What’s the Evidence for Efficacy in ED / PD

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I have no financial relationships with pharmaceutical or device companies relevant to this activity
Outline

• Platelet Rich Plasma (PRP)
  – What is it
  – Clinical use
  – Potential use
• Platelet Rich Plasma in ED
  – Evidence
• Platelet Rich Plasma in PD
  – Evidence
• Mission Statement of the SMSNA
  – AUA guideline
• Conclusion
Platelet Rich Plasma
Why use Platelets

• Platelets play a crucial role in:
  • Coagulation
  • Tissue repair
  • Vascular remodeling
  • Inflammatory and immune response

• Promoting wound healing following injury
  • Secretion of various growth factors, cytokines and chemokines

Epifanova and al, Sex Med Rev 2019;e1-8
Platelet Rich Plasma
What is it?

- Autologous blood plasma that contains platelet concentrations that exceed physiological standards by 3 to 7 fold.
  - centrifugation of the patient’s own blood

- Platelet count in the final cell product most be >1,000,000 U/mL to shows therapeutic effect

Epifanova and al, Sex Med Rev 2019;e1-8
Platelet Rich Plasma

• Potential Qualitative composition biologically active proteins
  – Growth factors
    • Vascular endothelial growth factor (VEGF)
    • Platelet-derived growth factor (PDGF)
    • Fibroblast growth factors (FGF)
    • Epidermal growth factor (EGF)
    • Insulin-like growth factor (IGF)
    • Transforming growth factor (TGF)-b

Epifanova and al, Sex Med Rev 2019;e1-8
Platelet Rich Plasma

- Regenerative potential
  - Restoring blood flow
    - Vasculogenesis
    - Angiogenesis
    - Endothelization
  - Stabilizing the composition
    - Extracellular matrix
    - Smooth muscle cells
    - Collagen formation
  - Tissue regeneration.

Epifanova and al, Sex Med Rev 2019;e1-8
Platelet Rich Plasma

• **Clinical use**
  – Absence or a minimum of adverse effects
    • Introduction in 1987
    • Use in:
      – Orthopedics / Sports medicine / Trauma surgery
      – Otolaryngology / Dentistry
      – Neurosurgery
      – Dermatology, Cosmetology / Plastic surgery
      – Cardiothoracic surgery
      – Ophthalmology

• **Effectiveness in?**
  • Its biological properties and effects of PRP remains poorly understood.

• **Unregulated Industry**
  • From a regulatory perspective, PRP injections are classified as minimal manipulation of tissue.

Epifanova and al, Sex Med Rev 2019;e1-8
Platelet Rich Plasma

- 1 studies listed on www.clinicaltrials.gov for PRP and ED - 9/2019

- Google “Platelet rich plasma”: 18,600,000 results - 10/2019

- Google “Platelet rich plasma, erectile dysfunction”: 210,000 results - 10/2019

- Cost: $1500 to $3000 cash per injection
Platelet Rich Plasma

• Absence of a standardized protocol for production of the cell product
  – The bioavailability of growth factors remains highly variable depending
    • Patient characteristics
    • Platelet, leucocyte and red blood cell concentration
    • Method of activation used.

• CLASSIFICATION: Dohan Ehrenfest 2009: nonstandardized nomenclature
  – based on presence or absence of blood cells and fibrin
    • pure platelet-rich plasma
    • leukocyte- and platelet-rich plasma
    • pure platelet-rich fibrin
    • leukocyte- and platelet-rich fibrin.

Epifanova and al, Sex Med Rev 2019;e1-8
Eppley & al, Plastic and Reconst Surg Vol. 114, No. 6, November 2004
Claims Made
The Priapus Shot or P-Shot

• “The Priapus Shot® is a medical procedure developed and trademarked by Dr. Charles F Runels....The Priapus Shot literally regrows new tissue and new blood vessels to rejuvenate men’s erections.”
Claims Made
The Priapus Shot or P-Shot

• ... It literally rejuvenates your penis: boosting sex drive.
• The P-Shot®: no chemicals or drugs, and requires no surgery.
  – P for PRIDE
• What Benefits Can a Man Have from the P-Shot®?
  – Stronger, firmer erections
    • Easier to achieve and maintain erections (i.e., improved sexual stamina)
    • Better overall blood flow to the penis
  – Increased penile length and girth
  – Improvement in or resolution of penile curvature from Peyronie’s Disease
  – Resolution of penile pain with erection
  – increasing sensation in the penis
Claims Made

• “Very helpful to restore sensation in patients who have had a prostatectomy or prostate cancer treatment with radiation”

• “Many men with peyronies disease….can be markedly improved with this treatment”

• “95% of men who have had a priapus shot saw increased firmness”

• “Greater than 70% of men had greater than ½inch increase in the length of their penis”

• “Greater than 50% grew more than an inch after one year”

• “Increase in girth and length is common after 2-3 weeks and lasts for 15-18 months”
Aggressive Direct to Consumer Marketing

PRP-SHOT
PENILE PLATELET RICH PLASMA INJECTION
For Erectile Dysfunction

For Men
 Longer, Harder & More Sustainable Erection
 Increase Sexual Stamina and Sensitivity
Platelet Rich Plasma in ED Evidence
The effect of platelet-rich plasma on cavernous nerve regeneration in a rat model

- 8 rats/group
- 3 months after cavernous nerves crushing injury
- Measurable neurotrophic effect of PRP on CN regeneration after crush injury in a rat model.

Figure 1. Example of Maximal intracavernous pressure (ICP) changes after electrostimulation of the cavernous nerves at 3 months. (A): Group 1; the pressure reached 100 cmH₂O. (B): Group 2; the pressure reached 38 cmH₂O. (C): Group 3; the pressure reached 92 cmH₂O.
Optimization of platelet-rich plasma and its effects on the recovery of erectile function after bilateral cavernous nerve injury in a rat model

The aim of this study was to optimize the PRP preparation method (human) and compare the effects of PRP from different preparation methods in restoration of erectile function in a rat model. Assessment 4 weeks later.

Safety and feasibility of platelet rich fibrin matrix injections for treatment of common urologic conditions

- **Use a matrix to avoid early washout: platelet rich fibrin matrix (PRFM)**
  - Assess safety and feasibility
  - 17 patients: 4 ED, 11 PD, 1 ED+PD, 1 SUI (female)
  - Mean of 2.1 injections per patient (1 to 8 inj /4-9 ml)
- **Post-procedural minor adverse events were seen in 3**
  - Well-tolerated, safe, and provides a feasible treatment for ED in humans
  - No patients experienced complications at follow-up.
- **No decline in IIEF-5**
  - IIEF-5 scores improved by an average of 4.14
  - In PD, 80% (4/5) initially reported subjective improvement in their degree of curvature.

The effectiveness of intracavernous autologous platelet-rich plasma in the treatment of erectile dysfunction.

- Article in Russian...
  - 3 groups of ED pts injected 3 times at weekly intervals.
    - PRP (30), PRP+PDE5i (30) and inactivated PRP (15)
    - Group 1 had the best results 1 month later but
      - IIEF and SEP improved in all group

- No long term data
- No placebo controls

Chalyj & al, Urologiia 2015:76-79.
Platelet Rich Plasma in PD

Evidence
The Effect of Platelet Rich Plasma on Peyronie's Disease in Rat Model

• 4 groups
  • Sham
  • PD
  • PD + PRP (day 15)
  • PRP (Day 0)

• Asses 45 days later
  • Significant changes in all three groups compared to the sham for:
    – fibrosis, collagen / smooth muscle ratio and type III / type I collagen ratio

• PRP has no therapeutic effect on PD
  – PRP shows PD-like effects in rats

Evaluation of the benefit of using a combination of autologous platelet rich-plasma and hyaluronic acid for the treatment of Peyronie’s disease

- 90 pts 8 ml of PRP combined with HA into the palque
  - repeated every 15 days for 2 months
  - Additional monthly sessions were done, if necessary
  - in addition, before the injection, fibrous or calcified plaques were punctured with a 22G or 18G needle

- Curve
  - Mean curvature of the penis of $44.37 \pm 15.93^\circ$
  - Mean final improvement was respectively $16.54 \pm 10.51^\circ$
    - $(39.65 \pm 24.83\% )$
      - Better result if the initial curve angulation was lower

- No Placebo group
- No analyze of the PRP composition
- Effect of the mechanical action of the needle?
SMSNA POSITION STATEMENTS ON RESTORATIVE THERAPIES FOR ED (2018)

• The SMSNA strongly supports the development of novel erectogenic therapies, given that many men with ED either fail currently available treatments or find them unpalatable.

• The society, however, recognizes the need for adequately powered, multicenter, randomized, sham/placebo-controlled trials in well-characterized patient populations to ensure that efficacy and safety are demonstrated for any novel ED therapy.
SMSNA POSITION STATEMENTS ON RESTORATIVE THERAPIES FOR ED

• Thus, given the current lack of regulatory agency approval for any restorative (regenerative) therapies for the treatment of ED and until such time as approval is granted
  – SMSNA believes that the use of PRP is experimental and should be conducted under research protocols in compliance with Institutional Review Board approval.
• Patients considering such therapies should be fully informed and consented regarding the potential benefits and risks.
• Finally, the SMSNA advocates that patients involved in these clinical trials should not incur more than basic research costs for their participation.
25- For men with ED, platelet-rich plasma (PRP) therapy should be considered experimental. (Expert Opinion)

- PRP should not be offered to men with ED unless it is administered in the context of an IRB-approved experimental clinical research protocol.
- At this time, no full-text peer-reviewed publications are available to constitute an evidence base. Therefore, reliable information about potential benefits and risks/burdens of PRP therapy is not available. Because of the absence of evidence and given the availability of multiple other proven treatment options, it is the Panel's expert opinion that PRP therapy is not appropriate for men with ED except as part of an IRB-approved research trial.
Conclusion

• Global presence of PRP clinics
• Regenerative medicine:
  – Active marketing
  – Public interest
    • desperate and vulnerable patients
• Lucrative
  – Ethical concern
• « No scientific evidence has been published to establish an evidence-based risk-benefit profile for PRP use for ED in humans »

Conclusion

• Limitations of the available data to support the use of PRP in the treatment of sexual dysfunction
  – Animal studies are required for better understanding of the mechanism of PRP
  – Need for proper clinical trial
    • Volume and frequency of injections
    • Quality of the PRP
    • Need of placebo controls
    • Large number
    • Follow-up: need long term data

• PRP: safe?
  – Does it justify its use and cost to the patient?
  – Interests outpacing clinical evidence despite a potentially legitimate therapeutic benefit\(^1\)

1-Scott & al, Sex Med Rev 2019;7:306e312
Two Test Positive for HIV After 'Vampire Facial'

Debbie Koenig
May 01, 2019
THANK YOU!