GUIDELINES ON CHRONIC PELVIC PAIN

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Introduction

"Chronic pelvic pain" is a non-malignant pain perceived in structures related to the pelvis. It can be difficult to manage because it is often impossible to identify the pathophysiological origin. There is no ideal classification for the conditions included in the set that constitutes chronic pain syndrome. The terms used in these guidelines follow the most recent recommendations for the terminology by the International Continence Society (ICS), and are based on the Axial Structure of the International Association for the Study of Pain (IASP) classification (Table 1).

Prostate Pain Syndrome

Background and diagnosis

The NIDDK system is the preferred classification, identifying four major subtypes of prostatitis (Table 2). In 5-10% of cases, prostatitis is shown to have a bacterial aetiology. In the remaining proportion the symptoms have been attributed to "Chronic non-bacterial prostatitis", "prostatodynia" or "chronic prostatitis" associated with "chronic pelvic pain syndrome." The lat-

ter is defined as discomfort or pain in the pelvic region with negative examination results. There is no evidence of any accompanying disease of the urinary tract. The aetiology and pathogenesis of this larger group of patients is extremely speculative and therefore the new term "prostate pain syndromes" seems more appropriate.

The diagnosis rests on a clinical history, symptoms evaluation, examination and analysis of urine and prostate-specific specimens (including semen, expressed prostatic secretions and urine collected after prostatic massage).

Table 1: Classification of chronic pelvic pain syndromes

Chronic pelvic pain (new definition)	Pelvic pain syndrome	Urological	Painful bladder syndrome	Interstitial cystitis	
			Urethral pain syndrome Penile pain syndrome (new definition)		
			Prostate pain syndrome (adopted from NIH)		
			Scrotal pain syndrome	Testicular pain syndrome (new definition)	
				Post-vasectomy pain syndrome (new definition)	
				Epididymal pain syndrome (new definition)	
		Gynaecological	Endometriosis-associated pain syndrome (new definition)		
			Vaginal pain syndrome		
			Vulvar pain syndrome	Generalized vulvar pain syndrome (ISSVD 1999)	
				Localized vulvar pain syndrome (ISSVD 1999)	Vestibular pain syndrome (ISSVD 1999)
					Clitoral pain syndrome (ISSVD 1999)
		Anorectal	Proctalgia fugax		
			Anorectal pain syndrome (new definition)		
			Anism		
		Neurological	Pudendal pain syndrome (new definition)		

		Muscular	Perineal pain syndrome
			Pelvic floor muscle pain syndrome (new definition)
	Well-defined conditions that produce pain, examples include:	Urological	Infective cystitis
			Infective prostatitis
			Infective urethritis
			Infective epididymo-orchitis
		Gynaecological	Endometriosis
		Anorectal	Proctitis
			Haemorrhoids
			Anal fissure
		Neurological	Pudendal neuropathy
			Sacral spinal cord pathology
		Other	Vascular
			Cutaneous
			Psychiatric

Table 2: Classification of prostatitis according to NIDDK/NIH

I. Acute bacterial prostatitis (ABP)
II. Chronic bacterial prostatitis (CBP)
III. Chronic pelvic pain syndrome (CPPS)
    A. Inflammatory CPPS: WBC in semen/EPS/voided bladder urine-3 (VB3)
    B. Non-inflammatory CPPS: no WBC semen/EPS/VB3
IV. Asymptomatic inflammatory prostatitis (histological prostatitis)

Treatment

Current treatment is directed at symptom management to improve life quality. Benefit may be wrought by alpha blockers, muscle relaxants and antibiotics. Patients who show a response to antibiotics should be maintained on them for at least six weeks. Should a relapse occur, continuous low-dose

antimicrobial treatment should be used. Although analgesics are given to most patients, efficacy data are sparse. Other options without evidence include non-steroidal anti-inflammatories (NSAIDs), immunotherapy, 5-alpha-reductase inhibitors and anticholinergics. Various physical therapies or heat therapy, such as microwave energy applied trans-urethrally or trans-rectally, have been reported to induce favourable effects in some patients. Surgical treatment is limited to circumstances where another indication for surgery exists.

Painful Bladder Syndrome (Interstitial Cystitis)

Background and diagnosis

The collective term "Interstitial cystitis" includes a variety of conditions most commonly identified by symptoms. The diagnostic criteria described by the NIDDK were formulated for research purpose and reach a diagnosis through exclusion, but are inappropriate in clinical care (Table 3). Since symptoms invariably define the clinical condition, the terms "painful bladder syndrome" (ICS 2003) or, alternatively, "bladder pain syndrome" are more apposite.

The aetiology is not known. Many hypotheses have been proposed but none of them have been tested properly and all have an invalid status.

The diagnosis is based on symptoms, examination, urine analysis and cystoscopy with hydro-distension and biopsy. All patients describe pain, urinary frequency and nocturia. The pain, which is sometimes extreme, typically increases with bladder filling and is located suprapubically, may radiate to surrounding areas, and is relieved by voiding although it soon returns.

Classical ulcer disease and non-ulcer bladder pain syndrome demonstrate different clinical presentations and age distribu-

Table 3: Research definition of interstitial cystitis described by NIDDK Workshop on IC August 1987

Automatic inclusions

- Hunner's ulcer

Positive factors

- Pain on bladder filling relieved by emptying
- Pain (suprapubic, pelvic, urethral, vaginal or perineal)
- Glomerulations on endoscopy
- Decreased compliance on cystometrogram

Automatic exclusions

- < 18 years old
- Benign or malignant bladder tumours
- Radiation cystitis
- Tuberculous cystitis
- Bacterial cystitis
- Vaginitis
- Cyclophosphamide cystitis
- Symptomatic urethral diverticulum
- Uterine, cervical, vaginal or urethral cancer
- Active herpes
- Bladder or lower ureteral calculi
- Waking frequency < five times in 12 hours
- Nocturia < two times
- Symptoms relieved by antibiotics, urinary antiseptics, urinary analgesics (for example phenazopyridine hydrochloride)
- Duration < 12 months.
- Involuntary bladder contractions (urodynamics)
- Capacity > 400 cc, absence of sensory urgency

tions. They can be discriminated non-invasively and respond differently to treatment. Classical ulcer disease is a destructive inflammation which in some patients leads to contracted, fibrotic bladders and upper tract outflow obstruction. This progression does not occur in non-ulcer bladder pain syndrome. The two conditions differ in their histopathology, immunology and neurobiology.

Biopsies help to support the clinical diagnosis and to exclude diseases like carcinoma *in situ* and tuberculous cystitis. The O'Leary-Sant symptom index aids diagnosis and helps to measure outcome.

Treatment

The treatment of bladder pain syndrome has yet to be defined from evidence. Tables 4 and 5 summarize the current literature on this subject.

Table 4: Level of evidence and grade of recommendation

Level	Type of evidence
1a	Meta-analysis of randomized trials
1b	At least one randomized trial
2a	One well-designed controlled study without randomization
2b	One other type of well-designed quasi-experimental study
3	Non-experimental study (comparative study, correlation study, case reports)
4	Expert committee, expert opinion
Grade	**Basis for recommendation**
A	Clinical studies of good quality and consistency including at least one randomized trial
B	Well-conducted clinical studies without randomized trials
C	Absence of directly applicable clinical studies of good quality

Table 5: Intravesical, interventional, alternative and surgical treatment of interstitial cystitis

	Level of Evidence	Nature of Recommendation	Comment
Analgesics (intravesical / oral)	2	C	Indications limited to cases awaiting further treatment
Corticosteroids	3	C	Corticosteroids not recommended as long-term treatment
Hydroxyzine	2b	B	Standard treatment
Cimetidine	1b	A	Preliminary data so far
Amitriptyline	1b	B	Standard treatment
Sodium pentosanpolysulphate (PPS)	1a	A	Standard treatment
Antibiotics	1b	A	Limited role in the treatment of IC
Prostaglandins	3	C	Insufficient data on IC, adverse effects
L-arginine	1b	C	Effect in IC uncertain
Immunosuppressants	3	C	Insufficient data on IC, adverse effects
Oxybutynin	3	C	Limited indication in IC
Tolterodine	3	C	Limited indication in IC
Gabapentin	3	C	Preliminary data so far

Suplatast tosilate	3	C	Preliminary data so far
Quercetin	3	C	Preliminary data so far
Intravesical anaesthetics	3	C	
Intravesical pentosanpoly-sulphate (PPS)	1b	A	
Intravesical heparin	3	C	
Intravesical hyaluronic acid	3	B	
Intravesical chondroitin sulphate	3	B	
Intravesical dimethyl sul-phoxide (DMSO)	1b	A	
Intravesical bacillus Calmet-te-Guérin (BCG)	1b	Not recom-mended beyond clinical trials	Data contradictory
Intravesical Clorpactin	3	Not recom-men-ded	Obsolete

Intravesical vanilloids	1b	Not recommended beyond clinical trials	Insufficient data on IC
Bladder distension	3	C	
Electromotive drug administration (EMDA)	3	B	
Transurethral resection (TUR) coagulation and Laser	n.a.	A/B	Hunner's ulcers only
Nerve blockades/epidural pain pumps	3	C	For crisis intervention, effect on pain only
Sacral neuromodulation	3	B	Not recommended beyond clinical trials
Bladder training	3	B	Patients without pain
Manual and physical therapy	3	B	
Diet	3	C	
Acupuncture	3	C	Data contradictory
Hypnosis		No data	
Psychological therapy	3	B	
Surgical treatment	n.a.	A	Ultima ratio, experienced surgeons

n.a. = not applicable

Urethral Pain Syndrome

Urethral pain syndrome is diagnosed in patients presenting with dysuria, with or without frequency, nocturia, urgency and urge incontinence in the absence of evidence of urinary infection.

It is germane that the methods typically used to identify urinary infection are extremely insensitive and some patients may have genuine infection that has not been recognized. Modern automated laboratory methods will not detect colony counts below 10^4 colony forming units per mL (cfu/mL) of urine, when in the presence of symptoms an appropriate diagnostic threshold should be 10^2 cfu/mL. Nearly one-third of acutely dysuric women with urinary infection caused by *Escherichia coli, Staphylococcus saprophyticus or Proteus spp.* have midstream urine colony counts in the range 10^2 to 10^4 cfu/mL. Urethral trauma arising from intercourse may cause pain and dysuria. Women with pelvic floor dysfunction describe the symptoms, as do postmenopausal women.

Scrotal Pain Syndrome

Background and diagnosis

Acute scrotal pain includes torsion of the testis and appendices and requires immediate diagnostic and therapeutic attention. In contrast, chronic scrotal pain is a symptom that has lasted at least six months.

In order to clarify the diagnosis, each component of the scrotum should be palpated and, if possible, the site of the pain should be localized. A digital rectal examination is mandatory and the integrity of the pelvis and spine should be checked. It is essential to perform ultrasonography of the scrotal contents to look for lesions within the testicular parenchyma and

epididymis. The urine should be analysed. The causes to consider include chronic epididymitis, painful cystic lesions, sequelae following trauma or orchitis, or pain referred from prostatitis, prostate cancer, anorectal disorders or distal ureteric stones. It is not unusual to be unable to find an explanation for chronic scrotal pain.

Treatment

The first-line treatments in chronic epididymitis are antibiotics and non-steroidal anti-inflammatory drugs (NSAIDs). Patients with extragenital disease are treated according to the cause. Patients without identifiable lesions have to be treated conservatively, using antibiotics and methods for managing chronic pain. A surgical procedure will cure an average of 50% of patients with an identifiable intrascrotal lesion, with superior results from painful hydrocele, spermatocele and varicocele. Postvasectomy pain may also be accessible to surgical management. In patients with chronic orchalgia where no cause has been found, surgery may be contemplated, but the results are not good. More favourable results have been reported from microsurgical testicular denervation.

Pelvic pain in gynaecological practice

Background and diagnosis

Pelvic pain presenting to the gynaecologist will feature a remedial cause in approximately 70% of cases, leaving 30% unexplained. Clues to the aetiology are provided by the history, including the nature, frequency and site of the pain, precipitating factors, effect of the menstrual cycle, a record of sexually transmitted diseases, vaginal discharge and sexual trauma. Abdominal and pelvic examination will exclude gross patho-

logy as well as demonstrating the site of any tenderness. Vaginal and endocervical swabs may identify pathogens. Pelvic ultrasound should always be used, magnetic resonance imaging (MRI) where indicated. Laparoscopy is the most useful invasive investigation.

Endometriosis is suggested by a history of secondary dysmenorrhoea and often dyspareunia, with reduced uterine mobility, and sometimes adnexal masses. The bladder, ureter and bowel may be involved. Endometriosis may be halted, but not cured, by hormone treatment. The best surgical results are achieved laparoscopically in specialist centres. Despite extensive surgery, pain may persist.

Chronic pelvic pain may arise from gynaecological malignancy or childbirth-related injuries.

Pelvic floor and pudendal nerve

Underactive pelvic floor muscles may result in urinary and faecal incontinence and pelvic organ prolapse. Overactive muscles may result in high outflow resistance producing low urinary flow rates, obstructed defecation and dyspareunia. Pelvic floor overactivity is also thought to be a major factor contributing to chronic pelvic pain. The cycle usually starts with increased muscle tension which may arise from several causes.

Pudendal nerve entrapment leading to chronic compression of the pudendal nerve can result in CPP. It is suggested by a one-sided, burning sensation, exacerbated by unilateral rectal palpation. Further information can be gained by a diagnostic nerve block or MRI investigation.

Psychological factors in chronic pelvic pain

Psychiatric disorders like somatization and somatoform disorders may be involved in some cases of chronic pelvic pain.

Depression is a state of significantly decreased emotional, psychological and social functioning with neurovegetative symptoms lasting at least two weeks. A subclinical depression is often overlooked and can worsen or prolong chronic pelvic pain. Physical or sexual abuse can give cause for chronic pelvic pain, and has consequences for the therapy chosen. On the other hand, chronic pelvic pain must not be used to stigmatize patients as being abused.

General treatment of chronic pelvic pain

Analgesia

Clinical trial evidence is signally lacking in this field. Whilst *paracetamol* should be considered for mild pain, research is needed to define its role in chronic pelvic pain.

There are very few data on the use of *NSAIDs* and even less on *COX2* selective drugs with studies focused on dysmenorrhoea. Non-selective, low potency NSAIDs should be used first and are most likely to be helpful when the pain has an inflammatory component. More potent NSAIDs should be used only when low-potency drugs have failed to be helpful. The benefits of the NSAIDs must outweigh the risks. All NSAIDs are contraindicated in active gastrointestinal ulceration/bleeding and renal disease and may seriously exacerbate asthma and produce fluid retention. If stronger analgesics are needed, NSAIDs may be continued because of their synergistic action with opioids in controlling pain.

Opioids have a role in chronic non-malignant pain but their use in urogenital pain is not well studied. All other reasonable treatments must have been tried and failed. Various safeguards must be followed and the decision to instigate long-term opioid therapy should be made by an appropriately trained specialist in consultation with another physician, preferably the patient's primary care doctor.

The neuropathic analgesics *tricyclic antidepressants* or *anticonvulsants* may be more helpful in patients with nerve injury or central sensitization. *Serotonin reuptake inhibitors* are less effective than tricyclic antidepressants. In some countries *gabapentin* is licensed for use in chronic neuropathic pain and is said to produce a more natural sleep state at night than the antidepressants.

The N-methyl-D-aspartate (NMDA) receptor complex is an important channel for development and maintenance of chronic pain. The NMDA antagonist *ketamine* may be helpful in nerve injury or central sensitization, opioid-resistant pain and intractable pelvic cancer pain. Ketamine is highly addictive and great care is required.

A change in the number, distribution and type of sodium channels can result in altered mechanosensitivity, thermosensitivity and chemosensitivity. Thus low plasma doses of the sodium channel blocker *lidocaine* have been used to reduce neuropathic pain and sensory phenomena without any effect on nociception. Infusions must be performed by trained practitioners. A single infusion may have benefit for several months.

Nerve blocks

These specialist procedures may be performed for diagnostic reasons and therapeutic benefit. Nerve blocks should be performed as part of a pain management package and not in isolation. Neurolytic blocks are rarely indicated for benign processes and to proceed with one may induce terrible consequences.

Transcutaneous electrical nerve stimulation (TENS)

Surface electrical nerve stimulation is thought to relieve pain by stimulating myelinated afferents, thereby activating segmental inhibitory circuits. Urinary frequency may also be reduced. In bladder pain syndrome suprapubic, vaginal-anal and tibial nerve sites have been tested using TENS, all with some success.

Sacral neuromodulation

Sacral nerve stimulation is based on the observation that electrical stimulation of sacral nerves modulates neural reflexes in the pelvis. It may benefit patients with refractory motor urge incontinence, urinary retention, chronic pelvic pain, neuropathic pain and complex regional pain syndromes as well as bladder pain syndrome, refractory pelvic floor dysfunction and pelvic pain.

Summary

Chronic pelvic pain encompasses a large number of clinical presentations and conditions. The aetiology and pathogenesis is often obscure. Successful management requires a detailed history, careful physical examination supported by appropriate laboratory testing and a cautious attitude to treatment, moving from less harmful treatment to more invasive procedures

according to established algorithms, contemplating surgery only when all other options have failed.

This short booklet text is based on the more comprehensive EAU guidelines (ISBN 90-70244-06-3), available to all members of the European Association of Urology at their website - http://www.uroweb.org.