The Role of Biologics: PRP and Stem Cells in Sports Medicine

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Disclosures

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(Embryonic Stem Cell)
Biologics: The Big 3

• **1. What is it?**
  - Platelet Rich Plasma (PRP)
  - Bone Marrow Aspirate Concentrate (BMC)
  - Amniotic Fluid Allograft (Embryonic Stem Cell)

• **2. Who does it benefit?**
  - Sports Injuries
  - Degenerative Joints

• **3. Does it work?**
  - Recent Studies
Tissue Regeneration - Mechanism of Action

Cell Proliferation Requires the Interaction of Three Biological Elements:

1. Recruitment of cells to the scaffold
2. Cell division within the scaffold
What is it?

**Platelet Rich Plasma (PRP)**

Peripheral blood is centrifuged to isolate platelets, growth factors and accessory cells to enhance tendon/muscle healing and reduce symptoms in DJD.

**Bone Marrow Aspirate Concentrate (BMAC)**

Bone marrow is aspirated from the hip bone and centrifuged to isolate stem cells to enhance tendon/muscle healing and reduce symptoms in DJD.

**Amniotic Fluid (Embryonic Stem Cell & Growth Factors)**

Cryopreserved, minimally processed amniotic fluid tissue product from human birth tissue (umbilical cord) from live, healthy c-section birth.
Let’s discuss PRP

- Literature shows clinical benefit for highly concentrated PRP

- Low concentration systems do not deliver the threshold of Platelets required for accelerated healing

- **Recovery high percentage** of cells from the total volume processed
  - Platelets, growth factors, and accessory cells
  - 1.5 – 3 Million Platelets/mL to stimulate angiogenesis
  - 3-5 x the initial concentration
What is the Optimal Composition of a Concentrated Platelet Product?

- **Platelets** Mediate cell to cell adhesion
- **G-Factors**
  - PDGF - Chemoattractive to stem cells
  - TGF-ß - Promotes cell mitosis and differentiation
  - VEGF - Stimulates angiogenesis
- **WBC’s** CD34+ cells as a marker for mononuclear cells
- **Cytokines**
  - SDF-1α - Actively modulates migration and homing of stem cells

These key cells are found in the Buffy Coat layer


A normal platelet count ...
Conclusions:

• Platelet Concentrate and VEGF stimulate chemotactic migration of hMSC’s in a dose-dependent manner.

• Platelet Concentrate stimulates proliferation of hMSC’s in a dose-dependent manner

Haynesworth, SE, Bruder, SP, et al; “Mitogenic Stimulation of Human Mesenchymal Stem Cells by PRP Suggests a Mechanism for Enhancement of Bone Repair”, Presented at 48th Orthopaedic Research Society Meeting, Dallas, TX, 2002
Unconcentrated Bone Marrow Aspirate

There are two principal multipotent stem cells in the marrow:

- One Stromal Stem Cell in every 250,000 cells in the marrow at age 35, but this ratio decreases with age.
- One Hematopoietic Stem Cell for every 10-15,000 cells in the marrow and does not decrease with age.

Issue: Unpredictable healing without concentration, particularly with healing impaired patients.
Biologic Components
Embryonic Stem Cells & Growth Factors (FloGraft Freedom)

• Secretion Components (Growth Factors)
  - PDGF: Chemoattractive to stem cells
  - TGF-β / α: Promotes cell mitosis and differentiation
  - EG-VEGF: Stimulates angiogenesis
  - Angiogenin: Angiogenesis, cell migration-invasion-proliferation
  - MCP-1: Mobilization & recruitment of mesenchymal stem cells
  - SDF-1α: Chemotactic factor for mesenchymal, endothelial stem cells

• Cellular Components
  - Amniotic fluid derived stem and progenitor cells
  - Amniotic epithelial cells
Does It Work?

In short... yes, no, sometimes

Evolving research and techniques

Pick the right patient and injury
Who Does It Benefit?

Acute Sports Injuries
Hamstring
Ankle Sprain
UCL (Tommy John Ligament)

Tendon Injuries (acute vs chronic)
Proximal Hamstring Tendon
Achilles Tendon
Patella Tendon
Lateral Epicondylitis (Tennis Elbow)

Degenerative Joint Disease
Osteoarthritis
Degenerative Labrum or Meniscus
PRP Research

• **Ankle Sprain** - 2014 issue of American Academy of Orthopedic Surgeons showed that PRP injections for ankle sprains got athletes back to their sport 10-days quicker.

• **Hamstring Tear** - October 2014 issue of American Journal of Sports Medicine showed that a single PRP injections combined with PT got athletes back to their sport 16-days quicker (26.7 days compared to 42.5 days in the control group). Full recovery for patients was 13-weeks faster with PRP injections (26 weeks compared to 39 weeks in the control group).
BMC & Cartilage Defects
(Equine Histologic)

- 15mm diameter full-thickness cartilage defects created on lateral trochlear ridge of femur (N=12)
- Defects treated with microfracture alone or microfracture + BMAC
  - **BMA rich with PDGF, TGF-β, VEGF - contained within alpha-granules of platelets and important for inducing effective chondrogenesis**
- 2nd look arthroscopy 3 mo and animals killed at 8 mo
- Healing - macroscopic and histological scoring; qMRI
- At 8 months:
  - Improvement in BMA+ vs microfracture alone
  - All scoring and MRI shows BMA+microfracture resulted
    - Increased fill of defects
    - Improved integration of repair tissue into surrounding normal cartilage
    - Greater type-II collagen content and improved orientation of the collagen
    - Significantly more glycosaminoglycan

Clinical outcome of autologous bone marrow aspirates concentrate (BMAC) injection in degenerative arthritis of the knee

BMC injection in 41 pts with knee OA, Mean age 60.7

Preoperative, 3, 6, and 12 months, pain score using visual analogue scale (VAS) and functional scales were used for evaluation.

Pts report significant improvements in OA grades I, II, and III (Kellgren-Lawrence) grade-IV modest improvement

BMC in Knee OA

Efficacy of autologous bone marrow concentrate for knee osteoarthritis with and without adipose graft.

840 procedures were performed, 616 without & 224 w/ adipose graft.

Statistically significant improvements in:
- Functionality (Lower Extremity Function Scale)
- Pain (Numeric Pain Scale)
- Subjective Percentage Improvement Rating.

No statistical difference between BMC and BMC w/adipose graft.

Embryonic Stem Cell OA

- Interim Analysis of Prospective, Multi-center Outcome Observational Cohort Registry of Amniotic Fluid Treatment of OA of the Knee

- First 181 pts in study designed for 470 pts
- Kellgren Lawrence Grade 1-3 OA
- Injected with minimally processed amniotic fluid tissue product

- VAS & WOMAC scores at 30, 60, 90 days
- 75% of pts with sustained improvement at 90-days
Elite Athlete Case #1

- 38-yo female, elite basketball player with moderate to advanced OA and degenerative labral tear. “Looking for one more season” before getting hip replacement.

- Failed PT and CSI

- BMAC with US guided hip injection

- Restarted PT at 4-weeks with minor discomfort

- 8-week graded return to running program

- At 12-week f/u complete resolution of pain with running. Returning to basketball training.
Bedside Bone Marrow Aspiration
Elite Athlete Case #2

- Elite Ironman Triathlete, Ranked #5 in the world. MRI diagnosed 90% tear of proximal hamstring. Ironman World Championship in Khona, HI in 9-months.
- Failed PT, NSAIDs, PO steroids, rest
- PRP injection under US guidance
- Started PT, graded biking & swim at 4-weeks
- 12-week return to run program at 6-weeks
- At 18-weeks back to regular running program
- Podium finish in Khona
Elite Athlete Case #3

- US martial arts National champion with ankle sprain and bone contusion 6-weeks from representing USA in International competition in Europe
- X-rays WNL, MRI: ATFL / CFL tear, Peroneal/Post tib tendon partial tear-tendonitis
- Failed 4-weeks of cam boot, PT, iontophoresis, topical/PO meds, rest, ice
- 18-days from competition, Embryotic Stem Cell injection into ATFL, joint capsule and peroneal tendon sheath
- 15th place in 2,200 International competitors
- Silver and Bronze medal the following week defending US title
Summary

Great results with appropriate patient and injury selection

PRP - Your US skills are everything

BMC - Your aspiration technique is everything

Manage expectations

Evolving research

Keeping you active.