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REVIEW

The efficacy and safety of intravesical platelet-rich plasma injections into the bladder for the treatment of interstitial cystitis/bladder pain syndrome: a systematic review and meta-analysis

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ABSTRACT

INTRODUCTION: Interstitial cystitis/bladder pain syndrome is a chronic bladder condition with a rising incidence that significantly impacts the lives of millions worldwide. The lack of understanding regarding the pathophysiology of this condition has resulted in a deficiency of effective treatment options. However, the development of regenerative medicine has brought platelet-rich plasma into our field of vision. Platelet-rich plasma may address unresolved inflammation in the interstitial cystitis/bladder pain syndrome bladder and facilitate the restoration of bladder and urethral barrier function through repeated injections, potentially reducing bladder pain. Our aim is to investigate the efficacy and safety of intravesical injection of platelet rich plasma in the treatment of interstitial cystitis/bladder pain syndrome.

EVIDENCE ACQUISITION: A comprehensive search was conducted across PubMed, EMBASE, MEDLINE, Cochrane Library, and Web of Science databases for studies on platelet-rich plasma injection for the treatment of interstitial cystitis/bladder pain syndrome, with a search cutoff date of August 7, 2024.

EVIDENCE SYNTHESIS: A total of 11 studies with 391 participants were included. The combined statistics indicated that the baseline interstitial cystitis symptom index score was 11.20±4.60, the interstitial cystitis problem index score was 10.81±3.51, and the pain score was 4.37±3.14. The results showed that compared to pre-treatment, the interstitial cystitis symptom index score decreased by 3.56 (95% CI -4.39 to -2.72, P<0.00001), the interstitial cystitis problem index score decreased by 3.24 (95% CI -3.90 to -2.58, P<0.00001), and the pain score decreased by 1.84 (95% CI -2.19 to -1.48, P<0.00001). Additionally, the average proportion of patients with a global response assessment score of ≥2 after treatment was 48% (95% CI 0.37 to 0.58, P<0.00001). Furthermore, the overall incidence of adverse events among patients was 2.9%.

CONCLUSIONS: Evidence-based statistical analysis results suggest that intravesical platelet-rich plasma treatment is effective and safe, potentially serving as a promising approach for managing interstitial cystitis/bladder pain syndrome.

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KEY WORDS: Platelet-rich plasma; Cystitis, interstitial; Meta-analysis.

Introduction

Interstitial Cystitis/Bladder Pain Syndrome (IC/BPS) is a chronic bladder condition with a rising incidence that significantly impacts the lives of millions worldwide.[1] Reported prevalence ranges from 0.06% to 30%, with a female-to-male ratio of 10:1.[2] The primary symptoms include bladder pain accompanied by urinary tract irritative symptoms, which frequently recur, ne-

cessitating repeated medical consultations and severely affecting quality of life.[3] Conventional treatments for IC/BPS include cystoscopic hydrodistension, intravesical hyaluronic acid instillation, non-steroidal anti-inflammatory drugs, intravesical botulinum toxin A injections, sacral nerve stimulation, and psychological therapy.[4] However, the lack of understanding regarding the pathophysiology of this condition has resulted in a deficiency of effective treatment options.[5] The most common finding in bladder biopsies from IC/BPS patients is epithelial denudation or thinning, suggesting alterations in urothelial homeostasis regulation.[6] Some studies hypothesize that the pathophysiology of IC/BPS may be related to the impaired regeneration of urothelial progenitor cells following trauma or infection.[7]

Recent advancements in regenerative medicine have led to the widespread use of autologous platelet-rich plasma (PRP) to promote wound healing and accelerate recovery.[8] PRP, also known as platelet-rich growth factor or platelet concentrate, is a concentrated protein extract derived from whole blood through centrifugation, which removes red blood cells. Platelets in PRP release a variety of growth factors, cytokines, and extracellular matrix modulators that regulate the wound healing process, including inflammation and tissue regeneration.[9] Additionally, PRP may address unresolved inflammation in the IC/BPS bladder and facilitate the restoration of bladder and urethral barrier function through repeated injections, potentially reducing bladder pain.[10, 11] PRP intravesical injection represents a novel treatment approach for refractory IC/BPS, with several studies already exploring its efficacy and reporting promising results. Despite these findings, further evidence is needed to substantiate the effectiveness of repeated PRP injections for treating IC/BPS. Therefore, this study aims to include more relevant research, analyze additional parameters, and investigate the efficacy of repeated PRP injections for IC/BPS, providing updated evidence for clinical practice.

Evidence acquisition

The results of this study are reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Guidelines.[12] This project did not require Institutional Review Board (IRB) approval as all data were sourced from publicly available studies. We have registered our research and obtained the CRD number as required by the PROSPERO website[13] (ID:CRD42024584089).

Search strategy

We performed the results according to the PRISMA guidelines. Records were identified through electronic databases, including PubMed, EMBASE, Web of Science, and the Cochrane Central Register of Controlled Trials up to 2024. The literature search was conducted independently by two authors in August 7, 2024. The retrieval strategy is as follows: (((((((Platelet-Rich Plasma[MeSH Terms])) OR (Platelet-Rich Plasma[Title/Abstract])) OR (Plasma, Platelet-Rich[Title/Abstract])) OR (Platelet Rich Plasma[Title/Abstract])) AND ((((((((((((((Cystitis, Interstitial[MeSH Terms])) OR (Cystitis, Interstitial[Title/Abstract])) OR (Cystitides, Interstitial[Title/Abstract])) OR (Interstitial Cystitides[Title/Abstract])) OR (Interstitial Cystitis[Title/Abstract])) OR (Cystitis, Chronic Interstitial[Title/Abstract])) OR (Chronic Interstitial Cystitides[Title/Abstract])) OR (Cystitides, Chronic Interstitial[Title/Abstract])) OR (Interstitial Cystitides, Chronic[Title/Abstract])) OR (Interstitial Cystitis, Chronic[Title/Abstract])) OR (Chronic Interstitial Cystitis[Title/Abstract])) OR (Painful Bladder Syndrome[Title/Abstract])) OR (Bladder Pain Syndrome[Title/Abstract])) OR (Bladder Pain Syndromes[Title/Abstract])) OR (Pain Syndrome, Bladder[Title/Abstract]))) AND (((((((((randomized controlled trial[Publication Type]) OR (controlled clinical trial[Publication Type])) OR (randomized[Title/Abstract])) OR (placebo[Title/Abstract]))) OR (drug therapy[MeSH Subheading])) OR (randomly[Title/Abstract])) OR (trial[Title/Abstract])) OR (groups[Title/Abstract]))) NOT (((animals[MeSH Terms]) NOT (humans[MeSH Terms])))). Additionally, reference lists from all relevant systematic reviews and potential studies in the field were screened to obtain further references.

Study selection

Studies focusing on evaluating the efficacy of injecting PRP for IC/BPS were included if they met the following criteria: 1) the study population consisted of patients with IC; 2) the intervention involved intravesical PRP injection; 3) outcome measures included, but were not limited to, symptom scores (*e.g.*, the Interstitial Cystitis Symptom Index [ICSI], the Interstitial Cystitis Problem Index [ICPI]), metrics from voiding diaries (*e.g.*, frequency of urination, nocturia), and urodynamic parameters (*e.g.*, maximum flow rate [Qmax], post-void residual volume [PVR]); 4) the study was published in English. Studies were excluded if they met any of the following criteria: 1) involved patients with other lower urinary tract dysfunctions or infections; 2) a type of reviews, meta-analyses, letters, case reports, or studies based on animal or pediatric subjects; 3) lacked the necessary outcome measures for analysis.

Data extraction

Two reviewers thoroughly examined the included studies using predefined forms and extracted data from studies meeting the inclusion criteria. Any discrepancies during data extraction were resolved either through consensus between the two reviewers or with the assistance of a third reviewer. The predefined form included the following information: study title, authors, publication year, sample size, study type, patient demographics, and outcome data.

Bias assessment

We assessed the risk of bias of cohort studies included in the analysis using the Newcastle-Ottawa Scale,[14] which comprises three categories: "selection of study groups," "comparability of groups" and "outcome assessment". This scale uses a star system for semi-quantitative evaluation, with a maximum possible score of 9 stars. For single-arm studies included in the analysis, we used the Methodological Index for Non-Randomized Studies (MINORS)[15] to evaluate quality. The MINORS criteria include: "clearly stated aims," "consecutive patient inclusion," "prospective data collection," "suitable outcome measures for the study objectives," "objective assessment of outcomes," "follow-up period appropriate to study aims," "lost to follow-up rate less than 5%" and "prospective calculation of sample size". MINORS assesses study quality using a scoring system where each item is rated 0-2 points: 0 point indicates no reporting; 1 point indicates partial reporting; and 2 point indicates complete and adequate reporting.

Outcomes

To evaluate the efficacy of injecting PRP in treating IC/BPS, we took the global response assessment (GRA), the ICSI, the ICPI, and the pain scores (PS) as primary outcome measures. It is worth noting that this PS includes the Visual Analogue Scale (VAS) and the Numeric Rating Scale (NRS). Secondary outcomes were urinary diary metrics and urodynamic parameters. The urinary diary metrics included the frequency of urination, nocturia, and functional bladder capacity (FBC). Urodynamic parameters involved Qmax, PVR, urine volume, and cystometric bladder capacity (CBC).

Statistical analysis

Review Manager 5.4 (Cochrane Collaboration, Oxford, UK) was used to perform all analyses. Means±standard deviations (M±SD) and mean difference (MD) were used for continuous variables to combine the statistics. Heterogeneity was assessed using the I^2 statistic, with significance set at $P<0.05$. I^2 values of 25%, 50%, and 75% typically represent low, moderate, and high degrees of variability, respectively. A fixed-effects model was used when I^2 was less than 50%, while a random-effects model was applied when I^2 exceeded 50%. If any results exhibited high heterogeneity, sensitivity analyses were performed to identify the source of heterogeneity. Additionally, subgroup analyses were conducted based on follow-up duration.

Evidence synthesis

A total of 124 records were initially identified through database searches, along with 11 additional references. After removing duplicates (N.=79), we excluded some articles based on

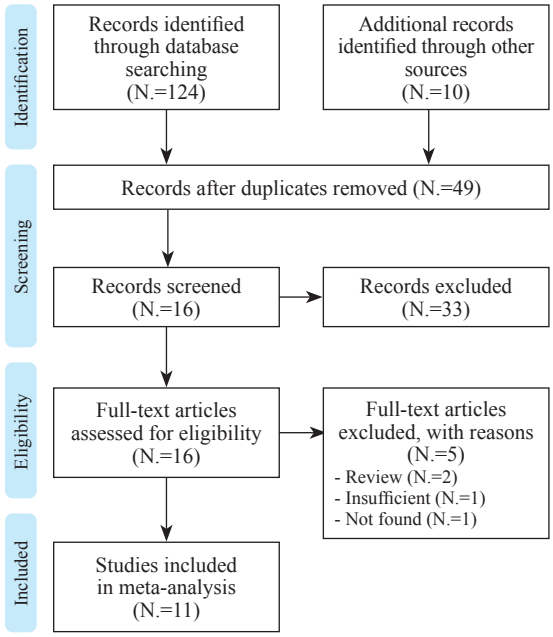


Figure 1.—PRISMA flow diagram for study selection.

titles and abstracts (N.=33) and conducted full-text reviews of the remaining 22 articles. 11 studies were ultimately included in our meta-analysis.[5, 7, 11, 16-23] The search and selection process were illustrated in Figure 1. The baseline characteristics of these 11 studies were summarized in Table I.[5, 7, 11, 16-23] No significant baseline differences were observed among the included studies. The included studies were primarily cohort studies and single-arm trials, with their quality assessed using the NOS scale and the MINORS criteria, as detailed in Supplementary Digital Material 1: Supplementary Table I, Supplementary Table II.[5, 7, 11, 16-23]

Considering that IC/BPS primarily presents with pain and urinary symptoms, and pain is a major factor affecting patients' quality of life, we focused on three key patient-reported outcome measures: the ICSI, ICPI, and the PS. These measures were selected as primary outcomes for their relevance to patient experience. Secondary outcomes included voiding diaries and urodynamic studies. Furthermore, since PRP injections are administered every 4 months, many studies measured these outcomes at each injection time point to better observe the effects. Therefore, our meta-analysis primarily employed subgroup analysis based on follow-up duration to evaluate the outcomes.

GRA

The GRA is a widely accepted scale for evaluating the efficacy of treatments for interstitial cystitis. The GRA is a 7-point symmetric scale used to assess the following possible responses: marked deterioration (-3), moderate deterioration (-2), mild deterioration (-1), no change (0), mild improvement (+1), moderate improvement (+2), and marked improvement (+3).[24] Most studies define a GRA score of ≥2 as treatment success, while scores below this threshold are considered indicative of suboptimal treatment outcomes.

A total of nine out of the eleven studies reported the number of patients with GRA ≥2, and our analysis focused on these nine studies. Our analysis shows significant statistical differences in GRA during injections (2nd injection: MD=0.44,

TABLE I.—*Characteristics of included studies.*[5, 7, 11, 16-23]

References	Study design	Simple size	Age	Injection	Follow-up	Outcome
Jhang JF *et al.*[5]	Cohort study	30	52.6±11.1	-	1mo, 3mo, 6mo	ICSS,VD,UD,GRA
Jiang YH *et al.*[7]	Cohort study	63	-	-	1mo, 3mo, 6mo	ICSS,VD,UD,GRA
Jhang JF *et al.*[11]	Single Arm Trial	19	55.6±15.8	4th	-	ICSS,VD,UD,GRA
Hung MJ *et al.*[16]	Single Arm Trial	6	46.3±4.7	-	6mo	ICSS,VD,UD,GRA
Jhang JF *et al.*[17]	Single Arm Trial	40	55.5±11.1	2nd, 3rd, 4th	1mo, 3mo	ICSS,VD,UD,GRA
Yang C[18]	Single Arm Trial	98	54.3±12.3	3rd	3mo	ICSS,VD,UD
Jhang JF *et al.*[19]	Cohort study	40	51.6±15.3	-	3mo	ICSS,GRA
El Hefnawy *et al.*[20]	Single Arm Trial	20	38.7±10.0	-	1mo, 2mo, 3mo	ICSS,UD
Jhang JF *et al.*[21]	Single Arm Trial	15	52.9±12.1	2nd, 3rd, 4th	1mo	ICSS,VD,UD,GRA
Shu-Yu W *et al.*[22]	Single Arm Trial	34	53.8±12.3	2nd, 3rd, 4th	1mo	ICSS,VD,UD,GRA
Lee YK *et al.*[23]	Single Arm Trial	26	58.6±14.2	3rd	-	ICSS,VD,UD,GRA

2nd: second injection; 3rd: third injection; 4th: fourth injection; 1mo: after one month follow-up; 2mo: after two months follow-up; 3mo: after three months follow-up; 6mo: after six months follow-up; ICSS: IC symptom scores; VD: voiding diaries; UD: urodynamics; GRA: global response assessment.

95% CI 0.31 to 0.57, P<0.00001; 3rd injection: MD=0.55, 95% CI 0.41 to 0.68, P<0.00001; 4th injection: MD=0.49, 95% CI 0.28 to 0.69, P<0.00001). Follow-up assessments also demonstrate significant results (1 month: MD=0.44, 95% CI 0.20 to 0.68, P=0.0004; 3 months: MD=0.53, 95% CI 0.43 to 0.62, P<0.00001; 6 months: MD=0.48, 95% CI 0.37 to 0.58, P<0.00001). The data reveal that the proportion of patients with GRA≥2 fluctuates around 50% both during and after injections, suggesting that PRP is an effective treatment for interstitial cystitis/bladder pain syndrome. The results are shown in Figure 2.[5, 7, 11, 17, 19-21, 23]

IC symptom scores

Based on the data presented, it is evident that, as expected, there are statistically significant differences in ICSI, ICPI, and PS both during the injection and in the follow-up period. Notably, during the injection phase, the symptom scores exhibit a more pronounced decline during the third injection, which then levels off. This may be closely related to the time required for the PRP injections to exert their effect. In the follow-up period after the injections, there is an overall trend of gradual symptom score reduction with increasing time, suggesting that PRP injections may have a positive impact on the improvement of interstitial cystitis symptoms. It is important to note that in the second-month follow-up, the symptom score decline was particularly steep. This could be due to the fact that only one study was included in the meta-analysis for the second-month follow-up, indicating that the accuracy of this data may need to be verified with additional data from follow-ups conducted at the second month.

ICSI

During the injection phase, there were significant statistical differences between the ICSI scores and baseline data for the second, third, and fourth injections (2nd injection: MD=-1.17, 95% CI -2.82 to -0.59, P=0.003; 3rd injection: MD=-3.06, 95% CI -3.85 to -2.26, P<0.00001; 4th injection: MD=-3.00, 95% CI -3.94 to -2.06, P<0.00001). In the follow-up data post-injection, significant statistical differences were observed between ICSI scores and baseline data across all follow-up months (1 month: MD=-3.07, 95% CI -3.74 to -2.40, P<0.00001; 2 months: MD=-11.0, 95% CI -12.16 to -9.39, P<0.00001; 3 months: MD=-3.71, 95% CI -5.23 to -2.19, P<0.00001; 6 months: MD=-6.02, 95% CI -11.55 to -0.50, P=0.030). The results are shown in Figure 3.[5, 7, 11, 16-23]

ICPI

The ICPI scores show a similar overall trend to the ICSI scores, with significant statistical differences observed both during the injection phase (2nd injection: MD=-1.77, 95% CI -2.88 to -0.66, P=0.002; 3rd injection: MD=-2.90, 95% CI -3.66 to -2.14, P<0.00001; 4th injection: MD=-2.55, 95% CI -3.49 to -1.61, P<0.00001) and in the follow-up period post-injection (1 month: MD=-3.17, 95% CI -3.79 to -2.56, P<0.00001; 2 months: MD=-7.80, 95% CI -9.09 to -6.51, P<0.00001; 3 months: MD=-3.42, 95% CI -4.58 to -2.25, P<0.00001; 6 months: MD=-5.15, 95% CI -9.84 to -0.46, P=0.030), compared to baseline data. The results are shown in Figure 4.[5, 7, 11, 16-23]

PS

For pain assessment in interstitial cystitis, most studies used the VAS, which requires patients to rate their pain from 0 to 10 (0="no pain" ; 10="worst pain imaginable"). Some studies employed the NRS, which similarly asks patients to rate their pain from 0 to 10 (0 indicating no pain, and 10 representing the worst pain). Since both scales aim to measure pain and have comparable definitions and ranges, we did not differentiate between them in our meta-analysis. Pain levels showed significant improvement both during the injection phase (2nd injection: MD=-1.07, 95% CI -1.75 to -0.40, P=0.002; 3rd injection: MD=-1.56, 95% CI -2.09 to -1.03, P<0.00001; 4th injection: MD=-1.87, 95% CI -2.46 to -1.28, P<0.00001) and in the follow-up period post-injection (1 month: MD=-1.75, 95% CI -2.40 to -1.09, P<0.00001; 2 months: MD=-3.25, 95% CI -4.10 to -2.40, P<0.00001; 3 months: MD=-2.02, 95% CI -2.90 to -1.15, P<0.00001; 6 months: MD=-2.78, 95% CI -5.78 to 0.23, P=0.070), with all improvements showing statistical significance. The results are shown in Figure 5.[5, 7, 11, 16-23]

Voiding diaries

As a diagnostic tool, the voiding diary allows for the definition of objective signs from patients' subjective symptoms.[25] It has been widely utilized in the diagnosis of various urinary disorders, such as overactive bladder and urinary incontinence in the elderly.[26, 27] The primary symptoms of IC/BPS include urinary frequency and urgency, among others. The voiding diary provides a clear depiction of the patient's daily voiding frequency and volume, which aids in the diagnosis of IC/BPS.[28]

Frequency

As a major symptom impacting patients' quality of life, frequency of urination can be significantly improved by PRP injections. We observed that PRP effectively alleviates urinary frequency symptoms in the short term (2nd injection: MD=-2.18, 95% CI -4.53 to 0.16, P=0.07; 3rd injection: MD=-2.05, 95% CI -3.79 to -0.31, P=0.02; 4th injection: MD=-3.92, 95% CI -5.96 to -1.88, P=0.0002; 1 month: MD=-1.96, 95% CI -3.25 to -0.67, P=0.003; 3 months: MD=-1.93, 95% CI -3.04 to -0.81, P=0.0007; 6 months: MD=-0.92,

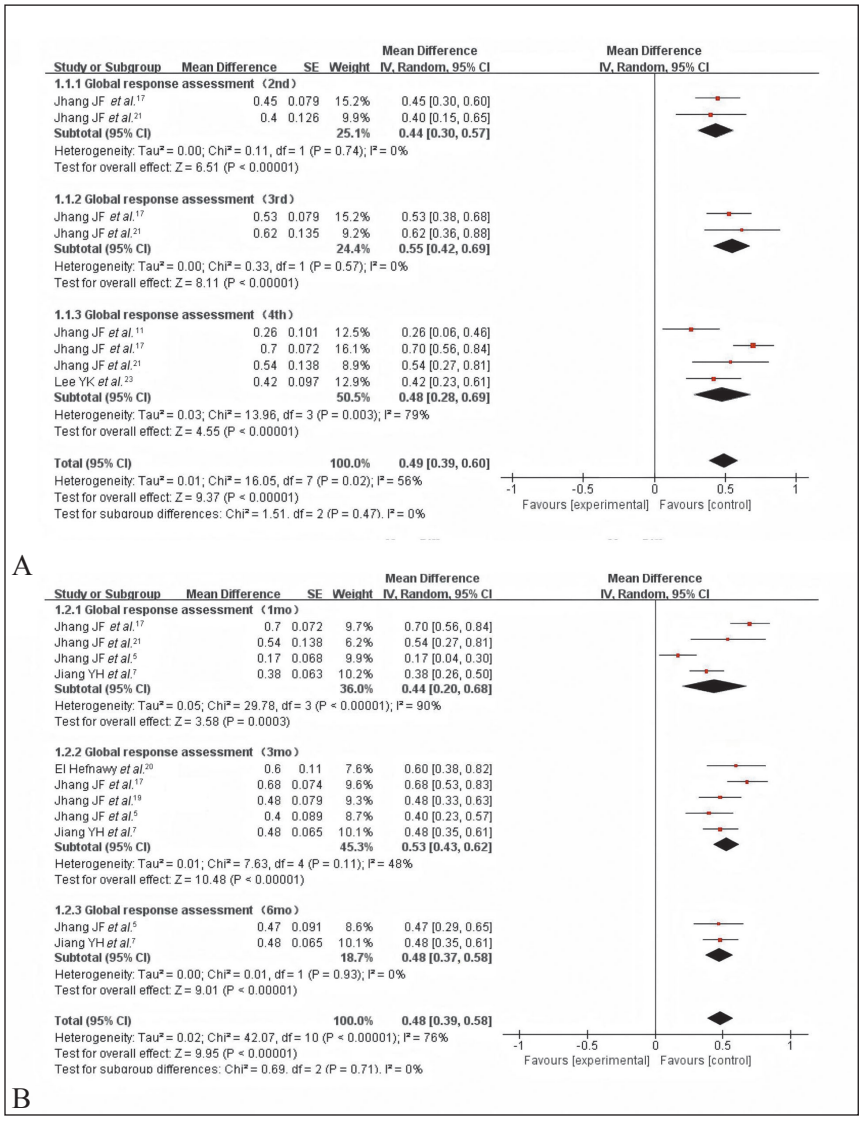


Figure 2.—Summary forest plot showing the MD of the GRA in injecting PRP (A, during injection; B, follow-up after injection).[5, 7, 11, 17, 19-21, 23]

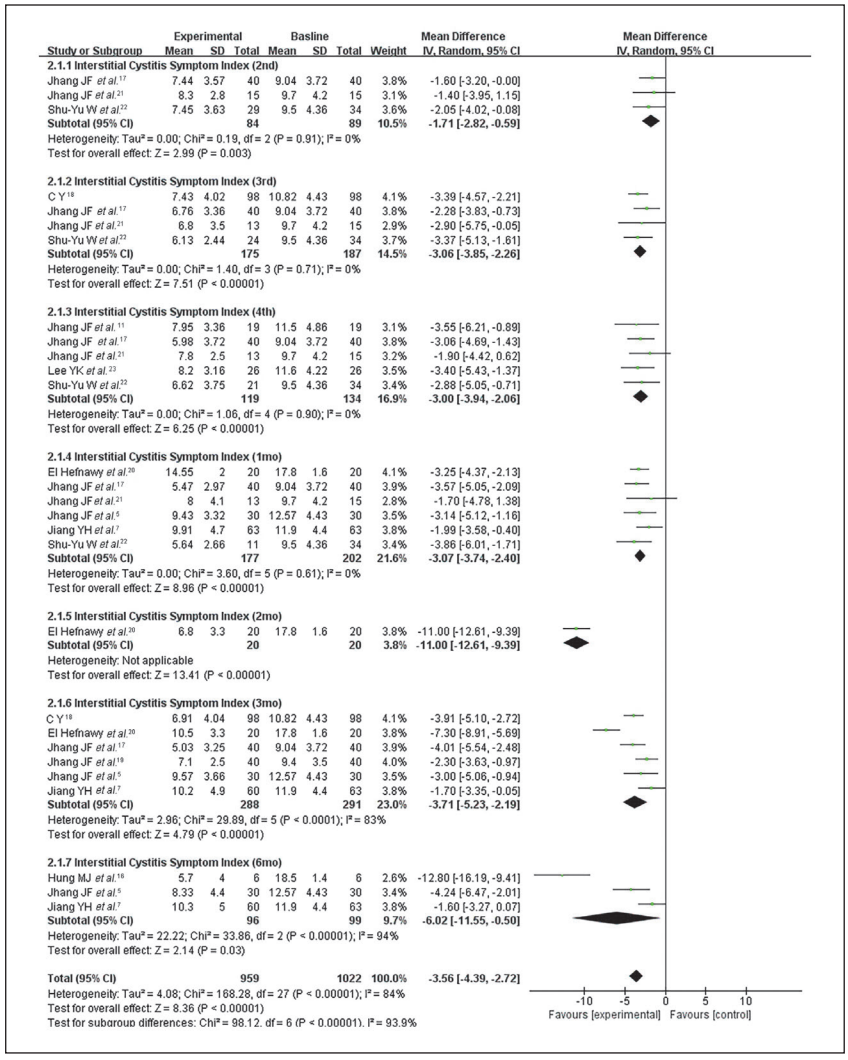


Figure 3.—Forest plots showing the MD of the ICSI in injecting PRP.[5, 7, 11, 16-23]

95% CI -2.44 to 0.60, P=0.23). However, the long-term effects on urinary frequency are less satisfactory, which may be related to the mechanism and duration of PRP action. The results are shown in Supplementary Digital Material 2, Supplementary Figure 1.[5, 7, 17, 18, 21-23]

Nocturia

Nocturia, a common complaint in IC/BPS, significantly impacts quality of life, including poor sleep, depression, decreased quality of life, and increased risks of morbidity, mortality, falls, and fractures. PRP injections have shown significant short-term improvements in nocturia symptoms (2nd injection: MD=0.02, 95% CI -0.41 to 0.45, P=0.94; 3rd injection: MD=-0.54, 95% CI -0.85 to -0.23, P=0.0006; 4th injection: MD=-0.49, 95% CI -0.91 to -0.06, P=0.03; 1 month: MD=-0.48, 95% CI -0.78 to -0.19, P=0.001; 3 months: MD=-0.67, 95% CI -0.93 to -0.40, P<0.00001; 6 months: MD=-0.41, 95% CI -0.83 to 0.01, P=0.05). However, long-term effects require further validation through additional research. The results are shown in Supplementary Digital Material 3, Supplementary Figure 2.[5, 7, 17, 18, 22, 23]

FBC

FBC is defined as the volume of urine that the bladder can effectively hold and expel, as reflected by the maximum single voiding volume

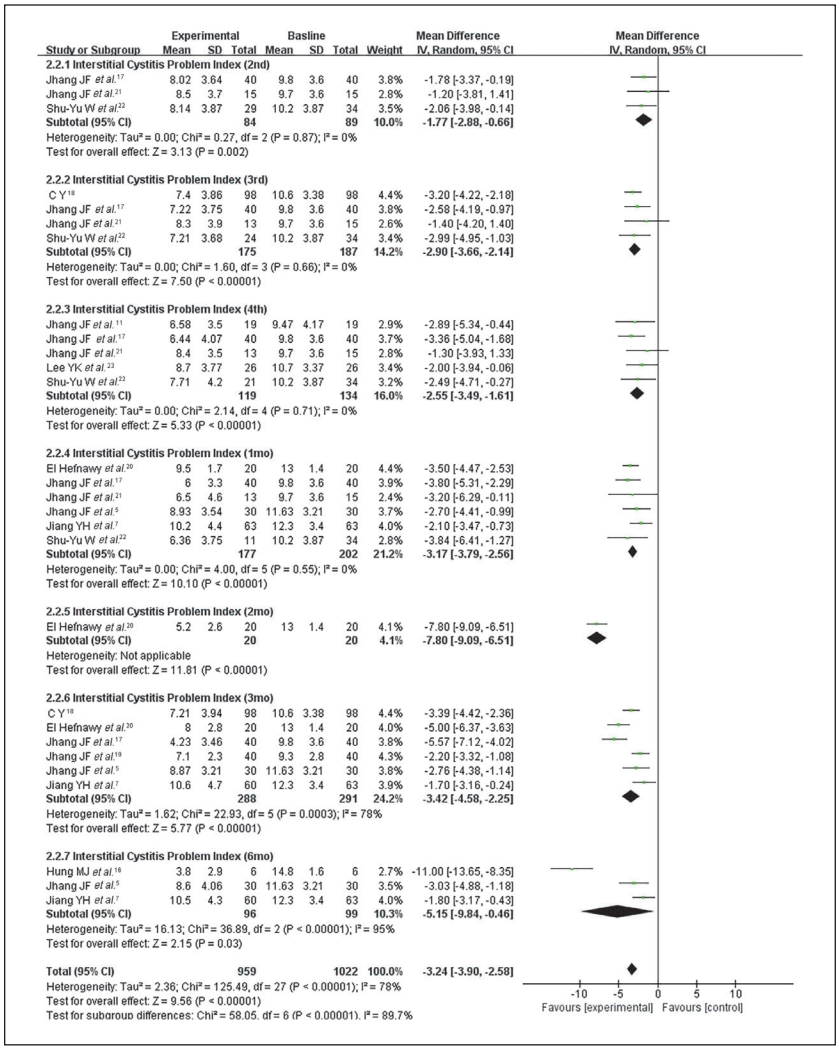


Figure 4.—Forest plots showing the MD of the ICPI in injecting PRP.[5, 7, 11, 16-23]

recorded in a voiding diary. A reduced functional bladder capacity often indicates dysfunction during the bladder storage phase. The effects of PRP injections on functional bladder capacity in patients with interstitial cystitis/bladder pain syndrome are most pronounced between the third injection and one month post-treatment (2nd injection: MD=16.82, 95% CI -19.84 to 53.48, P=0.37; 3rd injection: MD=34.35, 95% CI 8.58 to 60.12, P=0.009; 4th injection: MD=43.53, 95% CI 12.66 to 74.39, P=0.006; 1 month: MD=46.75, 95% CI 23.54 to 69.97, P<0.0001; 3 months: MD=22.98, 95% CI 1.81 to 44.14, P=0.003; 6 months: MD=21.91, 95% CI -8.51 to 52.33, P=0.16). The results are shown in Supplementary Digital Material 4, Supplementary Figure 3.[5, 7, 11, 17, 18, 21-23]

Urodynamic parameters

Urodynamic studies are a crucial component in the clinical evaluation of lower urinary tract dysfunction, encompassing bladder filling assessments, pressure-flow studies, urine flow rate measurements, urethral function tests, and electromyography.[29] A total of nine of the eleven studies we included reported urodynamic-related outcomes These tests provide physiological data on bladder function during filling and voiding, complementing clinical history and physical examination findings.[30] They play a significant role in the dif-

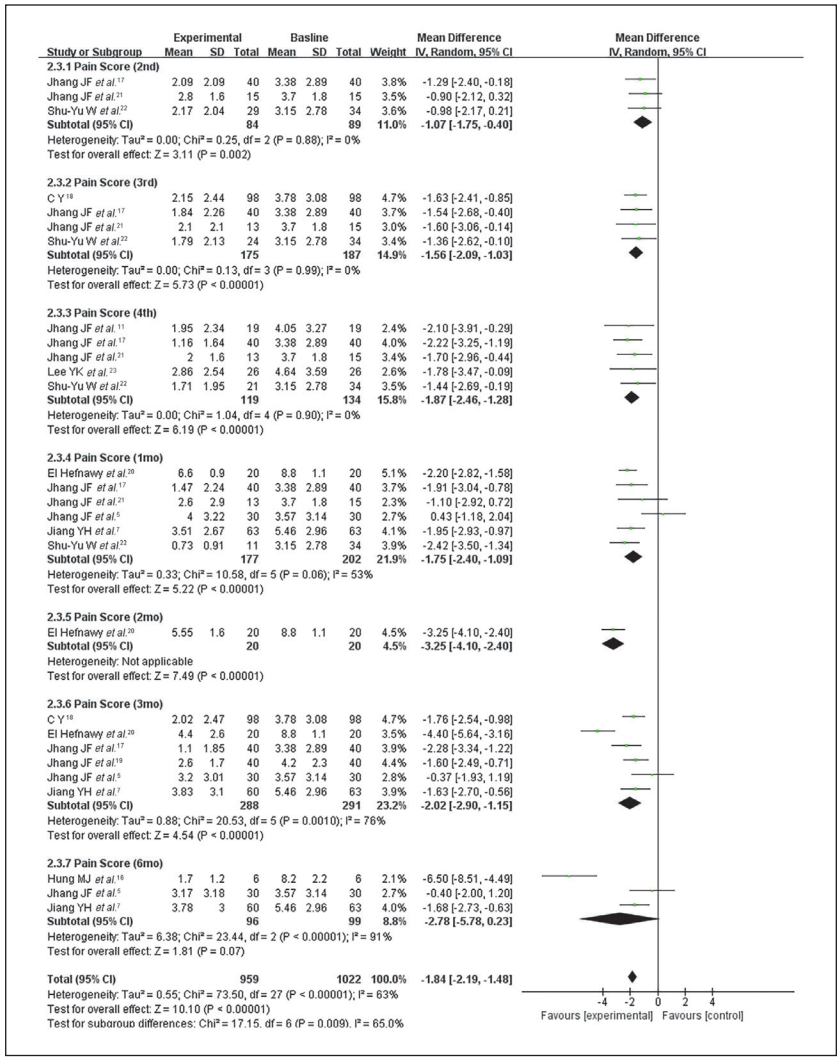


Figure 5.—Forest plots showing the MD of the PS in injecting PRP.[5, 7, 11, 16-23]

ferential diagnosis of interstitial cystitis/bladder pain syndrome. Our analysis of key urodynamic parameters revealed that PRP injection had statistically significant effects solely on PVR improvement (2nd injection: MD=-28.17, 95% CI -56.70 to 0.35, P=0.05; 3rd injection: MD=-20.67, 95% CI -39.58 to -1.76, P=0.03; 4th injection: MD=-16.88, 95% CI -41.30 to 7.54, P=0.18; 1 month: MD=-18.32, 95% CI -32.06 to -4.58, P=0.009; 3 months: MD=-15.02, 95% CI -27.58 to -2.47, P=0.02; 6 months: MD=7.16, 95% CI -16.62 to 30.94, P=0.56). The reduction in PVR was most pronounced within the first three months post-injection. However, at six months, PVR increased, possibly related to the duration of PRP's effects. Additionally, only two studies provided six-month follow-up, which may impact data reliability. Nine included studies also reported on Qmax, voided volume, and bladder compliance, but these parameters did not show significant statistical differences from baseline. These results are shown in Supplementary Digital Material 5, Supplementary Figures 4-7.[5, 7, 11, 16-18, 20-23]

Safety

Among the 11 studies included, 6 reported adverse events related to PRP, with half of these studies reporting zero adverse events. Although 3 studies reported adverse effects (difficulty uri-

nating, dysuria, urinary tract infections), these were largely isolated cases. These results provide reliable evidence for the safety of intravesical PRP injection. Specific data are presented in the Table II.[5, 7, 11, 16-23]

Although existing studies have indicated that PRP injection does not result in serious side effects, it is still important to consider its potential adverse effects. Autologous PRP, which is derived from the patient's own blood, may cause some discomfort during the blood collection process.[20] In our view, this is a normal physiological response, but further research is needed to pay attention to it. In addition, Intravesical injection is an invasive procedure that may lead to mucosal damage and inflammation, which could increase the risk of lower urinary tract symptoms such as pain and difficulty urinating. However, given that PRP possesses anti-inflammatory and analgesic properties,[31, 32] it may help mitigate the likelihood of these complications. Based on the current literature, we have observed that the incidence of adverse reactions to intravesical PRP injection is low and the procedure is generally considered safe. Nevertheless, larger-scale studies are needed to provide more robust and reliable evidence.

Discussion

IC/BPS or primary bladder pain syndrome (PBPS) is a chronic inflammatory condition that significantly impacts patients' quality of life. Treatment challenges for IC/BPS have long been a concern in the medical community. A review of the treatment history reveals that no single therapy has proven universally effective for all cases and many treatments are accompanied by adverse effects. Research dating back to 1967 investigated the treatment of IC/BPS, highlighting that most patients benefited from intravesical DMSO.[33] Since then, numerous studies have explored DMSO treatment for IC/BPS. Although high-quality RCTs suggest that DMSO is beneficial for improving urinary pain, urgency, and bladder capacity,[34] some studies indicate that patients may initially experience symptom exacerbation and suboptimal responses to DMSO.[35, 36] Subsequent research identified a subset of IC/BPS patients with a history of urinary tract infections,[37] leading to trials with antibiotics; However, these showed limited efficacy and concerns over microbial changes and antibiotic resistance.[38] With ongoing research, new medications have been introduced for IC/BPS. Hyaluronic acid, acting as an exogenous glycosaminoglycan to restore damaged epithelial cells,[39] has shown potential but is costly and often provides only temporary relief. BCG immunotherapy, originally used for non-muscle invasive bladder cancer, has been explored for IC/BPS due to its immunomodulatory properties.[40] However, current studies suggest that BCG has a minimal effect on IC/BPS with a low overall response rate.[41-43] Advances in regenerative medicine have directed attention towards PRP, an autologous plasma devoid of white blood cells, mixed with plasma proteins derived from the patient's own blood.[44] Research proposes that intravesical PRP injection could facilitate repair of urinary epithelial damage and regeneration of

TABLE II.—*Adverse event reports of PRP injection.*[5, 7, 11, 16-23]

References	Simple size	Number of adverse events			
		Dysuria	UTI	Hematuria	Micturition pain
Jhang *et al.*[5]	30	1	0	0	0
Jiang *et al.*[7]	63	0	0	0	0
Jhang *et al.*[11]	19	Not mention			
Hung *et al.*[16]	6	0	0	0	0
Jhang *et al.*[17]	40	0	0	0	0
Yang[18]	98	Not mention			
Jhang *et al.*[19]	40	Not mention			
El Hefnawy *et al.*[20]	20	0	3	0	0
Jhang *et al.*[21]	15	0	1	0	0
Shu-Yu *et al.*[22]	34	Not mention			
Lee *et al.*[23]	26	Not mention			

UTI: urinary tract infection.

epithelial cells in IC/BPS patients.[45] While numerous studies on PRP injection for IC/BPS have been conducted, findings are consistent but vary in specific outcomes. Therefore, we employ an evidence-based approach using systematic review and meta-analysis to synthesize data from included studies and further evaluate the efficacy and adverse events of intravesical PRP injection for IC/BPS, providing valuable insights for clinical decision-making.

From our combined statistics, we observed that intravesical PRP injection demonstrates significant short-term effects for IC/BPS patients. Although only 50% of patients had a GRA≥2, feedback on ICSI, ICPI, and PS was notably positive. These three parameters showed substantial improvement from baseline, and PRP was also effective in alleviating symptoms such as urinary frequency and nocturia. These findings support the use of PRP for IC/BPS treatment in the future. Furthermore, compared to other pharmacological treatments for IC/BPS, PRP has a clear safety advantage.

During the data extraction process, several issues were identified. First, half of the 11 studies included did not report adverse effects, which affects our assessment of the safety of PRP for IC/BPS patients. It is hoped that future studies will provide more comprehensive reporting in this regard. Additionally, during the full-text review and data extraction, one study only reported mean values, with missing data on standard deviations and ranges. This omission may impact our evaluation of the efficacy of PRP for IC/BPS patients. Future research should aim for more complete data reporting to facilitate accurate efficacy assessment.

Limitations of the study

This study has certain limitations. First of all, some of the included data exhibited high heterogeneity, which may be attributed to the varying ethnic distributions of the study populations. Despite this, significant differences were still observed with the random-effects model, suggesting that PRP treatment for IC/BPS patients may be effective. Second, the meta-analysis predominantly included cohort studies with a scarcity of high-quality randomized controlled trials, indicating a need for more high-quality, multicenter studies to strengthen the evidence base. Additionally, since PRP preparation is performed by researchers, variability in preparation techniques and processes may contribute to heterogeneity. Lastly, the extended follow-up periods in some studies may lead to recall bias in patients' symptom reporting, potentially affecting the study outcomes.

Conclusions

In summary, we conducted a statistical analysis of the literature on PRP injection for IC/BPS using evidence-based medicine. The results indicate that PRP injections show favorable short-term outcomes with a low incidence of adverse events and high safety, suggesting it could be a promising new approach for treating IC/BPS.

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Conflicts of interest
The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

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Authors' contributions
Hai-Rui Li, Ting Wang contributed equally. Hai-Rui Li: conceptualization, methodology; data curation and writing original draft preparation; Ting Wang: conceptualization, data analysis; Si-Hong Shen: visualization and investigation; Liao Peng: supervision. manuscript editing; all authors have participated to drafting the manuscript, Liao Peng revised it critically. All authors read and approved the final version of the manuscript.

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