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Chronic Pelvic Pain in Men

Abstracts

Chronic pelvic pain is a condition which receives less attention in men than in women. It is often difficult to diagnose and more difficult to treat. The new classification of prostatitis and its variants has introduced the term 'chronic pelvic pain syndrome' which underlines the difficulties in dealing with this disorder which may represent a variety of chronically painful conditions with a large functional component.

Introduction

Chronic pelvic pain as a medical condition is less common in men than in women and has therefore hitherto received less attention in the urological compared to the gynecological literature. A literature search on the topic yields about ten times as many references to the condition in females than in males.

In a recent US telephone survey amongst 17,927 households, of 5,263 women aged 18–50 years 14.7% reported to have suffered chronic pelvic pain over the last 3 months. Despite medical consultations the source of the pain was undetermined in 61% [1]. Similar data about the incidence or prevalence of chronic pelvic pain in men do not exist. However, there are a variety of chronically painful conditions in men which present to the urologist and often pose problems either because their underlying cause remains elusive or because treatment and cure prove difficult if not impossible.

Although one of the commonest chronically painful conditions in urological practice is chronic prostatitis there is more to chronic pelvic pain in men than chronic prostatitis.

Chronic Pain

Pain is the most frequent symptom of disease leading to a consultation with a physician. However, pain is not an objective symptom. It is more a perception than a sensation which undergoes a complex processing in the central nervous system. A nociceptive sensory impulse from the periphery is triggered by a local potentially tissue-damaging influence which leads to the release of substances (such as potassium, histamine, serotonin, prostaglandins) which stimulate free sensory nerve endings. The afferent nerve impulses thus generated are transmitted to the dorsal columns of the spinal cord, and reach the brain stem via the spinothalamic tracts [2]. Mainly in the thalamus pain is registered and processed consciously – its location, nature and intensity are noticed and compared with similar pain perceptions in one's experience. In the brain stem and parts of the formatio reticularis the autonomic and emotional processing of pain takes place which can lead to autonomic and emotional reactions (such as fear or nausea) and subconscious association with other levels of experience [3].

With chronic pain the intensity of the pain reaction is often out of proportion to the original stimulus which caused the pain. Social and psychological factors can influence chronic pain immensely, and typically variations in the character of the chronic pain and its relation to bodily functions occur.

In pain physiology, somatic pain generated by free nerve endings from the body surface is distinguished from visceral pain originating from deeper structures [4]. Pelvic pain by its nature is usually of the visceral type and thereby less well defined and usually not as clearly localizable as somatic pain. Pain referral to the

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dermatomes associated through the organization of our nervous system with pelvic organs is a frequent feature. Neuropathic pain, caused by the damage of nerves through, e.g., surgery or radiotherapy, can also occur.

Patients with chronic pain conditions are difficult to treat. After often a multitude of different treatments and numerous physician consultations without a cure or a clear diagnosis, these patients are frequently labelled as being chronically depressed [5]. However, the relationship between chronic pain and depression is twofold. While patients with long-lasting chronic pain often do develop depression, patients with endogenous depression also have a lower pain threshold and chronic pain conditions are more common in endogenous depression [6].

Chronic pain patients with depressive symptoms will often present a great degree of denial, but a careful history can elicit specific symptoms such as asomnia, loss of libido and adynamia. The psychosomatic differential diagnosis of chronic pain syndromes without an organic diagnosis includes in addition to the classic conversion neurosis a variety of so-called 'somatoform disorders' [7]. These include, for example, the 'pain prone syndrome', characterized by hypochondriacal pain perception, easy fatigueability and lack of resistance to stress.

However, the majority of chronic pelvic pain must be considered to be of organic origin. In urology, there are a number of clinical entities of unclear or at least incompletely understood etiology which are characterized by chronic pelvic pain. Examples are prostatodynia, stress prostatitis, chronic abacterial prostatitis, trigonitis, urethral syndrome and orchialgia. Many of these terms are descriptive in nature and have no clear clinical or pathophysiological correlate. They all have in common that they describe a condition associated with chronic pelvic pain in men.

In order to bring more clarity into an area of confusion the term 'chronic pelvic pain syndrome' (CPPS) has been introduced [8, 9]. This is defined as a condition of chronic or recurrent pelvic pain of more than 6 months duration. The CPPS is a descriptive diagnosis of exclusion and often will not yield a clear pathophysiological diagnosis either. However, the term is useful in describing a syndrome with probably multifactorial etiologies and multiple variants that have, however, common clinical symptoms and may respond to similar treatment strategies.

Characteristics of CPPS in Men

Zerman et al. [10] examined 103 men with CPPS (mean age 47 years). 45.6% suffered predominantly from perineally localized pain, 38.8% complained of scrotal and/or testicular pain, while only 5.5% each had mainly penile or suprapubic pain. The clinical and urodynamic investigation of these patients, who on average had already undergone 8.6 (ineffective) courses of antibiotic treatment, revealed a painful pelvic floor, normal bladder capacity, increased sphincter closing pressure, and reduced urinary flow in the majority of this group (88.3%).

This characterization of CPPS in men illustrates the salient features of this syndrome: chronic pain with predominantly perineal but variable location, and dysfunctional voiding with or without subjective micturition symptoms.

The variants of CPPS are several if not many. One of the commonest diagnoses in men with chronic pelvic pain of unexplained etiology is chronic abacterial prostatitis. While bacterial prostatitis is a clinical entity with a seemingly obvious etiology, the term 'abacterial prostatitis' is characterized by a lack of evidence concerning its etiology and effective treatment.

Yet chronic abacterial prostatitis is a well-used diagnosis, accounting for 8% of urology consultations and 1% of general physician visits in the USA [11]. A third of these patients is treated with antibiotics despite the absence of any evidence of infection.

In the age of evidence-based medicine, efforts have been made to put more proven facts behind the concept of chronic prostatitis [9]. The most common symptom in chronic abacterial prostatitis is that of chronic pain [12]. The pain localizations are similar to those described for CPPS [10], but patients with the diagnosis chronic prostatitis often report micturition symptoms (54%) and pain with ejaculation (58%) [12]. Taking into account newer concepts of approaching pelvic pain and prostatitis in men, in 1995 the National Institutes of Health devised a new classification of prostatic disorders (table 1). In this the term 'chronic pelvic pain syndrome' is substituted for the term 'chronic abacterial prostatitis', which should no longer be used. CPPS in this classification is further subdivided into inflammatory CPPS (with the presence of inflammatory cells in expressed prostatic secretions, urine after prostatic massage or the ejaculate) and noninflammatory CPPS (without evidence of prostatic inflammation).

Table 1. The National Institute of Health (NIH) definition of prostatic infections and the chronic pelvic pain syndrome (CPPS) [8]

Type of prostatic inflammation		Diagnostic criteria
I	Acute bacterial prostatitis	Acute bacterial prostatic infection
II	Chronic bacterial prostatitis	Recurrent bacterial prostatic infection
III	Chronic abacterial prostatitis/chronic pelvic pain syndrome	No evidence of bacterial prostatic infection
	IIIa Inflammatory CPPS	Increased white blood cells in prostatic secretions
IV	IIIb Non inflammatory CPPS	No white blood cells in prostatic secretions
	IV Asymptomatic inflammatory prostatitis	Asymptomatic, increased white blood cells in prostatic secretions or incidental histological diagnosis

The culture of bacteria from any of these fluids leads to the diagnosis of acute or chronic bacterial prostatitis.

Despite a multitude of studies into the microbiology and other features of the prostate in the condition known as chronic abacterial prostatitis (and now termed CPPS), its etiology remains largely unknown [13–19]. However, different variants of the condition were already described years ago, and newer neurourological concepts have helped to establish a broader understanding of the condition of chronic pelvic pain in men, for which the term CPPS is extremely useful.

In 1985, Hellstrom et al. [20] described 3 patients with chronic nonbacterial prostatitis, dysfunctional voiding with sphincter dyscoordination and radiologically detectable reflux into the prostatic ducts of the peripheral zone on micturition. The authors developed their theory of chronic focal prostatitis through intraprostatic reflux leading to pain and increased dysfunctional voiding with spasticity of the external sphincter segment as the underlying etiology of the chronic pelvic pain in these men who were treated successfully by sacral neuromodulation.

Similar findings of dysfunctional voiding were reported by Barbalias [21] in 1990. He undertook urodynamic investigations in 60 patients, who would be classified as inflammatory or noninflammatory CPPS today, and found normal bladder capacities and voiding pressures with increased urethral closing pressures and reduced flows in the majority of these patients. On micturition cysto-urethrogram, 84% of his patients showed an incomplete opening of the bladder neck and the distal prostatic urethral segment during voiding.

The clinical evidence of urethral sphincter/pelvic floor spasticity and dysfunctional voiding as a prominent feature of male CPPS has been further substantiated by advances in the understanding of the development of chronic pain. The neurourological concept of chronic pelvic pain proposed by Zerman et al. [10, 22] offers a concept which can explain many of the aspects

of chronic pelvic pain. In their hypothesis, a minor noxious stimulus (e.g. focal prostatitis) leads to painful stimuli which affect the complex and interactive innervation of the pelvic organs by altering and resetting effector pathways. The concept is based on the theories of neuronal plasticity (increase and change in synaptic properties, increase in sensibility of pain receptors ('wind-up'), increased central reception of painful stimuli), for which experimental evidence in animal physiology exists [23]. According to this concept, repetitive painful stimuli can lead to an increase in the central transmission of these stimuli, increased and over-proportional central processing and a change in the interactive and reflex coordination of effector pathways to the pelvic organs leading to pathological changes in the neuronal coordination. The latter is especially complex in the pelvic organs where coordinated contraction and simultaneous relaxation of autonomically and voluntarily innervated muscle groups is needed simultaneously. A chronic derangement of this coordination could explain how chronic painful conditions with dysfunctional voiding may develop out of initially rather minor painful stimuli.

Variants of CPPS

Although the neurourological concept of a common pathophysiology of the CPPS in men is very appealing, it can only serve as a basis for understanding and will not explain all aspects of the condition.

Sinaki et al. [24] and Segura et al. [25] described a variant of the syndrome, which was termed 'pelvic floor tension myalgia'. Patients are characterized by predominantly perineally located chronic pain and a relative lack of micturition symptoms. The common clinical finding is a painful and spastic muscular pelvic floor on examination, usually combined with an increased anal sphincter tone. The condition responds

Table 2. Interdisciplinary differential diagnosis of male chronic pelvic pain. The commonest causes in each field are given

<i>Urological</i>	
Acute inflammations	Prostatitis, cystitis, orchitis, epididymitis
Chronic inflammations	Prostatitis, epididymitis, chronic cystitis, interstitial cystitis
Functional disorders of micturition	Chronic sphincter dyssynergia, 'stress prostatitis'
Pelvic floor disorders	Spastic dysfunctional muscle disorders
Malignant	Carcinoma of the bladder, urethra, prostate
<i>Gastrointestinal/proctological</i>	
Inflammatory	Chronic inflammatory bowel disease, hemorrhoids, fissures, proctitis
Malignant	Rectal carcinoma, sigmoid carcinoma
<i>Neurological</i>	
Mononeuropathic	Secondary to surgery, radiotherapy
Polyneuropathic	Mixed, secondary to chemotherapy
Spinal	Localized spinal disease, root compression
<i>Orthopedic</i>	
Degenerative	Disc prolapse, spinal canal stenosis, chronic hip disorders
Disorders of bone metabolism	Osteoporosis, Paget's disease
Malignant	Pelvic bone metastases
<i>Psychosomatic</i>	
Somatoform disorders	Complex functional disorders
<i>Psychiatric</i>	
Affective disorders	Depression

well to physical therapy aimed at progressive relaxation of the habitually contracted pelvic floor muscles. Synonyms of this condition in the medical literature are coccygodynia, piriformis syndrome, levator ani syndrome and proctalgia fugax.

In 1988 Miller [26] described his experience with an aspect of chronic pelvic pain in men which he called 'stress prostatitis'. In a series of 134 patients with long-standing pelvic pain and a history of a multitude of diagnostic interventions and ineffectual treatments, he described a high degree of emotional stress (fear, anger, guilt). In these patients he described an 86% rate of marked improvement or cure with 'stress management' alone.

The different forms of chronic cystitis can also be a cause of chronic pelvic pain. Especially interstitial cystitis (IC) is a condition which is difficult to separate from other conditions with chronic pelvic pain [27] and can be associated with other disease entities [28]. IC is commonly defined as a condition with pain on bladder filling and/or painful micturition, reduced bladder capacity with only discrete inflammatory signs on urinalysis, a histologically evident chronic inflammation of the bladder with variable mast cell infiltration [28, 29]. 90% of patients diagnosed with IC are females [30]. In 86% of men diagnosed with IC the predominant

symptom is chronic pelvic pain with the frequency/dysuria syndrome [31] and the history typically includes several years of treatment efforts under the erroneous diagnoses 'chronic prostatitis' (48%) or benign prostatic hyperplasia (38%) before IC is eventually diagnosed by cystoscopy and histology [32]. It may therefore well be that IC is underdiagnosed in men and represents one of the conditions presenting as CPPS.

However, even chronic pelvic pain diagnosed as IC can be misleading. Gillespie et al. [33] reported a series of 10 patients with the clinical and histological characteristic findings of IC; in 9 of these 10 patients MRI examination showed lumbar dorsal root compression (L5). Pelvic pain and the symptoms and findings suggestive of IC were cured after neurosurgical decompression in these patients. The authors hypothesized on sympathetic dystrophy of the pelvic plexus causing the pelvic pain as well as the changes seen in the bladder.

Diagnostic Approach to the Patient with CPPS

In addition to the urological variants of CPPS, there is a long list of differential diagnoses of chronic pelvic pain which should be considered (table 2). Therefore, first of all, a careful history is required in order to pick

up any clues to possible defined disease entities. Gastrointestinal disorders ranging from hemorrhoids and chronic inflammatory bowel disease to rectal carcinoma can cause chronic pelvic pain. Neuropathic pain after pelvic surgery or radiation treatment can occur. The possibility of pain radiating from lumbar root compression, spinal canal stenosis or peripheral nerve entrapment [34] may require neurological consultation. Osteoporosis, a condition of increasing importance in ageing males, can cause diffuse as well as seemingly localized pain through undetected pathological or incomplete fractures. The diagnostic work-up of a patient with CPPS may therefore require the consultation of several specialists.

The urological diagnostic work-up requires a careful history with special reference to micturition, defecation, erection and ejaculation. In order to more objectively evaluate the main symptom, the pain, the use of a visual analog pain scale (VAS) in addition to a voiding diary is recommendable. The digital rectal examination is of central importance as it allows examination of the rectum, prostate, pelvic floor muscles and anal sphincter, looking for tenderness and muscle tone. In addition, physical examination should include evaluation of the relevant neuromuscular reflexes and sensation in the lumbar and sacral dermatomes.

As the diagnostic work-up in patients with CPPS needs to exclude other well-defined and treatable disease entities, i.e. inflammations and malignancies, investigations will have to include urinalysis, culture of prostatic secretions, prostate-specific antigen, urine cytology, cystoscopy and/or rectoscopy. Biopsies of the prostate or bladder should follow in case of suspicious relevant findings. With negative findings, a urodynamic investigation should then be done in patients with CPPS which will reveal dysfunctional voiding in many cases.

Therapeutic Approach to the Patient with CPPS

The patient with CPPS in the absence of other treatable diagnoses is often characterized by a long-standing history of pain and unsuccessful treatments by a number of physicians. The approach to such a patient should best be multidisciplinary as this facilitates the usually required multidisciplinary diagnostic work-up and increases the trust of the patient in the competence of the approach.

The aims of treatment in these patients who often take a multitude of medications should first be a reduction and simplification of the medication regimen. The second aim must be to increase the patient's understanding of and insight into his condition. The third long-term aim is to increase functional mobility and coordination.

In the context of the neuromuscular explanation of male CPPS this requires a 'wind-down' of hypersensitized neuronal pathways and a reorganization of disordered reflex coordination.

Therefore, treatment for the primarily urological CPPS should begin with effective and symptomatic pain relief by analgesic medication. This should begin at once, and in parallel to the often time-consuming diagnostic work-up, and should have enough analgesic potency to be effective.

Secondly, biofeedback treatment for the reeducation of the pelvic floor musculature is required in which the patient relearns voluntary and full relaxation and control of the pelvic floor.

The third component of the initial treatment approach is the use of medication which facilitates the effect of analgesics and the pelvic floor reeducation. α -Blockers can be used to improve sphincter and bladder neck relaxation, but this is purely empirical as there is as yet no evidence for their efficacy in this situation. In some patients, drugs acting on striated muscle tone such as baclofen may play a temporary role. In our experience, in addition to analgesic drugs the use of benzodiazepines with their effect on the spinal regulation of muscle tone plus their central sedative effect are useful initially.

There are a few other pharmacological options that have been tried on a largely empirical basis, were found to be beneficial in clinical trials and might therefore be useful in some patients: finasteride has been reported in a placebo-controlled trial to have some effect in men with the inflammatory variant of CPPS [35], and in noninflammatory CPPS, allopurinol was also found to have positive effects in a double-blind clinical trial [36].

Not all patients will respond to this treatment approach satisfactorily. In these cases the use of second-line treatments may be considered. With pathologically elevated sphincter tone the injection of botulinum toxin A into the external sphincter can be beneficial [37, 38]. Sacral neuromodulation can also be effective in otherwise refractory cases [20, 39].

Conclusion

Chronic pelvic pain in men can represent a variety of disorders that require a careful differential diagnosis in the approach to these patients. After exclusion of clearly defined organic disease entities, chronic functional voiding disorders should be considered which

may be amenable to biofeedback techniques of pelvic floor reeducation. However, the approach and treatment of men with chronic pelvic pain should be multidisciplinary and targeted at different levels of the problem.

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