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Anti-inflammatory bladder hydrodistension combined with pudendal nerve block in interstitial cystitis

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Introduction Interstitial cystitis/bladder pain syndrome (IC/BPS) is a chronic condition with unclear pathophysiology and limited standardized treatments. This retrospective analysis evaluates the association of a combined approach including prolonged hydrodistension, intravesical instillation, and bilateral pudendal nerve block with symptom improvement.

Material and methods Data from 64 patients, from December 2016 to June 2023, were analyzed, including demographic information, symptoms, intraoperative details, Interstitial Cystitis Symptoms Index (ICSI), Interstitial Cystitis Problem Index (ICPI), Visual Analogue Scale (VAS) for pain, and daily frequencies at baseline, 1 and 6 months. Patients underwent prolonged hydrodistension with intravesical prednisolone followed by instillation of $NaHCO_3$, bupivacaine, prednisolone, and heparin sulphate. A bilateral pudendal nerve block was then performed under fluoroscopic guidance.

Results Mean basal bladder capacity under general anaesthesia increased from 389.45mL to 537.34 ml and 629.91 ml after the first and second hydrodistension, respectively. Intravesical instillations and bilateral nerve block were performed in 90.6% and 95.3% of cases, respectively. ICSI decreased from 21.05 ±2.27 at baseline to 8.89 ±3.88 at 1 month and 13.87 ±5.42 at 6 months ($p < 0.0001$). ICPI showed similar improvement. VAS pain scores significantly decreased at follow-up. Symptom improvement correlated with increased bladder capacity and higher baseline ICPI, while pain reduction was predicted by higher ICPI and diurnal frequency, lower baseline bladder capacity, and increased capacity after the second hydrodistension.

Conclusions The combined approach of prolonged bladder anti-inflammatory hydrodistension and bilateral pudendal nerve block shows a short-term association with improvement in the management of IC/BPS. The observed early improvements in symptoms warrant further prospective studies with larger cohorts to confirm durability and to evaluate the role of repeat procedures.

Key Words: interstitial cystitis ‹› bladder pain syndrome ‹› bladder hydrodistension ‹› vesical instillations ‹› pudendal nerve block ‹› Hunner's lesion ‹› non-Hunner's IC/BPS

INTRODUCTION

Interstitial cystitis/bladder pain syndrome (IC/BPS) is a chronic condition characterized by pelvic, perineal and/or bladder pain, accompanied by symptoms of urinary urgency, frequency or nocturia [1]. Once considered uncommon, its prevalence is now estimated at >2% of females and 1.9% of males, with some reports suggesting rates exceeding 6%, particularly among women aged 50–59 years [2, 3]. The main characteristic of IC/BPS is the absence of an infective etiology or abnormal urine cytology [4].

IC/BPS is included within the broader classification of chronic pelvic pain, which also encompasses endometriosis and chronic prostatitis [5]. IC/BPS encompasses two distinct phenotypes: Hunner's lesion IC and non-Hunner's IC/BPS. Hunner's lesions are characteristic inflammatory patches or ulcers visible on cystoscopy, typically associated with a more localized inflammation and potentially distinct etiopathogenesis. Non-Hunner's IC/BPS, which lacks visible Hunner's lesions but may demonstrate glomerulations or petechial hemorrhages after hydrodistension, is now recognized as the more prevalent subtype, accounting for approximately 90% of IC/BPS cases in some series. These phenotypes may differ in their response to various treatments, necessitating clear differentiation in clinical studies [6].

The diagnosis of IC/BPS, which is typically established by the exclusion of other urinary tract diseases, remains a challenging endeavor, underscored by the incomplete understanding of its pathophysiology [7]. Although multiple therapeutic strategies have been proposed, ranging from behavioral interventions to pharmacologic and interventional treatments, no standardized approach has been established [8]. Recent advances of the American Association of Urology and the European Association of Urology guidelines have shifted IC/BPS management from a tiered stepwise model toward a multimodal, individualized pain strategy, reflecting the need for more effective therapies [9]. Bladder hydrodistension, first introduced in 1949, has long been used for diagnostic and therapeutic purposes, allowing identification of Hunner ulcers and glomerulations. However, these findings neither exclude nor reliably predict disease severity. Its mechanism of action has been linked to the disruption of sensory nerves present in the bladder, improving symptoms and quality of life in a subset of patients, with reported rates of improvement ranging from 30% to 54% at 1 month, 18% to 56% at 2 months and 0% to 7% at 6 months, although a sustained improvement of over 60% has been reported in other studies [10–12]. Peripheral nerve block, specifically targeting the pudendal nerves or the superior hypogastric plexus, has emerged as a promising alternative. These collectively mediate visceral pelvic pain and bladder control, making them plausible targets for intervention. While the use of pudendal nerve block and superior hypogastric plexus block in chronic pelvic pain associated with cancer and endometriosis is reported in several studies, their application in the management of IC/BPS remains relatively unexplored [13, 14]. In this manuscript we describe the technique and outcomes of a combined approach involving bladder hydrodistension and pudendal nerve block in the management of IC, contributing to the growing evidence supporting the feasibility and observed improvements of pudendal nerve block as a potential and alternative therapeutic modality.

MATERIAL AND METHODS

Study cohort characteristics

A retrospective analysis was conducted involving female patients affected by IC who underwent general anesthesia bladder hydrodistension followed by pudendal nerve block between December 2016 and June 2023. The study included only female patients because IC/BPS has a substantially higher prevalence in women (female-to-male ratio approximately 5–10 : 1), and no male patients presented during the study period. Data were extracted from both inpatient and outpatient electronic medical record systems. The collected baseline information included demographic data, presenting symptoms and baseline pain scores. The operative report was reviewed in order to obtain intraoperative information regarding the hydrodistension procedure, presence of glomerulation and performance of pudendal nerve block. Intraoperative cystoscopic findings were categorized as follows: 1) presence of Hunner's lesions (defined as circumscribed, reddened mucosal patches with small vessels radiating to a central scar or fibrin deposit) or 2) glomerulations (petechial hemorrhages) without Hunner's lesions or 3) normal appearing mucosa. Patients with Hunner's lesions were documented separately. Postoperative data collected included pain score, nocturnal and diurnal frequency, in addition to Interstitial Cystitis Symptoms Index (ICSI), Interstitial Cystitis Problem Index (ICPI) and Visual Analogue Scale (VAS) questionnaires performed at 1 month and 6 months.

Surgical technique

Cystoscopy is performed utilizing a 20-channel endoscope, under general anesthesia and in the lithotomy position. A schematic overview of the procedural steps is provided in Figure 1. The first step involves filling the bladder with saline solution until leaking is visualized from the urethra. The volume of saline solution is then measured and defined as "maximal bladder volume under general anesthesia". The second step involves, under cystoscopy monitoring, the filling of the bladder with saline solution and 250 mg of prednisolone, performing a bladder neck elevation using two fingers through the vagi-

na. This maneuver prevents reflux of the instillation into the lower ureters and maintains high intravesical pressure selectively on the bladder wall. During this filling, intravesical pressure is monitored, and the bladder is filled gradually, maintaining a stable intravesical pressure of 80 cmH_2O with manual elevation of the bladder neck. The hydrodistension is maintained for up to 15 minutes, and bladder capacity is then measured. Bladder wall glomerulation and submucosal petechial bleedings are observed. Thirdly, there is a repetition of bladder hydrodistension (a second hydrodistension is performed to maximize mechanical disruption of sensitized C-fibers and to further increase bladder capacity, because sustained pressure may recruit additional afferent fibers), via cystoscopy monitoring, performing the elevation of the bladder neck, maintenance of a stable pressure of 80 cmH_2O for 5 minutes, and then measurement of bladder capacity. Lastly, by using the resectoscope and bipolar cautery, bladder wall mucosal and submucosal tearing are fulgurated. Fulguration of visible mucosal tears is performed to prevent persistent submucosal bleeding and to remove potential nociceptive foci; this step is reserved for patients with visible lesions and is not performed routinely in all cases. Intravesical instillation is then performed for 30–40 minutes utilizing a mixture of 20 mEq $NaCHO_3$, 10 mg bupivacaine, 80 mg prednisolone, and 25,000 IU heparin sulphate. The choice of prednisolone 80 mg is based on prior studies of intravesical corticosteroid therapy (range 40–100 mg) and our institutional experience; the dose is equivalent to approximately 1 mg/kg for an average adult, providing local anti-inflammatory effect without significant systemic absorption. The same dose (80 mg) is used for a pudendal nerve block to achieve perineural anti-inflammatory action [15, 16]. The pudendal nerve block is performed, usually bilaterally, under fluoroscopic guidance using the ischial spine as a landmark and palpating it transvaginally. A 22-gauge, 12-cm spinal needle is advanced beneath the ischial spine toward the pudendal nerve, located under the sacrospinous ligament, and 10 mg bupivacaine with 80 mg prednisolone was injected.

Statistical analysis

Statistical analyses were performed with International Business Machines Corporation Statistical Product and Service Solutions (IBM SPSS) software for Windows (version 25.0, IBM Corp, Armonk, NY, USA). Descriptive statistics were used to present the baseline characteristics of the study population. Pertinent continuous variables were reported as mean and standard deviation (SD), while ordinal and categorical variables were reported as frequencies and percentages. The normal distribution of variables was assessed using the Kolmogorov-Smirnov test. Based on the results, continuous variables

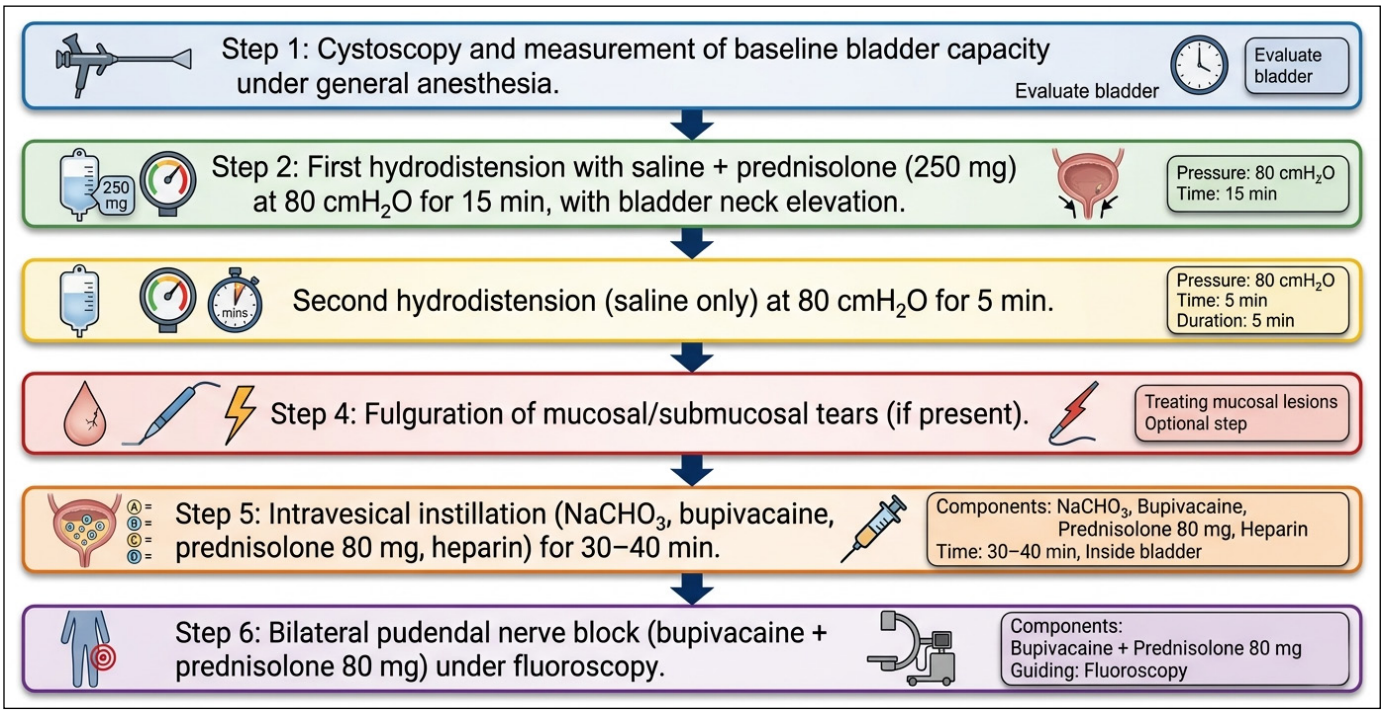

Figure 1. *Flow diagram of the combined procedure.*

were analyzed with the Mann-Whitney U test or the Kruskal-Wallis test, while the Chi-square test was used to compare categorical variables. The Friedman test for paired non-parametric variables was also used to compare the data obtained at the baseline, and at 1 month and 6 months. Statistical significance was considered for p-value <0.05. Lastly, clinically relevant variables were selected to perform multivariable linear regression modelling to identify independent predictors associated with variation in preoperative and postoperative one-month scores. Given the limited sample size (n = 64), we employed a stepwise forward selection procedure (entry criterion p <0.1, removal criterion p >0.1) to obtain parsimonious models and reduce the risk of overfitting. Collinearity was assessed using the variance inflation factor (VIF), with VIF values <5 considered acceptable.

Bioethical standards

This study was a retrospective review of anonymized clinical data collected during routine clinical practice. According to institutional regulations, formal approval by a Bioethics Committee/Institutional Review Board was not required for this type of retrospective study. Written informed consent for the procedures and for the use of anonymized clinical data and video recordings for research purposes was obtained from all participants. The study was conducted in accordance with the principles of the Declaration of Helsinki.

RESULTS

Description of the study cohort

During the defined time, 64 patients underwent bladder hydrodistension followed by a pudendal nerve block. Descriptive characteristics of the study population are reported in Table 1. Mean age at procedure and at diagnosis were, respectively, 51.40 ±14.43 years and 42.37 ±15.86 years. Regarding symptoms, mean reported diurnal and nocturnal frequencies were 13.86 ±7.73 and 8.02 ±5.09, with a reported mean routine VAS of 6.67 ±1.74. Notably, 56.3% (n = 36) of patients reported a previous hydrodistension, with an improvement of symptoms only in 25% (n = 16) of cases. Regarding cystoscopic findings (Table 2), 78.1% (n = 50) of patients demonstrated glomerulations without evidence of Hunner's lesions. No patient in this cohort presented with classic Hunner's lesions. Thus, our study population comprised exclusively patients with the non-Hunner's phenotype of IC/BPS.

Procedural characteristics

Intraoperative data are reported in Table 2. Mean basal bladder capacity under general anesthesia was 389.45 ±147.30 ml, which increased to 537.34

Table 1. *Descriptive characteristics of patients involved*

Characteristics of the study cohort	Mean	Standard deviation
Age at procedure (years)	51.40	14.436
Age at diagnosis (years)	42.37	15.859
Maternity	1.92	1.567
Nocturia	8.02	5.085
Diurnal Frequency	13.86	7.725
VAS Crisis	9.19	1.180
VAS Routine	6.67	1.737
Duration (months)	7.94	9.788
	Frequency (n)	Percentage (%)
Smoking	17	26.6
Bladder pain	61	95.3
Type of pain		
Burning	25	39.1
Stubbing	25	39.1
Both	14	21.9
Painful urine desire	60	93.8
Constipation	41	64.1
Dyspareunia	36	56.3
Previous hydrodistension	36	56.3
Improvement of symptoms after previous hydrodistension	16	25

VAS – Visual Analogue Scale

Table 2. *Intraoperative characteristics of patients involved*

Intraoperative variables	Mean	Standard deviation
Basal bladder capacity under general anaesthesia (ml)	389.45	147.299
Bladder capacity after first hydrodistension (ml)	537.34	182.763
Bladder capacity after second hydrodistension (ml)	628.91	228.752
Duration of first hydrodistension (min)	12.27	4.441
Duration of second hydrodistension (min)	5.11	2.183
	Frequency (n)	Percentage (%)
Glomerulation	50	78.1
Pudendal nerve block		
Monoliteral	3	4.7
Bilateral	61	95.3
Intravesical instillation	58	90.6

±182.76 ml and 628.91 ±228.75 ml after a first and a second hydrodistension, respectively. Intravesical instillations were performed in 90.6% (n = 58) of cases, while pudendal nerve block was performed bilaterally in 95.3% (n = 61) of cases, with only n = 3 (4.7%) monoliteral blocks.

Symptoms improvement

Significant improvements were observed at 1 and 6 months. Overall scores greatly improved postoperatively, reaching their nadir at one month before partially regressing to a plateau value at 6 months – a pattern consistent with transient benefit. In particular, the mean preoperative ICSI total score was 21.05 ±2.27, decreasing to 8.89 ±3.88 at one month and rising to 13.87 ±5.42 at 6 months postoperatively, whereas the mean preoperative ICPI total score was 17.17 ±2.53, decreasing to 7.16 ±3.37 at one month and increasing to 11.02 ±4.29 at 6 months (p <0.0001). VAS improved from 6.67 ±1.74 to 3.09 ±2.48 and 5.81 ±2.97, respectively (p <0.0001). A complete overview of the obtained results is reported in Table 3.

Table 3. *Results of hydrodistension plus pudendal nerve block evaluated through ICSI, ICPI, VAS, nocturia and diurnal frequency at baseline, 1 month and 6 months after treatment*

	Preoperative	1 month	6 months	P-value
ICSI Q1	5.59 ±0.706	2.28 ±1.327	3.20 ±1.605	<0.0001
ICSI Q2	5.33 ±1.070	2.11 ±1.183	3.59 ±1.743	<0.0001
ICSI Q3	5.17 ±1.032	2.52 ±1.208	4.06 ±1.531	<0.0001
ICSI Q4	4.95 ±0.452	1.98 ±1.105	3.02 ±1.363	<0.0001
ICSI TOTAL	21.05 ±2.271	8.89 ±3.876	13.87 ±5.417	<0.0001
ICPI Q1	4.61 ±0.809	1.87 ±1.120	3.09 ±1.455	<0.0001
ICPI Q2	4.22 ±1.188	1.89 ±1.129	2.87 ±1.609	<0.0001
ICPI Q3	3.52 ±1.309	1.42 ±0.752	1.69 ±0.941	<0.0001
ICPI Q4	4.83 ±0.380	1.97 ±1.181	3.36 ±1.429	<0.0001
ICPI TOTAL	17.17 ±2.530	7.16 ±3.372	11.02 ±4.285	<0.0001
VAS	6.67 ±1.737	3.09 ±2.480	5.81 ±2.970	<0.0001
Nocturia	8.02 ±5.085	3.02 ±1.830	3.98 ±2.579	<0.0001
Diurnal frequency	13.86 ±7.725	5.63 ±2.327	7.45 ±3.116	<0.0001

ICPI – Interstitial Cystitis Problem Index; ICSI – Interstitial Cystitis Symptom Index; VAS – Visual Analogue Scale

Table 4. *Multiple linear regression analysis for predictors of treatment response at 1 month*

Variables	Δ ICSI			Δ ICPI			Δ VAS		
	B	95% CI	p	B	95% CI	p	B	95% CI	p
Age	0.052	From –0.021 to 0.125	0.157	0.030	From –0.034 to 0.094	0.353	0.040	From –0.006 to 0.086	0.088
Smoking	1.024	From –1.485 to 3.532	0.417	1.070	From –1.126 to 3.265	0.333	1.556	From –0.025 to 3.137	0.054
Diurnal frequency	–0.063	From –0.200 to 0.075	0.365	–0.125	From –0.245 to –0.004	0.043	–0.099	From –0.186 to –0.012	0.026
Bladder pain	–2.231	From –6.870 to 2.408	0.339	–1.385	From –5.445 to 2.674	0.497	–1.917	From –4.841 to 1.006	0.194
VAS baseline	–0.088	From –0.965 to 0.789	0.841	0.040	From –0.727 to 0.807	0.918	0.382	From –0.171 to 0.934	0.172
Previous hydrodistension	–0.329	From –2.582 to 1.924	0.771	–1.030	From –3.001 to 0.941	0.299	0.064	From–1.355 to 1.484	0.928
ICSI baseline	0.457	From –0.124 to 1.038	0.121	–0.156	From –0.664 to 0.352	0.541	–0.142	From –0.508 to 0.224	0.441
ICPI baseline	0.322	From –0.194 to 0.839	0.216	1.140	From 0.689 to 1.592	<0.001	0.380	From 0.054 to 0.705	0.023
Basal bladder capacity – under GA (ml)	–0.006	From –0.015 to 0.002	0.132	–0.006	From –0.013 to 0.002	0.139	–0.007	From –0.013 to –0.002	0.007
Bladder capacity after 2nd HD (ml)	0.009	From 0.002 to 0.015	0.011	0.007	From 0.001 to 0.013	0.017	0.006	From 0.001 to 0.010	0.010

B – Unstandardized coefficient; CI – Confidence interval; GA – general anaesthesia; HD – hydrodistension; ICPI – Interstitial Cystitis Problem Index; ICSI – Interstitial Cystitis Symptom Index; VAS – Visual Analogue Scale

Predictors of treatment response at one month

Multivariable linear regression models evaluating associations between preoperative and intraoperative variables and the one-month change in symptom scores from baseline are presented in Table 4. Only an increasing bladder capacity after the second hydrodistension emerged as a significant predictor of ICSI improvement (B = 0.009; 95% CI: 0.002–0.015; p = 0.011). Regarding ICPI, greater improvement was associated with increased post-second hydrodistension bladder capacity (B = 0.007; 95% CI: 0.001–0.013; p = 0.017), higher diurnal frequency (B = −0.125; 95% CI: from −0.245 to −0.004; p = 0.043), and higher baseline ICPI score (B = 1.140; 95% CI: 0.689–1.592; p <0.001). Moreover, significant pain reduction (Δ VAS) was predicted by higher diurnal urinary frequency (B = –0.099; 95% CI: from –0.186 to –0.012; p = 0.026), higher ICPI baselines scores (B = 0.380; 95% CI: 0.054–0.705; p = 0.023), lower baseline bladder capacity under general anesthesia (B= –0.007; 95% CI: from –0.013 to –0.002; p = 0.007) and higher bladder capacity after second hydrodistension (B = 0.006; 95% CI: 0.001–0.010; p = 0.010).

Complications and safety assessment

No intraoperative or postoperative complications were recorded in any of the 64 patients. Specifically, there were no cases of bladder perforation, significant hematuria requiring transfusion or surgical intervention, urinary tract infection within 30 days, or post-procedural urinary retention beyond the immediate recovery period. No complications related to the pudendal nerve block were observed, including bleeding at the injection site, pelvic hematoma, local anesthetic systemic toxicity, or persistent motor or sensory deficits in the perineal distribution. Using the Clavien–Dindo classification, no adverse events of grade II or higher occurred; potential grade I events (e.g., transient mild discomfort at the injection site) were not reported by any patient during follow-up. However, given the retrospective design, minor or self-limited complications may be underreported.

DISCUSSION

A variety of medications and therapeutic approaches have been adopted for IC/BPS, reflecting the absence of a durable, standardized treatment [8, 17]. Although bladder hydrodistension has demonstrated benefit in a subset of patients, evidence remains limited, and it is mostly seen as part of diagnostic or multimodal treatment [18]. Given the increasing prevalence of IC/BPS, more effective therapeutic approaches are needed [3]. In the present study, we propose, in addition to bladder hydrodistension with a combination of saline solution and an anti-inflammatory agent (prednisolone), a synergistic approach combining intravesical instillation, high intravesical hydrostatic pressure and pudendal nerve block. Physiologically, bladder filling activates afferent Aδ fibers of hypogastric and pelvic nerves, promoting sympathetic-mediated detrusor relaxation [19]. In IC/BPS, chronic inflammation sensitizes C-fibers, leading to hyperexcitability with a reduced threshold and increased sympathetic tone, which causes pain during normal bladder distension. This process is associated with a marked edema, vasodilation, proliferation of nerve fibers, mast cells infiltration and increased expression of substance P – a major neurotransmitter of C-fibers [20]. Hydrodistension improves pain and urinary frequency in animal models by reducing C-fibers neurotransmission, although its efficacy alone in humans has not shown a significant therapeutic effect [21, 22]. Pudendal nerve block with glucocorticosteroid is widely used for the diagnosis and management of chronic pelvic pain and as regional anesthesia in gynecologic, obstetric and anorectal procedures [23–25]. The pudendal nerves arise from sacral roots S2–S4 and provide motor and sensory innervation to the perineum, external genitalia, anus, and external urethral and anal sphincters [26]. Damage or overactivity of these nerves can lead to visceral pelvic pain and urinary dysfunction [27, 28]. The rationale for combining hydrodistension with an anti-inflammatory agent and pudendal nerve block in IC/BPS resides in the neurogenic inflammation and pelvic floor hypertonia associated with the condition, which often correlate with chronic pelvic pain and lower urinary tract symptoms [29]. Additionally, a bidirectional neural cross-sensitization of the bladder and colon could support the neurogenic etiology of IC/BPS and explain the overlapping pain patterns with chronic pelvic pain [30, 31]. Few data are available regarding the use of pudendal nerve blocks in IC/BPS, as current evidence is limited to small case series and extrapolation from chronic pelvic pain literature. Kalava et al. [13] performed the procedure in addition to superior hypogastric plexus blocks in three cases, reporting improvement in pain, urinary symptoms, and functionality. Another retrospective study by Patil et al. [14], involving 84 patients, reported an improvement in pain after six weeks of weekly pudendal nerve blocks, with a statistically significant

difference in VAS scores pretreatment (6.23 ±2.68) and post-treatment (3.90 ±2.63). Our findings are consistent with this limited literature. Beyond pain reduction assessed by VAS, the use of ICSI and ICPI questionnaires allowed a more comprehensive evaluation of symptom burden and quality-of-life impact following the combined approach of hydrodistension, intravesical instillations and pudendal nerve block. The multi-step nature of our protocol warrants discussion regarding standardization and reproducibility. Each component was selected based on mechanistic rationale: 1) double hydrodistension maximizes mechanical stretch-induced desensitization of C-fibers and increases bladder capacity, as sustained or repeated pressure may enhance afferent modulation; 2) intravesical instillation provides topical anti-inflammatory (prednisolone), anesthetic (bupivacaine), and mucosal protective (heparin) effects; 3) pudendal nerve block targets pelvic floor hypertonia and visceral afferent pathways. Bladder neck elevation, while unconventional, is a maneuver to prevent reflux and maintain effective intravesical pressure. Fulguration of mucosal tears is reserved for visible lesions and is derived from the concept of removing irritable foci, though its routine use remains unvalidated. We acknowledge that this complex protocol may be difficult to standardize across centers; a detailed procedural schematic (Figure 1) is provided to enhance reproducibility. Walker et al. [32] evaluated how lower bladder capacity while under anesthesia was related to higher symptom scores and increased urinary frequency, suggesting bladder capacity as a key factor in IC/BPS' pathophysiology. Similarly, in our cohort, greater bladder capacity after the second hydrodistension predicted symptom improvement, underscoring its potential role in treatment response. Patients with more severe baseline problems, especially those with higher ICPI scores and urinary frequency, experienced more substantial benefits. This paradoxical association was also described by Yu et al. [33], reporting how patients with lower baseline capacity were often characterized by more severe mucosal or neurogenic involvement, which may have made them more responsive to the therapeutic intervention, potentially explaining their greater symptomatic improvement after treatment. No adverse events or complications were reported, confirming the feasibility and safety of the procedure. Nevertheless, several risks inherent to the procedure deserve explicit mention. Bladder hydrodistension carries a risk of bladder perforation, mucosal laceration with bleeding, and post-procedural dysuria or urinary tract infection. Pudendal nerve block, while generally safe when performed under fluoroscopic guidance, may be associated with bleeding (especially in anticoagulated patients), infection, local anesthetic systemic toxicity, inadvertent intravascular or intraneural injection, and temporary motor weakness of the pelvic floor or lower limb. In this series, none of these events was documented. However, because our retrospective chart review may not have captured all minor or transient adverse events, the true incidence of grade I complications may be underestimated. The observed partial regression of symptoms at 6 months suggests that the therapeutic effect is predominantly short-term, similar to the well-known transient benefit of bladder hydrodistension alone. Previous studies report improvement ranges from approximately 30–60% at 1 month, but drops to less than 10–20% at 6 months in many series providing bladder hydrodistension alone [34, 35]. Accordingly, this temporal pattern mirrors the trajectory observed in our cohort, despite reporting greater load of improvement (e.g. ICSI, ICPI and VAS scores), suggesting a potential additive and synergistic role of a combined approach. Consistent with this observation, more than an half of patients underwent prior bladder hydrodistension with limited benefit, thus experiencing clinically meaningful improvement following combined intervention.

This finding has important clinical implications. First, the combined approach may be best suited as a "rescue" or intermittent therapy rather than a one-time definitive treatment. Second, repeat procedures at regular intervals (e.g., every 6–12 months) or maintenance strategies such as periodic pudendal nerve blocks or self-administered intravesical instillations could be considered to prolong symptom control, although this hypothesis requires prospective evaluation. Third, the optimal timing for retreatment remains unknown and should be addressed in future studies. Furthermore, the waning effect at 6 months underscores that this intervention, while promising, does not provide durable remission for most patients. Clinicians should counsel patients accordingly and consider scheduled repeat treatments or adjunctive therapies to sustain improvement.

We must acknowledge several important limitations. First and foremost, the retrospective, non-comparative design with no control group (e.g., hydrodistension alone, nerve block alone, or a sham procedure) is the major limitation of this study. Without a control group, we cannot determine whether the observed improvements are attributable to the combined intervention, to one of its components, or to a placebo effect. Second, the in-

tervention was heterogeneous: 90.6% of patients received intravesical instillations and 95.3% received pudendal nerve block, but not all patients received all components, making it impossible to isolate the additive or synergistic effects of each component or to establish causal inference. Therefore, our results should be interpreted as associations with improvement rather than evidence of efficacy. Third, the lack of long-term follow-up beyond 6 months limits our understanding of durability. Fourth, the single-center design and relatively small sample size may limit generalizability. Fifth, our multivariable analysis included up to 10 predictors with only 64 patients, raising a potential risk of overfitting. Although we performed stepwise variable selection and collinearity diagnostics (all VIFs <2.5), these exploratory results should be interpreted cautiously and require validation in larger independent cohorts. Sixth, our study included only female patients, limiting the generalizability to male IC/BPS patients, although the lower prevalence of this condition in men. Lastly, we did not systematically record prior treatments and patients were not stratified by symptom phenotype – due to the limited sample size. Despite these limitations, the observed improvements are promising and warrant further investigation in prospective, controlled trials.

Another important consideration in interpreting our findings is the phenotypic composition of our study cohort. All 64 patients demonstrated non-Hunner's IC/BPS, characterized by glomerulations without classic Hunner's lesions on cystoscopic examination. This distinction is clinically relevant, as Hunner's lesion IC and non-Hunner's IC/BPS may respond differently to various therapeutic interventions. Patients with Hunner's lesions, for instance, often show favorable responses to fulguration or laser coagulation, whereas non-Hunner's patients may derive greater benefit from hydrodistension and neuromodulatory approaches such as pudendal nerve block. Therefore, our findings should be considered specifically applicable to the non-Hunner's IC/BPS population. Future studies should prospectively stratify patients by phenotype to determine whether treatment responses differ between these subgroups. Nevertheless, given the major limitations described above, the promising results presented in this manuscript should be viewed as hypothesis-generating. Further prospective studies with larger cohorts and control groups are needed to validate the findings and explore the long-term sustainability of the observed improvements and to determine the optimal retreatment interval.

CONCLUSIONS

The combined approach of prolonged bladder hydrodistension, intravesical instillation and pudendal nerve block shows a short-term association with improvement in symptoms and quality of life in patients with non-Hunner's IC/BPS. No major complications were observed in this retrospective series, but the absence of reported adverse events should be interpreted cautiously, given the study design. Given that our cohort consisted exclusively of patients with non-Hunner's IC/BPS, these results are particularly relevant to this prevalent phenotype. However, the partial regression of benefit at 6 months indicates predominantly transient efficacy, consistent with the known effects of hydrodistension. Future research should focus on prospective randomized trials to confirm short-term benefit, to define the optimal retreatment interval, and to explore maintenance strategies (e.g., repeat nerve blocks, home instillations) that may extend symptom control, while further research is warranted to evaluate whether patients with Hunner's lesions derive similar benefits from this combined approach.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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