

RESEARCH ARTICLES

ASSESSMENT OF TREATMENT OUTCOMES OF INTERSTITIAL CYSTITIS WITH SODIUM HYALURONATE BY THE O'LEARY-SANT INTERSTITIAL CYSTITIS SYMPTOM INDEX (ICSI) AND INTERSTITIAL CYSTITIS PROBLEM INDEX (ICPI)

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ABSTRACT

Background: Interstitial cystitis is a syndrome characterized by symptoms of urgency and frequency. The prevalence of interstitial cystitis varies widely with ranges from 0.06% to 30%. Interstitial cystitis is more common in women than men. Bladder instillation using sodium hyaluronate is considered an acceptable treatment for interstitial cystitis. A scoring system with The O'Leary-Sant symptom index can help describe the symptoms and the treatment outcomes. This study wants to assess the treatment outcome of interstitial cystitis with sodium hyaluronate (cystistat) instillation by O'Leary-Sant interstitial cystitis symptom index (ICSI) and interstitial cystitis problem index (ICPI).

Methods: From January 2019 to October 2020, 11 patients diagnosed with interstitial cystitis were treated with sodium hyaluronate (cystistat) instillation. Each patient was assessed using the O'Leary-Sant interstitial cystitis symptom index (ICSI) and interstitial cystitis problem index (ICPI) before and after therapy. The data were analyzed by univariate analysis and paired t-test with SPSS ver 23.0.

Results: The number of interstitial cystitis patients who completed the instillation program in this study was 11 patients. In the assessment of interstitial cystitis symptom index (ICSI), there was a significant clinical improvement in each of the symptoms, which are urgency, frequency, nocturia, and bladder pain, with statistical test results obtained p-value (0.002, 0.003, 0.003, and 0.003) consecutively. In the interstitial cystitis problem index (ICPI) study, clinical improvements were obtained from each symptom in the form of urgency, frequency, nocturia, and bladder pain with statistical test results obtained p-value (0.002, 0.003, 0.003, and 0.003) consecutively.

Conclusion: In all interstitial cystitis patients who were treated with sodium hyaluronate instillation in this study, there was a significant difference in the values of O'Leary-Sant interstitial cystitis symptom index (ICSI) and interstitial cystitis problem index (ICPI) before and after therapy. This shows that sodium hyaluronate (cystistat) instillation therapy is very effective for interstitial cystitis patients.

Keywords: interstitial cystitis, sodium hyaluronate, O'Leary-Sant interstitial cystitis symptom index (ICSI) and interstitial cystitis problem index (ICPI)

INTRODUCTION

Interstitial cystitis is a syndrome characterized by symptoms of urgency and frequency, which is accompanied by pelvic pain and urination at night, without bacterial infection or other pathological causes.¹ Several studies have associated interstitial cystitis with painful bladder syndrome. This refers to the international society for the study of bladder pain syndrome (ESSIC).² Interstitial cystitis can be confirmed by performing cystoscopy, hydrodistension, and tissue biopsy. The international society for the study of bladder pain syndrome (BPS) divides interstitial cystitis into several subtypes.³

The prevalence of interstitial cystitis varies widely,

with recent reports saying the prevalence of interstitial cystitis ranges from 0.06% to 30%.⁴ Interstitial cystitis is more common in women than men with a ratio of 10: 1.⁵ Initially, interstitial cystitis is caused by an unidentified bladder failure resulting in an inflammatory, endocrine, and nervous process.⁶ Several aetiologies and pathophysiological mechanisms are thought to be responsible for interstitial cystitis, however, there is no evidence that they are directly related to the infectious process.⁷ Cystoscopy and biopsy findings have shown consistent results in the form of defects in the urothelial glycosaminoglycan (GAG) layer, exposing submucosal structures to urinary components causing a cytotoxic effect.⁸ Damage to the GAG layer of the urothelium and the effects of urinary toxins lead to a cavity of sensory nerves, inflammation of the bladder,

and fibrosis of the detrusor muscle which are potential pain sensations and urinary retention symptoms in women with interstitial cystitis.⁹

Bladder instillation using sodium hyaluronic is a replacement therapy for damaged GAG layers and is considered an acceptable treatment for interstitial cystitis. Despite its invasiveness, this therapy is still used because it has a very safe profile.¹⁰ The use of this method has been in use for twenty years. Bladder instillation still rarely known by the public, so most patients who completed this therapy have previously been treated in various ways but have not received significant results. This refers to studies that reported that sodium hyaluronic instillation was effective in replacing glycosaminoglycan (GAG) in interstitial cystitis patients who were resistant to other therapies.¹¹

Recent meta-analyses confirm that the repair of the GAG layer improves symptoms of interstitial cystitis.¹² Instillation of sodium hyaluronate therapy is carried out by injecting it directly into the bladder at a dose of 40mg / 50 ml. Solution sodium hyaluronate 50 ml enter into the bladder through catheter then clamp at the end of the urine bag. After the fluid entered, the patient was asked to sit in sitting position for 15 minutes, the patient was asked to lie down for 15 minutes, the patient was asked to be on his right side position for 15 minutes, and finally the patient was asked to be on his left side for 15 minutes. Then the nurse discharges catheter and the patient is asked to drink 1 until 1.5 liters of water and hold on to urination for 30 minutes. After completion of the procedure, the patient is asked to urinate normally. The frequency of therapy is once to four times a week and continued once a month for four months.²

A scoring system can help describe the symptoms and the treatment outcomes. The O'Leary-Sant symptom index (ICSI) has been validated as a diagnostic tool for BPS.² Meanwhile, the interstitial cystitis problem index (ICPI) is

also a tool for problems experienced by interstitial cystitis patients. This questionnaire is very useful for dealing with complaints and problems of patients with interstitial cystitis.¹³

MATERIAL DAN METHODS

This study used data from patients diagnosed with interstitial cystitis through cystoscopy and hydrodistension in the urology section of Graha Medika hospital and has completed instillation therapy program from January 2019 to October 2020. After data collection, 11 patients have met the criteria. The inclusion criteria in this study were patients has completed this therapy during 6 months or 8 times instillation. Each patient was interviewed and assessed by the O'Leary-Sant interstitial cystitis symptom index and interstitial cystitis problem index before and after therapy.

Both instruments of the O'leary-Sant questionnaires have been validated for diagnosis patients with interstitial cystitis. Scoring system of this instruments show quantitative evaluation of the therapies for patients with interstitial cystitis.² Furthermore, the data were analyzed by univariate analysis and paired t-test. $P < 0.05$ indicates a significant statistical value, the software used is SPSS ver 23.0.

RESULTS

There were 11 patients diagnosed with interstitial cystitis who has completed instillation therapy with sodium hyaluronate during 6 months or 8 times instillation. All patients were assessed using the O'Leary-Sant interstitial cystitis symptom index (ICSI) and interstitial cystitis problem index (ICPI) questionnaires before and after treatment.

Table 1. Observation With Interstitial Cystitis Symptom Index (ICSI)

Variable		Score					
		0	1	2	3	4	5
Q1	Before	0	0	0	2 (18 %)	7 (64%)	2 (18%)
	After	1(9 %)	8 (73%)	2 (18 %)	0	0	0
Q2	Before	0	0	0	2 (18 %)	6 (55%)	3 (27%)
	After	2 (18 %)	8 (73%)	1 (9%)	0	0	0
Q3	Before	0	0	0	2 (18 %)	3 (27 %)	6 (55 %)
	After	0	4 (36 %)	7 (64 %)	0	0	0
Q4	Before	0	0	1 (9 %)	3 (27 %)	7 (64 %)	0
	After	3 (27 %)	7 (64 %)	1 (9 %)	0	0	0

Abbreviations: ICSI, O'Leary-Sant Interstitial Cystitis Symptom Index Q1 until Q4. Question 1-4 of ICSI.

Table 1 shows the symptoms experienced by patients with interstitial cystitis, in the form of an improvement in the frequency of urination without warning in daily life less than 5 times a day before treatment 64% to 73% after therapy. Improvement in frequency of frequent trips to the bathroom in less than 2 hours before treatment was 55% to 73% after

therapy. Other complaints by patients such as urinating at night 5 times a night (55%) experienced improvement to one to two times a night (64%). Meanwhile, the feeling of pain and burning in the bladder area that was previously felt very often (64%) became less (73%) after therapy completion.

Table 2. Outcome of Complaints Before and After Treatment (ICSI)

	Variable	Mean	SD	95% CI	p-value
Q1	Before	4,00	0,6325	3,58-4,42	0,002
	After	1,091	6,5394	0,73-1,45	
Q2	Before	4,091	0,7006	3,62-4,56	0,003
	After	0,909	0,5394	0,55-1,27	
Q3	Before	4,364	0,8090	3,82-4,91	0,003
	After	1,636	0,5045	1,30-1,98	
Q4	Before	3,545	0,6876	3,08-4,01	0,003
	After	0,818	0,6030	0,41-1,22	

Abbreviations: ICSI, O'Leary-Sant Interstitial Cystitis Symptom Index; Q1 until Q4. Question 1-4 of ICSI. SD, standard deviation. CI, confidence interval.

Table 2 shows a summary of the ICSI statistical values of interstitial cystitis patients who have received interstitial cystitis therapy 8 times during 6 months of treatment. The mean ICSI score of patients with interstitial cystitis showed significance after therapy compared to before therapy. The mean values of complaints of urgency, frequency, nocturia,

and bladder pain before therapy were 4.00, 4.091, 4.364, and 3.545, respectively, to 1.091, 0.909, 1.636, and 0.818 after therapy. Based on the statistical test with paired t-test, significant results were obtained with p values (0.002, 0.003, 0.003, and 0.003).

Table 3. Observation With Interstitial Cystitis Problem Index (ICPI)

Variable		Score				
		0	1	2	3	4
Q1	Before	0	0	0	2 (18 %)	9 (82 %)
	After	2 (18 %)	7 (64 %)	1 (9 %)	1 (9 %)	0
Q2	Before	0	0	0	4 (36 %)	7 (64 %)
	After	2 (18 %)	7 (64 %)	2 (18 %)	0	0
Q3	Before	0	0	0	4 (36 %)	7 (64 %)
	After	4 (36 %)	5 (46 %)	2 (18 %)	0	0
Q4	Before	0	0	1 (9 %)	2 (18 %)	8 (83 %)
	After	4 (36 %)	8 (83 %)	1 (9 %)	0	0

Abbreviations: ICPI O'Leary-Sant Interstitial Cystitis Problem Index, Q1 until Q4. Question 1-4 of ICPI.

Table 3 shows the changes in quality of problems that often occur in interstitial cystitis patients before and after treatment. The frequency of urination during the day was categorized as a very big problem (82%), being a very minor problem (64%) according to the patient after treatment. The feeling of being awake at night to urinate was also considered a major problem (64%), being a very minor

problem (64%) after treatment. Problems wanting to urinate with little warning of wanting to urinate which was a major problem (64%) became very minor problems according to patients (46%) after treatment. While problems such as burning, pain, discomfort, and pressure in the bladder which are major problems (83%) become very minor problems (83%) after treatment.

Table 4. Outcome of Problems in Interstitial Cystitis (ICPI) Patients

	Variable	Mean	SD	95% CI	p-value
Q1	Before	3,818	0,4045	3,546-4,090	0,002
	After	1,091	0,8312	0,532-1,649	
Q2	Before	3,636	0,5045	3,297-3,975	0,003
	After	1,000	0,6325	0,575-1,425	
Q3	Before	3,636	0,5045	3,297-3,975	0,003
	After	0,818	0,7508	0,314-1,323	
Q4	Before	3,636	0,6742	3,182-4,089	0,003
	After	0,727	0,6467	0,293-1,162	

Abbreviations: ICPI, O'Leary-Sant Interstitial Cystitis Problem Index Q1 until Q4, question 1-4 of ICPI. SD, standard deviation. CI, confidence interval.

Table 4 shows the statistical changes in problems experienced by patients with interstitial cystitis before and after administration of sodium hyaluronic therapy 8 times. The mean values of urgency, frequency, nocturia, and bladder pain before therapy were found to be 3,818, 3,636, 3,636, and 3,636 to be 1,091, 1,000, 0.818, and 0.727 after therapy. Based on the statistical test with paired t-test it was found that the p-value was significant with their respective values (0.002, 0.003, 0.003, and 0.003).

DISCUSSION

The diagnosis of interstitial cystitis was carried out using cystoscopy and hydrodistension procedures.³ All patients in this study completed cystoscopy and hydrodistension procedures to first diagnose interstitial cystitis before intravesical sodium hyaluronate instillation. From January 2019 to October 2020, 11 patients had been diagnosed and agreed to undergo the sodium hyaluronic instillation procedure. All patients in this study were female, in line with the prevalence of interstitial cystitis which was more prevalent in female patients with a ratio of 10: 1 between women and men.⁵

To date, several therapies have been developed for interstitial cystitis patients. Management of interstitial cystitis generally consists of behavioral management, non-pharmacological, pharmacological, intra-bladder therapy, surgery, and management with limitations.¹⁴ The therapy chosen in this study used intra-bladder sodium hyaluronate at a dose of 40 mg / 50 ml a frequency of once a week up to four times a month followed by up to 8 treatments.²

Therapy using intravesically sodium hyaluronate instillation is still rarely known by the public, so most patients who completed this therapy have previously been treated in various ways but have not received significant results. This refers to studies that reported that sodium hyaluronic instillation was effective in replacing glycosaminoglycan (GAG) in interstitial cystitis patients who were resistant to other therapies.¹¹

Therapy using sodium hyaluronate is a safe and effective therapy for interstitial cystitis patients. Patients who had completed therapy for 6 months experienced significant clinical improvement.¹⁵ All patients in this study showed clinical improvement, especially regarding the improvement of their symptoms and problems. This indicates that the intravesical sodium hyaluronic therapy used in this study was satisfactory and safe for the patient. This is supported by research from Raymon et al from Current Urology which states that intravesical instillation with sodium hyaluronate can be used in interstitial cystitis patients with satisfactory results and minimal side effects.¹⁶

To evaluate the results of the intravesical sodium hyaluronic therapy evaluation procedure in each patient in

this study, the researchers used an O'Leary-Sant questionnaire consisting of interstitial cystitis symptom index (ICSI) to assess perceived symptoms and interstitial cystitis problem index (ICPI) to assess the problems experienced by the patient. Both questionnaires have been validated from previous studies.¹² Also, based on the 2019 perennial bladder pain guide which states the scoring system on the O'Leary-Sant interstitial cystitis symptom index (ICSI) and interstitial cystitis problem index (ICPI) can be used as a diagnostic tool and a tool to evaluate the results of the therapy that have been done.² In this study, the questionnaire is used as a quantitative indicator of the treatment outcome of therapy by sodium hyaluronate. According to Barua, JM said in a meta-analytical review that there was a positive effect on intravesical glycosaminoglycan (GAG) therapy as interstitial cystitis therapy, and there was a significant improvement in the patient's complaints.¹⁷ This is consistent with this study which showed a significant improvement in the ICSI and ICPI values before and after therapy. The mean value of each item assessed, including urgency, frequency, nocturia, and bladder pain, showed significant improvement in complaints and problems. This is supported by the results of statistical tests in this study which get the p-value for each of these items (p-value <0.05). Although the study was conducted in a small number, this study showed an improvement after being given therapy, so the next step was to develop a study with a larger number of participants or a different hospital.

CONCLUSION

In all interstitial cystitis patients who were treated with sodium hyaluronic instillation in this study, it was found that there were significant differences in the values of O'Leary-Sant interstitial cystitis symptoms and problem indices before and after therapy. This shows that sodium hyaluronic instillation therapy is effective for interstitial cystitis patients.

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