Archives of Clinical Trials

Original Article

Interstitial Cystitis: Etiology, Pathophysiology, and the Potential Role of Platelet-Rich Plasma Instillation and Predictive Value of Potassium Chloride Sensitivity Test

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- Received Date: 06 Nov 2025
- Accepted Date: 17 Nov 2025
- Publication Date: 1 Dec 2025

Keywords

Interstitial cystitis, platelet rich plasma, hydrodistention, chronic pelvic pain, urinary incontinence, painful bladder syndrome, nocturia, potassium chloride sensitivity test.

Abstract

Background and aims: *To confirm platelet rich plasma with hydrodistention facilitates healing of the barrier function of the urothelium and subsequently relieves symptoms of pain urgency frequency confirmed by the potassium chloride sensitivity test.*

Methods: *Patients with diagnosis of interstitial cystitis were recruited to the study. The patient completed the O'Leary Sant symptom and problem index and then underwent potassium chloride sensitivity testing. After treatment with hydrodistention with platelet rich plasma instillation the testing was repeated at 1 month and 3 months.*

Interstitial cystitis is proposed to be caused by a defect in the gag layer of the urothelium which can be identified by potassium chloride sensitivity test which is proposed to leak into the suburothelial layer and stimulate subepithelial nerves and cause inflammation and subsequent urinary frequency urgency and pain with bladder filling. Platelet rich plasma infusion has been shown in previously published study by author to effectively treat interstitial cystitis. This study objective is to use the potassium chloride sensitivity test to predict success of hydrodistention with platelet-rich plasma.

Materials and methods: *The patients recruited for the study completed a validated questionnaire O'Leary-Sant Symptom and Problem Index (OSPI) and underwent potassium chloride sensitivity test. The testing was repeated at 1 month and 3 months. The analysis at 1 month showed 80% responsive with 90% responsive in the positive potassium chloride sensitive test and 50% responsive in the negative potassium chloride sensitivity test. As described in a previous paper 60 cc of autologous blood was collected from the patient by phlebotomy and processed to provide 10 cc of platelet rich plasma. The patient was placed in the dorsolithotomy position and after general anesthesia was induced the bladder was visualized with cystoscopy and the bladder was distended with 80 cm of water pressure for 3 minutes. The bladder was drained and the platelet rich plasma was infused. The patient was instructed to maintain the plasma rich plasma in the bladder for 2 hours. In the post procedure month all patients were instructed to continue their usual medications and to avoid bladder irritants specifically caffeine alcohol tobacco spicy foods and citrus. In accordance with University of Virginia ethical principles for the protection of human subjects of biomedical behavioral research we adhered to the 3 principles underlying the ethical conduct of research: respect for persons, beneficence and justice. Consent was obtained from all participants.*

Results: *The median age of patients was 52.2 years old with the range of ages being 23-83.The potassium sensitivity test was positive for 95%. At 3 months 92% had a negative potassium chloride sensitivity test and low OSPI score.*

Conclusion: *Hydrodistention with platelet rich plasma is successful in treating patients with a positive potassium chloride sensitivity test which aids in identifying patients with Interstitial cystitis. The potassium chloride sensitivity test has an 95% predictive value for success of hydrodistention with PRP In reducing urinary frequency urgency and pain with full bladder.*

Introduction

Interstitial cystitis (IC), also known as painful bladder syndrome (PBS), is characterized by a compromised glycosaminoglycan (GAG) layer in the urothelium. This defect disrupts the urothelium's watertight function, thereby impairing the bladder's capacity to effectively store urine. [1,2].In a normally functioning bladder, distention occurs at low pressure until micturition is socially appropriate, at which point the pontine micturition center facilitates bladder contraction. [3] Patients with IC experience bladder dysfunction leading to symptoms such as pain, urgency, nocturia, and relief upon urination [4].

Citation: Hardy TJ, Afrifie P. Interstitial Cystitis: Etiology, Pathophysiology, and the Potential Role of Platelet-Rich Plasma Instillation and Predictive Value of Potassium Chloride Sensitivity Test. Arch Clin Trials. 2026;6(1):011.

This bladder dysfunction is a complex interplay of four key mechanisms:

1. **Urothelial Defect:** The compromised GAG layer facilitates the diffusion of urinary irritants into the bladder wall.[1]
2. **Inflammation:** This infiltration triggers inflammation of the suburothelium and suburothelial nerves.[1]
3. **Frequent Bladder Contractions:** Detrusor overactivity, typically suppressed in a healthy bladder, can contribute to symptoms.[4]
4. **Central Sensitization:** Heightened stress and anxiety can exacerbate symptoms through central sensitization, leading to a dysfunctional bladder state.[5,6]

While conditions like overactive bladder (OAB), acute urinary tract infection (UTI), and substance abuse (e.g., ketamine) can precede or contribute to interstitial cystitis (IC), its precise underlying cause or inciting mechanism remains unknown. [7] Without proper treatment, this condition can progress to interstitial cystitis. The concept of urothelial dysfunction and disruption of the glycosaminoglycan (GAG) layer is supported by research, such as that by Truschel S.T. et al., who detailed the dynamic nature of apical umbrella cells within the urothelium. [8]These umbrella cells expand their surface area through membrane unfolding and new membrane formation, a process stimulated by bladder stretch and involving the incorporation of subapical vesicles. Following bladder emptying, this added membrane is internalized and reincorporated into vesicles for subsequent filling cycles. This intricate process, essential for maintaining the urothelial barrier and its uroplakin surface proteins, is energy-dependent and needs cyclic AMP. The newly added urothelium from the apical vesicles of the umbrella cells contain uroplakin which is part of the GAG layer to aid in maintaining bladder impermeability.

Maintaining this impermeable barrier requires energy at the cellular level mediated by cyclic AMP.[8] Studies suggest that in Interstitial Cystitis (IC), there's a defect in the urothelial lining, specifically the glycosaminoglycan (GAG) layer, that makes it "leaky".[9] The "leaky bladder" theory is supported by the Potassium Chloride Sensitivity Test, which shows increased sensitivity to potassium chloride in many IC patients due to its leakage into the bladder wall.[9]The compromised GAG/ urothelial layer allows potentially irritating substances (solutes like potassium chloride) in the urine to leak into the subepithelial layer.[9]This leakage stimulates bladder nerves and triggers an inflammatory response.[10]The inflammatory response leads to an increase in inflammatory cells like leukocytes and macrophages, as well as the release of inflammatory mediators like leukotrienes, histamine, substance P, and vascular endothelial growth factor (VEGF)[10].While inflammation aims to heal the urothelial defect, it can also contribute to dysfunction with bladder spasms , decreased bladder capacity, and increased sensitivity, perpetuating the IC symptoms. Chronic stress may worsen IC symptoms by potentially reducing blood flow to the bladder, impacting the healing process and growth factors essential for repair[11].

Statistical analysis

Patients were categorized into 2 groups: potassium chloride sensitivity test positive group and potassium sensitivity test negative group according to the initial test. Statistical analysis compared the initial test with post test 1 month and 6 months. Using the Fisher exact test.

Secondary analysis was performed with logistic regression analysis.

Results

The median age of the patient was 52.2 years. All patients were female. The average time of initiation of symptoms to treatment was 60 months. Previous treatments included Elmiron amitriptyline heparin intravesical instillations and hydroxyzine.. The analysis at 1 month showed 80% responsive .The analysis at 3 months showed 92% responsive using the positive potassium chloride sensitive test. Table 1 shows individual patient's symptom trajectory before and after the procedure with an overall trend towards improvement which was statistically significant. Table 2 shows confidence interval for the mean symptom level with the average symptom levels showing a significant statistical improvement at 3 months after procedure. Table 4 shows a significant 90% improvement at 3 months using composite symptom score of pain urgency and frequency. Table 5 shows a downward trend in symptoms score after hydrodistention with PRP treatment at 3 months.

Table 1. *Spaghetti plot*

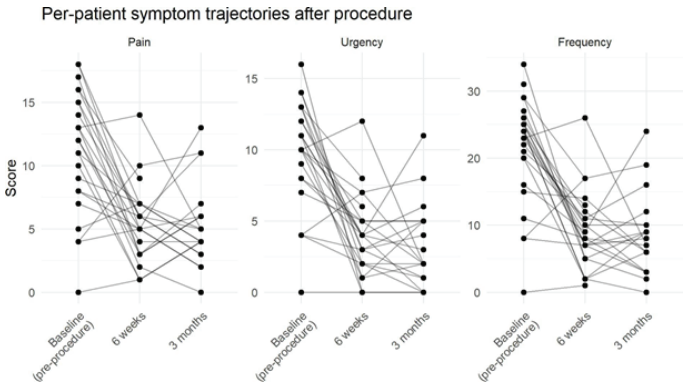
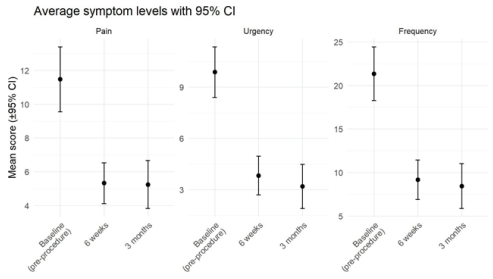


Table 2. *Confidence interval for mean symptom level*



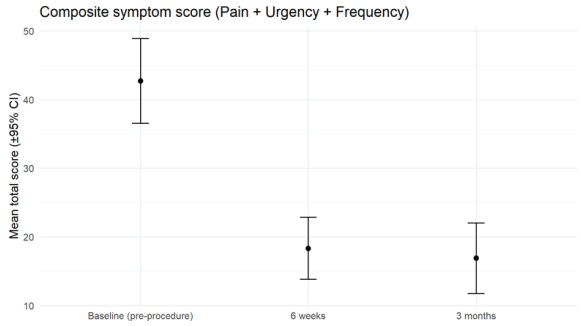
Summary: There is sufficient statistical evidence that on average the patient's symptom levels were higher pre-procedure compared to three months after surgery.

Paired t-test

measure	comparison	n_pair	mean_diff	t_pvalue	w_pvalue
Pain	Baseline vs 6 weeks	24	-5.875000	2.407359e-05	2.506164e-04
Urgency	Baseline vs 6 weeks	24	-5.916667	3.217260e-06	9.112805e-05
Frequency	Baseline vs 6 weeks	24	-11.791667	3.097207e-06	1.206413e-04
Pain	Baseline vs 3 months	20	-6.450000	7.442686e-05	6.177349e-04
Urgency	Baseline vs 3 months	20	-6.950000	1.198412e-06	2.629434e-04
Frequency	Baseline vs 3 months	20	-13.400000	5.670199e-06	3.688361e-04

Summary: There is sufficient statistical evidence that on average the patient's symptom levels were higher pre-procedure compared to 6 weeks and three months after surgery.

Table 3. *Confidence interval for mean composite symptom level*



Summary: There is sufficient statistical evidence that on average the composite symptom levels are higher pre-procedure compared to three months after procedure.

Paired t-test

comparison	n_pair	mean_diff	d_paired	t_pvalue	w_pvalue
Baseline vs 6 weeks	24	-23.58333	-1.247795	3.097207e-06	0.0001206413
Baseline vs 3 months	20	-26.80000	-1.390381	5.670199e-06	0.0003688361

Summary: There is sufficient statistical evidence that on average the composite symptom levels were higher pre-procedure compared to 6 weeks and three months after surgery.

Table 4. *Exploring Percentage improvement:*

comparison	measure	n_pair	pct_improved
Baseline → 6 weeks	Pain	24	79.2%
Baseline → 6 weeks	Urgency	24	87.5%
Baseline → 6 weeks	Frequency	24	87.5%

comparison	measure	n_pair	pct_improved
Baseline → 3 months	Pain	20	90%
Baseline → 3 months	Urgency	20	90%
Baseline → 3 months	Frequency	20	90%

Exploring composite improvement

comparison	n_pair	pct_improved
Baseline → 6 weeks	24	88%

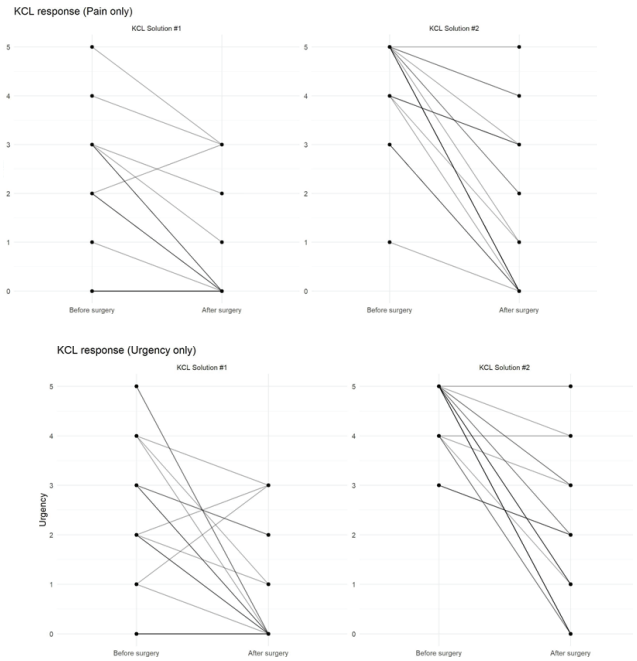
comparison	n_pair	pct_improved
Baseline → 3 months	20	90%

KCL Solution Analysis5

Discussion

Interstitial cystitis/bladder pain syndrome affects up to 6% of women and causes immense suffering. There is an overlap between patients who have overactive bladder and painful bladder syndrome. As mentioned by CHUNG ET AL treatment should be tailored to effectively relieve all of the patient's symptoms.[12] Interstitial cystitis is difficult to treat as it is often associated with comorbidities including endometriosis Vulvodynia,fibromyalgia anxiety depression and autoimmune disorders. [13]This study provides further evidence to support the primary defect of interstitial cystitis is a defect in the Glycosamino- glycan layer. As a third line therapy, hydrodistention with platelet rich plasma can be an effective treatment that relieves pain and urgency symptoms that lasts longer than hydrodistention alone. In some cases over 3 years in a previously published study by the author. Potassium chloride sensitivity test before and after the procedure provides evidence for effectiveness of restoring the integrity of the urothelium and providing evidence for the effectiveness of the potassium chloride sensitivity test to determine appropriate candidates for

Table 5. *XXXXXXXXXXX*



Summary: Overall, the symptom scores are trending downwards for KCL Sol # 1 after procedure

the treatment. Further studies are necessary to confirm these findings

References

1. Vij M, Srikrishna S, Cardozo L. Interstitial cystitis: diagnosis and management. Eur J Obstet Gynecol Reprod Biol. 2012;161(1):1-7. doi:10.1016/j.ejogrb.2011.12.014.
2. Moskowitz MO, Byrne DS, Callahan HJ, Parsons CL, Valderrama E, Moldwin RM. Decreased expression of a glycoprotein component of bladder surface mucin (GP1) in interstitial cystitis. J Urol. 1994;151(2):343-345. doi:10.1016/s0022-5347(17)34944-3.
3. Fowler CJ, Griffiths D, de Groat WC. The neural control of micturition. Nat Rev Neurosci. 2008;9(6):453-466. doi:10.1038/nrn2401.
4. Butrick CW. Interstitial cystitis and chronic pelvic pain: new insights in neuropathology, diagnosis, and treatment. Clin Obstet Gynecol. 2003;46(4):811-823. doi:10.1097/00003081-200312000-00011.
5. Lowe EM, Anand P, Terenghi G, Williams-Chestnut RE, Sinicropi DV, Osborne JL. Increased nerve growth factor levels in the urinary bladder of women with idiopathic sensory urgency and interstitial cystitis. Br J Urol. 1997;79(4):572-577. doi:10.1046/j.1464-410x.1997.00097.x.
6. Marcu I, Campian EC, Tu FF. Interstitial cystitis/bladder pain syndrome. Semin Reprod Med. 2018;36(2):123-135. doi:10.1055/s-0038-1676089.
7. Akiyama Y, Luo Y, Hanno PM, Maeda D, Homma Y. Interstitial cystitis/bladder pain syndrome: the evolving landscape, animal models and future perspectives. Int J Urol. 2020;27(6):491-503. doi:10.1111/iju.14229.
8. Truschel ST, Wang E, Ruiz WG, et al. Stretch-regulated exocytosis/endocytosis in bladder umbrella cells. Mol Biol Cell. 2002;13(3):830-846. doi:10.1091/mbc.01-09-0435.
9. Parsons CL. Interstitial cystitis and lower urinary tract symptoms in males and females: the combined role of potassium

and epithelial dysfunction. Rev Urol. 2002;4(Suppl 1):S49-S55.

10. Theoharides TC, Kempuraj D, Sant GR. Mast cell involvement in interstitial cystitis: a review of human and experimental evidence. Urology. 2001;57(6 Suppl 1):47-55. doi:10.1016/s0090-4295(01)01129-3.
11. Goldstein DS. Adrenal responses to stress. Cell Mol Neurobiol. 2010;30(8):1433-1440. doi:10.1007/s10571-010-9606-9.
12. Chung KH, Liu SP, Lin HC, Chung SD. Bladder pain syndrome/interstitial cystitis is associated with anxiety disorder. Neurourol Urodyn. 2014;33(1):101-105. doi:10.1002/nau.22382.
13. Nickel JC, Tripp DA, Pontari M, et al. Interstitial cystitis/painful bladder syndrome and associated medical conditions with an emphasis on irritable bowel syndrome, fibromyalgia and chronic fatigue syndrome. J Urol. 2010;184(4):1358-1363. doi:10.1016/j.juro.2010.06.005.