Original Article

In what type of interstitial cystitis/bladder pain syndrome is DMSO intravesical instillation therapy effective?

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Background: Dimethylsulfoxide (DMSO) is the most-used agent for intravesical instillation. We conducted this retrospective clinical study to determine in what type of the interstitial cystitis (IC)/bladder pain syndrome (BPS) DMSO was effective.

Methods: We combined DMSO with hydrodistension in 2003 and from 2004 we performed hydrodistension alone. Hydrodistension had been performed in 7 cases of IC/BPS with Hunner's lesions (H group) and 7 cases of IC/BPS without Hunner's lesions (non-H group), and they served as the control group (C group; n=14). There was also a DMSO group (D group; n=14) that consisted of an H group of 7 cases and an non-H group of 7 cases in which the hydrodistension had been immediately followed by intravesical instillation of 50% DMSO 50 mL. Before, and 2, 6, 12, 18, and 24 months (M) after the intervention, the patients were asked to complete a 4-day frequency-volume chart (FVC) and the O'Leary-Sant IC symptom index (ICSI) questionnaire and IC problem index (ICPI) questionnaire, and to rate their pain on a visual analogue scale (VAS).

Results: All parameters were improved after hydrodistension in both the C group and the D group. However, comparison of the C group and D group according to whether Hunner lesions were present showed that there were no significant differences in any of the postoperative parameters between the non-H groups in the C group and D group, but in the H groups, average and maximum voided volume were significantly higher and the ICSI, ICPI, and VAS scores were lower in the D group. Moreover, the significant differences increased with the duration of the postoperative period.

Conclusions: DMSO intravesical instillation therapy was useful in both maintaining and improving the effectiveness of hydrodistension in IC/BPS with Hunner lesions. However, DMSO did not have any particular efficacy in the treatment of IC/BPS in the absence of Hunner lesions.

Keywords: Interstitial cystitis (IC); dimethylsulfoxide (DMSO); intravesical instillation therapy; Hunner lesion

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Introduction

The etiology of interstitial cystitis (IC)/bladder pain syndrome (BPS) is unclear, and there is no definitive method of treatment. There are two types of IC/BPS, i.e., IC/BPS with Hunner lesions and IC/BPS with glomerulation alone. IC/BPS with Hunner lesions is thought to be an independent disease, and IC/BPS with glomerulation alone is thought to have many phenotypes.

Hydrodistension followed by transurethral resection and fulguration is known to be an effective means of treating Hunner lesions (1). While the recommendation level of intravesical instillation of dimethylsulfoxide (DMSO) as a method of intravesical instillation therapy is high, which type of IC/BPS it is effective against has been rarely reported (2).

Materials and methods

Hydrodistension followed by transurethral coagulation

(TUC) has been performed to treat IC/BPS with Hunner lesions at our hospital since 2005. We therefore conducted a retrospective study of consecutive cases of IC/BPS in which first-instance hydrodistension had been performed in 2003-2004, when transurethral fulguration was not yet being performed. We combined DMSO with hydrodistension in 2003 and from 2004 we performed hydrodistension alone.

Hydrodistension had been performed in 7 cases of IC/BPS with Hunner lesions (H group) and 7 cases of IC/BPS without Hunner lesions (non-H group), and they served as the control group (C group; n=14). There was also a DMSO group (D group; n=14) that consisted of an H group of 7 cases and an non-H group of 7 cases in which the hydrodistension had been immediately followed by intravesical instillation of 50% DMSO 50 mL, which is a solution of 50% DMSO diluted by distilled water, retained in the bladder for 10 to 20 minutes (3), once a week for a total of 8 times, once every 2 weeks for a total of 8 times, and once every 4 weeks thereafter.

Before, and 2, 6, 12, 18, and 24 months (M) after the intervention, the patients were asked to complete a 4-day frequency-volume chart (FVC) and the O'Leary-Sant IC symptom index (ICSI) questionnaire and IC problem index (ICPI) questionnaire, and to rate their pain on a visual analogue scale (VAS). We analyzed these data backward and report them.

Table 1 Baseline patient characteristics

Characteristics	Control group	DMSO group	P value
Number	14	14	
Age (years)	57.0±6.9	61.6±5.9	N.S.
Average voided volume (mL)	98±36	70±32	P<0.04
Maximum voided volume (mL)	178±59	134±54	P<0.05
IC symptom index	12.6±3.7	16±3.6	P<0.02
IC problem index	11.9±3.7	13.4±2.5	N.S.
Pain on VAS	5.6±2.6	5.6±3.1	N.S.

DMSO, dimethylsulfoxide; IC, interstitial cystitis; VAS, visual analogue scale.

Results

The mean age of the patients was 59.3±6.4 years (range: 28-78 years). Between 6 and 12 M there was a recurrence in 1 case each in the non-H group of both the C group and D group. Between 12 and 18 M there was a recurrence in 1 case in the H group of the C group, and between 18 and 24 M there was a recurrence in 1 case in the H group of the D group.

Preoperative average voided volume (AVV) was 98±36 mL in the C group and 70±32 mL in the D group (P<0.04), and maximum voided volume (MVV) was 178±59 mL in the C group and 134±54 mL in the D group (P<0.05)

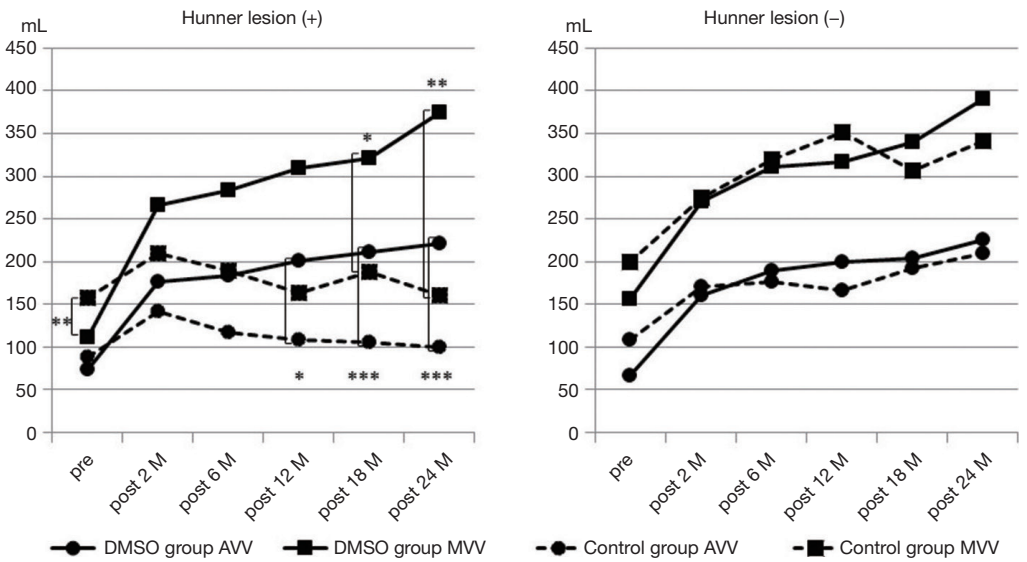

Figure 1 AVV/MVV in DMSO group *vs.* control group. M, months; AVV, average voided volume; MVV, maximum voided volume; DMSO, dimethylsulfoxide; *, P<0.05; **, P<0.04; ***, P<0.02.

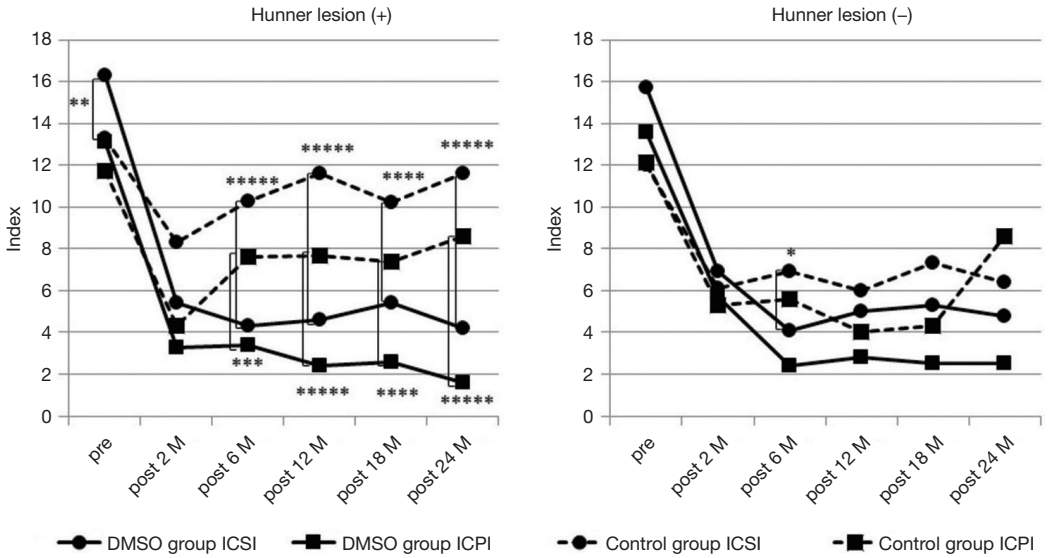

Figure 2 ICSI/ICPI in DMSO group *vs.* control group. M, months; ICSI, interstitial cystitis symptom index; ICPI, interstitial cystitis problem index; DMSO, dimethylsulfoxide; *, P<0.05; **, P<0.03; ***, P<0.03; ****, P<0.02; *****, P<0.01.

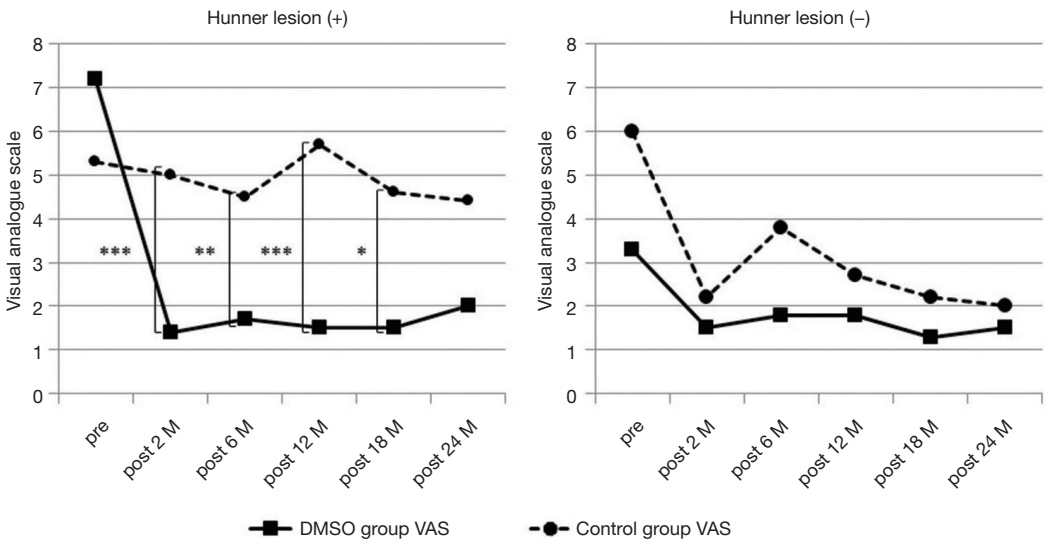

Figure 3 VAS for pain DMSO group *vs.* control group. M, months; VAS, visual analogue scale; DMSO, dimethylsulfoxide; *, P<0.04; **, P<0.02; ***, P<0.01.

(*Table 1*). Both the AVV and MVV values in the D group were significantly higher than before hydrodistension throughout their course, but in the C group the differences in MVV from 12 M after hydrodistension onward were not significant in comparison with before hydrodistension.

The preoperative ICSI score was 12.6±3.7 in the C group and 16±3.6 in the D group (P<0.02), and the ICPI score was 11.9±2.9 in the C group and 13.4±2.5 in the D group (*Table 1*). The ICSI score and ICPI score in both groups had significantly improved after hydrodistension in comparison with before hydrodistension. From 6 M after hydrodistension onward both the ICSI scores and ICPI scores were significantly lower in the D group than in the C group.

The preoperative pain score on the VAS was 5.6±2.6 in the C group and 5.6±3.1 in the D group (*Table 1*), and with the exception of the C group at 12 M after hydrodistension,

the scores had significantly improved in both groups throughout their course.

In the H group, both the AVV and MVV values in the D group tended to be higher. At 24 M after hydrodistension, AVV and MVV were 99±32 and 160±55 mL in the C group and 221±98 and 374±213 mL in the D group, respectively (P<0.02, P<0.04). However, there were no significant differences in AVV and MVV between the non-Hunner group in the D group and the C group (*Figure 1*).

In the H group at 24 M after hydrodistension, the ICSI and ICPI were 11.6±3.0 and 8.6±1.3 in the C group and 4.2±3.3 and 1.6±1.8 in the D group, respectively (P<0.01, P<0.01). However, there were no significant differences in the ICSI and ICPI between the non-Hunner group in D group and C group (*Figure 2*). In the H group, the VAS score of the pain at 18 M after hydrodistension was 4.6±0.5 in the C group and 1.5±2.4 in the D group (P<0.04). However there was no significant difference between the non-H group in the D group and C group (*Figure 3*).

Discussion

In intravesical instillation treatment, there are DMSO, heparin and/or pentosan polysulfate sodium, hyaluronic acid, chondroitin sulfate, and lidocaine cocktail with steroid and/or bicarbonate etc. In the interstitial cystitis data base (ICDB) study experience (4), PPS and/or heparin and DMSO were the most-used agents for intravesical instillation therapy. In the clinical guideline in Asia (5), grade of recommendation of DMSO is B with level of evidence of efficacy 2. Actually, DMSO was the most-used agent for bladder instillation, at 20 out of 62 institutions, in a survey on clinical practice of IC in Japan (6), nevertheless DMSO has not been approved in Japan.

DMSO appears to have anti-inflammatory, analgesic, muscle relaxant and collagenolytic effects. It prompted nitric oxide release from dorsal ganglion neurons and urinary bladder (7). In two randomized (2,8) and some non-randomized (9-12) studies, an approximately 75% efficacy has been reported (13). However, there are only one report (2) that showed the difference in effect of DMSO between Hunner lesion and non-Hunner lesion in IC/BPS. Peeker *et al*. (2) showed that DMSO had no positive effect on maximal functional capacity but resulted in a significant reduction in pain and urinary frequency, only in IC patients with Hunner lesions. In addition, it is not a randomized study, but Ek *et al*. (10) reported that the pain and the urinary frequency by the patient interview were improved in 12 out of 17 IC patients with Hunner lesions, although the bladder capacity in the cystometry was not improved.

In our study, all parameters were improved after hydrodistension in both the C group and the D group. However, comparison of the C group and D group according to whether Hunner lesions were present showed that there were no significant differences in any of the postoperative parameters between the non-H groups in the C group and D group. However, in the H groups, AVV was significantly higher and the ICSI, ICPI, and VAS scores were lower in the D group. Moreover, the significant differences increased with the duration of the postoperative period.

IC/BPS is a chronic pelvic pain syndrome and the etiology is not well known. Furthermore, the definition of IC/BPS has not been unified. Many urologists have noticed that some IC/BPS patients present different behavior towards the treatments. In the American Urological Association Guideline (14), cystoscopy is the third-line treatment, but transurethral fulguration is recommended as a "should-be-performed" treatment for Hunner lesion. In the standardization of terminology in Chronic Pelvic Pain, which will be published by the International Continence Society in the near future, IC/BPS will be divided into three groups: (I) without glomerulation; (II) with glomerulation; and (III) Hunner lesion. It is possible that IC/BPS without Hunner lesion is heterogeneous (15).

The small number of cases, the fact that the data analysis of only recurrence-free cases may not have reflected the true situation, and the fact that it was a retrospective study were limitations of this study. Because there are garlic-like odor and bladder pain after the bladder infusion of DMSO, it is difficult to do the randomized control trial (RCT) with placebo control. However, it is expected that a RCT comparing IC/BPS with and without Hunner lesion will be carried out, and that it will therefore become clear as to which IC/BPS patients DMSO is useful for.

Conclusions

DMSO intravesical instillation therapy did not have any particular efficacy in the treatment of IC/BPS in the absence of Hunner lesions, but it was useful in both maintaining and improving the effectiveness of hydrodistension in IC/BPS with Hunner lesions.

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None.

Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

Patient Consent: Written informed consent was obtained from the patient for publication of this article.

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