Original article

Chronic pelvic pain syndrome in women. Review and preliminary results with low-energy extracorporeal shock wave therapy

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Abstract. *Introduction:* Chronic Pelvic Pain Syndrome (CPPS) is a highly prevalent and very debilitating clinical condition, with a significant impact on the social, working and family activities, negatively affecting the quality of life. Currently there is not yet an satisfying treatment. Several therapeutic options have been proposed and experimented with some results, but in certain patients they are all ineffective. Extracorporeal Shock Wave Therapy (ESWT) could be a new secure and promising approach for this condition. *Aim of the study:* To describe our experience about the effects of three cases of female CPPS. *Materials and Methods:* Three women suffering from CPPS underwent four weekly sessions ESWT (3000 SW, 3 Hz, 0,25 mJ/mm2) with the aim to reduce their pain. Basal and 2 follow-up assessments were conducted using NRS pain score and recording the consumption of medications. Results: In one case we observed a partial improvement on pain, in the second one no benefit and in the last one an almost complete disappearance of the pain. No adverse events were registered. *Discussion and Conclusions:* Although our result are discordant, Low-energy ESWT could represent a new promising treatment for CPPS as it is simple, non-invasive, painless, well tolerated, apparently secure, but more studies are needed to discover the mechanisms through which ESWT acts on the pain and to define the optimal parameters and the better approach to use in clinical practice.

Keywords: Woman's pelvic pain; Chronic pelvic pain syndrome; ESWT; Shock wave therapy; Quality of life.

INTRODUCTION

Chronic pelvic pain Syndrome (CPPS) is a highly prevalent condition which can present a major challenge to health care providers due to its complex aetiology and poor response to therapy.[1,2] Much of the research examining chronic or recurrent pelvic pain in women has been hampered by the lack of a consistent definition.[2]

CPPS is a very debilitating clinical condition with a significant impact on the social, working and family activities, negatively affecting the quality of life.

There is a great variability of prevalence in literature,[3] from 2.1[4, 5] to 43.4%,[6] due to the definition used, the characteristics and quality of the studies and the cultural characteristics of the population studied.

Pelvic pain is an understated and major problem. The best available figures suggest the number of women in the UK with chronic pelvic pain as 1 million (compared with 1.6 million adults with low back pain).[7] CPPS is the reason of 10% outpatient gynaecological visits, 40% diagnostic laparoscopy and 10-15% hysterectomy in the USA[8]. Amongst males, CPPS can affect 10%-15% of the population and results in nearly 2 million outpatient visits each year.[9]

Diseases characterized by pain have a documented higher prevalence in females.[10, 11] In particular abdominal and perineal pain syndromes are sharply more frequent among women, because of anatomy, hormonal conditions, and reproductively aspects.[12] Besides epidemiological studies have shown differences between women and men's pain perception.[10]

TERMINOLOGY AND DEFINITIONS

The International Association for the Study of Pain (IASP) defined pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage".[13, 14]

Definitions and classifications of *chronic pelvic pain* (CPP) have evolved from the mid-1990s under the thrust of expert groups and scientific societies involved on this type of pain. Indeed, classic definitions and classifications were based on the notion of organ disease and usual medical process (infectious, inflammatory, metabolic) and did not allow a proper understanding of functional pathologies.[15]

Apte G et al.[16] define *pelvic pain* as pain arising from the visceral or somatic system and encompasses structures supplied by the nervous tissue from the 10th thoracic spinal level and below. When this pain is recurrent or persistent and associated with symptoms, suggesting involvement of the musculoskeletal, gynecological, urological or gastrointestinal systems and the absence of inflammation or other specific pathology we have a *pelvic pain syndrome*, while *chronic pelvic pain* (CPP) is defined as non-malignant pain perceived in the structures related to the pelvis that has been present for more than 6 months or has a non-acute pain mechanism of shorter duration.[16]

The definition of a chronic pelvic pain theoretically assumes that three components are present: the same pain, its chronic character and pelvic-perineal topography. Nevertheless the definition is more complex and overcomes these three aspects because chronic pain is not only a symptom based on a notion of duration but a syndrome associating various conditions, the chronic pain syndrome.[15]

More recently the European Association of Urology has defined *chronic pelvic pain* as chronic or persistent pain perceived in structures related to the pelvis of either man or woman, that is often associated with negative cognitive, behavioral, sexual and emotional consequences as well as with symptoms suggestive of lower urinary tract, sexual, bowel, pelvic floor or gynecological dysfunction.

CPP is a frequent and difficult problem because, despite the quality and diversity of diagnostic procedures, no relevant aetiology will be found in 30 to 40 % of all cases.[17]

Indeed chronic pelvic pain may be subdivided into "*specific disease-associated pelvic pain*", if it is related to a well-defined classical pathology (such as infection or cancer) and "*chronic pelvic pain syndrome*" when it is not associated to an obvious pathology. Hence CPPS is the occurrence of CPP,

often associated with negative cognitive, behavioral, sexual or emotional consequences (depression, anxiety, fears about pain or its implications, unhelpful coping strategies, and distress in relationships, catastrophic interpretation of pain, sense of helplessness), as well as with symptoms suggestive of lower urinary tract, sexual, bowel or gynaecological dysfunction, in the absence of proven infection or other obvious local pathology that may account for the pain.[1]

Confusingly, a patient may have a well-defined pelvic condition concurrently with chronic pelvic pain syndrome.[7,18]

Pain perception in CPPS may be focused within a single organ, more than one pelvic organ and even associated with systemic symptoms such as chronic fatigue syndrome (CFS), fibromyalgia (FM) or Sjögren's syndrome. When the pain is localised to a single organ, some specialists may wish to consider using an endorgan term such as prostate pain syndrome, bladder pain syndrome, urethral pain syndrome, chronic anal pain syndrome. When the pain is localised to more than one organ site, the term CPPS should be used.

As more information is collected suggesting that the CNS is involved, and indeed may be the main cause of many CPP conditions (e.g., bladder, genitalia, colorectal or myofascial), there is a general tendency to move away from end-organ nomenclature.

Perineal pain syndrome should be mentioned: it is a neuropathic-type pain that is perceived in the distribution area of the pudendal nerve, and may be associated with symptoms and signs of rectal, urinary tract or sexual dysfunction; in this condition there is no proven obvious pathology. It should be distinguished from pudendal neuralgia which is a specific disease associated with pelvic pain that is caused by nerve damage.[1]

We report below (Table 1) the EAU classification of chronic pelvic pain syndromes,[1] set up according to the axis system used by IASP; it may be a useful tool for clinical purpose:

TABLE 1. – The EAU classification of chronic pelvic pain syndromes.

Axis I **Region**		**Axis II** **System**	**Axis III** **End-organ as pain syndrome as identified from Hx, Ex, Ix**	**Axis IV** **Referral characteristics**	**Axis V** **Temporal characteristics**	**Axis VI** **Character**	**Axis VII** **Associated symptoms**	**Axis VIII** **Psychological symptoms**
Chronic Pelvic Pain	Specific disease associated pelvic pain OR Pelvic Pain Syndrome	Urological	Prostate Bladder Scrotal Testicular Epididymal Penile Urethral Post-vasectomy	Suprapubic Inguinal Urethral Penile/ clitoral Perineal Rectal Back Buttocks Thighs	ONSET Acute Chronic ONGOING Sporadic Cyclical Continuous TIME Filling Emptying Immediate post Late post TRIGGER Provoked Spontaneous	Aching Burning Stabbing Electric	UROLOGICAL Frequency Nocturia Hesitance Dysfunctional flow Urge Incontinence GYNAECOLOGICAL Menstrual Menopause GASTROINTESTINAL Constipation Diarrhoea Bloatedness Urge Incontinence NEUROLOGICAL Dysaesthesia Hyperaesthesia Allodynia Hyperalegesie SEXUOLOGICAL Satisfaction Female dyspareunia Sexual avoidance Erectile dysfunction Medication MUSCLE Function impairment Fasciculation CUTANEOUS Trophic changes Sensory changes	ANXIETY About pain or putative cause of pain Catastrophic thinking about pain DEPRESSION Attributed to pain or impact of pain Attributed to other causes Unattributed PTSD SYMPTOMS Re-experiencing Avoidance
		Gynaecological	Vulvar Vestibular Clitoral Endometriosis associated CPPS with cyclical exacerbation Dysmenorrhoea					
		Gastrointestinal	Irritable bowel Chronic anal Intermittent chronic anal					
		Peripheral nerves	Pudendal pain syndrome					
		Sexological	Dyspareunia Pelvic pain with sexual dysfunction					
		Psychological	Any pelvic organ					
		Musculo-skeletal	Pelvic floor muscle Abdominal muscle Spinal					
			Coccyx					

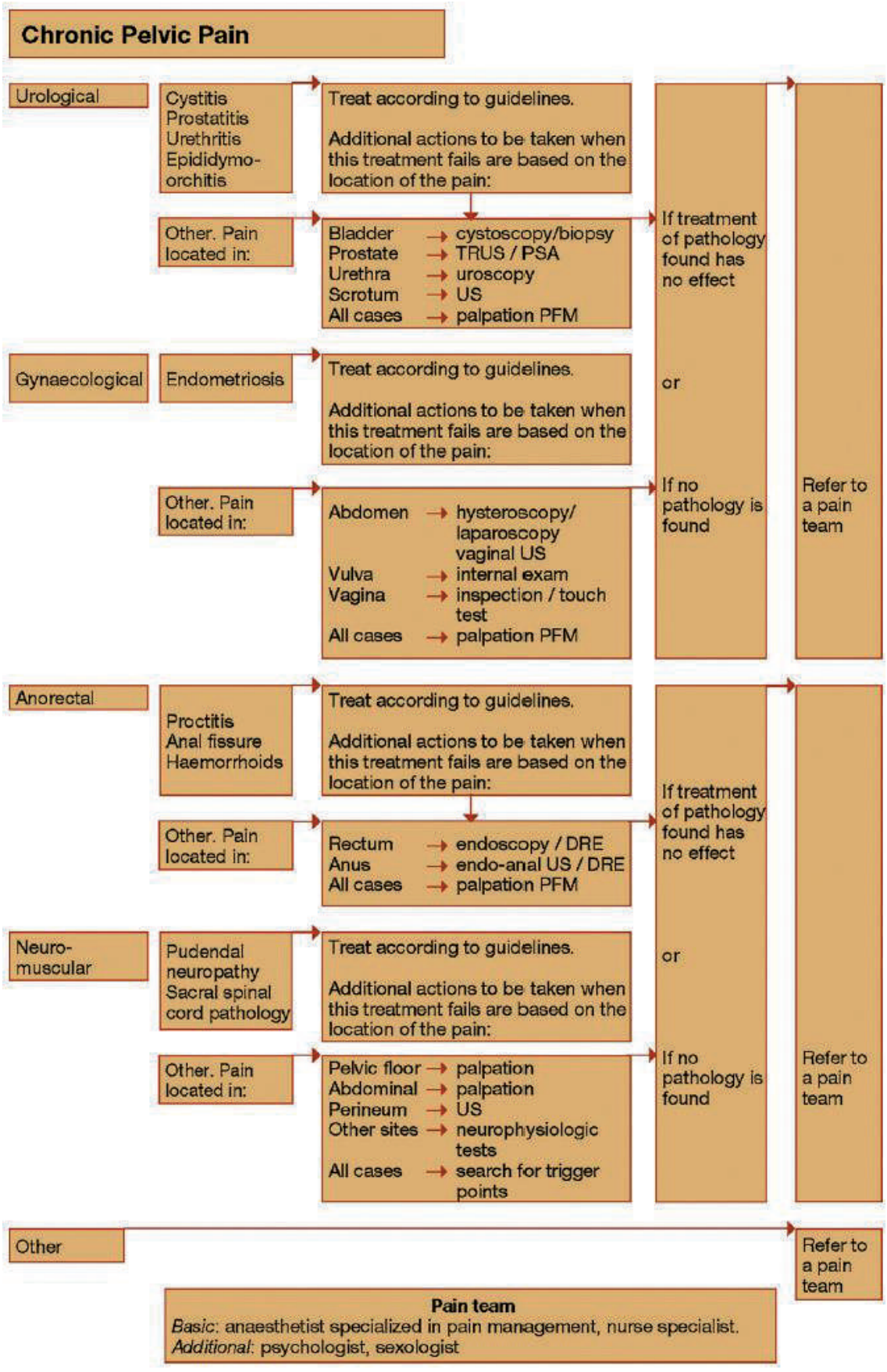

Figure 1. – Algoritm for the diagnosis and treatment of CPP:[46] DRE = digital rectal examination; PSA = prostate-specific antigen; US = ultrasound; PFM = pelvic floor muscle; TRUS = transrectal ultrasound.

Physiopatology of CPPS

Pain in the pelvic region can arise from musculoskeletal, gynecologic, urologic, gastrointestinal, and/or neurological conditions. Such pain can involve both the somatic (T12-S5) and visceral (T10-S5) systems, making the differential diagnosing challenging.[16]

CPP mechanism may involve:

1. Ongoing acute pain mechanisms[19] (such as those associated with inflammation or infection), which may involve somatic or visceral tissue.
2. Chronic pain mechanisms, which especially involve the central nervous system.[20,21]
3. Emotional, cognitive, behavioural and sexual responses and mechanisms.[22-25]

In most cases of CPP, ongoing tissue trauma, inflammation or infection is not present.[26-29] However, recurrent trauma, infection or ongoing inflammation may result in CPP in a small proportion of cases. For this reason the early stages of assessment include looking for these pathologies.[30]

A nociceptive event actives acute pain mechanisms (direct activation of the peripheral nociceptor transducers), but could also generate a sensitisation of the nociceptor transducers, thus magnifying the afferent signalling. There may be activation of the so-called silent afferents. The increased afferent signalling is often a trigger for the chronic pain mechanisms that maintain the perception of pain in the absence of ongoing peripheral pathology.[31,32]

Possible mechanisms by which the peripheral transducers may exhibit an increase in sensibility are:

1. modification of the peripheral tissue, so the transducers become more exposed to peripheral stimulation;
2. increase in the chemicals that stimulate the receptors of the transducers;[33]
3. modifications in the receptors that make them more sensitive.

In general, the first two mechanism lower the threshold of activation of transducers, the third one increases responsiveness to external stimuli.[1]

At the spinal level three processes are involved in central sensitization:

– Changes in existing protein activity (post-translational processing);
– changes in genetic transcription of proteins;
– structural changes in neuron connectivity.

The first process is the earliest (within minutes); the latter two processes may occur within days.[34,35]

The result is that a stimulus produces a magnified evoked response in these neurons.[1]

CPPS is probably manifested as a myofascial pain syndrome with an abnormal tone of the pelvic floor muscles, and a neurological component has become increasingly apparent, associated with dysfunctional effects.[36,37,38] Myofascial dysfunction of the pelvic floor has been implicated in CPP conditions as both a causative and associated factor responsible for pain.[36-40]

Many of the complaints are closely connected to the autonomous nervous system, and the interplay between smooth and cross-striated muscles. Acute and chronic inflammations occurring via the sympathetic endplate might be involved, leading to the endogenous generation of pain via nociceptive nerve endings and receptors. Certain kinds of psychological stress can lead to abnormal electromyographic activity and to myofascial pain syndromes.[41]

Anymore, in the pain syndromes, the role of the nervous system in generating the sensations is thought to be pivotal, but the term "syndrome" indicates that, although peripheral mechanisms may exist, CNS neuromodulation may be more important and systemic associations may occur; "syndrome" takes into account the emotional, cognitive, behavioural, sexual and functional consequences of the chronic pain.[1]

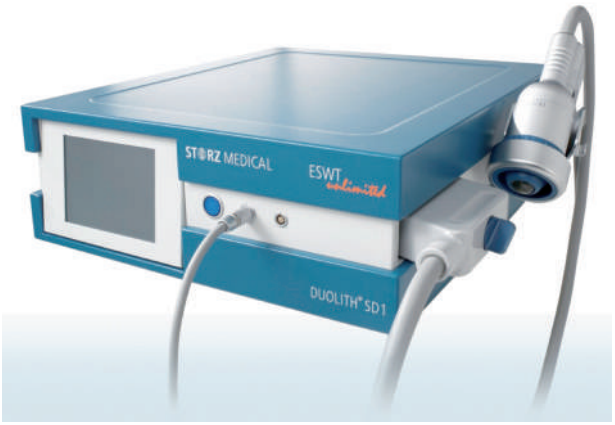

Figure 2. – Duolith SD1 Storz Medical.

Diagnosis of CPPS

Diagnosis of CPPS is based on symptoms and on exclusion of obvious diseases than could cause pain.[42]

The presenting symptoms for many of the known causes of chronic pelvic pain (CPP) are often similar and non-specific, making it difficult to differentiate between causes.[1,2] Chronic infection, inflammation, neuropathy, pelvic floor muscle dysfunction, autoimmune disease, and neurobehavioral disorders are among the postulated etiologies, although no single factor is thought to be the cause.[43]

At any rate, to identify the cause of dysfunction, a systematic approach to examination is essential. Such an approach provides the practitioner the best ability to: (1) appraise relevant historical findings; (2) clinically examine their patients by anatomical region; (3) identify specific mechanical and motor control dysfunctions; (4) determine the level of nervous system sensitization; and (5) evaluate the extent of biopsychosocial involvement in the patient's condition.[16]

While the history may indicate pain from a pelvic source, consideration for referred pain from structures outside the pelvic region should not be overlooked.[1,44]

System investigations should be guided by the medical history and examination to exclude and/or identify end organ pathology.[45] Laboratory, imaging, neurophysiological studies, endoscopy and laparoscopy can help the physician to make a diagnosis.[46]

Fall et al.[46] proposed an algorithm for diagnosis and management of chronic pelvic pain (Figure 1).

Treatment of CPPS

Various drugs are used individually and in various combinations to reduce pain and improve quality of life in patients with CPPS:[1,46] simple analgesics and NSAIDs, opioids, antidepressants, anticonvulsivants, antibiotics, a-receptor blockers, and 5a-reductase inhibitors (5-ARIs). A certain group of patients may benefit from these therapies, but often side-effects may predominate over possible treatment effects, thus minimising the benefit to the patient.[46,47] Other therapeutic options are represented by nerve blocks. Sacral neuromodulation, Botulinum toxin, TENS, trigger-points' massage, electromagnetic treatment, acupuncture, cognitive behavioural therapy, and biofeedback and relaxation training, hyperthermia, and phytotherapy.[43,46,47]

In the latest years some studies have proposed ESWT for treatment of CPPS.[43,47,48,49,50]

Low-energy ESWT could affect CPPS by several mechanisms, such as reducing passive muscle tone, hyperstimulating nociceptors, interrupting the flow of nerve impulses, or influencing the neuroplasticity of the pain memory. Human data for the indication of CPPS are not available for any of these mechanisms. The number of shock waves and the energy level chosen were purely empirical, and many technical questions (eg. the impact of prostate volume) remain unanswered.[47,49]

Despite this limits, this approach might represent an advance in the treatment of CPPS, thanks to its benefits: the possibility of outpatient execution, no need for anaesthesia, lack of side-effects, easy repeatability.[47]

ESWT-associated pain alleviation based on hyperstimulation of nociceptors was intended to interrupt the flow of nerve impulses.[51,52] Furthermore, ESWT-induced revascularization processes can alleviate pain and help to heal tissue.[47,53] The stimulation of microvascularization and reduction in muscle tone after applying SWs is demonstrated.[54]

ESWT possibly influence the neuroplasticity of the 'pain memory'.[48] The prolonged lack of effective pain therapy could lead to a reinforcement of negative impulses (pain) in the brain. Long-term fixation of these impulses could result in the development of a particular pain memory. By minimal pain impulses, ESWT could break through this negative-conditioned pain memory and induce a sort of "reprogramming", resetting the pain.[55] This theory might explain, for example, why it is possible to influence an area of pain located some distance from the treatment locus.[47,48]

The periprostatic pelvic floor muscles are also influenced by the therapy, therefore local muscle relaxation could be causing the disorder improving as the result of a reduction in functional muscle shortening.

Zimmerman et al. supported the hypothesis that the underlying effective mechanisms are not just local alterations, but associated with many factors, because the pain reduction by SWs remained effective over a period of several weeks.[47]

PATIENTS AND METHODS

We treated three women suffering from CPPS with four weekly sessions ESWT with the aim to reduce their pain (all three patients reported a pain intensity 9/10 at NRS). After giving to each patient detailed information about potential benefits and risks of the procedure, treatment was conducted using a standard electromagnetic SW device (DUOLITH SD1, Storz Medical Tägerwilen, Switzerland) (Figure 2), following a protocol based on literature parameters: 3000 focused shock waves, frequency 3 Hz, energy level 0,25 mJ/mm2.[47] Follow-up assessment was carried out one week and eight months after treatment.

All three patients had already tried several common treatment (drugs, infiltrations, anesthetic blockade, sacral neuromodulation, dilatation, acupuncture, supplements) before coming to our attention. Other information about these patients is reported below:

S.M.A., 49 years-old, BMI 23,1, previous appendicectomy, sphincterotomy for anal fissure complicated by abscess, two vaginal deliveries (the first with episiotomy, the second with lacerations), normal intestinal function, regular menstrual cycle. Reported symptoms: intense anal and gluteal pain, lasting for 6 years, absent at night and increasing during the course of the day, worsening during menstrual cycle, associated with anal pricking, daily rectal tenesmus and anxiety. Physical examination, in particular rectal exploration, pointed out tenderness in the region between anus and right ischiatic spine and in correspondence of tendineous centre of perineum. No abdominal, genital and anal alterations were found at physical examination, anoscopy and sigmoidoscopy, except for scars of previous surgery.

P.G., 69 years-old, BMI 18,3, regular intestinal function, previous colecistectomy, surgery for anal fissure, exeresis of an anal polipo, a vaginal delivery, hysterectomy and ovariectomy. Reported symptoms: chronic intense bruising anal pain (mostly during defecation), associated with rectal tenesmus and anxiety.

Physical examination revealed abdominal bloating, painful trigger points of the levator ani, no other perineal, anal, genital abnormalities.

M.Z., 60 years-old, BMI 20,3, regular intestinal function, two vaginal delivery (both with episiotomy), dysmenorrhoea before the first pregnancy, previous appendicectomy, hysterectomy for endometriosis, surgical treatment for crural hernia, exeresis mammary nodule, exeresis pulmonary hamartoma, osteoporosis, laminectomy for lumbar stenosis (L4-L5). Reported symptoms: intense bruising anal and low-back pain, associated with pollachiuria, urgence, vescical tenesmus (rare rectal tenesmus), intestinal bloating, flatulence, anxiety. Physical examination showed abdominal bloating, tenderness in correspondence of coccyx and ischiatic spine, vulvar and vestibular pain, no other perineal, anal, genital abnormalities.

In literature, all studies on ESWT in CPPS describe a perineal approach (patients were supine and the probe was positioned on the perineum). Indeed, we wanted to try a new approach: patients were positioned in lateral decubitus and the probe on the most painful point for half treatment (1500 SW) and then on the gluteal region (at the emergence of pudendal nerve from pelvis both in left then in right part) for the second half treatment (1500 SW), with the intent to interfere with the pudendal nerve transmission.

The pudendal nerve comprises the anterior branches of the ventral rami from S2 to S4. It exits the pelvis through the greater sciatic foramen and reenters the pelvis through the lesser sciatic foramen, passing between the sacrospinous ligament anteriorly and sacrotuberous ligament posteriorly, while wrapping behind the ischial spine. Once in the perineal area, the pudendal nerve travels within the Alcock's (pudendal) canal, a tunnel created by the overlying parietal fascia covering the obturator muscle. The nerve is accompanied by the pudendal artery and, vein, and nerve to the obturator internus through the pudendal canal. The pudendal canal is located on the medial aspect of the obturator internus covered by the obturator fascia. Once the nerve reenters the pelvis it divides into three branches that are named for the structures they innervate.

The first branch of the pudendal nerve, the nerve to the levator ani, arises just proximal to the pudendal canal and supplies motor function to the external anal sphincter and perianal skin. The second branch, also known as the perineal branch, provides sensation to the perineal skin,vaginal tissues,and vestibule, as well as motor fibers to the external urethral sphincter. The third branch innervates the anal sphincters. The pudendal nerve provides sensory innervation to an area defined by the inferior pubic ramus, labio-crural folds, and the intergluteal fold. The pudendal nerve converges on the area of the dorsal horn shared with the cervix, uterosacral, and vulvovaginal area. The pudendal nerve is a mixed sensory and motor nerve, often lending to concurrent motor and sensory symptoms.[16]

RESULTS

In the first case NRS before ESWT was 9/10; at one-week follow up was 9/10; at the 8 months follow-up it was variable from 5/10 (during the day) to 8/10 (in the evening). It was referred that, although pain was intense at certain times of the day, no analgesic drugs were taken.

In the second case NRS before ESWT was 9/10 and did not change at the follow-up assessments. Pharmacological therapy remained the same compared to before treatment.

In the third case NRS before therapy was 9/10 and gradually decreased during the treatment; at one week follow-up NRS was 2/10 and kept the same at 8 months, with no need to assume analgesic drugs.

No adverse effects occurred altogether.

DISCUSSION

Chronic pelvic pain (CPP) is a highly prevalent and debilitating clinical condition with a significant impact on the social, working and family activities of women, negatively affecting their quality of life.

Identifying the pain generators and effectively treating this condition is a formidable challenge and this explains the tendency for pelvic pain to become chronic.[1] Numerous patients face frustration from the inadequate effects of treatment following multiple repeated attempts to cure this disorder. Recently, multi-modal treatment approaches and the utilization of complementary and alternative medicine (CAM) strategies have been suggested as potential treatment options for CP/CPPS.[43]

Some recent studies have suggested the potential role of ESWT within the therapeutic pathway for CPPS. Actually five studies[43,47,48,49,50] on male and just one[56] on female CPPS have been issued in literature. The authors reported promising results of this kind of treatment, with an important reduction of pain and an improved quality of life.

In our experience three women with CPPS have been treated with ESWT, using parameters based on Vahdatpour's work (4 sessions, 3000 SW, 3 Hz, 0,25 mJ/mm2).[50] All three women suffered from intense pain (NRS score pre-treatment 9/10). According to literature, no pain or discomfort was felt by patients (no anaesthesia was required), and no apparent side-effects or complications occurred, suggesting that this therapy is painless, secure and well tolerated.

Results at follow-up assessment were different between the three patients: the first one reported a partial pain reduction (as demonstrated by lower NRS score in some hours of the day and suspension of pharmacologic therapy), the second one had no effect from ESWT, while the third one obtained an important improvement of her pain (NRS score post-treatment 2/10).

It would take a wider sample to obtain meaningful data, just three cases are too few. Thus we formulated some assumptions about the possible reasons of such different effects: the pain in the three patients could have a different origin and mechanism (let think about the variability in patients' histories), therefore a same therapy could be effective in some cases but not in other; the parameters used (determined empirically) were maybe inadequate for at least one of the three patients, that means that therapy should be customized on patient; besides 4 sessions could be too few to obtain a significant result, in fact in other experiences until 11 sessions were given; the original transgluteal approach, that was thought to have the effect of modulate the transmission of the pudendal nerve, could be more effective than the classic perineal one in some patients but not in all of them, probably because in "non-responders" the pudendal nerve is not heavily involved in the pain mechanisms, but pain originates in other anatomical structures, such as muscles or bowels.

CONCLUSIONS

CPPS is a frequent condition, often associated with negative cognitive, behavioral, sexual or emotional consequences, compromising the quality of life. Between various therapeutic approaches, most of the time ineffective, ESWT represents a new promising treatment for CPPS: it is simple (it is an outpatient procedure), non-invasive, painless (it does not require anaesthesia), well tolerated, apparently secure. Although our results are discordant, some studies in literature report benefits of this treatment in patients with CPPS (both males and females). It means that some effect of ESWT on CPPS exists, but more studies are needed to discover the mechanisms through which ESWT acts on the pain and to define the optimal parameters and the better approach to use in clinical practice

DISCLOSURES

The Authors declare that there are no conflicts of interest.

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