What are the risks of these treatments?**
There are no known risks to these injections. We have had nothing but positive outcomes for our patients.

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**ACL Tears**

70% of ACL tears can be healed without surgery
So, what is it?

- **Stem Cells:**
  - Different from minimally manipulated cell-based therapies
    - Stem Cells are capable of dividing and renewing for long periods
    - Unspecialized (pluripotent)
    - Can give rise to specialized cell types
In the US, we are using minimally manipulated cell based therapies derived from bone marrow (BMAC), fat, blood.

- These do contain stem and progenitor cells. Concentration of these cells increases with preparation at the point of care, however, stem and progenitor cells are the least abundant cells in the preparations.

- Embryonic Stem Cells remain ethically controversial and are not used for MSK purposes in the US.

- Nomenclature is better as: “Cell based therapy”, less so “Stem Cell Therapy.”
So, what is it?

- **PRP (Platelet Rich Plasma)**
  - Autologous mixture of highly concentrated platelets and associated growth factors produced by centrifugal separation of whole blood.
  - Promotes cell recruitment, proliferation and angiogenesis.
  - PRP preparations vary widely in the type of growth factors, mediators, leukocyte count, platelet count etc.

### Table 1

Commercially available PRP systems and their PRP preparations

<table>
<thead>
<tr>
<th>System</th>
<th>Company</th>
<th>Blood volume required (mL)</th>
<th>Concentrated volume produced (mL)</th>
<th>Processing time (min)</th>
<th>PPP produced?</th>
<th>Increase in [platelets] (times baseline)</th>
<th>Platelet capture efficiency (% yield)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukocyte-rich PRP</td>
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<tr>
<td></td>
<td>Biologics/Arterioscule</td>
<td></td>
<td></td>
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<tr>
<td>Leukocyte-poor PRP</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clear PRP</td>
<td>Harvest</td>
<td>54^a</td>
<td>6.5^a</td>
<td>18^a</td>
<td>+</td>
<td>3–6^a</td>
<td>62 ± 5%^a</td>
</tr>
<tr>
<td>Pare PRP</td>
<td>EmCyte</td>
<td>50^a</td>
<td>6.5^a</td>
<td>8.5^a</td>
<td>+</td>
<td>4–7^a</td>
<td>76 ± 4%^a</td>
</tr>
</tbody>
</table>

^aData obtained from manufacturers’ promotional literature or internal studies
Complicating factors of PRP

- Many manufacturers of kits; independent preparation
- Leukocyte rich (LR-PRP)
- Leukocyte poor (LP-PRP)
- Activation of the PRP prior to injection
  - Form of calcium, thrombin
- Platelet concentration varies widely
- Growth factor and cytokine concentrations vary by age, health, sex, processing methods in addition to variability when obtaining samples from the same patient at different times of day.
- This leads to complications in interpretation of literature

So why are the cool kids doing it?
Achilles

- Several historical trials failed to show benefit of PRP vs placebo injection when combined with an eccentric program.
- Additional studies have suggested benefit
- Based off of current literature, PRP in achilles tendinopathy is not supported.

Lower extremity

- Achilles-tear
  - Paucity of high quality studies
  - Conflicting data, currently not recommended for surgical augmentation of a tendon repair.

Lower extremity

- Patellar Tendon
  - Overall, a small number of high quality studies are available
  - Of these, the data tends to supports usage of LR-PRP
    - Dry needling alone vs PRP with improvement in PRP at 12 weeks, no difference at >26 weeks.
    - PRP vs ECSWT showing similar at 2 months, PRP favored at 6 and 12 months.

Lower extremity

- ACL
  - No high quality studies in setting of acute rupture
  - Partial tears with several studies, one performed intraligamentous PRP suggesting improved return to play time for professional athletes.

Lower extremity

- ACL repair
  - 1. Osteoligamentous integration in the tunnels
  - 2. Maturation of the articular portion of the graft
  - 3. Harvest site healing and pain reduction

Findings have shown some early results on donor site pain and healing
No significant clinical effect on graft integration or maturation

Plantar Fasciitis

Studies have typically had a low n, but several recent meta-analyses have shown equivocal to superior results to a control of corticosteroid.

Obvious benefit over cortisocosteroid in setting of fat pad atrophy and rupture of the plantar fascia.

Ankle Sprains

- Low quality evidence
- Of the reasonable studies, PRP has not shown effectiveness in the setting of an acute ankle sprain

Upper extremity

- Lateral epicondylitis and medial epicondylitis
  - Stronghold of tendon research is in lateral epicondylitis
  - High quality evidence available with majority showing both short-term and long-term efficacy
  - Studies suggest LR-PRP as treatment of choice
  - Corticosteroid may have long-term negative effect

“How can I have tennis elbow?”
Upper extremity

- Tenex
  - Recent head to head of PRP vs Tenex
    - No statistically significant difference found between the 2 groups
    - Both produced clinically and statistically significant improvements in pain, function and quality of life.

Upper extremity

- Rotator cuff
  - Most studies have been performed with PRP into the subacromial space
  - Of these, the results are largely equivocal. Safety profile is reasonable, further studies needed
  - Studies need to be performed with injection into the tendinopathic portion

Upper extremity

- Rotator cuff repair
  - High quality studies have been performed
    - Majority of studies show little to no difference between the PRP/PRFM augmented repairs vs repair alone
    - Some limited data that it may reduce perioperative pain
  - Study performed at the U of U was aborted 2/2 lack of noted improvement and 2 cases of PRFM augmented repairs with infection noted.

Muscle injuries

- Use in acute muscle injuries is common in professional sports
  - 28 patients with grade 2 hamstring muscle injuries comparing LR-PRP with rehab vs rehab alone. RTP was 26.7 vs 42.5.
  - Structural improvements not achieved. Placebo?

Shout out to the joints

- **Knee**
  - Level 1 evidence is in support of usage in mild to moderate OA.
  - Leukocyte poor preparations appear to be most efficacious
  - Long-term efficacy unknown

- **Hip**
  - Limited data. Head to head with HA favors PRP early, similar at 12 months
My recommendations

- There is a serious need for more options for those suffering from chronic orthopedic issues. We need to move forward and encourage research and application of ortho biologics.

- All involved in ortho biologics should maintain a registry.

- Costs should be stated and controlled. PRP of 600 vs 3,000. BMAC of 2,000 vs 10,000.

- Utility of imaging guidance

- Further research is needed, and should follow the recommendations as outline by the recent consensus from the AAOS.

- Transparency in advertising, direct to consumer marketing.

Thank you!