Research Article

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Combined low-intensity extracorporeal shock wave therapy and platelet-rich plasma in acute-phase Peyronie's disease

Akut faz Peyronie hastalığında düşük yoğunluklu ekstrakorporeal şok dalga tedavisi ve trombositten zengin plazma kombinasyonu

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Abstract

Purpose: To evaluate the efficacy, safety, and tolerability of combined low-intensity extracorporeal shock wave therapy and platelet-rich plasma in patients with acute-phase Peyronie's disease.

Materials and methods: This retrospective single-center study included 42 men with acute-phase Peyronie's disease treated between January 2025 and January 2026. The acute phase was defined as a symptom duration of less than 6 months. All patients received daily tadalafil, six sessions of low-intensity extracorporeal shock wave therapy, and three intralesional platelet-rich plasma injections. Penile curvature, plaque size, penile pain, and erectile function were assessed before treatment and 3 months after treatment. Penile pain was evaluated with a visual analog scale, and erectile function was assessed using the International Index of Erectile Function. Paired comparisons were performed according to data distribution.

Results: The median pain score decreased significantly from 7.00 to 3.50 (p<0.001). Erectile function also improved significantly, with the mean score increasing from 16.59±4.51 to 20.88±5.51 (p<0.001). Mean penile curvature decreased from 33.89±10.49 degrees to 31.53±13.26 degrees, but this change was not significant (p=0.058). Mean plaque size changed from 1.58±0.45 cm to 1.56±0.46 cm without statistical significance (p=0.594). No major adverse events were observed. Minor local complications included mild ecchymosis in 11.9% and transient edema in 4.8% of patients.

Conclusion: Combined low-intensity extracorporeal shock wave therapy and platelet-rich plasma appears to be a safe and effective conservative treatment option in acute-phase Peyronie's disease. The protocol provided significant pain relief and improved erectile function, while stabilizing penile curvature and plaque size.

Keywords: Peyronie's disease, platelet-rich plasma, shock wave therapy, erectile dysfunction, penile induration.

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Öz

Amaç: Bu çalışmanın amacı, akut faz Peyronie hastalığında düşük yoğunluklu ekstrakorporeal şok dalga tedavisi ile trombositten zengin plazma kombinasyonunun etkinliğini, güvenliğini ve tolere edilebilirliğini değerlendirmektir.

Gereç ve yöntem: Bu retrospektif tek merkezli çalışmaya, Ocak 2025-Ocak 2026 tarihleri arasında tedavi edilen akut faz Peyronie hastalığı tanılı 42 erkek hasta dahil edildi. Akut faz, semptom süresinin 6 aydan kısa olması olarak tanımlandı. Tüm hastalara günlük tadalafil, altı seans düşük yoğunluklu ekstrakorporeal şok dalga tedavisi ve üç intralezyonel trombositten zengin plazma enjeksiyonu uygulandı. Penis eğrilik açısı, plak boyutu, penil ağrı ve erektil fonksiyon tedavi öncesinde ve tedaviden 3 ay sonra değerlendirildi. Penil ağrı görsel analog skala ile, erektil fonksiyon ise Uluslararası Erektil Fonksiyon İndeksi ile değerlendirildi. Eşleştirilmiş karşılaştırmalar veri dağılımına göre yapıldı.

Bulgular: Ortanca ağrı skoru 7.00'den 3.50'ye anlamlı olarak azaldı (p<0,001). Erektil fonksiyonda da anlamlı iyileşme saptandı ve ortalama skor 16,59±4,51'den 20,88±5,51'e yükseldi (p<0,001). Ortalama penis eğrilik açısı 33,89±10,49 dereceden 31,53±13,26 dereceye geriledi, ancak bu değişiklik anlamlı değildi (p=0,058). Ortalama plak boyutu 1,58±0,45 cm'den 1,56±0,46 cm'ye değişti ve bu fark istatistiksel olarak anlamlı bulunmadı (p=0,594). Majör yan etki gözlenmedi. Minör lokal komplikasyonlar hastaların %11,9'unda hafif ekimoz ve %4,8'inde geçici ödemdi.

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Sonuç: Düşük yoğunluklu ekstrakorporeal şok dalga tedavisi ile trombositten zengin plazma kombinasyonu, akut faz Peyronie hastalığında güvenli ve etkili bir konservatif tedavi seçeneği gibi görünmektedir. Bu protokol anlamlı ağrı azalması ve erektil fonksiyonda iyileşme sağlamış, penis eğriliği ile plak boyutunda ise stabilizasyon oluşturmuştur.

Anahtar kelimeler: Peyronie hastalığı, trombositten zengin plazma, şok dalga tedavisi, erektil disfonksiyon, penil indürasyon.

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Introduction

Peyronie's disease (PD) is an acquired, localized connective tissue disorder of the penis characterized by the development of fibrotic plaques within the tunica albuginea [1]. The fibrotic accumulation leads to inelastic penile deformities, curvature, shortening, and painful erections, which frequently cause severe psychological distress and erectile dysfunction (ED) [2, 3].

The clinical progression of PD is classically divided into two distinct stages: an acute inflammatory phase and a chronic stable phase [3]. The acute phase, which can last up to 18 months, is marked by active inflammation, progressive penile curvature, and pain in both the flaccid and erect states [4]. Once the disease transitions to the chronic phase, the plaque stabilizes, pain typically subsides, and the deformity becomes permanent [4, 5]. While surgical intervention is considered the definitive treatment for correcting severe curvature, it is generally reserved for the chronic, stable phase and carries risks such as penile shortening and worsening ED [6, 7]. Therefore, conservative and minimally invasive treatments are the primary focus during the acute phase, aiming to alleviate pain, halt disease progression, and limit deformity [8, 9].

Recently, regenerative modalities such as low-intensity extracorporeal shock wave therapy (Li-ESWT) and platelet-rich plasma (PRP) have emerged as promising, less-invasive alternatives [10, 11]. Li-ESWT utilizes acoustic wave energy to induce targeted microtrauma, which stimulates angiogenesis, increases local blood flow, and promotes tissue remodeling via the release of vascular endothelial growth factor (VEGF) and endothelial nitric oxide synthase [12]. Furthermore, Li-ESWT has been widely recognized for its efficacy in reducing penile pain through its neuroprotective and anti-inflammatory effects [13].

Concurrently, PRP is an autologous biologic therapy that delivers a supraphysiological concentration of platelets and essential growth factors directly to the injured tissue. The bioactive proteins in PRP, including Vascular Endothelial Growth Factor (VEGF), platelet-derived growth factor (PDGF), and fibroblast growth factor (FGF), play a critical role in modulating the inflammatory response, enhancing angiogenesis, and promoting natural wound healing while inhibiting aberrant fibrotic pathways. Given its regenerative and immunomodulatory properties, PRP has been successfully utilized across various medical fields and is gaining significant traction in urology for its potential to reverse fibrotic changes in PD [14].

Although both therapies have shown individual benefits, their combination provides a strong synergistic therapeutic rationale. The mechanical disruption and neovascularization induced by Li-ESWT can be substantially enhanced by the regenerative growth factors provided by PRP, potentially accelerating tissue repair and plaque remodeling [11]. Despite the theoretical advantages and promising initial outcomes of this multimodal approach, robust clinical data specifically evaluating the combination of Li-ESWT and PRP during the early, active inflammatory phase of PD remain limited.

Therefore, the primary objective of this study was to evaluate the overall clinical efficacy, safety, and tolerability of a combined Li-ESWT and PRP treatment protocol specifically in patients

with acute-phase PD. By comprehensively assessing clinical outcomes, we aimed to determine the therapeutic potential and safety profile of this multimodal regenerative approach in halting disease progression.

Materials and methods

Prior to data collection, the study protocol was reviewed and permission was obtained from the Pamukkale University Non-Interventional Clinical Research Ethics Committee for the study (approval date and number: 09.10.2025 E.764107). The medical records of patients diagnosed with PD and treated at a single institution between January 2025 and January 2026 were retrospectively analyzed. A total of 42 male patients meeting the strict inclusion criteria for the acute inflammatory phase of the condition were enrolled. The primary inclusion criterion was defined as the onset of disease symptoms, specifically the development of penile curvature, palpable tunical plaque, or painful erections, within the preceding 6 months. Patients were systematically excluded if they presented with chronic stable disease lasting more than 6 months, heavily calcified plaques, congenital penile curvature, use of antiplatelet or anticoagulation, hourglass deformity, ventral curvature of the penis, any contraindication for the use of daily tadalafil 5 mg or a history of prior penile reconstructive surgeries or intralesional injection therapies.

Comprehensive baseline and final evaluations were performed for all 42 participants to determine objective and subjective clinical modifications. The penile curvature angle was objectively measured using a medical goniometer following the induction of an artificial erection via an intracavernosal injection of a vasoactive agent. Additionally, plaque dimensions and anatomical locations were documented using penile duplex Doppler ultrasonography. To quantify symptomatic modifications, the intensity of penile pain was recorded utilizing a 10-point Visual Analog Scale (VAS). Furthermore, erectile function and sexual satisfaction were assessed utilizing the validated International Index of Erectile Function (IIEF) questionnaire. Throughout the observation period, all potential complications related to the treatment were monitored and documented to establish the safety profile of the protocol. All patients were administered tadalafil 5 mg daily. Patients were evaluated with VAS, IIEF, curvature angle, and plaque size before and 3 months after the intervention.

The PRP was prepared under sterile conditions following a standardized autologous blood processing protocol. During each session, 10 mL of venous blood was drawn from the patient into collection tubes containing an appropriate anticoagulant. The collected whole blood was immediately processed in a centrifuge at 3000 revolutions per minute for 10 minutes to effectively separate the platelet-poor plasma and red blood cells from the platelet-rich fraction. Subsequently, the highly concentrated plasma was carefully extracted into a sterile syringe for immediate intralesional administration.

All patients received ESWT (DUOLITH® SD1 ultra; STORZ MEDICAL AG, Tägerwilen, Switzerland - focused shockwaves produced by an electromagnetic generator with a cylindrical coil) in an outpatient setting, without local or general anesthesia. The treatment time of each Li-ESWT session was approximately 15 minutes. The treatment was performed perpendicularly on the penile shaft exactly on the top of the plaque with 1,500 pulses in the right side of the plaque and then 1,500 in the left side (A total of 3,000 hits). An energy density of 0.25 mJ/mm2 and emission frequency of 4–6 Hz were set according to the manufacturer's recommendation and according to previous studies. All patients received a total of six treatment sessions, twice a week for 3 weeks, with a 1-week interval. All patients received 0.5 mL of PRP injections into the penile plaque area and around once a week for a total of three injections at interval weeks of ESWT session. Totally, each patient received three sessions of PRP and six sessions of Li-ESWT and the treatment regimen lasted for 6 weeks.

Statistical analyses were performed using SPSS version 26.0 software. Descriptive statistics were utilized to summarize baseline demographic and clinical characteristics. Continuous variables were expressed as means and standard deviations. Comparisons between initial and final clinical parameters, including curvature degree, plaque size, VAS, and IIEF scores, were conducted using the

paired Student t test or Wilcoxon signed rank test, depending on the normality of the data distribution. A *p* value of less than 0.05 was considered to denote statistical significance.

Results

A total of 42 male patients who met the inclusion criteria for the acute inflammatory phase of PD were evaluated in this study. The baseline demographic and clinical characteristics of the study cohort are comprehensively summarized in Table 1. The mean age of the participants was 51.57±7.57 years, ranging from 37 to 68 years. The mean body mass index of the cohort was calculated as 26.99±2.93 kg/m^2, with a range between 21 and 32 kg/m^2. Regarding lifestyle habits, a history of smoking was present in 14 patients (33.3%), and regular alcohol consumption was reported by 9 patients (21.4%). The evaluation of medical comorbidities revealed that hypertension was the most prevalent condition, identified in 16 patients (38.1%), followed by hypercholesterolemia in 11 patients (26.2%), and diabetes mellitus in 2 patients (4.8%). Confirming the acute nature of the condition, the mean duration of the disease prior to the intervention was 3.34±1.48 months (range 1.00 to 5.80 months).

Regarding the initial objective clinical parameters, anatomical assessment of the fibrotic plaques revealed that the dorsal aspect of the tunica albuginea was the most frequent location, observed in 17 patients (40.5%). Other documented plaque locations included the left lateral aspect in 9 patients (21.4%), the left dorsolateral aspect in 6 patients (14.3%), the right dorsolateral aspect in 6 patients (14.3%), and the right lateral aspect in 4 patients (9.5%). The mean baseline penile curvature angle was measured at 33.89±10.49 degrees (range 10.00 to 57.80 degrees). The mean plaque size, as determined by ultrasonography, was 1.58±0.45 cm (range 0.80 to 2.42 cm). For the subjective assessments, the initial intensity of penile pain was notably high, with a median VAS score of 7.00 (interquartile range 2.00). Furthermore, the baseline erectile function of the patients was compromised, as reflected by a mean IIEF score of 16.59±4.51 (range 7.00 to 25.00).

The detailed clinical outcomes and comparative statistical analyses before and after the treatment protocol are presented in Table 2. Regarding subjective symptom relief, a highly significant reduction in penile pain was observed following the treatment protocol. The median VAS score demonstrated a substantial decrease from an initial 7.00 (interquartile range 2.00) to a final measurement of 3.50 (interquartile range 3.00). Based on the Wilcoxon signed rank test, all 42 patients experienced a decrease in VAS scores, yielding a statistically significant improvement (p<0.001). Furthermore, the evaluation of erectile function demonstrated a substantial recovery. The mean IIEF score increased from a baseline of 16.59±4.51 to a final score of 20.88±5.51. This positive modification was determined to be statistically significant (p<0.001).

Conversely, the objective physical measurements of the penile deformities did not exhibit statistically significant alterations. The mean penile curvature angle exhibited a slight decrease from an initial 33.89±10.49 degrees to a final measurement of 31.53±13.26 degrees; however, this reduction did not reach statistical significance (p=0.058). Similarly, the anatomical evaluation of the fibrotic tissue revealed a marginal reduction in mean plaque size from 1.58±0.45 cm to 1.56±0.46 cm at the end of the observation period, which was also not statistically significant (p=0.594).

Regarding the safety profile of the combined treatment protocol, no major adverse events or systemic complications were observed throughout the study period. The safety profile and documented local complications are detailed in Table 3. A total of 35 patients (83.3%) completed the therapeutic regimen without experiencing any adverse effects. Minor and self-limiting local complications were recorded in a small fraction of the study population. Specifically, mild ecchymosis at the injection and application sites was noted in 5 patients (11.9%), while transient edema was observed in 2 patients (4.8%). These minor local reactions resolved spontaneously within a few days without the need for additional medical intervention.

Table 1. Baseline demographic and clinical characteristics

Characteristics	Value
Total Patients, n	42
Age (years)	
Mean ± SD	51.57±7.57
Range	37 to 68
Body Mass Index (kg/m²)	
Mean ± SD	26.99±2.93
Range	21 to 32
Disease Duration (months)	
Mean ± SD	3.34±1.48
Range	1.00 to 5.80
Medical Comorbidities, n (%)	
Hypertension	16 (38.1%)
Hypercholesterolemia	11 (26.2%)
Diabetes Mellitus	2 (4.8%)
Lifestyle Habits, n (%)	
Smoking history	14 (33.3%)
Regular alcohol consumption	9 (21.4%)
Plaque Location, n (%)	
Dorsal	17 (40.5%)
Left lateral	9 (21.4%)
Left dorsolateral	6 (14.3%)
Right dorsolateral	6 (14.3%)
Right lateral	4 (9.5%)

Table 2. Clinical outcomes before and after treatment

Parameters	Initial Evaluation	Final Evaluation	Test Statistic	*p* value
Penile Curvature (degrees)				
Mean ± SD	33.89±10.49	31.53±13.26	t=1.953	0.058*
Plaque Size (cm)				
Mean ± SD	1.58±0.45	1.56±0.46	t=0.537	0.594*
Erectile Function (IIEF score)				
Mean ± SD	16.59±4.51	20.88±5.51	t=-10.124	<0.001*
Penile Pain (VAS score)				
Median (IQR)	7.00 (2.00)	3.50 (3.00)	Z=-5.709	<0.001**

p values calculated using paired Student t test (*) and Wilcoxon signed rank test (**). VAS: Visual Analog Scale; IIEF: International Index of Erectile Function; SD: Standard Deviation; IQR: Interquartile Range

Table 3. Safety profile and complications

Complications	Number of Patients (n)	Percentage (%)
None (No adverse effects)	35	83.3%
Mild ecchymosis	5	11.9%
Transient edema	2	4.8%
Total	42	100.0%

Discussion

The primary objective in the clinical management of the acute inflammatory phase of PD is to halt disease progression, alleviate penile pain, and prevent severe anatomical deformities [15]. Although various conservative modalities are utilized during this active stage, an unequivocal gold standard therapeutic approach remains elusive [16]. Recently, regenerative therapies utilizing Li ESWT and autologous PRP have gained significant attention for their potential to synergistically modulate the inflammatory response, enhance angiogenesis, and promote tissue repair [17]. The present study evaluated the efficacy and safety of combining targeted Li ESWT with intralesional PRP injections specifically in patients presenting with acute-phase PD. The clinical outcomes demonstrated that this multimodal protocol provided a highly significant reduction in subjective pain symptoms and a substantial improvement in erectile function, alongside the successful stabilization of penile curvature and plaque dimensions. Furthermore, the combination therapy exhibited a highly favorable safety profile, with only minor and self-limiting local reactions observed.

The alleviation of penile pain and the restoration of erectile function are considered paramount clinical objectives during the active inflammatory phase of PD. In the present evaluation, a highly significant reduction in penile pain was achieved, accompanied by a substantial recovery in erectile capacity. These favorable outcomes align strongly with recent literature evaluating regenerative modalities. Karakose and Yitgin [18] investigated a similar multimodal protocol combining Li ESWT and PRP for acute phase PD, documenting statistically significant enhancements in both VAS and IIEF scores. Similarly, Achraf and colleagues demonstrated that isolated intralesional PRP injections effectively diminished penile pain and improved erectile function, emphasizing the potent tissue repair mechanisms of autologous growth factors [19]. Furthermore, a comprehensive meta-analysis conducted by Li and colleagues confirmed that Li ESWT significantly facilitates pain relief, although its independent efficacy on overall sexual function remains a subject of debate [20]. The robust subjective improvements documented in the current study suggest that the analgesic and neuroprotective properties of Li ESWT are synergistically amplified by the bioactive proteins delivered via PRP, leading to a comprehensive functional recovery. Consequently, the combination of Li ESWT and intralesional PRP demonstrated a highly favorable safety and tolerability profile in the clinical management of acute phase PD.

The primary objective of conservative management during the acute inflammatory phase of PD is the cessation of disease progression and the stabilization of penile deformity, rather than the complete eradication of the fibrotic tissue [18]. In the present analysis, while the objective measurements of penile curvature and plaque size exhibited marginal decreases that did not achieve statistical significance, the absence of further anatomical deterioration signifies a highly successful clinical stabilization. It is documented in the literature that without medical intervention, penile curvature progressively worsens in nearly half of the patients during the active phase of the condition [18]. Therefore, halting this active fibrotic process through the combined application of Li ESWT and PRP represents a substantial therapeutic benefit. These findings

are consistent with previous clinical evaluations of regenerative modalities, where interventions such as isolated Li ESWT or intralesional injection therapies frequently resulted in disease stabilization without complete anatomical reversal [6, 21]. By effectively arresting the inflammatory cascade and preventing the exacerbation of the curvature, this multimodal approach preserves penile anatomy and potentially eliminates the future necessity for complex surgical corrections, which are typically reserved for the chronic stable phase of the disease [18, 22].

Regarding the safety and tolerability of the therapeutic interventions, an exceptionally favorable profile was demonstrated by the combination of Li ESWT and autologous PRP. In the present evaluation, the protocol was completed by the vast majority of the participants without the occurrence of any adverse effects. Documented complications were strictly confined to minor local reactions, specifically mild ecchymosis and transient edema, which resolved spontaneously without the need for further medical assistance. These observations are highly consistent with the existing literature. Similar minor local events, such as ecchymosis and hematomas, were previously reported in a small fraction of patients in comparable studies, with an absolute absence of major systemic complications [23]. Furthermore, the safety and feasibility of PRP injections in an outpatient setting were confirmed by recent evaluations, wherein exclusively mild and self-limiting injection site reactions were noted [22]. The favorable safety profile observed in our study is also consistent with previous reports evaluating other intralesional treatments, including hyaluronic acid and verapamil, which were generally associated with mild and manageable adverse events [24].

Patient-centered outcomes are important in Peyronie's disease, as anatomical changes may not directly reflect functional recovery or satisfaction. Baser et al. [25] reported that penile shortening, erectile dysfunction, comorbidities, and symptom recurrence negatively affected satisfaction after Peyronie's disease surgery. Although their study involved surgically treated patients in the stable phase, it supports the clinical importance of preserving erectile function and managing patient expectations. Accordingly, the improvements in pain and erectile function observed in our study may represent meaningful patient-centered benefits despite the absence of significant anatomical changes.

Despite the promising clinical outcomes, the present study is subject to certain limitations. The primary limitation is the retrospective design of the clinical evaluation, coupled with a relatively small sample size. Furthermore, the absence of a placebo or control arm prevents a definitive comparative analysis, which is a frequently acknowledged constraint in existing literature regarding regenerative modalities. Additionally, the follow-up duration was relatively short, which inherently restricts the ability to ascertain the long-term durability of the therapeutic benefits and the potential occurrence of late-onset complications. Finally, the reliance on subjective tools such as the IIEF questionnaire introduces a degree of subjectivity, while the objective ultrasonographic assessments of plaque dimensions might be influenced by interoperator variability. Consequently, the execution of well-designed, randomized, placebo-controlled multicenter trials with extended follow-up periods is highly recommended to comprehensively validate these findings.

In conclusion, an effective, safe, and feasible conservative approach is constituted by the clinical management of acute phase PD utilizing a combined protocol of targeted Li ESWT and intralesional PRP injections. A highly significant alleviation of penile pain and a substantial restoration of erectile function were achieved by this therapeutic regimen. Although statistically significant alterations were not exhibited by the objective measurements of penile curvature and plaque dimensions, a critical clinical achievement during the active inflammatory stage was represented by the successful stabilization of the fibrotic process and the prevention of further anatomical deterioration. Characterized by an excellent safety profile with exclusively minor and transient local reactions, this multimodal therapy is proposed as a promising alternative to halt disease progression, whereby the future need for complex surgical reconstructions is potentially minimized.

Ethics committee approval: Permission was obtained from the Pamukkale University Non-Interventional Clinical Research Ethics Committee for the study (approval date and number: 09.10.2025 E.764107).

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