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**A Randomized Double-Blind Placebo Controlled Trial of Autologous Platelet Rich Plasma Intradermal Injections for the Treatment of Vulvar Lichen Sclerosus.**

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**Conflicts of Interest:**

Andrew Goldstein: Dr. Goldstein is on the Board of Directors of the Gynecologic Cancers Research Foundation.  
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Vaishnavi Govind reports no conflict of interest.

Leia Mitchell reports no conflict of interest.

Debra Heller reports no conflict of interest.

*To the Editor:* We performed a randomized, double-blind, placebo controlled trial to evaluate the efficacy and safety of autologous platelet rich plasma (PRP) for the treatment of vulvar lichen sclerosus (LS). Thirty patients (mean age 52.6 years, 29 Caucasians, 1 Hispanic) with biopsy proven active LS were recruited. One participant withdrew after randomization, but before treatment, and 29 completed the study. Patients were randomized to receive either placebo (saline injections) (10 subjects) or two separate treatments of PRP separated by 6 weeks (20 subjects). There was no statistically significant difference between the participant age or duration of symptoms between PRP and placebo groups. Each treatment consisted of 5 ml of PRP injected sub-dermally and intra-dermally, infiltrating the areas affected by LS. The PRP was prepared using a FDA cleared, centrifuge which uses a laser to isolate the platelet rich fraction of 60ml of whole blood [Magellan® Autologous Platelet Separator System.] The PRP was collected in a blackened syringe so that neither the physician administering the PRP, nor the study participants, were aware if they were receiving the PRP or placebo. The primary efficacy variable was determined by a pathologist with expertise in vulvar pathology (DH) who was blinded to the treatment arms, who evaluated the inflammatory infiltration on the pre and post treatment biopsies (0 to 3 scale). A secondary endpoint was change in the “Clinical Scoring System for Vulvar Lichen Sclerosus” (CSS) a validated instrument that assesses both the investigators and patients’ impression of the severity of the LS.<sup>1</sup> Of the 19 women receiving PRP, 5 had improvement in histopathologic inflammation between pre-and-post treatment biopsies, 10 had no change, and 4 had more inflammation. Of the 10 women receiving placebo, 5 had improvement, 4 had no change, and 1 had more

inflammation  $U=109.0$ ,  $p=0.542$  (Mann-Whitney). Mean difference in the CSS patient domain between initial and final visit was -7.74 for patients receiving PRP and -9.44 for patients receiving placebo,  $U=80.50$ ,  $p=0.654$  (Mann-Whitney). Bruising was the only adverse event reported.

A recent pilot study performed by our group showed that PRP reduced histopathologic inflammation in 7 of 12 patients with vulvar lichen sclerosus.<sup>2</sup> However, the main limitations of that study was its lack of placebo control. In addition, Tedesco et al. studied PRP injection in 31 LS patients.<sup>3</sup> They reported that 62% of patients have improvement in their LS but their study was not placebo controlled, did not use validated measures of subjective or objective improvement, and did not include histopathologic evaluation. As LS is a premalignant condition, and a reduction in inflammation with optimal use of corticosteroids lowers the rate of malignant transformation, it is essential that all studies of LS use reduction in inflammation as the primary efficacy measure.<sup>4</sup> One of the strengths of our current study is that it used this objective criterion as its primary endpoint. Additional strengths of our study are that it was blinded, placebo-controlled, and used the validated CSS. A sample size calculation was performed prior to the onset of the study and determined that our study sample was powered to show a clinically significant effect of a 50% reduction in inflammation with a two-sided significance of 0.05 and a power of 0.8. In conclusion, until further well-designed, controlled studies with appropriate endpoints show positive results, the negative results of this study suggest that autologous PRP does not adequately treat vulvar LS.

**Statement of Authorship:**

Andrew Goldstein was responsible for study design, data collection, interpretation of data, and manuscript preparation.

Vaishnavi Govind was responsible for data collection, statistical analysis, and interpretation of data, manuscript preparation.

Leia Mitchell was responsible for data collection, interpretation of data, manuscript preparation.

Debra Heller was responsible for data collection, manuscript preparation.

All authors had access to the data.

### References

1. Gunthert AR, Duclos K, Jahns BG, et al. Clinical scoring system for vulvar lichen sclerosis. *J Sex Med.* 2012;9(9):2342-2350.
2. Goldstein AT, King M, Runels C, Gloth M, Pfau R. Intradermal injection of autologous platelet-rich plasma for the treatment of vulvar lichen sclerosis. *J Am Acad Dermatol.* 2017;76(1):158-160.
3. Tedesco M, Pranteda G, Chichierchia G, et al. The use of prp (platelet-rich plasma) in patients affected by genital lichen sclerosis: clinical analysis and results. *J Eur Acad Dermatol Venereol.* 201
4. Lee A, Bradford J, Fischer G. Long-term Management of Adult Vulvar Lichen Sclerosis: A Prospective Cohort Study of 507 Women. *JAMA Dermatol.* 2015;151(10):1061-1067.