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Commentary

Chronic Pelvic Pain in Women: Sharing Interdisciplinary Experience

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INTRODUCTION

Chronic pelvic pain (CPP) is a common, burdensome, and costly condition that disproportionately affects women. Touching an estimated more than 20% of people worldwide or approximately 1 in 7 women,¹ CPP is a common problem. In one study of reproductive-aged women in primary care practices, the reported prevalence rate of pelvic pain was 39%.² Of all referrals to gynecologists, 10% are for pelvic pain.³

Ten percent (10%) of the world's population - approximately 60 million people - endure chronic pain⁴ and fairly reliable estimates in individual countries and regions indicate chronic pain prevalence closer to 20-25%.^{5,6} Primary care facilities in Asia, Africa, Europe, and in the Americas have patients reporting persistent pain prevalence of 10-25%. Consistent estimates of chronic pain prevalence in the U.S. range from 12-25%, and a prevalence of 20% has been noted in Europe.⁷ The World Health Organization (WHO) has estimated that as many as 1 in 10 adult individuals are newly diagnosed with chronic pain each year.⁸

Chronic pelvic pain differs from acute pelvic pain in several important ways. Acute pain typically arises from an inflammatory, infectious, or anoxic event or traumatic injury that resolves over time with treatment and recovery. When pain persists, a chronic stress phenotype may emerge and is characterized by a vicious cycle of physical and psychological consequences. Prolonged activity restriction can lead to physical deconditioning. Continued fear, anxiety, and distress can lead to long-term psychosomatic deterioration and social isolation. Although mood symptoms are ubiquitous in chronic pain syndromes, criteria for major depression are met in approximately 12-33% of women across samples of women living with or seeking care for CPP.

Diagnosis and initial management of CPP in women are within the operative scope of specialists mainly in obstetrics

and gynecology. In reality, the complexity of the muscular and osteopathic structures and pelvis innervation with the anatomical proximity of pelvic viscera means this condition frequently overlaps traditional medical specialties and could benefit from complementary medicine such as osteopathy, physiotherapy, or traditional Chinese medicine. A multidisciplinary approach which includes complementary and alternative medicine techniques in managing CPP in women seems to yield the best results.⁹ Although very few of these approaches have been evaluated in formal clinical trials so far, they have much to offer to those with chronic pain in terms of enhancing quality of life and pain-related coping, as well as reducing disability and pain-related interference with functioning.

CHRONIC PELVIC PAIN

Because CPP is often multifactorial, most patients will have multiple pain generators and comorbid conditions. Although many conditions are associated with CPP, determining how pain changes with sexual activity, menstruation, urination, and defecation is a good starting point. Patients often focus on visceral etiologies, yet neuromuscular issues such as myofascial trigger points may be more common and are often overlooked.⁹ Single-digit or swab palpation for tenderness of pelvic floor muscles, or palpation of the abdomen and the lower back, including the sacroiliac joints that generates pain can identify possible neuromuscular conditions. In one small study, pelvic floor muscle tenderness or a positive flexion, abduction, and external rotation test identified 85% of patients with chronic neuromuscular pelvic pain. Other clinical signs were statistically significantly associated with long-term pelvic chronic pain in women: these include suicidal risk, alcoholism, smoking, psychotropic drug use, psychosomatic and sleep disorders, post-traumatic stress disorder, vaginal discharge, pelvic pain, sexual disorders, diarrhea and chest pain.

A detailed medical history and physical examination, with particular attention to the abdominal and pelvic neuro musculo-

skeletal examination, are recommended for the evaluation of CPP. Subtle physical sensitivity that increase the likelihood of neuro musculoskeletal contributors to CPP include pelvic floor muscle tenderness and abdominal wall tenderness that stimulate a reaction of pain in the patient.

Psychosocial factors play a role in all types of pain and can affect symptom severity and prognosis. Pelvic pain and dyspareunia are more prevalent in women with a history of abuse, mental illness, lack of support, social stressors, and relationship discord. These comorbidities do not alter the visceral or neuro musculoskeletal pain generators but may worsen the associated symptom burden and psychological effects. Treating psychosocial factors as separate but equally important pain contributors can increase the woman's awareness of her conscious and unconscious perception of pain and facilitate her recovery. Female genital mutilations should not be forgotten during the process of diagnosis and treatment.

As follows, CPP should receive greater attention as a global health care priority for women, particularly in developing countries. In order to be able to provide adequate, inexpensive care and treatment for this condition, pain management must be recognized as a human right, and access to this care for vulnerable populations must be a priority. All health care systems must engage in their obligation to provide this access to all women.

The non-exhaustive list of pelvic pain disorders encompasses many conditions: dyspareunia, cystalgia, bladder hyperexcitability, coccygodynia, dysmenorrhea and hypofertility, interstitial cystitis, vulvodinia, endometriosis, pelvic floor tension, sacral pain, lumbar pain, inter-discal pain, abdominal pain, with associated symptoms such as insomnia, headaches, nausea, and gastro-intestinal dysfunctions, trauma (e.g. secondary to vaginal delivery), surgery (e.g. any abdominal wall incision including caesarean section), pelvic floor muscle pain syndrome, vaginal muscle spasms, neuralgia from nerve entrapment or irritation, pain arising from the lower part of the spine (e.g. from sprains, strains, fractures, degenerative disease, disc lesions), sacroiliac joint dysfunction, symphysis pubis dysfunction, coccygeal pain, piriformis syndrome, myofascial pain syndrome, and abdominal migraines.

RECOMMENDATIONS

The main recommendations for the management of pelvic pain vary from woman to woman depending on her personal life story. Recommendations are often based on listening to and understanding the needs of women with this complex condition. The time required to treat these women varies according to the time spent on clinical evaluation and the means available to physicians for their treatment. The cost of the consultation also rests a choice to be made regarding the spectrum of the general clinical evaluation and the orientations granted according to the location of the pathology. The total cost of care will differ from one country to another depending on the level of training of the caregivers and the treatments available. Practical assessment of pain levels measured by type, myofascial pain, medications and surgical interven-

tions, principles of opioid management, increased use of magnetic resonance imaging (MRI), documentation of the extent of disease seen through surgery, non-conventional therapies (acupuncture, osteopathy, pelvic reduction through electrostimulation), access to multidisciplinary models of care with components of physiotherapy, posturology, psychological and psychiatric care for trauma, in conjunction with other medical disciplines, such as gynecology and anesthesia also play a significant role in the causal orientation of this type of pathology.

CONCLUSION

The organization Formations Sans Frontières-International Health Care Education¹⁰ has been working since 2004 to sensitize health authorities as well as national and local associations to promote training in sexual and reproductive health.

Considering broad measures in favor of the creation of multidisciplinary teams through advanced training of health professionals in its sectors strengthens local capacities to ensure the management of this pathology.

The evidence-based literature on the treatment of CPP remains limited. The majority of treatments are too often focused on symptomatic pain relief, due to a lack of multidisciplinary working capacity of health care providers and financial resources for training and treatment. The approach to the treatment of chronic pelvic diseases should be focused on the pathology and the history of the person, taking into consideration the co-morbidity factors of the individual in their medical history and life circumstances. If, however, the origin of the pelvic pain remains unknown, it is recommended that the patient undergo further evaluation with alternative approaches such as osteopathy, traditional Chinese medicine, yoga, breathing exercises, hypnosis, and eye movement desensitization and reprocessing (EMDR) – especially if the case may be traumatic, following rape and/or abusive touching that is often perpetuated (and/or unspoken) during medical consultations.

Multidisciplinary management of chronic pain should be offered to women with CPP within the public health care system of each country. The strengthening of training programs for health care providers should be systematically considered in health care centers and should systematically include a program in medical and paramedical universities. Raising women's awareness from an early age through sex education campaigns in school programs is also essential to increasing early detection and improving treatment of this condition and to apply preventive measures such as training in posture, hygiene, exercise and breathing.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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Commentary

The Preventive Effect of Dietary Antioxidants on Viral Infection (Coronavirus Disease-2019, Influenza and Human Papillomavirus) and the Development of Cervical Carcinogenesis

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Viral infections cause the production of radicals and reactive oxygen species (ROS) in cells. Disbalance between ROS generation and elimination results in oxidative stress. Oxidative stress plays an important role in pathogenesis.¹ Thus, oxidative processes cause virus replication in infected cells, decrease cell proliferation and induce cell apoptosis,² leading to chain reactions and subsequently damaging the cells of organisms.³ In contrast, an antioxidant is any substance that significantly inhibits or delays the oxidation of a substance.⁴ The role of antioxidants is also to complete chain reactions and prevent the damage of cellular components due to free radicals and associated chemical reactions.^{3,4} Beck also insisted that the antioxidant selenoenzyme, glutathione peroxidase-1, was found to be critically important, as glutathione peroxidase knockout mice developed myocarditis, when infected with a benign strain of myocarditis.⁵ This work points to the importance of host nutrition in not only optimizing the host immune response, but also preventing viral mutations that could increase viral pathogenesis.

Coronaviruses (CoVs) are single-stranded ribonucleic acid (RNA) viruses which cause respiratory, gastrointestinal, hepatic and neurologic disease.⁶ Above all, coronavirus disease-2019 (COVID-19) disease began to spread from Wuhan, China, in December 2019.^{7,8} On March 11, 2020, the World Health Organization (WHO) announced the world wide COVID-19 pandemic only 2-months after the official disclosure from the Chinese government. Oxidative stress and lipid oxidation are involved in the pathogenesis of COVID-19-related pulmonary damage.⁹

Curcumin, a polyphenol (one of antioxidants), has been shown to target multiple signaling molecules while also demonstrating activity at the cellular level, which has helped to support its multiple health benefits.¹⁰ Moreover, curcumin has been reported to bind to severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2); the virus that causes COVID-19 target receptor.¹¹ Curcumin could therefore be a potential treatment option for patients with COVID-19.¹² In addition, it has been reported that the combination of vitamin C, curcumin and glycyrrhizic acid, promotes the production of interferons and regulates the inflammatory response, suggesting that the combination of these compounds may be useful in modulating the immune response to counteract the SARS-CoV-2 infections.¹³ Vitamin D induces cathelicidins and defensins which can lower viral replication rates and reduce concentrations of pro-inflammatory cytokines, which produce the inflammation that injures the lining of the lungs, leading to pneumonia, as well as increase the concentrations of anti-inflammatory cytokines can also reduce risk of infection.¹⁴ Therefore, vitamin D can reduce risk of viral infection. Grant et al¹⁴ suggested that vitamin D supplementation may decrease the risk of contracting influenza and COVID-19 infections. In a nutritional protocol for COVID-19 patients, the supplementation of 25-hydroxyvitamin D (25(OH)D) is planned.¹⁵

De Alencar et al¹⁶ reported a double-blind, randomized, placebo-controlled trial with N-acetylcysteine (NAC) as an antioxidant for the treatment of severe acute respiratory syndrome caused by COVID-19. However, no difference was observed in secondary endpoints between 67 patients in the placebo group and

68 patients in the NAC group. Thus, the administration of NAC in high doses did not affect the evolution of severe COVID-19.

It has been reported that influenza virus (IV) infection also leads to the induction of oxidative stress or ROS damage and the development of the clinical outcome.¹⁷ Mouse models and cell lines infected with IVs showed the enhanced ROS levels, together with an imbalance of antioxidant protection.^{18,19} These models indicated the relevance of the redox homeostasis induced by IVs.²⁰ During IV infection, the cellular metabolism of the host cells could be affected, leading to the dysregulation of redox homeostasis. Antioxidant therapies have been proposed to decrease the viral load and counteract the lung injuries caused by the overproduction of ROS induced by viruses.²¹ Some antioxidants are effective in this protection against infection through the nuclear erythroid 2-related factor 2 (Nrf2) pathway.²² However, the direct clinical use of antioxidant drugs for IV-infected patients has never been reported.

Persistent infection by high-risk human papillomavirus (HPV) types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 and 68) genotypes has been recognized as a necessary step in the development, maintenance, and progression of cervical intraepithelial neoplasia (CIN) and cervical cancer.²³

HPV is a small, non-enveloped deoxyribonucleic acid (DNA) virus that infects the skin or vaginal mucosal cells.²⁴ The circular, double-stranded viral genome is approximately 8-kb in length.

During recent decades, the important role of antioxidants in preventing the development of cervical carcinogenesis has been received much attention.^{25,26} Antioxidants can act as efficient scavengers of free radicals and oxidants to prevent free-radical damage to DNA.²⁷ Moreover, if free radicals and oxidants are not neutralized by antioxidant molecules, the inflammatory processes caused by HPV infection could lead to extensive damage to DNA proteins.²⁸ The major product of DNA oxidation is also correlated with increased HPV infection, viral-host integration, and the development of dysplasia.²⁹ Thus, apoptosis is hindered by the disruption of many regulator pathways, which results in altered cellular proliferation.³⁰

Different antioxidants may have differing abilities to intervene in the natural history of cervical diseases associated with HPV infection. The intake of carotenoids may inhibit early events of cervical cancer development (HPV infection).^{31,32} The intake of vitamin A and D may also inhibit early events (from HPV infection to the development of CIN 1).³³⁻³⁶ The intake of folate was reported to potentially inhibit the events from HPV infection to the development of various grades of CIN.³⁷⁻³⁹ Furthermore, the intake of vitamin C and E may widely inhibit cervical cancer development (from HPV infection to the development of CIN 1, 2 and 3, as well as cervical cancer).^{23,40-42} However, the intake of antioxidants cannot inhibit cervical cancer development without chemotherapy and radiation therapy.²⁶

We suggest that the intake of antioxidants may prevent both RNA and DNA virus infection and persistent infection. However, we do not consider them to be sufficiently effective for the treatment of advanced stage disease.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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