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Chronic Pelvic Pain Syndrome, General Conservative and Medical Management and Palmitoylethanolamide (PEA) Efficacy

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ABSTRACT

Chronic pelvic pain syndrome is a condition of pelvic and perineal pain, not releated to other known pathologies, that lasts more than three months.

It is a disease that influences a lot people's quality of life.

Currently there are several types of management, including conservative, medical and surgical approaches.

About medical therapy the management with phytotherapics has shown a good efficacy on pain reduction, in particular palmitoylethanolamide (PEA) has demonstrated to have a role for its anti-inflammatory and analgesic properties.

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Introduction

Chronic Pelvic Pain Syndrome (CPPS)

Pain is referred to as negative sensory experience associated with the potential or real presence of tissue damage. Currently clinical research have indicated that in addition to the peripheral-end-organ mechanisms, such as inflammatory or infective conditions there are many mechanisms based within the central nervous system (CNS). Although infection or other peripheral stimulus may initiate the start of a CPPS condition, this condition may become self-perpetuating as a result of CNS modulation [1].

Chronic pain seriously affect the quality of people's social, family, and working lives in all the world [2].

CPPS is characterized by a history of pelvic and perineal pain lasting more than 3 months in absence of other recognizable underlying diseases.

Risk Factors for Chronic Pelvic Pain

Risk factors include recurrent physical trauma, genetic, psychological and endocrine factors.
Increased susceptibility to stress is thought to be in part due to increased corticotrophin-releasing hormone (CRH).

There is evidence that the sex hormones also modulate both nociception and pain perception. Stress can also induce long-term biological changes which may be related to chronic pain syndromes [3].

Genetics also play a role in assessing the risk of developing chronic pain. [4].

There is some evidence for a specific relationship between fibromyalgia, functional gastrointestinal disorders and CPPPS [5]; Another association was found between patients who have experienced physical or sexual abuse and pelvic pain [6, 7].

Processes Underlying Chronic Pelvic Pain

-Acute inflammation or infection which may involve somatic or visceral tissue: Although a peripheral stimulus such as infection may initiate the start of a CPPPS condition, the condition may become self-perpetuating as a result of central nervous system modulation.
-Chronic pain mechanisms, which involve the central nervous system. [8]
-Cognitive, psychological and emotional mechanisms: Each individual phenomenon needs to be addressed in its own right through multi-specialty and multi-disciplinary care [9, 10].
Chronic pain mechanisms may include altered resting state neuromotor connectivity, for example in men with chronic prostatitis/CPPPS [11].

Relation of Pelvic Pain and Musculo-Skeletal System Alterations
Trigger points may be implicated as a source of urogenital pain syndromes.

Inflammation of the ligaments and tendons to the bones (enthesitis) and of the bursa (bursitis) may be trigger points of chronic pelvic pains syndrome [12, 13]. Stress can be a trigger for the onset of pelvic myalgia and also a maintenance factor.

Diagnosis of Chronic Pelvic Pain Syndrome
General Evaluation
It is important the history and physical evaluation of the patient in order to assess the pain in the region of the pelvis and perineum and the absence of other pathologies (such as bacterial infection, cancer and other primary anatomical or functional diseases) for a minimum of three months.

Assessment of the psychological state to possibly find problems such as anxiety, depression.

Urological symptoms can be releated with pain so it is important to pay attention to the influence of micturition on the pain's experience.

Primary Prostate Pain Syndrome
Primary prostate pain syndrome is diagnosed from a history of pain in the region of the prostate , but often reported in other pelvic areas outside the prostate such as perineum, rectum, penis, testicles and abdomen for a minimum of three months in absence of other LUTS [14].

Primary Bladder Pain Syndrome
Primary bladder pain syndrome is the term that replaced "Interstitial cystitis" and is used to define a disease diagnosed based on pain, or feeling of pressure or discomfort releated with the urinary bladder, associated by at least one other symptom, such as pollakiuria, nocturia, and after the exclusion of other diseases as the cause of symptoms, also using cystoscopy if necessary [15].

It is important to investigate gynaecological aspects such as menstrual problems, vaginal discharge, story of gynaecological pelvic surgery and gastrointestinal aspects such as pain related to their bowel habits, or to defecation, to possibly assess criteria for primary chronic anal pain syndrome (chronic proctalgia), fissure, haemorrhoids [16].

Management
In most cases the management must be multifactorial and personalised, including self-management, psychology, physioterapy, drugs and more invasive treatments.

The conservative management includes pain education of the patient and also physiotherapist approach [17].

The physiotherapist plays an important role on pelvic floor iperactivity management. For patients with chronic pelvic pain and dysfunction of the pelvic floor muscles, it is important to relax the muscles, breaking the circle of pain-spasm-pain.

It could be also important to treat sexual dysfunctions releated to chronic pelvic pain [18].

Medical Management
Drugs
The non-steroidal anti-inflammatory agents (NSAIDs), in particular a trial with colecoxib reported a reduction in pain but limited to the duration of the therapy [19].

The α-blockers has demonstrated a role in the reduction of Primary Prostate Pain Syndrome (PPPS) [20] [21].

The antibiotics in long term protocols, such as the class of fluoroquinolones also gave good results in PPPS management [22].

Tricyclic antidepressant such as amitriptyline, immunosuppressants such as azathioprine have proven effective for Primary Bladder Pain Syndrome (PBPS/IC) [23].

In the treatment of PBPS the intravescical treatments with local anaesthetics such as intravesical lidocaine , but also Hyaluronic acid and chondroitin sulphate intravescical have shown a relief from painful symptomatology releated to PBPS [24] [25].

Phytotherapy
Phytotherapy seems to be a good option for the management of chronic pelvic pain also due the low rate of side effects.

For example flower pollen extract compounds have shown to reduce pain and symptoms releated to PPPS [26].

Palmitoylethanolamide (PEA)
Palmitoylethanolamide (PEA) is an andogenous fatty acid amide-signaling cannabinoid that, among the phytotherapeutic options, has demonstrated to be a good choice for chronic pelvic pain thanks to its anti-inflammatory and analgesic characteristics which also include action on the neuropathic pathway [27, 28].

In a case presentation it was shown the efficacy of a PEA approach for a pain due to a metastatic prostate cancer with a regimen of PEA 600 mg twice daily. In the same case series another case presentation showed a successful therapy with PEA using the same protocol as in the previous case for an old girl with pelvic pain related to a vaginal lichen sclerosis [29].

A compound based on a micronized-palmitoylethanolamide (400 mg) and polydatin (40 mg), administered twice daily, demonstrated a significant pain relief ($p<0,0001$) in 32 patients suffering from interstitial cystitis/bladder pain syndrome (IC/BPS) and a significant storage symptoms reduction ($p=0,013$), evaluated with the PUF questionnaire, after two months of treatment [30].

A case study which investigated the efficacy of a PEA and magnesium based product in patients suffering from pelvic pain due to several urological diseases proved a significant reduction of pelvic pain of about five points of VAS scale (Visual Analogue Scale) after 1 month of therapy ($p<0,001$) (Figure 1) and of about six points of VAS scale after three months protocol ($p-<0,001$) (Figure 2). Moreover it was reported a significant improvement of the Quality of life after 1 and 3 months of treatment. In this manuscript the protocol used consisted of PEA 1200 mg plus Magnesium 140 mg once daily for twenty-eight days and PEA 600 mg plus Magnesium 70 mg once daily for other fifty-eight days [31].

Both of the studies mentioned above showed a good safety profile of PEA.

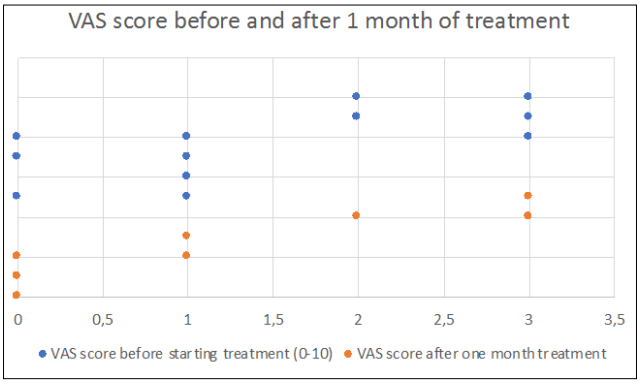

Figure 1: VAS Score Reduction after 1 Month of Treatment with PEA Plus Magnesium Compound

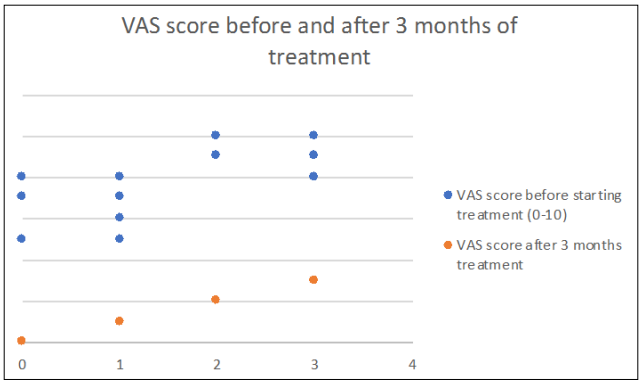

Figure 2: VAS Score Reduction after 3 Months of Treatment with PEA Plus Magnesium Compound

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