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UPCOMING ISSUES

What Does Pain Hurt?

Opioid Abuse Risk

Cancer Pain

Chronic Pelvic and Urogenital Pain Syndromes

Chronic pelvic and urogenital pain is a common and debilitating problem that has a significant impact on the quality of life of patients. These types of pain are some of the most common presenting symptoms for primary care doctors and fall within the practice of most medical specialties, but particularly urology, gynecology, and gastroenterology. Many urological, gastrointestinal, and gynecological disorders appear to cause or are associated with chronic pelvic pain, which often produces a diagnostic dilemma. Pain localized to the lower abdomen and the pelvic and perineal region can be a warning sign of acute or chronic tissue injury to the abdominal and pelvic organs, or it can be a chronic condition without identifiable pathology.

Although patients seek medical care because they are looking for help to alleviate their pelvic discomfort and pain, in clinical practice much emphasis has been placed on finding a specific etiology and specific pathological markers for pelvic disease. These patients typically undergo many diagnostic tests and procedures. However, often the examination and workup remain unrevealing, and no specific cause of the pain can be identified.

Many health care providers question the existence of chronic pelvic and urogenital pain, especially if the diagnostic workup does not reveal any pathology to explain the pain complaint. In these cases, it is important to recognize that pain is not simply a symptom of pelvic or urogenital disease, but that the patient is suffering from chronic pain, where pain is the prominent symptom of a chronic visceral pain syndrome.¹ In addition, pain complaints localized to areas that are related to sexual function, defecation, and urination are often considered taboo and are complicated by psychological and unique physiological issues. Falvey has proposed that health care providers who work with patients with chronic pelvic pain make a conceptual shift in relation to the emotional aspects of chronic pelvic pain and consider the psychological disturbances as a result of the disease rather than the cause.²

Definitions: What Are Chronic Pelvic and Urogenital Pains?

Definitions are important if a body of reliable information is to be built up in the scientific literature, which will eventually lead to a better understanding of the pathophysiology of chronic pelvic and urogenital pain. At present, one of the major problems of clinical research into chronic pelvic and urogenital pain is the lack of agreed definitions, which would allow comparison between studies. On the other hand, the lack of understanding of the pathophysiological mechanisms of these syndromes makes it difficult to decide on criteria to define chronic pelvic and urogenital pain conditions.³

Pain is defined by the International Association for the Study of Pain (IASP) as an “unpleasant sensory and emotional experience associated with

actual or potential tissue damage or described in terms of such damage.”⁴ There is no generally accepted definition of chronic pelvic pain. IASP defines chronic pelvic pain without obvious pathology as chronic or recurrent pelvic pain that apparently has a gynecological origin but for which no definitive lesion or cause is found.⁴ This definition is problematic from a clinical perspective, since it implies absence of pathology, which might not necessarily be the case—for example, many patients with endometriosis suffer from pelvic pain. The definition also excludes cases where pathology is present, although it may not necessarily be the cause of pain. As in many other pain conditions, the relationship of the pain complaint to the presence of pathology is often unclear in patients with chronic pelvic pain. The proportion of women with chronic pelvic/urogenital pain and a specific diagnosis (or diagnoses) varies greatly in the literature. A large primary care study from Great Britain found that diagnoses related to urinary and gastrointestinal tracts are more common than gynecological causes (30.8% are urinary, 37.7% gastrointestinal, and 20.2% gynecological). Further, 25–50% of women with chronic pelvic pain who received medical care in primary care practices have been given more than one diagnosis.^{5,6}

Epidemiological studies have documented that chronic pelvic and urogenital pain syndromes in men and women are indeed quite prevalent. These studies have prompted an increased effort by several medical societies, spearheaded by urologists and gynecologists, to revise and extend the rudimentary taxonomy of these pain syndromes. These efforts were driven by the need to establish a common terminology to result in better patient diagnosis and care.⁷

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One of the earliest consensus committees on the terminology of urogenital pain focused on vulvodynia. Hyperesthesia of the vulva was described in American and European gynecological textbooks more than 100 years ago. Surprisingly, despite early detailed reports, chronic vulvar dysesthesia almost disappeared from the medical literature until the mid-1970s. In 1976, the International Society for the Study of Vulvovaginal Disease (ISSVD) identified idiopathic vulvar pain as a unique entity and introduced the term “burning vulva syndrome,” based on the observation that most women describe the pain as a hot, burning sensation. The ISSVD subsequently coined the term “vulvodynia” to describe this disorder.^{8,9} Subsequently, two subsets of vulvodynia were identified. One subgroup of patients complained about entrance dyspareunia (pain with tampon insertion and pain at vaginal penetration during sexual intercourse), rather than diffuse vulvar pain. The term “vulvar vestibulitis” was introduced for this subset of vulvodynia. The other main subgroup of patients with vulvodynia presented with generalized, spontaneous vulvar pain occurring in the absence of physical findings. The term “dysesthetic” (or “essential”) vulvodynia

was suggested for this symptom complex. Based on the concern that the suffix “-itis” in vulvar vestibulitis incorrectly implies an inflammatory etiology, the term “vestibulodynia” has been suggested.⁹ The ISSVD’s most recent revision of the terminology of vulvodynia was published in 2004.⁹ This classification suggests categorizing a generalized form of vulvodynia and a localized form (vestibulodynia, clitorodynia, hemivulvodynia, etc.) and differentiating subgroups within those two categories based on the observation as to whether the vulvar pain is provoked, unprovoked, or mixed (provoked and unprovoked).

The International Continence Society (ICS) has defined the urogenital pain syndromes as follows.¹⁰ Genitourinary pain syndromes are all chronic. Pain is the major complaint, but there may be concomitant complaints related to the lower urinary tract or bowel, or of a sexual or gynecological nature. Seven pain conditions were introduced: painful bladder syndrome, urethral pain syndrome, vulvar pain syndrome, vaginal pain syndrome, scrotal pain syndrome, perineal pain syndrome, and pelvic pain syndrome. Pelvic pain syndrome was defined as the occurrence of persistent or recurrent episodic pelvic pain associated with symptoms suggestive of lower urinary tract, sexual, bowel, or gynecological dysfunction in the absence of proven infection or other obvious pathology.¹⁰ The European Association of Urology has suggested extending this definition by considering two subgroups based on the presence or absence of well-defined conditions that produce pain.¹¹ In the gynecological literature, chronic pelvic pain is often referred to as pelvic pain in the same location for at least 6 months. The American College of Obstetricians and Gynecologists has proposed the following definition, limited to females: chronic pelvic pain is noncyclic pelvic pain of at least 6 months’ duration that localizes to the anatomical pelvis, the anterior abdominal wall at or below the umbilicus, the lumbosacral back, or the buttocks and is of sufficient severity to cause functional disability or lead to medical care. A lack of physical findings does not negate the significance of a patient’s pain, and normal examination results do not preclude the possibility of finding pelvic pathology.¹²

Definitions of chronic pelvic and urogenital pain will probably continue to be revised as knowledge about the pathophysiology of these pain syndromes increases based on basic science and clinical research.

Epidemiology

Chronic pelvic and urogenital pain is more common than previously thought. Epidemiological data show that 14.7% of women of reproductive age reported chronic pelvic pain and that the estimated number of female pelvic pain sufferers is 9.2 million in the United States alone.¹³ Analysis of a large primary care database from the United Kingdom demonstrated that the annual prevalence of chronic pelvic pain in women is 38/1000, which is comparable to the prevalence rate of asthma and low back pain.⁶ Although this study found a high prevalence of pain, many women had never had the condition diagnosed.¹⁴ Irritable bowel syndrome (IBS) accounts for 12% of primary care visits and 28% of gastroenterological practice.¹⁵ While prevalence estimates vary widely, experts have suggested that somewhere between 450,000¹⁶ and 1 million¹⁷ people

in the United States have interstitial cystitis (IC) or IC-like conditions. When the Nurses' Health Study (NHS) I and II cohorts were used as a study population, the prevalence of IC in NHS II was reported as 67/100,000 and in NHS I as 52/100,000.¹⁸

Prostate pain syndrome without demonstrated infectious or inflammatory etiology is the most common urological diagnosis among men under age 50, and the third most common in those over 50, with an estimated 6 million men affected in the United States.¹⁹ Community studies suggest that vulvar pain is common, and prevalence rates as high as 18% have been reported.²⁰ Vulvar vestibulitis has been described in up to 15% of gynecological outpatients.²¹ While initial reports postulated that vulvodynia affects primarily Caucasian women, a recent survey of ethnically diverse women showed similar lifetime prevalences of chronic vulvar burning pain or pain on contact.²²

Careful clinical history and examination show that patients with pelvic and urogenital pain often suffer from "more than one pain." The clinical observations are supported by epidemiological data. Data from the Interstitial Cystitis Data Base Study²³ show that 93.6% of patients enrolled with a diagnosis of IC reported having some pain in some part of their body. Of the patients having pain, 80.4%, 73.8%, 65.7%, and 51.5% reported having pain in their lower abdomen, urethra, lower back, and vaginal area, respectively. Increasing clinical and epidemiological evidence attests to the comorbidity of several pelvic and urogenital pain syndromes in the same patient, as well as the co-occurrence of pelvic and urogenital pain with chronic pain syndromes, such as fibromyalgia, in other body areas. Such evidence raises the question of systemic alterations of pain modulatory mechanisms rather than local organ-based mechanisms.^{24–26}

Sex, Gender, and Gonadal Hormonal Status

A distinguishing feature of several of the pelvic and urogenital pain syndromes is the overwhelming burden reported by women of reproductive age. For example, population prevalence estimates in patients with IC indicate a female-to-male ratio of 9:1.¹⁷ There is growing evidence from studies in animals and humans that the response to noxious stimuli may be influenced by the gonadal hormonal milieu and that it varies across different phases of the estrous cycle (in rodents) or menstrual cycle (in women).²⁷ Clinical research studies have demonstrated a menstrual cycle effect on sensory function in women with urogenital pain,^{28,29} suggesting a potential role for hormone modulation as a therapeutic option.

The Future: Challenges, Opportunities, and Clinical Implications

The chronic urogenital and pelvic pain syndromes have previously been neglected and underestimated.¹ They have only reached clinical and scientific recognition in the last 15–20 years, due to the overwhelming evidence of recent epidemiological data highlighting the widespread existence of these pain syndromes. Increasing evidence has emerged to show that different urogenital and pelvic pain syndromes, as well as pain syndromes in other body regions, often occur

together in the same patient. Thus, efforts to understand the pathophysiology of pelvic and urogenital pain and to design therapeutic modalities have recently shifted from an organ-based approach to a more global approach. For example, the U.S. National Institute of Diabetes and Digestive and Kidney Diseases recently held an international symposium on "Defining the urologic chronic pelvic pain syndromes."³⁰

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Current treatment strategies for pelvic and urogenital pain range from acupuncture to physical therapy to psychological interventions to local and systemic drugs to nerve blocks and neuromodulation. Clinical studies that have tried to refine or test existing therapies in these patient populations have often obtained frustrating results, and it appears that many therapies are effective in only a subset of patients.³¹ Thus, a key issue will be to identify subsets of patients who respond to particular therapeutic approaches. Since multiple different pathogenic pain mechanisms may coexist in patients presenting with chronic pelvic and urogenital pain, a combination of different pharmacological agents or treatment modalities might be required to obtain an optimal result. It is encouraging to see the growing interest in the pharmaceutical industry in expanding basic science and clinical research efforts for this underserved patient population, based on the convincing epidemiological data documenting high prevalence rates of these pain syndromes. The European Agency for the Evaluation of Medicinal Products has suggested including patients with chronic visceral pain in their 2002 recommendations, "Guidance on clinical investigation of medicinal products for treatment of nociceptive pain."³² Thus, there is a possibility that drugs will be evaluated specifically for chronic pelvic and urogenital pain. As pointed out above, many patients present with additional pain syndromes. It will be important to keep track of these comorbidities for clinical trial design, because the pathophysiological mechanisms in subjects with different comorbidities might be different.

In conclusion, a great deal of progress has occurred in the last 15 years in recognizing the chronic pelvic and urogenital pain syndromes as a clinical entity.³³ The challenge in the next decade will be to identify effective treatment modalities. Given the many comorbidities observed in this patient population, it will be important to assess which patients will be at risk to develop other chronic pain syndromes and to design strategies for early intervention.

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