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A Pilot Study of the Effect of Localized Injections of Autologous Platelet Rich Plasma (PRP) for the Treatment of Female Sexual Dysfunction

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Abstract

Currently, accepted treatments for Female Sexual Dysfunction (FSD) are limited to psychological, behavioral, hormonal and psychopharmacologic interventions. Because of the complex and multifactorial nature of FSD, current therapeutic options may leave a subset of women suffering with sexual dysfunction without clinical improvement. As a simple, safe, and natural alternative therapeutic option for treating female sexual dysfunction, a pilot study was undertaken to test the effect, if any, of vaginal and clitoral injections of autologous Platelet Rich Plasma (PRP) on women desiring treatment for painful intercourse or anorgasmia. Two standardized sexuality tests, the Female Sexual Function Index and the Female Sexual Distress Scale, were administered before and after treatment and were used to measure the response to this therapeutic intervention. Our data indicated some degree of improvement in FSD, including positive changes in isolated sexual difficulties and in the reduction of levels of sexual distress. However, the limited number of participants in this pilot study restricts conclusions. Our initial observations do suggest that further investigation of PRP therapy for the treatment of female sexual dysfunction is indicated.

Keywords: Dyspareunia; Platelet rich plasma; Female sexual dysfunction; Female sexual arousal disorder; Female orgasmic disorder; Hypoactive sexual arousal disorder; Anorgasmia; Injection

Introduction

Because of the many possible etiologic factors involved in female sexual dysfunction and the variability in the response to existing treatment modalities, this area requires research to develop new safe and effective therapeutic alternatives [1]. A recent review of treatment options, when surgically correctable pathology has been ruled out, listed psychological therapeutics and short-term testosterone as the only Level A therapies [1]. A woman with normal hormonal levels or a contraindication to hormonal therapy and no surgical pathology has only psychological therapies as Level A choices for all four classes of sexual dysfunction (i.e. for hyposexual desire disorder, arousal disorder, orgasmic disorder, and dyspareunia) [1]. Although psychological therapies do help many women, there are no other Class A therapeutic alternatives. This indicates that there is a need for further research in this area.

As one possible strategy, a variety of materials have been injected in the periurethral area to treat both sexual dysfunction and urinary incontinence [2]. For example, Calcium Hydroxyapatite Crystals (CHAC) are FDA approved (Coaptite®) for periurethral injection in the treatment of urinary incontinence. However, such therapy may create a discrete constriction that can be associated with urinary obstruction, erosion, infection, and granuloma formation requiring surgical removal [2-6]. With CHAC, no reports show improvement in sexual dysfunction.

Similarly, the injection of hyaluronic acid fillers (the "G-Shot") has been used as a treatment to enhance orgasmic intensity by the amplification of a controversial anatomical area in the anterior vaginal wall (the Graffian Spot). Due to the potential incidence of granuloma formation by hyaluronic acid fillers at the injection site, this therapy has been condemned by the American College of Obstetrics and Gynecology [2-4].

Since investigators have studied the injection of various substances into the vaginal or periurethral areas for treatment of both urinary incontinence and sexual issues, the mechanics and technique of injection into these anatomic sites appears to be safe and well tolerated. The limiting factor seems to be finding a material that, when injected, produces the desired therapeutic effect without causing untoward side effects.

In contrast to the above mentioned synthetic materials, Platelet Rich Plasma (PRP) has been demonstrated to be effective and without serious side effects in multiple studies in the areas of wound care, orthopedics, dental surgery and in a variety of cosmetic procedures [7-9]. PRP activates pluripotent stem cells in the area of injection, resulting in rejuvenation and even enhancement of damaged or undamaged tissue [10-12]. Moreover, the medical literature contains many articles demonstrating the safety of PRP, with no reports of granuloma formation, infection, or any other serious side effects when FDA approved preparation kits are used [13,14]. Should the PRP be prepared using improperly sterilized tubes, there is the potential for a serious local inflammation or life threatening sepsis. Since PRP is completely autologous, there are no known contraindications to its administration. Technically, PRP injection also offers the advantage of flowing into tissue as a non-viscous liquid and not as a gel (as with hyaluronic acid fillers) or as a particulate slurry (as with calcium hydroxyapatite). The aqueous nature of PRP allows injection through a small bore needle and an even distribution throughout the tissue surrounding the injection site.

Considering the precedent of PRP use in clinical practice, as well as its proven safety, women who presented with complaints of dyspareunia or other symptoms related to sexual dysfunction were offered PRP injections into the periurethral area of the Skenes glands and the clitoris and were observed for their responses to this treatment.

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This pilot study measures the responses of women with varying degrees of sexual dysfunction who received this intervention.

Methods

Eleven females, ages 24-64, presenting with complaints associated with female orgasmic disorder, hypoactive sexual arousal disorder, anorgasmia, or dysparunia, participated in the study. The patients were seen in clinical private practices and were not paid either to receive the procedure or to complete the survey. All patients were fully informed of the innovative therapeutic and experimental nature of the localized PRP injection and consented to the procedure.

The materials and equipment included the following: (1) 5cc syringes, (2) 27 gauge needles, (3) two separate centrifuges with proprietary collection systems, (4) calcium chloride 10% (for activation of PRP), (5) and a topical anesthetic cream compounded with a base that prevents irritation and promotes absorption through the vaginal mucosa. Active ingredients were as follows: bupivicaine, lidocaine, and tetracaine with percent concentrations of 20/8/8 respectively.

First, a topical anesthetic cream was applied to the anterior vaginal wall. The clitoral hood was retracted and cream applied to the clitoris. Delaying the PRP injection for 20 minutes after anesthetic application achieved complete or near complete analgesia for the procedure. Peripheral blood was drawn from the arm and centrifuged to yield 5 cc of PRP. One of either of two FDA-approved, proprietary collection systems were used according to the standard recommendations for each system: (1) Regen® or (2) TruPRP® [15,16]. Both systems use centrifugation to separate and concentrate PRP. The TruPRP® system concentrates 5 ml of PRP from 60 ml of whole blood using a laser device that visualizes the buffy coat to separate the PRP from RBC's. The Regen® system concentrates 5ml of PRP from 10 ml of whole blood using a gel separator.

After isolation of the PRP, calcium chloride (0.5ml) was added to the 5 ml of PRP isolate to activate the thrombin cascade, thereby causing degranulation of platelets, releasing growth factors and cytokines, and starting the transformation of the PRP to platelet rich fibrin matrix (PRFM) [17]. Before the PRFM became too gelatinous for passing through a needle (less than 10 minutes), two injections were given through a 27-gauge needle, one injection into each of two specific sites: (1) the anterior vaginal wall into a space between vagina and urethra most distal from bladder), and (2) into the clitoris. All authors were trained by Dr. Runels and agreed to perform the procedure in a uniform manner.

Exclusion criteria

Patients presenting with pregnancy, infection, prior genital tract surgery, malignancy or inappropriate affect were not considered eligible for the procedure.

Ethics

This study falls in the category of Medical Practice and Innovative Therapy, which describes an activity that is designed solely to benefit individual patient(s) and does not require IRB review (University of Virginia Institutional Review Board Health Science for Health Science Research).

Data collection

Two standardized tests to monitor the effects of the procedure on sexual function were employed: (1) the standardized Female Sexual Function Index (FSFI) questionnaire and (2) the Female Sexual Distress Scale Revised (FSDS-R) [18,19]. The FSFI questionnaire measures arousal, desire, pain, orgasm, satisfaction, and lubrication [18]. The FSDS-R questionnaire measures sexually related distress in Females With Sexual Dysfunction (FSD) [19,20]. The FSFI and the FSDS-R were administered before and after the procedure by the patient. Data was obtained at the time of the injection and at 12-16 weeks after receiving treatment.

Previous PRP studies of other tissue types suggests that collection of follow up data at approximately twelve weeks after the procedure allows adequate time to observe therapeutic effects attributed to stem activation and transformation [7-11]. The outcomes measured were the patients' responses to the FSDS-R and FSFI surveys prior to and after receiving the intervention.

Results

Eleven females presenting with dysparunia (not related to vulvodynia or vaginismus) or with one of the previously mentioned categories of sexual dysfunction, ages 24-64, were included the pilot study group. Of the 11 patients treated, seven (64%) demonstrated some degree of improvement (Table 1). Five of the 7 women who started with elevated levels of sexual distress in the FSDS-R, in which the threshold of distress is defined as a score of 11 or more, dropped their scores to less than 11. Therefore, according to the test criteria, 71% of the women improved from being "distressed" to being "not distressed" after the procedure.

Two patients (18%) showed no change in their levels of distress, but both of these women started with low distress levels. Interestingly, two women (18%), according to their FSDS-R, actually became more distressed after treatment. One of the two who reported more distress subsequent to her PRP injection attributed the worsening of her distress to the loss of her sexual partner. The other woman who reported increased distress explained that after the procedure, her libido increased to a point that it exceeded the ability of her partner to satisfy her.

The mean FSDS-R score dropped 10 points, from 17 to 7 (p=0.04) (Table 2). Nine (82%) of 11 women showed improvement in total FSFI scores. Two (18%) did not experience improvement. The range of improvement in total FSFI scores was from 1.6 to 14.3. The difference between the mean pre-treatment and post-treatment totals was 5.5 (p=0.01) (Table 2). The mean scores for arousal improved by 1.2 (p=0.009), for lubrication improved by 1.28 (p=0.002), for desire 0.82 (p=0.06) and orgasm 1.08 (p=0.05). Since the pre-injection and post-injection scores are observed from the same individual (a repeated-measures design), a paired sample t-test was used, assuming that the

Patient #	PRE-Shot	POST-shot
1	31	2
2	2	2
3	21	35
4	1	2
5	7	4
6	30	4
7	3	3
8	34	14
9	28	0
10	21	7
11	12	7

Table 1: Results for Female Sexual Distress Scale: A score of ≥ 11 effectively discriminates between women with FSD and no FSD.

	Pre PRP Injection		Post PRP Injection*		Difference	
	n	Mean	n	Mean	P value**	95% CI
		Score		Score		
FSDS-R	11	17.27	11	7.27	0.04	-19.57 to -0.43
FSFI (Total)	11	24.13	11	29.63	0.01	1.48 to 9.52
Desire	11	3.60	11	4.42	0.06	0.03 to 1.67
Arousal	11	3.95	11	5.18	0.009	0.39 to 2.07
Lubrication	11	4.17	11	5.45	0.002	0.57 to 1.99
Orgasm	11	4.11	11	5.19	0.05	0.02 to 2.14
Satisfaction	11	4.04	11	4.40	0.28	-0.35 to 1.08
Pain	11	4.25	11	4.98	0.25	-0.59 to 2.04

*10-16 weeks post treatment **unadjusted

Table 2: Mean scores before and after injection with Plate-Rich Plasma (PRP) of the Female Sexual Distress Scale Revised (FSDS-R) and the Female Sexual Function Index (FSFI). The FSFI individually measures Desire, Arousal, Lubrication, Orgasm, Satisfaction, and Pain. The Wilcoxon signed rank sum test was used to assess the difference between the Pre PRP Injection and Post PRP Injection scores.

differences between paired observations are normally distributed. When breaking down the FSFI into the individual domains: desire, arousal, lubrication, and orgasm were significantly increased after injection with PRP. There was no statistically significant effect on satisfaction and pain, although there was a trend toward improvement in those domains.

Side effects

Extreme sexual arousal occurred in 2 patients and included the following: sexual arousal with urination, continuous sexual arousal, ejaculatory orgasm, and spontaneous orgasm. Except for ejaculation, these responses only lasted 1 to 2 weeks and occurred in younger patients who received the procedure with an initial score indicating minimal dysfunction. Other than ejaculatory orgasm, these side effects resolved without further treatment. No other unfavorable side effects were reported.

Discussion

Our results suggest that some cases of female sexual dysfunction, manifested by decreases in sexual desire, arousal, lubrication and orgasmic responsiveness, may be treated with specifically directed injections of autologous Platelet Rich Plasma (PRP) in the area of the Skene's glands and the clitoris. The issue of female sexual dysfunction is quite common. Data shows that sexual difficulties may be experienced by more than 40% of the sexually active adult female population at some time in their lives [21,22]. This percentage represents a sub-set of women who are psychologically distressed by their dysfunction, but do not necessarily consult a physician. Consequently, this statistic may actually be under reported and the condition under-diagnosed because data indicates that only 14% of women may have a conversation with their physician about their sexuality [1]. For sexually dysfunctional women who have not responded to hormonal or psychologic therapies, previous attempts to develop an effective injectable therapy to treat dyspareunia, female orgasmic difficulties, and urinary incontinence have been limited by complications related to the material injected. Autologous PRP injections, on the other hand, have been shown to be safe in other therapeutic areas, since PRP is nonantigenic and contains no synthetic agents that could cause an untoward local or systemic reactions. From our literature search, we could find no reports of granuloma formation, infection, or local tissue necrosis with the use of any of the kits approved by the FDA for preparation of PRP. Since PRP is derived from the patient's own blood, with no foreign or synthetic substances employed, the body will not react to it immunologically [12]. Hence, there are no reports of allergic reactions to PRP injection.

Studies have demonstrated that PRP induces regrowth of new tissue by of the activation of pluripotent stem cells that are indigenous to most parts of the body. These cells are capable of differentiating into several tissue types, when stimulated by growth factors produced by activated platelets [4-7]. We therefore postulate that when PRP is activated and injected into the anatomic areas involved in sexual responsiveness, growth factors and cytokines may cause differentiation of pluripotent stem cells resulting in neoangiogenesis, fibroblast growth, glandular proliferation (Skene's glands), and new neuronal growth—resulting in improved physiologic responsiveness. Improved vascularity and neuronal regrowth in the vagina and in the clitoral area could restore or possibly enhance sexual responsiveness and sensitivity by increasing blood flow to the area, especially in cases where hormonally independent vaginal atrophy contributes to FSD. In addition to increased blood flow, collagen and sensory nerve regrowth might relieve coital discomfort as well as enhance vaginal sensitivity. Also, increased blood flow in the clitoris, if induced by PRP injections, could also lead to improved arousal and orgasm.

The extreme sexual arousal observed in two of our patients may have resulted from a volumetric effect of the PRP injection, causing continuous pressure on the urethra and the Skene's glands. This effect can result from Platelet Rich Fibrin Matrix (PRFM), in which the PRP interacts with thrombin to form a matrix. If Platelet Rich Fibrin Matrix in the periurethral tissue behaves as it does in the dermis of the arm, then this matrix would resolve within 2 weeks to become replaced over the following 8 weeks with new tissue growth [12].

There are certain obvious limitations to this study. Because of the small number of patients in this pilot study, the statistical power of this study is limited and, as such, only suggests a possible effect of our intervention. Furthermore, due to the complexity of the female sexual response and the importance of emotional factors in sexual responsiveness, a placebo effect must be considered when evaluating our findings. Another possible limitation of our pilot study is its observational and subjective nature, despite the use of standardized diagnostic questionnaires. Despite the potential methodologic problems inherent in a pilot study involving female sexuality, because of the patient's positive response to our intervention, without the incidence of complications, future prospective, placebo controlled studies are planned.

Conclusions

The preliminary results of this pilot study suggests that specifically placed intravaginal and intraclitoral PRP injections could be an effective method to treat certain types of female sexual dysfunction, especially in the areas of desire, arousal, lubrication and orgasm. Improvement in satisfaction and pain were noted, but were not statistically significant.

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