PRP, Growth Factors and Stem Cells – Role of Regenerative Medicine in Dermatology

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Conflicts of Interest Disclosure

- Abbvie
- Allergan
- Amgen
- Anacor
- Aqua
- Bayer
- Castle
- Celgene
- Dermira
- Eclipse
- Galderma
- Genentech
- GSK/Stiefel
- Intraderm
- ISDIN

- Janssen
- Leo
- Menlo
- Novartis
- Pharmaderm
- Pfizer
- Ranbaxy
- Regeneron
- Scibase
- Suneva
- TEVA
- Valeant/Ortho Dermatologica
- Verrica
- Xoft

- Digital editor for CUTIS
Outline

• What is regenerative medicine?
• Dermatologists already practice regenerative medicine
• Role of Platelet Rich Plasma (PRP) in dermatology
• Role of Growth Factors (Amniotic) in dermatology
• Role of Stem Cells in dermatology
What is regenerative medicine?

- *Regenerative medicine is the process of creating living, functional tissues to repair or replace tissue or organ function lost due to age, disease, damage, or congenital defects.*

- National Institute of Health

What is regenerative medicine?

- Regenerative medicine research translates fundamental knowledge in biology, chemistry and physics into materials, devices, systems and a variety of therapeutic strategies that augment, repair, replace or regenerate organs and tissues.

  - Alliance for Regenerative Medicine

https://alliancerm.org/page/promise-and-potential
Dermatologists already practice regenerative medicine

• Medical dermatology:
  – Alopecia
  – Vitiligo
  – Inflammatory dermatoses
  – Actinic keratosis

• Cosmetic dermatology:
  – Epidermal regeneration with topical therapy, laser, and other devices
  – Collagen regeneration with fillers, laser, ultherapy, and other devices
Platelet Rich Plasma (PRP)

- What is PRP
- Uses of PRP in Dermatology
- How to use PRP in Dermatology
Platelet Rich Plasma (PRP)

- **Autologous preparation of plasma with high concentrations of platelets derived from whole blood**
  - Whole blood => Centrifugation
    - Separation into 3 layers: platelet-poor plasma, PRP, and erythrocytes
    - Platelet count of at least 1,000,000/µL in a 5-mL volume
  - Most PRP – concentrations 4-8 times higher than that of normal blood
Platelet Rich Plasma (PRP)

• MOA:
  – High concentration of platelets release proteins containing a multitude of growth factors, chemokines, and cytokines, resulting in the promotion of cell proliferation and differentiation
    • More than 20 growth factors
      – platelet derived growth factor (PDGF)
      – transforming growth factor (TGF)
      – epidermal growth factor (EGF)
      – vascular endothelial growth factor (VEGF)
      – insulin-like growth factor (IDGF)
      – interleukin 1 (IL-1)
# Platelet Rich Plasma (PRP)

| Platelet- derived growth factor- (PDGFαα, PDGFαβ, PDGF ββ) | - Chemotactic for fibroblasts, macrophages, and neutrophils  
- Mitogenic for fibroblasts, smooth muscle cells, endothelial cells, mesenchymal cells, and osteoblasts  
- Promotes synthesis of collagen and other proteins, regulates collagenase secretion |
| --- | --- |
| Transforming growth factor - (TGF-β1, TGF-β2, TGF-α) | - Promotes angiogenesis  
- Regulation of cell proliferation, differentiation, and apoptosis  
- Chemotactic for fibroblasts, keratinocytes, and macrophages  
- Mitogenic for fibroblasts, smooth muscle cells  
- Inhibits endothelial cells, keratinocyte, lymphocyte, and macrophage proliferation  
- Regulates matrix proteins production (collagen, proteoglycans, fibronectin, and matrix degrading proteins)  
- Proliferation of undifferentiated mesenchymal cells |
| Vascular endothelial growth factor- (VEGF) | - Stimulates angiogenesis and vessel permeability  
- Chemotactic and mitogenic for endothelial cells |
Platelet Rich Plasma (PRP)

<table>
<thead>
<tr>
<th>Growth Factor</th>
<th>Effects</th>
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</table>
| Fibroblast growth factor- (FGF-2, FGF-9) | - Involved in tissue regeneration  
- Stimulates growth and differentiation of mesenchymal  
  cell, chondrocytes, osteoblasts |
| Epidermal growth factor- (EGF) | - Heavily involved in regulating cell proliferation,  
  differentiation, and survival  
- Stimulates angiogenesis  
- Mitogenic for fibroblasts, endothelial cells,  
  mesenchymal cells, and keratinocytes  
- Promotes endothelial chemotaxis  
- Regulates collagenase secretion |
| Insulin like growth factor- (IGF-1) | - Regulates cell metabolism  
- Stimulates proliferation and differentiation in  
  osteoblasts (bone formation)  
- Chemotactic for fibroblasts  
- Stimulates protein synthesis |
| Connective tissue growth factor- (CTGF) | - Promotes angiogenesis, chondral regeneration,  
  fibrosis, and platelet adhesion |
# Platelet Rich Plasma (PRP)

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<tr>
<th>PRP Uses in Dermatology</th>
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PMID: 29130636

PMID: 29118521

PMID: 29103820


Best matches for prp androgenetic alopecia:

New investigational drugs for androgenetic alopecia.

Study of platelet-rich plasma injections in the treatment of androgenetic alopecia through an one-year period.

Platelet-rich plasma for androgenetic alopecia: a pilot study.

Switch to our new best match sort order
Platelet Rich Plasma (PRP)

- Androgenetic alopecia
  - Anagen associated angiogenesis and neovascularization
    - Vascular endothelial growth factor (VEGF)
    - Alpha granules
    - Platelet derived angiogenesis factor (PDGF)
    - Platelet derived endothelial factor
Platelet Rich Plasma (PRP)

- **Induction of dermal papilla cell proliferation**
  - B- catenin
  - Extracellular signal-related kinase (ERK)
  - Akt signaling

- **Anti-apoptotic effects**
  - Activation of Bcl-2
  - Phosphorylation of Akt (pAKT)

- *Dermal papilla cells are protected from premature breakdown and remain active, thereby extending the anagen phase of the hair cycle and delaying induction into catagen and telogen phases*
A Spilt Head Study of Efficacy of Placebo versus Platelet-rich Plasma Injections in the Treatment of Androgenic Alopecia

Dilip Kachhawa, Gauri Vats, Durgesh Sonare, Pankaj Rao, Sandeep Khuraiya, and Rohit Kataiya

Results:

Hair loss reduced with evidence of new hair growth. Digital image analysis showed an overall improvement in hair density and quality as lanugo-like hair became thicker, normal hair. An improvement in hair density, quality and thickness on trichoscopy was noted.

Conclusion:

Our data suggest that PRP injections have therapeutic effect on male pattern hair loss with no major side effects and high patient satisfaction overall.
Subjects and Methods:

Fifty patients with AGA were selected on the basis of inclusion and exclusion criteria. These patients were randomly divided into two groups of 25 patients each and were given following treatment: (i) Group A: topical minoxidil (5%) alone and (ii) Group B: topical minoxidil (5%) + microneedling with platelet-rich plasma (PRP).

Statistical Analysis Used:

Patients were assessed before starting the treatment and at the end of 6 months on the basis of (a) Patient's self-assessment based on standardized seven-point scale compared with baseline (b) Physician's assessment based on standardized seven-point scale of hair growth compared with baseline.

Results:

There was a significant improvement ($P < 0.05$) in both patients' assessment and investigator's assessment in Group B as compared to Group A at the end of 6 months.

Conclusions:

Microneedling with PRP is safe, effective, and a promising tool for the management of AGA.
Platelet-rich plasma for androgenetic alopecia: Does it work? Evidence from meta analysis

Salvatore Giordano MD PhD¹,²  |  Marco Romeo MD PhD³  |  Petteri Lankinen MD PhD⁴

Conclusions: Local injection of PRP for androgenic alopecia might be associated with an increased number of hairs and some hair thickness improvement in the treated areas with minimal morbidity. The results of this meta-analysis should be interpreted with caution as it consists of pooling many small studies. Larger randomized studies can verify this perception.
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More Information
Platelet Rich Plasma (PRP)

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Microneedling Therapy With and Without Platelet-Rich Plasma

Peter W. Hashim, MD, MHS; Zachary Levy; Joel L. Cohen, MD; Gary Goldenberg, MD

PRACTICE POINTS

• Microneedling is an effective therapy for skin rejuvenation.
• Preliminary evidence indicates that the addition of platelet-rich plasma to microneedling improves cosmetic outcomes.
Growth Factors

• Dehydrated human amnion/chorion composite graft
  – Contains numerous growth factors
  – Recruiting endogenous stem cells
  – Low immunogenicity


Dehydrated human amnion/chorion membrane treatment of venous leg ulcer [J Wound Care. 2015]

Dehydrated Human Amnion/Chorion Membrane as Ad [Ostomy Wound Manage. 2015]

Dehydrated human amnion/chorion composite graft

- platelet derived growth factor AA (PDGF-AA)
- transforming growth factor b1 (TGFb1)
- vascular endothelial growth factor (VEGF)
- fibroblast growth factor 2 (FGF-2)
- angiopoietin-2 (ANG-2)
- epidermal growth factor (EGF)
- basic fibroblast growth factor (bFGF)
- heparin binding epidermal growth factor (HB-EGF)
- hepatocyte growth factor (HGF)
- platelet derived growth factor BB (PDGF-BB)
- placental growth factor (PIGF)
- promote fibroblast and endothelial cell proliferation
- recruit mesenchymal stem cells (MSC)
- promote growth factor expression in native cells
- support perimatrix neovascularization
Potential uses of Stem cells

- Stroke
- Traumatic brain injury
- Learning defects
- Alzheimer's disease
- Parkinson's disease
- Baldness
- Blindness
- Deafness
- Amyotrophic lateral-sclerosis
- Myocardial infarction
- Muscular dystrophy
- Diabetes
- Spinal cord injury
- Bone marrow transplantation (currently established)
- Osteoarthritis
- Rheumatoid arthritis
- Wound healing
- Missing teeth
- Crohn's disease
- Multiple sites: Cancers
Stem Cells

- **Totipotent** – may develop into any primary germ cell layer (ectoderm, mesoderm or endoderm) of the embryo and extraembryonic tissue (trophoblast => gives rise to the placenta)

- **Pluripotent** (embryonic) – differentiate into any derivative of the three germ cell layers, but not trophoblast
Stem Cells

- **Multipotent** – differentiate into multiple cell types from similar lineages
  - Mesenchymal stem cells (MSCs) – differentiate into adipogenic, osteogenic, chondrogenic, and myogenic cells

- **Unipotent** – can only self-replicate
  - Lowest differentiation potential

  - **Adults lack totipotent or pluripotent cells**
  - **Have multipotent or unipotent cells only**
Stem Cells

- Multipotent stem cells (MSCs)
  - Bone marrow, umbilical cord, adipose tissue, dermis, or hair follicle bulge
Stem Cells

- Multipotent stem cells (MSCs)
  - Autologous multipotent hematopoietic bone marrow cells
  - First successfully used for the treatment of chronic wounds

Due to invasive nature of extracting bone marrow stem cells and their declining number with age, other sources of MSCs are now favored.
Stem Cells

• Multipotent stem cells (MSCs)
  – Umbilical cord blood
    • Surgical intervention is not necessary
      – Retrieved after umbilical cord clamping

» Advantages:
  • high regenerative power
  • low immunogenicity
    • newborn is immunologically immature
Stem Cells

• Multipotent stem cells (MSCs)
  – Adipose derived stem cells (ASCs)
    • Mid face contouring, lip augmentation, facial rejuvenation, facial scarring, lipodystrophy, penile girth enhancement and vaginal augmentation
    • Harvested from lipoaspirate of the abdomen
      – Combined with supportive mechanical scaffolds such as hydrogels
    • Scaffold for autologous fat transfer to increase viability of transplanted tissue
      – Cell-assisted lipotransfer (CAL)

» Number of MSC depends on various host factors
  • Age, health, smoking history, etc.
Stem Cells

- Multipotent stem cells (MSCs)
  - Autologous human fibroblasts
    - Treatment of wrinkles, rhytids, and acne scars
    - FDA approved azficel-T (2011) – autologous fibroblast injection
      - Fibroblasts harvested from a patient’s own postauricular skin
      - Culture expanding them in vitro for 3 months
      - Reinjecting cells into the desired area of dermis in a series of treatments

Regenerative Medicine in Cosmetic Dermatology – MS submitted for publication.
Stem Cells

- Multipotent stem cells (MSCs)
  - Follicular bulge – rich in epithelial and melanocytic stem cells
  - Potential for treating androgenic alopecia and vitiligo
Clinical Applications of Mesenchymal Stem Cells in Soft Tissue Augmentation

Summer E. Hanson, MD; Karol A. Gutowski, MD; and Peiman Hematti, MD

Abstract
Based on a variety of preclinical studies showing that mesenchymal stem cells (MSC) play a significant role in tissue repair and homeostasis, MSC have rapidly moved into a phase of clinical trials investigating their efficacy as a cell-based therapeutic modality for a diverse group of applications. An emerging body of evidence shows that in addition to being a progenitor cell population with self-renewing and multipotent differentiation capabilities, MSC have unique immunomodulatory properties, making them even more attractive for regenerative medicine. Emerging discoveries in stem cell biology have revealed a multitude of mechanisms through which MSC could potentially augment the current techniques in aesthetic surgery. In this article, the authors review the clinical advances in cell-based therapies relevant to aesthetic surgery, including tissue augmentation, rejuvenation, and regeneration.

Keywords
mesenchymal stem cells, fat grafting, cosmetic augmentation, immune modulation

Accepted for publication February 23, 2010.
Stem Cells

• Cell-assisted lipotransfer (CAL)
  – Scaffold for autologous fat transfer to increase viability of transplanted tissue
    • Some studies showing better clinical improvement but data is mixed

• Wound therapy
  – Topical wound dressing
    • Data is mixed and limited

• Skin rejuvenation
  – Injection into mid dermis showed some improvement and thickening of collagen bundles in one study
Future Directions

• Combination treatment for aesthetic patient with other modalities
• Medical dermatology implications?
Conclusions

• Regenerative medicine
• Dermatologists already practice regenerative medicine
• Role of Platelet Rich Plasma (PRP) in dermatology
• Role of Dehydrated human amnion/chorion composite graft
• Role of Stem Cells in dermatology
References - PRP

References – Dehydrated human amnion/chorion composite graft


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• Gellhorn AC, Han A. The Use of Dehydrated Human Amnion/Chorion Membrane Allograft Injection for the Treatment of Tendinopathy or Arthritis: A Case Series Involving 40 Patients. PM&R. 2017 Dec;9(12):1236-1243.
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