

The Efficacy of Chondroitin Sulphate in Treating Interstitial Cystitis

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Abstract

Objectives: To test in an open label study the response to chondroitin sulphate in patients with the interstitial cystitis syndrome and a positive potassium test.

Patients and Methods: Eighteen patients with interstitial cystitis based on NIH symptom criteria were enrolled in the study. Patients received 40 ml chondroitin sulphate 0.2% instilled intravesically once a week for four weeks and then once a month for 12 months. Quality of life scores, pain and voiding indices were measured baseline and at the final visit. Frequency of voiding was recorded in diaries.

Results: 13/18 (66.7%) patients responded with improvement of symptoms, 6/18 (33%) either showed no response or withdrew from the study.

Conclusion: Intravesical chondroitin sulphate seems to demonstrate beneficial effects in the treatment of interstitial cystitis patients that have a positive potassium stimulation test.

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Keywords: Interstitial cystitis; Potassium test; Chondroitin sulphate

1. Introduction

Interstitial cystitis (IC) is a puzzling, chronic inflammatory condition of the bladder that causes frequent, urgent and painful urination and pelvic discomfort. IC is categorized by type, but there is considerable variation in the manifestation of the disease. Frequency of urination varies from 10 to more than 50 times a day in severe cases. Some people experience chronic pelvic pain, while others do not. Though not curable, IC is treatable and most patients find some relief with treatment and lifestyle changes.

Interstitial cystitis is a disease of unknown etiology which to date has eluded effective treatment. 70% of patients are thought to have a defective GAG layer [1–5]. This damage causes epithelial leaks, which allows urinary solutes to gain access to subepithelial tissues and induces an inflammatory response. The knowledge that many IC patients have damaged GAG layers has led to treating these patients by replenishing the mucus lining with GAG products. A potassium stimulation seems to be able to segregate those patients who have a defective

GAG layer. Intravesical instillation of potassium has been used to objectively detect abnormal epithelial permeability of the bladder [6–8].

We conducted a pilot study, attempting to determine whether or not chondroitin sulphate relieves symptoms induced by potassium stimulation test and, as well, to investigate the effectiveness of chondroitin sulphate in treating interstitial cystitis patients with a positive potassium stimulation test that had been relieved by the instillation of chondroitin sulphate just after potassium provocation.

2. Patients and methods

18 patients (1 man, 17 women) were enrolled in the study. Most patients were newly diagnosed with IC and had not received previous treatment for this condition. The National Institute of Health criteria were utilized to establish a diagnosis of interstitial cystitis and once the patients were diagnosed, they were subjected to a potassium stimulation test and if the potassium stimulation test was positive, the patients were entered in the study.

Two of the 18 patients were diagnosed with Hunner's ulcer. Five of the 18 patients had incidental voiding volumes 350 ml per 24 hours as recorded in their voiding diaries but they were included in the study on the basis of all other criteria.

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We had chosen the potassium stimulation test (PST) as most of the individuals with IC are PST positive. The PST detects abnormal epithelial permeability by exposing the bladder surface to two solutions, sterile water for injection and potassium chloride. The two test solutions were instilled into the bladder for 3 minutes. Solution 1 was sterile water for injection, USP (WFI) and solution 2 was 40 ml of potassium chloride solution 3.0%. After instilling solution 1, patients were asked to rate their symptoms on a scale of 1 to 5.

Solution 1 was removed and solution 2 was instilled and again patients were asked to rate their symptoms on a scale of 1 to 5. Patients who stated that potassium chloride was causing their symptoms to increase (a rating of 2 or higher) were considered to have a positive test result. No response implied that the patient did not have GAG deficiencies and might not respond to GAG replacement therapies.

Patients with a positive potassium stimulation test had any residual test fluid removed from their bladder and 40 ml solution of sterile sodium chondroitin sulphate 0.2% was instilled. Patients were then asked to rate their symptoms using the same scale of 1 to 5. Symptom reduction of 2 or better was considered a positive response and these patients were eligible for the study.

Patients in this study received the chondroitin sulphate (0.2%) as a bladder instillation weekly for 4 weeks and then monthly for 1 year.

All patients completed the Quality of Life Questionnaire at their initial visit and final visit. However, the Quality of Life Questionnaire was not specific for the bladder, and was deemed to be of little value as a monitoring tool for this study. A patient evaluation was carried out utilizing the O'Leary/Sant Interstitial Cystitis Symptom and Problem Index (ICSP) as it is specific for interstitial cystitis.

3. Results

The patient problem and symptom scores are outlined in Table 1. Thirteen patients completed the study. You will note that one patient (a non-responder) failed to complete the final visit.

The response to treatment is outlined in Table 2. The average response time was 3–12 weeks. 46% of patients fell into the good response category, 15.4% into a fair

Table 2

The efficacy of chondroitin sulphate in treating interstitial cystitis

Response to treatment		
Number	Response type	Improvement in score from baseline to 13 months
6/13 (46.2%)	good	8 to 13 points for symptoms scores and 5 to 14 points for problem scores
2/13 (15.4%)	fair	2 to 3 points for symptoms scores and 3 to 5 points for problem scores
4/13 (30.8%)	partial	1 point for symptom score or 1 to 4 points for problem scores
1/13 (7.7%)	None	none

response category and 30.8% into the partial response category. 7.7% of patients did not respond. The average time to treatment was 3 to 12 weeks.

Nearly half of the patients showed a good response. 2 Patients withdrew from the study due to increased pain after 1 month. 1 patient withdrew from the study due to pregnancy and two others withdrew for unspecified reasons.

Intravesical treatments may act by targeting the bladder mucosa or bladder layer, leading to symptomatic relief of pain, frequency and urgency. Intravesically applied medications have the benefit of establishing high concentrations of a therapeutic agent at the intended target tissue along with a low risk of systemic side effects. In this study bladder instillations were well tolerated and there was a very good overall response rate. The data illustrates that 12 out of 13 patients (92.3%) responded, at least partially, to treatment and 8 of 13 (61.5%) had a good to fair response. Some patients demonstrated significant improvement in their problem index scores, although their symptom index scores did not decrease correspondingly. This may be due to the pain scores not being able to differentiate between levels of pain/discomfort.

As we followed these patients out beyond a year all the patients on study elected to stay on monthly instillations and it is interesting to note that approximately half of those patients who were in the fair response group migrated into the good response group and about 25% of those in the partial response group migrated into the fair response group.

Another interesting aspect was focused in this study: although it is difficult to measure, the urology nurse undoubtedly had an impact on patient's treatment. It has been reported in other studies that a trusting relationship between IC patients and caregivers can facilitate the management of this disease. All patients in the study were treated and managed by an experienced, caring urology nurse who provided individual attention and support regarding self-care techniques, stress reduction

Table 1

The efficacy of chondroitin sulphate in treating interstitial cystitis O'Leary/Sant Interstitial Cystitis Symptom and Problem Index scores (ICSP)*

Patient	Baseline		Month 13		Change	
	Symptom	Problem	Symptom	Problem	Symptom	Problem
1	11	7	11	3	0	-4
2	14	13	15	12	1	-1
3	10	8	1	1	-9	-7
4	12	12	3	2	-9	-10
5	15	12	3	2	-12	-10
6	9	9	6	4	-3	-5
7	11	8	10	10	-1	2
8	18	16	16	13	-2	-3
9	13	14	0	0	-13	-14
10	14	13	4	2	-10	-11
11	14	10	6	5	-8	-5
12	17	13	17*	13*	0	0
13	11	9	10	9	-1	0

* 12 months only; no end point measured.

and modifications to diet. This interaction may have introduced a significant placebo effect.

4. Conclusion

It would appear that chondroitin sulphate seems to offer effective treatment for interstitial cystitis patients

whose symptoms are brought on by potassium stimulation and subsequently relieved at the time of potassium stimulation by the instillation of chondroitin sulphate.

This is a small pilot study and larger properly conducted double blind placebo controlled studies are planned in an attempt to verify these encouraging results.

References

- [1] Parsons CL, Lilly JD, Stein P. Epithelial dysfunction in nonbacterial cystitis (interstitial cystitis). *J Urol* 1991;145:732–5.
- [2] Parsons CL, Dell J, Stanford EJ, Bullen M, Kahn BS, Willems JJ. The prevalence of interstitial cystitis in gynecologic patients with pelvic pain, as detected by intravesical potassium sensitivity. *Am J Obstet Gynecol* 2002;187(5):1395–400.
- [3] Parsons CL, Dell J, Stanford EJ, Bullen M, Kahn BS, Waxell T, et al. Increased prevalence of interstitial cystitis: previously unrecognized urologic and gynecologic cases identified using a new symptom questionnaire and intravesical potassium sensitivity. *Urology* 2002; 60(4):573–8.
- [4] Hurst RE, Roy JB, Min KW, Veltri RW, Marley G, Patton K, et al. A deficit of chondroitin sulfate proteoglycans on the bladder uroepithelium in interstitial cystitis. *Urology* 1996;48(5): 817–21.
- [5] Hurst RE. Structure, function, and pathology of proteoglycans and glycosaminoglycans in the urinary tract. *World J Urol* 1994;12(1):3–10.
- [6] Gregoire M, Liandier F, Naud A, Lacombe L, Fradet Y. Does the potassium stimulation test predict cystometric, cystoscopic outcome in interstitial cystitis? *J Urol* 2002;168(2):556–7.
- [7] Parsons CL, Stein PC, Bidair M, Lebow D. Abnormal sensitivity to intravesical potassium in interstitial cystitis and radiation cystitis. *Neurol Urology* 1994;13:515–20.
- [8] Parsons CL, Zupkas P, Parsons JK. Intravesical potassium sensitivity in patients with interstitial cystitis and urethral syndrome. *Urology* 2002;60:573–8.

Chondroitin Sulphate in the Treatment of Interstitial Cystitis and Chronic Inflammatory Disease of the Urinary Bladder

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Abstract

Objective: To test chondroitin sulphate in patients with interstitial cystitis (IC).

Patients and Methods: 24 female patients with the symptom complex frequency/urgency and pain caused by interstitial cystitis were enrolled in the study. Patients suffered between 1 and 20 years from the disease and were all pretreated (hydrodistension, pentosanpolysulphate, anticholinergica). Patients underwent a potassium test as a means of identifying a leaking mucus barrier.

Results: Out of 20 patients still under treatment in this ongoing study 12 patients are treated ≥ 12 months. Improvement of symptoms was reported by all, on average symptom score improved 73%.

Conclusion: Chondroitin sulphate was beneficial in patients with pretreated IC.

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Keywords: Interstitial cystitis; Chondroitin sulphate; Potassium test

1. Introduction and background

Interstitial cystitis (IC) is a chronic inflammation of the bladder wall of unknown etiology. There is no

single treatment that provides symptomatic relief for all IC patients, nor is there a known cure. Patients suffering from IC have some or all of the following symptoms:

- Frequency of urination (up to 60 times a day).
- Sense of urgency to urinate immediately which may also be accompanied by pain, pressure and spasms.

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