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# HISTOPATHOLOGY OF INTERSTITIAL CYSTITIS - HYDRODISTENSION MATTERS?

#### Hypothesis / aims of study

Most investigations on histopathology of interstitial cystitis (IC) have used post-hydrodistension biopsy specimens, because it is presumed that hydrodistension may cause little change in bladder histology but cause adverse events such as the bladder perforation. However, there is no definite evidence for the presumptions. We examined the effect of hydrodistension on histopathology and morbidity associated with pre-hydrodistension biopsy.

### Study design, materials and methods

IC patients who were compatible with the NIDDK criteria were included. They completed O'Leary and Sant's symptom index and problem index, and underwent cystoscopy followed by biopsy and hydrodistension under spinal anesthesia. The bladder was fully examined by cystoscopy for any abnormal lesions including hyperemia, Hunner's ulcer, scars and tumors. Pre-hydrodistension biopsy specimen was taken from bladder wall by cold cup forceps. In ulcer type IC patients, ulcerative lesion and/or apparently normal retrotrigonal area was biopsied, while in non-ulcerative IC patients only retrotrigonal mucosa was taken. Then, the bladder was filled with 3% sorbitol solution at a pressure of 80 cm H2O until the full distension was attained, left distended for 3 minutes, and drained through a cystoscope channel. The bladder lumen was continuously monitored by cystoscopy for the possible bladder bleeding and raptures. Immediately after bladder drainage, post-hydrodistension biopsy specimen was taken from the bladder wall which was close to the post-hydrodistension biopsy sites. Electro-coagulation was performed to control the bleeding. The biopsy specimens were fixed in 20% phosphate-buffered formalin and stained with H&E, toluidine blue, and c-kit. The histological slides were examined by 2 blinded investigators for epithelial denudation, cellular atypia, submucosal congestion, and submucosal edema. These findings were graded by a score from 0 (none), 1(a little), 2(moderate), 3(severe). The density (number per 1 square mm) of inflammatory infiltrates including mast cells was counted under microscopy. Data were analyzed using the Wilcoxon signed-rank test and Mann-Whitney U test.

## Results

A total of 29 patients (21 ulcer type patients and 8 non-ulcer type patients) were collected (Table 1). The mean age was 64.8 years old (range 27-79), and the mean symptomatic period before diagnosis was 52 months. O'Leary and Sant's symptom index was 13.6 on average (range 7-20) and problem index was 5.48 (3-15). Table 2 summarizes histological findings of the pre- and post-hydrodistension biopsy specimens.

In both pre- and post-hydrodistension biopsies, ulcerative lesions showed higher scores of denuded epithelium, submucosal congestion and higher density of infiltrates of eosinophiles, and mononuclear cells as compared with retrotrigonal biopsy. Apparently normal mucosa obtained from retrotrigonal area demonstrated little histological abnormalities in both ulcer and non-ulcer type IC.

Comparison of pre- and post-hydrodistension biopsies showed a tendency to increase in scores of denuded epithelium, submucosal edema and infiltration of eosinophiles for ulcerative lesions but not for retrotrigonal area. Numbers of submucosal mast cells stained with c-kit or toluidine blue were unchanged by hydrodistension.

No adverse event including bladder wall rupture was observed during or after hydrodistension.

## Interpretation of results

Ulcerative lesions associated with IC showed characteristic histopathological features including denudation of epithelium, submucosal inflammation, and congestion and edema. Hydrodistension is likely to pronounce denudation of epithelium, edema and eosinophile infiltration, but this is limited to ulcerative lesions. These results suggest that histopathological specimens obtained from sites of ulcer lesions might be modified by hydrodistension. Performing biopsy before hydrodistension has been said to cause complications such as bladder wall rupture; however we found no complications in this study. During hydrodistension, bladder wall, especially the biopsy sites, was carefully watched for possible cracks or perforation, and this procedure may enables 'safe' hydrodistension.

# Concluding message

Pre-hydrodistension biopsy in IC patients does not seem to increase the morbidity of the procedure but may affect histopathological findings of ulcer lesions. Pre-hydrodistension specimen may be needed for more precise histological evaluation.

 Ulcertype
 Non-ulcertype

 No(F/M)
 21 (19/2)
 8(6/2)

 Age
 69(27-79)
 62(32-78)

 OSSI
 14.2(9-20)
 13.1(7-20)

 OSPI
 5.52(4-15)
 5.38(3-15)

Table 1 Background of the patients

OSSI: O'Leary and Sant's symptom index

OSPI: O'Leary and Sant's problem index

Table 2 Histopathology of biopsy specimens of IC

Histology	Pre-hydrodistension			Post-hydrodistension			Pre vs. Post (P)	
	Ulcer	RTM*	Р	Ulcer	RTM	Р	Ulcer	RTM

Denuded epithelium	1.69	0.75	0.018	2.39	0.88	<0.01	0.075	0.635
Congestion	0.23	0.56	0.067	0.15	0.69	0.026	0.317	0.779
Submucosal edema	0.46	1	0.279	0.77	0.81	0.293	0.067	0.374
Mononuclear cell								
infiltration	2.08	1.44	0.019	1.61	1.38	0.524	0.109	0.735
Eosinophil infiltration	0.69	0.25	0.005	1.08	0.13	0.001	0.068	0.179
Cellular atypia	0.15	0.19	0.430	0	0.06	0.05	0.179	0.108
No. of mast cell / mm <sup>2</sup>	116.9	78.1	0.029	90.0	83.4	0.367	0.889	0.127

# RTM: retrotrigonal mucosa

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Is this a clinical trial?	Yes
Is this study registered in a public clinical trials registry?	No
What were the subjects in the study?	HUMAN
Was this study approved by an ethics committee?	Yes
Specify Name of Ethics Committee	Japan Red Cross Medical Center Ethics Committee
Was the Declaration of Helsinki followed?	Yes
Was informed consent obtained from the patients?	Yes