A Comparative Study of the Efficacy of Two Different Bladder Intravesical Hyaluronic Acid Treatments, Cystistat® and Hyauro®, in the Management of Interstitial Cystitis: A Retrospective Analysis, single center study

Chun Shuo Hsu

1. Institute of Medicine of Chun Shan Medical University, Taichung, Taiwan
2. Department of Obstetrics and Gynecology, Dalin Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Tzu Chi University, Chiayi 622, Taiwan
3. School of Medicine, Tzu Chi University, Hualien City, Taiwan

introduction

Interstitial cystitis/bladder pain syndrome (IC/BPS) is a chronic bladder condition characterized by inflammation and pain of the bladder lining, often accompanied by symptoms such as urinary frequency, urgency, and pelvic pain. The European Society for the Study of Interstitial Cystitis (ESSIC) defines BPS based on chronic (>6 months) pelvic pain, pressure, or discomfort perceived to be related to the urinary bladder, accompanied by at least one other urinary symptom such as persistent urge to void or frequency.One treatment modality for IC/BPS involves intravesical instillation of hyaluronic acid. Cystistat®, produced by the Irish company Mylan, is an internationally recognized hyaluronic acid bladder instillation medication. Cystistat® is a solution containing 40 mg of sodium hyaluronate in a 50 ml vial, used to treat bladder conditions such as interstitial cystitis (bladder lining inflammation). It aims to enhance the glycosaminoglycan (GAG) layer on the surface of the bladder, providing a protective barrier.However, since the onset of the COVID-19 pandemic in 2019, the importation of Cystistat® into Taiwan has been disrupted. Consequently, our institution has adopted Hyauro®, a hyaluronic acid product from Taiwan's Scivision Biotechnology Co., Ltd. (approved by TFDA in 2017), as an alternative treatment. Hyauro® is produced in Taiwan and contains the same active ingredient as Cystistat®, with 40 mg of sodium hyaluronate in a 50 cc bottle, maintaining the same concentration of hyaluronic acid.From January 2019 to the end of 2023, our institution treated approximately one hundred patients with hyaluronic acid therapy. All patients completed full treatment cycles with both Cystistat® and Hyauro® for six months each, showing stable clinical outcomes during both treatment periods.

Study design, materials and methods

Research Objective:
To retrospectively analyze patient medical records and post-treatment questionnaire surveys, aiming to investigate the differences in efficacy between Cystistat® and Hyauro® hyaluronic acid treatments for interstitial cystitis.

Trial Methods:
(1) Number of Subjects:
This study is a retrospective analysis involving a total of 101 participants.

(2) Inclusion and Exclusion Criteria:
Inclusion Criteria:
Patients diagnosed with interstitial cystitis between 2019 and 2023, who underwent full treatment cycles of both Cystistat® and Hyauro® hyaluronic acid treatments for six months each, and remained stable during treatment with Cystistat®.

Exclusion Criteria:

Below 18 years of age
Suspected malignant tumors during treatment
Allergy to hyaluronic acid
Patients who did not complete full treatment cycles of both Cystistat® and Hyauro® hyaluronic acid treatments.
(3) Trial Design and Methods:
Data Collection Methods:
Patient medical records were retrieved using the hospital's medical prescription system between January 1, 2019, and December 31, 2023. Patients diagnosed with interstitial cystitis and treated with both Cystistat® and Hyauro® hyaluronic acid treatments were included in the study if they remained stable during both treatment periods and completed six months of treatment each. Starting September 1, 2023, researchers approached participants during gynecology outpatient visits, explained the contents of the informed consent form, and invited them to participate in the study. Relevant medical records were accessed upon obtaining consent and signed informed consent forms from participants.

(4) Evaluation and Statistical Methods:
From January 1, 2019, to December 31, 2023, we selected 101 patients with interstitial cystitis who underwent bladder instillation of hyaluronic acid. These patients were not newly diagnosed but were stable and had not experienced any recurrence. They had already received Cystistat instillations for at least six months. Due to a shortage of Cystistat, they were switched to Hyauro and received at least six months of instillations.
We conducted detailed questionnaires, including the O'Leary–Sant Interstitial Cystitis Symptom Index (ICSI), O'Leary–Sant Interstitial Cystitis Problem Index (ICPI), visual analog scale (VAS) for pain, GRA score before switching from Cystistat to Hyauro. After six months of Hyauro instillations, we conducted the same questionnaires again and compared the results to analyze the differences between the two sets of questionnaires.(Fig1)

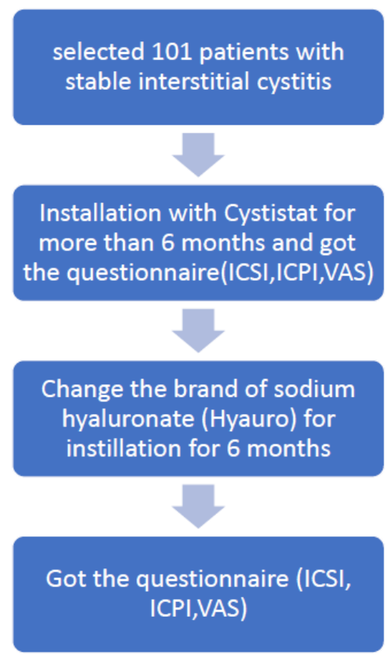

Fig 1:
Study flow chart

Results and interpretation

Results
The average scores of the Interstitial Cystitis (IC) Symptom Index were 3.18 and 3.79 for Cystistat® and Hyauro® respectively. Paired t-test analysis revealed no significant difference in the IC Symptom Index scores between the two different medications (t=-0.15; p=0.88). Similarly, paired t-test analysis showed no significant difference in the IC Problem Index scores between the two medications (t=-0.06; p=0.95). Regarding the comparison of IC bladder pain Visual Analog Scale (VAS) scores, the statistical results indicated no significant difference between the two medications (t=0.61; p=0.54). Furthermore, for the Global Response Assessment (GRA) scores, the average scores were 2.00 and 2.25 for Cystistat® and Hyauro® respectively. Paired t-test analysis revealed a significant difference between the two groups (t=-2.84; p=0.005). (table 1)

Discussion
Interpretation of results
The scores of the Interstitial Cystitis Symptom Index (ICSI) and Interstitial Cystitis Problem Index (ICPI), as well as a pain visual analog scale (VAS), were statistically analyzed, showing no significant differences between Cystistat® and Hyauro®. This indicates that the effectiveness of Cystistat ®and Hyauro®, two brands of hyaluronic acid, is consistent in real-world scenarios. As for the Global Response Assessment (GRA), the variation might be due to the experimental design where patients initially received Cystistat® intravesical therapy followed by Hyauro ® intravesical therapy. While this design reduces questionnaire errors within the same patient, it's possible that patients who received Hyauro ® intravesical therapy after Cystistat ®had already undergone multiple cycles of bladder instillation of hyaluronic acid, potentially resulting in greater improvement. Therefore, GRA may favor Hyauro ®over Cystistat ®.

Comparison of	Cystistat ® and Hyauro ® intravesicle therapy(N=101)		
	Cystistat ®	Hyauro ®	
ICSI	10.50±3.17	10.54±3.79	P=0.884
ICPI	10.17±3.63	10.19±3.84	P=0.956
Pain -VAS	6.24±1.82	6.12±1.90	P=0.541
GRA	2.00±0.81	2.24±0.69	P=0.05

VAS: visual analog score (range 0-10); ICSI: interstitial cystitis symptom index (range 0-20); ICPI: interstitial cystitis problem index (range 0-16); GRA: Global Response Assessment

Table 1.

Conclusions

This is the first real-world comparison of Cystistat ®and Hyauro ®in hyaluronic acid instillation therapy. Essentially, the effects of these two brands of hyaluronic acid are similar with no significant differences.

References

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佛教大林慈濟醫院
Buddhist Dalin Tzu Chi Hospital