Case Reports

EFFICACY OF LOW DOSE AMITRIPTILYNE IN A 37 YEARS OLD MAN WITH CHRONIC PELVIC PAIN SYNDROME: A CASE REPORT

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Summary

Chronic pelvic pain syndrome (CPPS) is a poorly studied health problem with prevalence rate exceeding 10% of the adult population. The majority of affected patients are seen in urologic practice presenting clinically with urethral, prostate, scrotal or penile pain syndrome. Chronic non-bacterial prostatitis is the leading cause of CPPS. A2-blockers and antidepressants have shown greatest efficacy in CPPS. The tricyclic antideprssant amitriptyline is among the most prescribed drugs for CPPS and other neuropathic pain syndromes. Its recommended doses are between 50 and 150 mg. Below we report a clinical case of 37 years old male with persistent testicular pain. The patient was referred from an urologist with diagnosis CPPS/chronic prostatitis after unsuccessful treatment with a combination of antibacterial drug and α_2 -agonist. We started treatment with amitriptyline 12.5 mg daily with subsequent increase to 25 mg daily. As a result, pain began to decrease gradually on day 4 of treatment and completely disappeared on day 10. During a six month follow up period, no relapse of symptoms was reported. It can be concluded that at least in some cases, amitiptyline might be an effective treatment for CPPS even in lower than usually used daily doses.

Key words: amitriptyline, chronic pelvic pain syndrome, chronic prostatitis

Introduction

Chronic pelvic pain is a complex, poorly understood health problem with prevalence rates ranging from 10 to 16 % for both sexes [1, 2, 3]. The European Association of Urology and the International Continence Society define chronic pelvic pain as a non-malignant pain, perceived in structures related to the pelvis of either men or women and associated with symptoms suggesting lower urinary tract, sexual, bowel or gynaecological dysfunction, without evidence of infection or other obvious pathology, with a constant or recurring course over a period of ≥ 6 months [4]. Representing a public health burden comparable to congestive heart failure, Crohn disease, and diabetes mellitus [5], chronic pelvic pain is better viewed as a functional syndrome involving multiple sites, aetiologies and mechanisms. Table 1 lists the more commonly diagnosed conditions that cause chronic pelvic pain.

The majority of affected patients are seen in urologic practice presenting clinically with urethral, prostate, scrotal or penile pain syndrome. These cases are often combined under the universal term "Urologic Chronic Pelvic Pain Syndrome" (UCPPS). As generally accepted treatment for this condition is still lacking, multiple symptomatic pharmacotherapy approaches have been tried with different degree of efficiency.

Herein, we present a clinical case of a young male with CPPS (persistent testicular pain) whose complaints were successfully relieved by a small dose of tricyclic antidepressant (amitriptyline).

Case report

We report a clinical case of 37 years old male with CPPS whose primary symptom was persistent testicular pain with 4 month duration. The patient denied having had similar symptoms in the past. He did not have history for an urologic disease either or any concomitant somatic of psychiatric illnesses. The patient was referred from an urologist with diagnosis "chronic non-bacterial prostatitis" after unsuccessful treatment course with a combination of antibacterial drug (ciprofloxacin 1000 mg daily) and α_2 -agonist (tamsulosin 0.40 mg per day). Based on his complaints and on our previous experience with tricyclic antidepressants in chronic pain syndromes, we started treatment with amitriptyline 12.5 mg once daily. As the patient tolerated this dose well, we increased it to 25 mg daily (12.5 mg b.i.d.). Subjective pain was assessed with a 10 point visual-analog scale. Upon treatment initiation, level of pain was perceived by the patient as 7.0. It began to decrease gradually as early as on day 4 of treatment and completely disappeared on day 10 (VAS=0). We continued the medication for two months and after that a six months follow up period was performed. During the two months of amitriptyline treatment and the follow up period no relapse of symptoms was reported.

Discussion

As most of the patients with chronic pelvic pain

are seen in urological practice, in 2007 the US National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) began using the umbrella term Urologic Chronic Pelvic Pain Syndromes (UCPPS), for research purposes, to refer to pain syndromes associated with the bladder (i.e. interstitial cystitis/painful bladder syndrome, IC/PBS) and the prostate gland (chronic prostatitis, subdivided into inflammatory or IIIa and non-inflammatory or IIIb type depending on whether white blood cells are found in the expressed prostatic secretions of the patient) [6]. Although having different aetiologies, these conditions share similarities in symptoms and treatment modalities. Clinically, patients usually present with urethral, prostate, scrotal or penile pain syndrome.

The leading cause of UCPPS in men is the non-bacterial chronic prostatitis (NIH category IIIb) [7], which affects approximately 10 to 16%of men [2, 3]. Its key presenting symptom is pelvic or perineal pain without evidence of urinary tract infection [8], lasting longer than 3 months [9, 8]. However, symptoms may vary from case to case. For example pain may range in intensity from mild discomfort to a debilitating state. Sometimes it radiates to back and rectum, making sitting difficult. Dysuria, arthralgia, myalgia, unexplained fatigue, abdominal pain, constant burning pain in the penis, and frequency may all be present. Frequent urination and increased urgency may suggest interstitial cvstitis (inflammation centered in bladder rather than prostate). Post-ejaculatory pain, mediated by nerves and muscles, is a hallmark of the condition and serves to distinguish CP/CPPS patients from those with benign prostate hyperplasia [10]. Some patients report low libido, sexual dysfunction and erectile difficulties.

The aetiology of chronic prostatitis is largely unknown. The bacterial infection hypothesis that held sway in this field for a long was proved nonvalid [11]. It appears that CP is a result from an interplay between psychological factors and dysfunction in the immune, neurological and endocrine systems. Aetiological theories of today include stress-driven hypothalamic-pituitaryadrenal axis dysfunction and adrenocortical hormone (endocrine) abnormalities [12], neurogenic inflammation [13, 14, 15], and myofascial pain syndrome [16, 17]. According to the neurogenic inflammation hypothesis, a presumable dysregulation of the local nervous system leads to an inflammation, mediated by substances released by nerve cells (such as substance P). The prostate (but also bladder, urethra and/or testicles) may become inflamed by the action of the chronically activated pelvic nerves on the mast cells at the end of the nerve pathways. Similar stress-induced genitourinary inflammation has been shown experimentally in other mammals [17]. The upregulation of the sensory nerves in the end organ is transmitted to the spinal cord and central nervous system via a central sensitization process involving C fibers [18]. It results in pain wind-up so that pain is perceived as visceral allodynia and hyperalgesia in the bladder and adjacent pelvic organs, defining a visceral pain syndrome.

In accordance with the above mentioned mechanism, Wise et al. [19] assume that pelvic pain syndrome is neurologically induced problem possibly leading to inflammation in the bladder wall and surface or distortion of the glycosaminoglycan (GAG) layer. They suggest that the pain syndrome results from a continuous and unconscious process of muscle tension engaging perineal musculature (for example m. levator ani), which on its turn is driven by autonomic nervous system dysregulation. The cause of the latter may be emotional (i.e. chronic inner tension, anxiety etc) or physical stress (such as bladder infection, childbirth, hemorrhoids, hernias, trauma etc.). Drawing a parallel between the increased muscle tone that is found in CPPS patients and in patients with migraine headache (in shoulder and upper neck muscles), these authors introduce the term "headache in the pelvis".

Effective treatment for the chronic pelvic pain syndrome is still uncertain. Factors complicating the management of this condition include its probably multifactorial pathogenesis, the lack of a gold standard for diagnostic testing, and the methodological limitations of many treatment studies. Thus far, strategies have focused on symptomatic relief. Non-pharmacological treatment options for chronic pelvic pain include dietary modifications, different mind-body approaches (psychotherapy, acupuncture, relaxation techniques etc.), biofeedback, physical therapy and neuromodulation. Available pharmacological treatments for CPPS are summarized on Tabl. 2.

Among all other pharmacological treatment options, alpha blockers and pain modulators (including antidepressants) are the ones with most empirical support for efficacy [7, 18].

The analgesic properties of antidepressant drugs, regarded as independent of their antidepressant effects were first reported more than 40 years ago. Today they are widely used for chronic and neuropathic pain [20-22]. Of all available antidepressants, amitriptyline belonging to the older generation of three tricyclic antidepressants (TADs), has shown greatest efficacy in CPPS and other neuropathic pain syndromes. Based on limited number of studies, its recommended daily doses in CPPS are between 50 and 150 mg [21].

System	Differential diagnosis
Gastrointestinal	Celiac disease, colitis, colon cancer, inflammatory bowel disease, irritable bowel syndrome
Gynecologic	Adhesions, adnexal cysts, chronic endometritis, dismenorrhea, endometriosis, gynecologic malignancies, leiomyomata, pelvic congestion syndrome, pelvic inflammatory disease
Musculoskeletal	Degenerative disk disease, fibromyalgia, levator ani syndrome, myofascial pain, peripartum pelvic pain syndrome, stress fractures
Psychiatric/neurologic	Abdominal epilepsy, abdominal migraines, depression, nerve entrapment, neurologic dysfunction, sleep disturbances, somatization
Urologic	Bladder malignancy, chronic urinary tract infection, interstitial cyctitis, radiation cystitis, painful bladder syndrome, urolithiasis, benign prostatic gland hypertension
Other	Familial Mediterranean fever, herpes zoster, porphyria

Table 1. Selected differential diagnoses of chronic pelvic pain by organ system

* from Schaeffer J. 2003 [9]

Antibiotics	Quionolones; Cotrimoxazole
Anti-inflammatory a gents	Rofecoxib
Immunomodulators	Prednisone; Cyclosporine
Glycosaminoglycans	Pentosan polysulfate sodium
α-blockers	Tamsulosin; Terazosin; Alfuzosin
Antihistamines	Hydroxyzine; Montelukast
Neuropathic pain modulators	Tricyclic ntidepressants (Amitript yline,
	Nortriptyine); Gabapentin, Pregabalin
Phytotherapy	Quercetin; Cernilton
Muscle relaxants	Cyclobenzapryne; Tizanidine; Clonazepam

Table 2. Non-invasive therapeutic modalities for the treatment of urologic pelvic pain syndromes

*Adapted from Wise D, Anderson R., 2003 [19]

Conclusion

In accordance with other studies [21], we found that the tricyclic antidepressant amitriptyline is an effective treatment for CPPS. Besides, at least in some cases, this medication may work in lower than reported in literature daily doses.

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