BLADDER PAIN SYNDROME/
INTERSTITIAL CYSTITIS
Studies on classic BPS/IC, ESSIC type 3C, with special reference to the role of nitric oxide

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av
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II. Ýr Logadottir, Ingrid Ehrén, Magnus Fall, N. Peter Wiklund, Ralph Peekler. Intravesical nitric oxide production discriminates between classic and nonulcer interstitial cystitis. J Urol, 2004;171: 1148-1151.


IV. Ýr Logadottir, Catharina Lindholm, Pernilla Jirholt, Inger Gjertsson, Magnus Fall, Dick Delbro, Ralph Peekler. Cytokine responses in BPS/IC Type 3C. Manuscript.
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ABSTRACT

Patients presenting with symptoms of Bladder Pain Syndrome (BPS) are challenging to the urologist. Previously known as Interstitial Cystitis (IC), this syndrome has been extensively debated and investigated. IC mainly affects women, only 1 or 2 out of 10 patients are males. There is a need of consensus on classification since there are quite diverging opinions. BPS/IC is divided in two main subgroups, classic ulcerative and non-ulcerative forms, which have different histopathological, immunological and neurobiological features and respond differently to a variety of treatments. The symptoms are similar, with chronic pain related to bladder filling and urinary frequency. The International Society for the Study of BPS (ESSIC) has proposed diagnostic criteria, classification and nomenclature based on how the diagnosis was established. Classic IC is now referred to as BPS Type 3C, which indicates that the patient has a Hunner lesion, is diagnosed with cystoscopy, bladder hydrodistention under general anaesthesia, and histopathological examination of bladder tissue sample. For simplicity, the remaining group will here be referred to as non-Hunner BPS patients.

The aims of this thesis were; to further describe a patient population with the diagnosis of BPS/IC, to investigate the nitric oxide (NO) production in the BPS/IC urinary bladder, to analyse the source of NO production, to localise the presence of the iso-enzyme, inducible Nitric Oxide Synthase (iNOS), and to survey inflammatory mediators in the bladder tissue of BPS ESSIC Type 3C/classic IC patients compared to healthy controls.

The hallmark of BPS Type 3C compared to non-Hunner BPS patients is the ulceration in the mucosa and the inflammation in the bladder wall, including increased mast cell count. This is not found in the non-Hunner group of patients. The Hunner BPS Type 3C patients are older by 10 to 20 years at diagnosis and have markedly smaller bladder capacity when measured under general anaesthesia. The end stage is a fibrotic small bladder. This does not happen in non-Hunner BPS.

We have shown that the BPS Type 3C bladder produces large quantities of NO, which is not the case in non-Hunner BPS patients or healthy controls. The iso-enzyme iNOS, believed to be the catalyst in NO production, is found in large amounts within the inflammatory infiltrate of the BPS Type 3C bladder, as well as in the urothelial cells, in both BPS groups and healthy controls. The spectrum of inflammatory markers in the bladder wall of BPS Type 3C patients indicates that the inflammation is similar to what is seen in certain diseases believed to be of autoimmune origin. The paper on cytokine responses in BPS/IC Type 3C, with increase in mRNA expression of interleukin-17, opens up novel research avenues with expectations for new pharmacological targets for the treatment of this condition.

Key words: Bladder Pain Syndrome (BPS), Interstitial Cystitis (IC), Nitric Oxide (NO), Nitric Oxide Synthase (NOS), Inflammatory mediators, Interleukin-17, Mast cells.