

出國報告（出國類別：討論式海報發表）

參加第45屆國際尿控學會(ICS)心得
報告
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服務機關：衛生福利部豐原醫院

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摘 要

藉由參與 ICS 與各國做學術上的交流，不同方向的實驗研究讓我們對間質性膀胱炎有更突破性的見解，從不同的研究觀點也可帶入自己的研究中，引起我們深切的思考。

海報口頭報告發表中，讓各國了解台灣對間質性膀胱炎付出的心力及現況，探討議題的方向讓在場人士都能有所思考並提出發問，在這過程中，審視自己未注意到的部分並了解下一步的方向。除了吸收世界各地優秀學者所提供的研究資訊之外，對於這種直接面對面交流與觀摩的機會，與會者提出的最新成果和交流思想對提升間質性膀胱炎新的研究開發和應用都能促進更多概念的提升也更能夠提升國內的研究水準，並提高台灣在國際學術研究上的能見度。

(第四十五屆國際尿控協會年度會議)

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本 文

目的

藉由參與 ICS 與各國做學術上的交流，不同方向的實驗研究讓我們對 IC 有更突破性的見解，並讓各國了解 IC 在台灣的現況、研究及未來方向。

過程

從103年蒐集資料、實驗、整理、分析到結論，以下報告發表一至發表三。在發表過程中，除了吸收世界各地優秀學者所提供的研究資訊之外，對於這種直接面對面交流與觀摩的機會，與會者提出的最新成果和交流思想對提升間質性膀胱炎新的研究開發和應用都能促進更多概念的提升也更能夠提升國內的研究水準。

此次會議，邀請了許多國家權威學者與會演講，參加的以歐洲與亞洲的學者為最多數，每場演講後的討論正是各國學者意見互相交流的時間，可以相互激發思慮。

簡列此次大會的主要學術會程如下：

(1) 演講者：日本專家 Yukio Homma

題目：Hypersensitive bladder – its clinical and biological implication

內容大致為：間質性膀胱炎和膀胱過度活動症過敏膀胱的概念。膀胱傳入的致敏之間的關係，中樞神經系統的途徑和慢性膀胱疼痛增強的興奮性。

(2) 演講者：Matthias Oelke

題目：Treatment of nocturnal LUTS - increasing bladder capacity or decreasing nocturnal urine production?

內容大致為：本次研討會提供了一個上夜間下尿路症狀（LUTS）的最新知識全面的概述。夜間的LUTS有分為夜尿，夜間尿失禁尿床。此次Workshop不僅僅是討論這些症狀的診斷和治療，並簡化了大家的臨床思維。並瞭解夜尿是一個麻煩的症狀，疾病與發病率和死亡率的相關性。

(3) 演講者：Lori Birder

題目： Conceptualising Causes, Diagnosis and Therapy of Nocturnal LUTS Workshop

內容大致為：解釋和理解上膀胱疼痛目前的研究現狀及其對臨床研究的影

響，並察看其子類型中對的間質性膀胱炎疼痛表現的概念，進而增加醫療界對間質性膀胱炎治療的質與量。

- (4) 其他：各國相關口報發表—Pelvic Pain Syndromes Podium Short Oral Session
- A. Behind the Ulcer Type IC – An Analysis of the Correlation among Clinical Symptoms, Immunochemical Study, Computerized Tomography, and Histopathology Findings between Ulcer and Non-ulcer Type IC/BPSTreatment of nocturnal LUTS - increasing bladder capacity or decreasing nocturnal urine production?
 - B. Participant experiences of ketamine bladder syndrome (KBS)
 - C. Hydrodistention of the Bladder for the Treatment of Painful Bladder Syndrome/Interstitial Cystitis (PBS/IC)
 - D. A Phase 2 Study in Women with Interstitial Cystitis/Bladder Pain Syndrome (IC/BPS) of the Novel P2X3 Antagonist AF-219
 - E. Clinical Comparison of Intravesical Hyaluronic Acide and Chondroitin Sulphate Therapy for Bladder Pain Syndrome/Interstitial Cystitis
 - F. Painful Bladder Filling and Painful Urgency Are Distinct Characteristics in Men and Women with Urologic Chronic Pelvic Pain Syndromes (UCPPS) – A MAPP Research Network Study
 - G. PDF AbstractDisclosureIntrapelvic nerve entrapments – a neglected cause of perineal pain and urinary symptoms
 - H. STRAINING TO VOID IS ASSOCIATED WITH FEMALE DYSPAREUNIA
 - I. Bladder detrusor endometriosis – where does it come from?
 - J. EFFECTS OF CONNECTIVE TISSUE MANIPULATION IN PRIMARY DYSMENORRHEA: A RANDOMIZED CONTROLLED TRIAL

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發表一 : Interstitial Cystitis / Bladder Pain Syndrome (IC/BPS) is not
Related to Bladder Cancer: A Nationwide Population-based, Propensity
Score – Matched Cohort Study

Objective

IC/BPS patients who present with comorbid disease would be evaluated with more physician visits and may be more likely to have an incidental bladder cancer detected, such as during routine urinalysis. Therefore, we re-examined the risk of bladder cancer in a large population based cohort of individuals with a new diagnosis of IC/BPS to assess a potential detection bias because of poor controlled confounding factor (comorbid disease) or inadequate matched non-IC/BPS cohort group.

Methods

We performed a retrospective cohort study of Longitudinal Health Insurance Database 2000 with newly diagnosis of IC/BPS from 2002 through 2010. After limiting our sample to patients with IC/BPS diagnosis (ICD-9 code 595.1 at least once during the study period), we identified an IC/BPS cohort. We then excluded patients with diagnosis of bladder cancer (ICD-9 codes, 180-189) before IC/BPS diagnosis. This process yielded an IC/BPS cohort comprising 1684 patients without bladder cancer before. Subjects free from diagnosis of IC/BPS were extracted with a total 927,726 patients without bladder cancer before as non-IC/BPS cohort.

The primary outcome was the event of bladder cancer, determined by the record with ICD-9 codes, 180-189 after the entry dates. Next, we measured pre & post existing comorbidity during the study period for propensity score-matching. We adopted the propensity score – matching method to minimize the detection bias and selection bias from confounding factor. Subjects with IC/BPS were matched on a one-to one basis with subjects with non-IC/BPS. Next, we compared primary outcome (events of bladder cancer) between IC/BPS and non-IC/BPS cohort using multiple logistic regression.

Result

After adjusted with propensity score-matching, we identified 1642 patients with diagnosis of IC/BPS and 1642 patients with non-IC/BPS cohort. During the study period, 20 (1.2%)

IC/BPS patients and 30 (1.8%) non-IC/BPS patients were diagnosed as having bladder cancer. Chi-square test showed no difference of bladder cancer incidence between IC/BPS and non-IC/BPS cohort (p=0.2)

			Bladder Cancer		Total
			No	Yes	
IC/BPS	No	Count (Percentage)	925198 (99.7%)	2528 (0.3%)	927726 (100%)
	Yes	Count (Percentage)	1664 (98.8%)	20 (1.2%)	1684 (100%)
Total		Count (Percentage)	926862 (99.7%)	2548 (0.3%)	929410 (100%)

<Table1> Before matching, Chi-square tests between IC/BPS & non-IC/BPS cohort

			Bladder Cancer		Total
			No	Yes	
IC/BPS	No	Count (Percentage)	1612 (98.2%)	30 (1.8%)	1642 (100%)
	Yes	Count (Percentage)	1622 (98.8%)	20 (1.2%)	1642 (100%)
Total		Count (Percentage)	3234 (98.5%)	50 (1.5%)	3284 (100%)

<Table2> After matching, Chi-square tests between IC/BPS & non-IC/BPS cohort

	B value	P value
IC/BPS	-0.23	0.447
Age*	0.02	0.005*
Sex	0.59	0.056
Urolithiasis	14.44	0.999
Urinary tract infection	0.69	0.999

<Table3> Multiple logistic regressions estimating the risk of bladder cancer showed no significant association among IC/BPS, sex, urolithiasis, and urinary tract infection except age (B=0.02, p=0.005).

Conclusion

Within the first year after IC/BPS diagnosis, bladder cancer incidence in the IC/BPS cohort was 12/20 (60%). The process during diagnosis of IC/BPS maybe exist a delayed diagnosis of bladder cancer.

IC/BPS is not related to bladder cancer. The detection bias from previous study may be the results of either an inadequate matching non-IC/BPS cohort or poor controlled confounding factor.

發表二 : Severe Pain Perception Predict Systemic Phenotype of Interstitial

Cystitis / Bladder Pain Syndrome (IC/BPS)

Objective

The purpose of this study was to examine association between functional, anesthetic bladder capacity and non-bladder conditions in a physician diagnosed of women with IC/BPS.

Methods

Of 175 female patients who were compatible with AUA/SUFU criteria including unpleasant sensation (pain, pressure, discomfort) perceived to be related to bladder with duration >6 weeks were included. All of IC/BPS patients were assessed by cystoscopic hydrodistension and all of them have different severity of glomerulations. These patients were assessed by validated questionnaire including O'Leary-Sant Symptom (ICSI) and Problem Index (ICPI) was used to objectify subjective symptoms. Pelvic Pain and Urgency/Frequency (PUF) questionnaire and VAS pain and urgent score were also completed. Validated voiding diary and anesthetic bladder capacity during 2-minutes hydrodistension were also measured. All patients completed medical history questionnaire for non-bladder condition. Symptomatic duration was also asked. We separated IC/BPS patients into two groups: pure IC/BPS and IC/BPS with comorbid disease. These data were analyzed using independent T test.

Results

There is no association between symptomatic duration and symptom, voiding diary parameter, and anesthetic bladder capacity. There is no difference between ICSI, ICPI, PUF, urgent score and comorbid disease. However, systemic IC/BPS showed more severe pain perception than pure IC/BPS (6.00 ± 2.61 vs 4.90 ± 3.04 , $P=0.02$). According to validated voiding diary, the mean value of daytime frequency, daytime average voided volume, nocturnal frequency, and nocturnal average voided volume are 14.58 ± 6.91 , 103.74 ± 61.9 ml, 3.92 ± 1.86 , 101.96 ± 83.53 ml. Systemic IC/BPS showed more day-time voiding volume than pure IC/BPS (120.38 ± 51.3 ml vs 102.87 ± 63.1 ml, $P=0.05$). However, there is no significant association between daytime, night-time frequency and comorbid disease. During cystoscopic hydrodistension, there is no difference between anesthetic bladder

capacity and comorbid disease. Multiple linear regression model revealed more severe pain predicted systemic type IC/BPS (B=0.02, P=0.04).

	Pure IC/BPS	Systemic IC/BPS	P value
VAS Pain	4.90 ± 3.04	6.00 ± 2.61	0.02*
VAS Urgency	6.44 ± 2.38	7.02 ± 2.06	0.12
ICSI	13.04 ± 3.46	13.20 ± 3.58	0.78
ICPI	11.57 ± 2.93	12.17 ± 3.44	0.28
PUF	19.44 ± 5.74	20.17 ± 6.09	0.47

<Table1> Subjective symptoms between pure and systemic IC/BPS using independent T test

	Pure IC/BPS	Systemic IC/BPS	P value
Day-time frequency	14.46 ± 6.44	14.00 ± 7.51	0.69
Night-time frequency	2.52 ± 2.64	1.91 ± 1.60	0.06
Day-time voiding volume	102.87 ± 63.1	120.38 ± 51.2	0.05*
Night-time voiding volume	111.35 ± 78.2	129.80 ± 97.2	0.21
Anesthetic bladder capacity (2 min)	594.49 ± 173.4	605.89 ± 187.7	0.70

<Table2> Objective findings between pure and systemic IC/BPS using independent T test

Conclusion

It is also demonstrated from evidence of voiding diary that systemic IC/BPS showed as same as day-time and night-time frequency to pure IC/BPS. Moreover, even systemic IC/BPS showed more pain than pure IC/BPS, there is no difference in anesthetic bladder capacity during cystoscopic hydrodistension.

Systemic IC/BPS showed more severe pain perception than pure IC/BPS but not

lower urinary tract symptoms. However, systemic IC/BPS did not showed smaller anesthetic bladder capacity than pure IC/BPS.

發表三 : The Prevalence of Non-bladder Condition in patients with ketamine abuse and IC/BPS

Objective

Recreational ketamine abuse cause lower urinary tract symptoms including dysuria, urinary frequency, urgency, urge incontinence and hematuria. As with similarly presenting interstitial cystitis, several studies investigated the pathophysiology as purinergic neurotransmission of ketamine induced uropathy. The aim of this study is to investigate the prevalence of non-bladder condition in ketamine induced uropathy compared to ketamine abusers without bothering lower urinary tract symptoms (LUTS) and IC/BPS patients.

Methods

This was a retrospective cross-sectional study. Of 32 patients who were admitted due to severe lower urinary tract symptoms with recreational ketamine abuse history more than one year and 27 female age-matched IC/BPS patients who were compatible with AUA/SUFU criteria. All of patients with ketamine induced uropathy and IC/BPS patients were assessed by cystoscopic hydrodistension and all of them have different severity of glomerulations or post-dilated hemorrhage. Moreover, we collected 44 ketamine abusers without LUTS with the duration than one year of their ketamine abuse. The definition of ketamine abusers without bothering LUTS was 1.no pelvic pain (VAS pain score=0) 2.mild LUTS (ICSI+ICPI <6). All these three groups completed measures of pain severity (Visual Analog Scale), bladder symptom severity (IC Symptom Index, IC Problem Index) and non-bladder condition as medical history questionnaire including etiology unknown disease, such as FM, IBS, allergy and depression. These data were analyzed using point bi-serial correlation for ANOVA and chi-square to evaluate symptoms and comorbid disease in these three patient' s groups.

Results

There is no difference in age between ketamine abuser without bothering LUTS and ketamine induced uropathy. Age-matched IC/BPS showed more severe LUTS than ketamine induced uropathy and ketamine abusers without bothering LUTS (ICSI: 13.00 vs 9.72 vs 1.11, $p<0.001$; ICPI: 11.73 vs 7.13 vs 0.27, $p<0.001$). More severe pain perception

in IC/BPS and ketamine induced uropathy groups were found than ketamine abuser without bothering LUTS (VAS pain: 5.40 vs 4.16 vs 0, p<0.001).

	Ketamine abusers without bother LUTS (N=44)	Ketamine induced uropathy (N=32)	Age-matched IC/BPS (N=27)	P value
Age	26.81 ± 3.7	26.58 ± 4.4	26.54 ± 2.4	0.98
VAS Pain	0.00 ± 0.0	4.16 ± 2.8	5.40 ± 2.9	<0.001
ICSI	1.11 ± 1.2	9.72 ± 6.8	13.00 ± 3.0	<0.001
ICPI	0.27 ± 0.7	7.13 ± 5.5	11.73 ± 2.7	<0.001

<Table1> Age and subjective symptoms between three groups using ANOVA

There is no difference in IBS and FM between these three groups. However, ketamine induced uropathy had more severe depression and allergy history than age-matched IC/BPS and ketamine abuser without bothering LUTS (Depression: 53.1% vs 7.4% vs 9.1%, p<0.001; Allergy: 62.5% vs 37% vs 25%, p=0.004).

	Ketamine abusers without bother LUTS (N=44)	Ketamine induced uropathy (N=32)	Age-matched IC/BPS (N=27)	P value
IBS	1 (2.3%)	1 (3.1%)	2 (7.4%)	0.53
FM	1 (2.3%)	3 (9.4%)	2 (7.4%)	0.39
Depression	4 (9.1%)	17 (53.1%)	2 (7.4%)	<0.001
Allergy	11 (25%)	20 (62.5%)	10 (37%)	0.004

<Table2> Comorbid disease between three groups using chi-square

Conclusion

Ketamine induced uropathy have more diagnosis of depression and allergy history than IC/BPS and ketamine abuser without bothering LUTS. Further study need to evaluate causality and pathogenesis between comorbidity and uropathy induced by ketamine

心得及建議

除了吸收世界各地優秀學者所提供的研究資訊之外，會議中各國學者針對間質性膀胱炎這難纏的疾病，各國仍致力研究，也發表了不少的新概念。各國與會者提出的最新成果和交流思想對提升間質性膀胱炎新的研究開發和應用都能促進更多概念的提升，也希望藉由這次的發表，亦能更提高台灣在國際學術研究上的能見度。

照 片











