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ORAL ADMINISTRATION OF STEROID FOR ULCER TYPE INTERSTITIAL CYSTITIS

Hypothesis / aims of study

Interstitial cystitis (IC) is a disease of myth. The nomenclatures, diagnosis procedures and treatment modalities remain to be standardized[1)]. Oral administration of anti-inflammatory steroids is not a recommended treatment option for IC because of concern on adverse events. However, its possible efficacy for ulcer type IC is suggested[2)].

Study design, materials and methods

Twenty-three patients (22 women and 1 man) who were diagnosed as ulcer type IC and treated by oral steroid were retrospectively analyzed. The average age was 67.9 years [range: 45 to 84], and the average time from the onset of symptoms and steroid treatment was 7.6 years [range: 2 to 28]. The diagnosis was based on the guideline for IC and hypersensitive bladder syndrome[1)], which comprises 1) lower urinary tract symptoms such as bladder hypersensitivity, urinary frequency, bladder discomfort and bladder pain; 2) Hunner's ulcer confirmed by cystoscopy ; 3) exclusion of confusable diseases such as infection, malignancy and calculi of the urinary tract. The patients were also compatible with National Institute of Diabetes and Digestive Kidney Diseases (NIDDK) consensus inclusion and exclusion criteria for clinical trials. These patients had been treated with transurethral resection or fulguration for the ulcerative lesions for 1 to 7 times (average: 2.6 times), yet recurred the symptoms. The average interval from the transurethral surgery to steroid treatment was 8.1 months [range: 2 to 30]. Oral betamethazone of 0.75mg to 0.5mg was given daily for 1 to 2 months, then tapered to 0.5mg or 0.25mg according to symptom relief, and continued for an average period of 11.3 months [range: 1 to 48]. The symptoms were evaluated by the O'Leary-Sant's Symptom Index (OSSI) [range: 0 to 20] and Problem Index (OSPI) [range: 0 to 16], Visual Analogue Scale (VAS) for pain [range: 0 to 10] and the Core Lower Urinary Tract Symptom Score (CLSS), an assessment tool that can evaluate symptoms in a non-disease-specific manner [range: 0 to 30][3)]. Quality of Life (QoL) was measured by QoL Index (QoLI) of International Prostate Symptom Score [range: 0 to 6]. Overall efficacy was evaluated by Global Response Assessment by patients' subjective impressions (GRA) as either of markedly improved, moderately improved, slightly improved, unchanged, slightly worsened, moderately worsened, and markedly worsened [range: 0 to 6]. The patients were assigned to clinical progression by any of 1) invasive therapy such as transurethral resection and intravesical instillation, 2) increased analgesic ladder or 3) GRA of slightly worsened or worse. Paired t-test was used for analysing treatment-related change. P value less than 0.05 was considered to be significant.

Results

Twelve patients (52%) reported improvement by GRA, 2 of whom had ceased steroid (Table 1). The remaining 11 patients were unchanged, which included 7 cases deemed to clinical progression because of transurethral resection (n=5) and intravesical instillation (n=2). The assessment results of pre- and post-treatment were summarized in the Table 2. Significant improvement was noted for all the variables evaluated, especially for VAS (Table 2A), and it was pronounced for cases without clinical progression (Table 2B). Those with clinical progression showed slight worsening in the variables (Table 2C). Adverse events included weight gain more than 2 kg in 7 subjects; however, no steroid-related cessation occurred. The pre-treatment backgrounds between those with clinical progression and without showed no significant difference except younger age in those free of progression (Table 3).

Interpretation of results

Oral administration of steroid has been almost abandoned as a treatment option for IC. However, out results suggested that it could be an option for painful ulcer type IC of relatively young ages. The limitation of the study included the small sample size, short-term observation period, retrospective nature of analysis (thus without concurrent control), and no assessment by biomarkers and cystoscopy. Further study is warranted for the possible usefulness of oral steroid therapy for this intractable disease.

Concluding message

Oral administration of steroid could be a therapeutic option for ulcer type IC, and this possibility mandates further studies.

Table 1: Number of patients according to Global Response Assessment (GRA)

	Markedly improved	Moderately improved	Slightly improved	Unchanged	Slightly worsened	Moderately worsened	Markedly worsened
No	3	1	8	11(7)*	0	0	0

*Those with clinical progression (n=7) were included in "unchanged".

Table 2: The average values of assessment variables pre- and post-oral steroid therapy
Table 2A: All subjects (n=23, treatment period: 11.3 months)*

	CLSS	OSSI	OSPI	VAS	QoLI
Pre	17.0	12.7	11.1	6.1	4.9
Post	14.9	10.9	9.1	4.0	4.4
Post/Pre	88%	86%	82%	66%	90%

Table 2B: Those without clinical progression (n=16, treatment period: 13.6 months)*

	CLSS	OSSI	OSPI	VAS	QoLI
Pre	16.6	12.3	10.8	6.0	4.8
Post	13.1	9.5	7.7	2.8	3.9
Post/Pre	79%	77%	71%	47%	81%

Table 2B: Those with clinical progression (n=7, treatment period: 6.4 months)+

	CLSS	OSSI	OSPI	VAS	QoLI
Pre	18.0	13.4	11.7	6.4	5.1
Post	18.7	14.0	12.1	6.4	5.4
Post/Pre	104%	104%	103%	100%	106%

*All variables in Table 1A and Table 1B showed significant improvement.
OSSI: O'Leary- Sant's Symptom Index (range: 0 to 20), OSPI: O'Leary- Sant's Problem Index (range: 0 to 16), VAS: Visual Analogue Scale for pain (range: 0 to 10), CLSS: Core Lower Urinary Tract Symptom Score (0 to 30), QoLI: Quality of Life Index of the International Prostate Symptom Score (0 to 6)
+Reasons for clinical progression: transurethral resection (5) and intravesical instillation (2)

Table 3: Pre-treatment backgrounds with or without clinical progression

clinical progression	Age	Affected period (y)	Capacity (ml)	No of TUR	CLSS	OSSI	OSPI	VAS
No progression	65.8	7.8	409	2.8	16.6	12.3	10.8	6.0
progression	72.7	7.3	614	2.2	18.0	13.4	11.7	6.4

No significant difference except age

References

1. Int J Urol. 16: 597-615, 2009
2. J Urol. 173: 841-3, 2005
3. Int J Urol. 15: 816-20, 2008

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Is this a clinical trial?	**No**
What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**No**
This study did not require ethics committee approval because	**it is a retrospective study**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**No**