COMMENT

Commentary on: Safety and feasibility of percutaneous needle tunneling with platelet-rich plasma injections for Peyronie's disease in the outpatient setting: a pilot study

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In the article titled 'Safety and Feasibility of Percutaneous Needle Tunneling with Platelet-Rich Plasma Injections for Peyronie's Disease in the Outpatient Setting: A Pilot Study,' Zugail et al. [1] presented data from a non-randomized, prospective pilot study that investigated the antifibrotic effects of platelet-rich plasma (PRP) injection combined with percutaneous needle tunneling (PNT) and followed by vacuum erection device (VED) application for the treatment of Peyronie's disease. In this prospective study, 54 patients were enrolled and the main outcome was the improvement in penile curvature. In 87.04% of the patients upon consultation, the curvature of the penis became stable. When they compared the mean curvature angle before (53.98 ± 23.19) and after the use of VED following PNT/PRP (30.09 ± 20.61), they observed a significant improvement ($p = 0.001$) in the curvature.

The rationale behind this treatment approach is the utilization of injected PRP to modulate fibrosis in Peyronie's disease. PRP contain various mediators responsible for modulating tissue integrity remodeling, including growth factors, chemotactic molecules, and angiogenic mediators [2].

However, it's worth noting that the mediators in PRP solution can have controversial effects on fibrotic tissues. PRP contains fibrotic mediators in its composition, including TGF-β, PDGF, and FGF2, which have the potential to induce fibrosis [3]. To use PRP in wound healing modulation, agents that inhibit these fibrotic mediators are necessary, as scar tissue and fibrosis, which are complications of wound healing, need to be prevented and treated. For this reason, using Suramin and TGF-β inhibitor antibodies were recommended to prevent the fibrosis that may result from PRP treatment in the literature [3–5]. In the study conducted by Culha and colleagues, the naive application of PRP injections, without considering fibrosis-inducing mediators such as TGF-β, actually demonstrated the induction of fibrosis rather than its prevention [6]. Furthermore, PRP injection not only stems from its content but also induces TGF-β expression from the applied tissue [7]. To ensure the safety of using PRP in fibrotic diseases, it must be applied after purification from fibrotic mediators or by inhibiting fibrotic mediators because it can potentially induce fibrosis by activating FAP+ fibroblasts [8] already found in fibrotic tissue, making the situation more complicated.

Moreover, in diseases like Peyronie's disease and other fibrotic conditions, the role of the immune system is unquestionably significant. The dominance of M2-type macrophages, which stimulate fibroblast activation through the secretion of cytokines and mediators, is essential for the formation of fibrotic tissue [9]. To treat fibrotic diseases, it is essential to repolarize macrophages from an anti-inflammatory and fibrotic M2 type to an inflammatory character. Stimulation of inflammation is required for the transformation of M2-type macrophages into M1 type [10]. In this study, the authors used the PNT technique, which, as evident from the text, leads to penile ecchymosis in 75.93% of patients, potentially indicating trauma [1]. This trauma is triggered by the release of damage-associated molecular patterns (DAMPs) from cells, initiating inflammation induction and potentially facilitating the transformation of M2-type macrophages, which contribute to fibrosis, into M1 type macrophages [11, 12]. Therefore, the authors should have certainly compared the PNT and PNT/PRP groups to enable a more reliable assessment of PRP's effectiveness.

Also, it is essential to highlight some other limitations in the study. First, PNT was performed by urologists with equivalent levels of experience, followed by intralesional PRP injections through the tunnels, and VED application was conducted afterward. Nevertheless, the authors did not explain how they standardized the experience levels when referring to "equivalent experience level" urologists. Additionally, the inclusion of VED application in their study, introduces bias into their assessment of the effectiveness of PRP injection in Peyronie's disease. Besides, researchers in their study do not provide information on whether Peyronie's plaques are in the active or stable phase. This lack of information does not provide sufficient insight into whether the PRP/PNT treatment regimen should be used during the active or stable phase for treating Peyronie's plaques.

Despite these limitations, this study adds to the ever-growing body of literature demonstrating the potential benefit of injecting PRP in the plaque for Peyronie's disease treatment. This procedure could be a promising treatment option for patients who do not respond to the currently available oral and topical pharmacotherapies; however, further clinical studies involving large cohorts are needed to establish the characterization of PRP injection therapy for Peyronie's disease treatment.

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ADDITIONAL INFORMATION

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