Afferent Neurourology: An Epidemiological Perspective

J. Quentin Clemens*

From the Department of Urology, University of Michigan Medical Center, Ann Arbor, Michigan

Abbreviations and Acronyms

CP = chronic prostatitis

CPPS = chronic pelvic pain syndrome

GU = genitourinary

IC = interstitial cystitis

LUTS = lower urinary tract symptoms

NHS = Nurses' Health Study

NIH = National Institutes of Health

OAB = overactive bladder

PBS = painful bladder syndrome

Submitted for publication September 22, 2009.

* Correspondence: Department of Urology, University of Michigan Medical Center, 1500 East Medical Center Dr., Ann Arbor, Michigan 48109-5330 (telephone: 734-232-4881; FAX: 734-936-9127; e-mail: qclemens@umich.edu).

Supplementary material for this article can be obtained at http://www.med.umich.edu/urology/research/ManuscriptAppendices/index.html.

Purpose: Multiple urological conditions are characterized by bothersome sensations such as pain or urinary urgency. There is significant confusion about the etiology and pattern of these symptoms.

Materials and Methods: The term afferent neurourology is introduced to describe the study of sensory processing related to the genitourinary tract. Epidemiological studies related to afferent neurourology are reviewed and unique challenges to our understanding of these disorders are described.

Results: Afferent urological disorders are characterized by urological pain or urinary urgency. Conceptually these afferent disorders can be differentiated from efferent urological disorders and structural urological abnormalities. Afferent urological disorders are common in men and women, although symptom severity is variable. Study of the entire disease spectrum may provide insight into pathogenesis and prevention. The natural history of these symptoms is poorly understood. Afferent urological disorders commonly co-occur with other poorly understood somatic symptoms, suggesting that symptoms may be due to a systemic disorder in certain individuals. Mechanisms responsible for these sensory abnormalities are poorly understood and may arise from central and peripheral abnormalities.

Conclusions: Urinary pain and urgency are common, bothersome symptoms that are currently understood poorly and managed ineffectively. Intentional recognition of sensory urological abnormalities as a separate field of study may enhance research efforts into these conditions and improve treatment outcomes.

Key Words: urinary bladder; cystitis, interstitial; pain; prostatitis; epidemiology

NEUROUROLOGY encompasses the study of lower urinary tract neurophysiology and the functional urological abnormalities that result from neurological dysfunction, disease or injury. Multiple neurological disorders can adversely affect urinary tract function. Management principles focus on preserving continence and preventing upper urinary tract complications by decreasing detrusor overactivity and maintaining low bladder storage pressure. Therefore, the focus is on identifying and treating abnormal motor (efferent) neurological activity.

AFFERENT NEUROUROLOGY

A Novel Paradigm

A different type of abnormality exists in which bothersome sensations of pain or urinary urgency are the defining complaints. For these conditions the concept of afferent neurourology has been introduced.[1] This term refers to the field of study concerned with the processing of sensory information related to the GU tract. This review expands on this concept to discuss specific epidemiological data that are relevant to the field of afferent

0022-5347/10/1842-0432/0
THE JOURNAL OF UROLOGY®

Vol. 184, 432-439, August 2010
Printed in U.S.A.
DOI:10.1016/j.juro.2010.04.012

neurourology. This information may focus attention and research on this poorly understood field.

Defining Characteristics of Disorders

The abnormal processing of sensory information that characterizes afferent neurourology results in pain and urinary urgency symptoms. Pain may be described by patients as pressure or discomfort but such symptoms still meet the accepted definition of pain, that is an unpleasant sensory or emotional experience associated with actual or potential tissue damage, or described in terms of such damage.[2] Urinary frequency and nocturia are often but not always present. However, frequency and nocturia are behaviors, rather than sensory experiences, that are caused by urinary urgency, pain and many other factors, such as fluid intake, medical conditions, medication etc. Therefore, frequency and nocturia are not considered defining characteristics in the afferent neurourology paradigm.

Clinical Syndromes

Urological pain and urgency result in clinically recognized conditions such as IC/PBS, CP/CPPS, OAB, LUTS, chronic epididymitis and orchialgia. Each is a syndrome (collection of symptoms) without objective markers. It is common for individuals to have symptoms that meet the criteria for more than 1 of these conditions. OAB can be subcategorized into OAB dry (urgency without urge incontinence) and OAB wet (urgency with urge incontinence). These 2 subgroups are typically considered part of an OAB disease spectrum but to my knowledge it is unknown whether they in fact share the same underlying pathophysiology. It is also unclear to what extent those with OAB dry progress to OAB wet. Furthermore, the mechanism responsible for converting the afferent symptom of urgency to the efferent symptom of urge incontinence is not well understood.

Afferent symptoms and disorders can be differentiated from efferent abnormalities (eg detrusor failure, decreased bladder compliance and detrusor overactivity) and structural abnormalities (eg stress incontinence, prolapse and anatomical bladder outlet obstruction) (see Appendix). Efferent and structural abnormalities tend to be better understood because each has an objective diagnostic test that can be done to confirm the diagnosis and quantify severity. Conversely the lack of objective markers for afferent disorders has hampered our ability to confirm the diagnosis, identify patient subgroups or provide prognostic information. Furthermore, multiple afferent, efferent and structural disorders may be present in an individual.

LOWER URINARY TRACT SYMPTOMS

Traditionally the term LUTS has referred to symptoms attributable to benign prostatic hyperplasia. However, there is growing recognition that a more expansive underlying pathophysiology than the prostate alone is responsible for these symptoms.[3] For example, LUTS are equally common in men and women.[4] The LUTS concept combines various symptoms that are typically subcategorized as voiding symptoms (incomplete bladder emptying, intermittence, slow stream and straining to void) and storage symptoms (frequency, urgency and nocturia). This concept is fairly comprehensive of common urological symptoms and LUTS symptoms are commonly quantified and used to measure symptom severity. However, the LUTS paradigm ignores pain, which is often present in patients with LUTS.[5,6] Furthermore, subcategorization into voiding and storage symptoms implicitly acknowledges the disparate nature of these symptom types. Thus, 2 patients with the same degree of LUTS based on a symptom score may show completely different symptom characteristics. Also, the more specific subcategory of storage symptoms includes a symptom (urgency) and behaviors (frequency and nocturia) that may be completely unrelated, as explained. In the afferent neurourology paradigm urgency and pain symptoms are isolated as unique sensory abnormalities.

AFFERENT UROLOGICAL DISORDER PREVALENCE

Generally prevalence studies of afferent urological disorders have been done in 1 of 5 ways. Collectively an impression about the overall prevalence of these conditions can be formed. 1) Surveys have been done that ask participants whether they have ever been diagnosed with a condition of interest (self-report studies). Such studies are subject to recall bias and depend on accurate clinical diagnoses being communicated to patients. 2) Questionnaires have been administered to identify symptoms suggestive of the condition of interest (symptom assessments). These studies are often subject to response bias since individuals with the symptoms may be more likely to complete the questionnaire. Also, identifying symptoms is not the same as diagnosing a specific medical condition, and to our knowledge the sensitivity and specificity of various questionnaire definitions for these conditions are unknown. 3) Administrative billing data have been used to identify individuals in a population with a specific diagnosis indicating an afferent urological disorder (clinician diagnosis). These studies require an accurate clinician diagnosis and are limited by the categorization schemes that are inclusive in billing data. 4) Clinical records