Chronic Pelvic Pain

AN INTEGRATIVE APPROACH

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Chronic pelvic pain (CPP) is characterised as pain perceived in the pelvic area, occurring for at least six months duration, irrespecrive of both menstruation and intercourse. CPP may affect both genders, however, it primarily occurs in women. Globally, up to 26% of women experience CPP for greater than a one-year duration.[1]

CPP is usually non-gynaecological[2] with no pelvic disease identified in approximately ONE THIRD of individuals.[3]

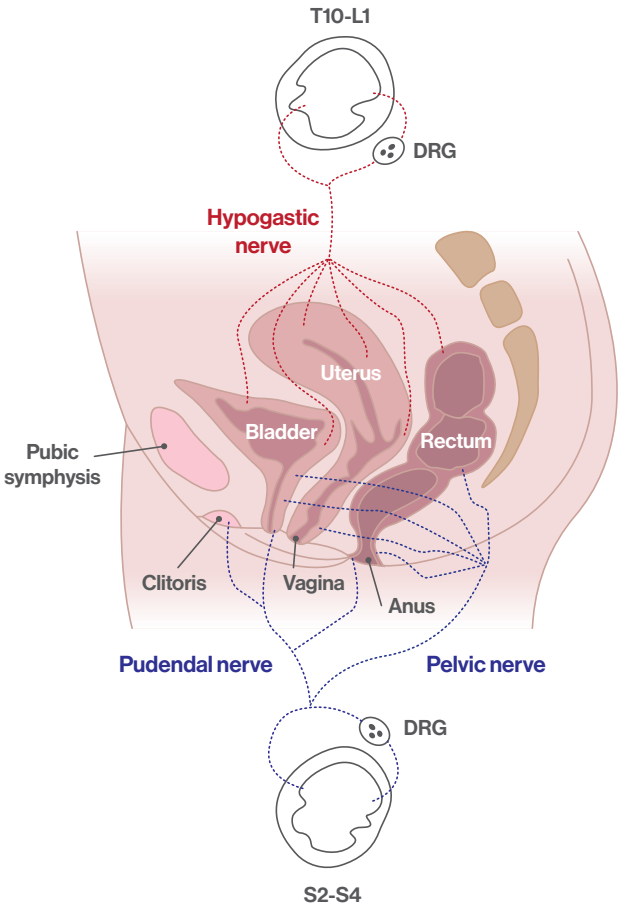
Pain may originate from any of the urogynecological, gastrointestinal, pelvic, musculoskeletal, neurological, and/or psychological systems - highlighting that a single-organ pathological approach should be avoided. As with most pain conditions, CPP negatively impacts quality of life and is associated with an increased risk of depression and anxiety, as well as a decrease in sexual satisfaction.[4]

CPP comorbidities

CPP is commonly associated with several conditions including Irritable bowel syndrome (IBS), endometriosis, and bladder pain syndrome. Often these conditions coexist because of the neuroanatomy of the pelvis. Sensory information from organs within the pelvis such as the rectum, bladder, and vagina converge on the same spinal cord neural circuits resulting in neural cross-sensitisation (see Figure 1).[5] For example, there is a two-fold increased risk of IBS in women with endometriosis compared to women without.[6]

- 1 in 5 in individuals with CPP has IBS
- 1 in 5 individuals with CPP has interstitial cystitis
- 1 in 5 individuals with CPP has depression

Figure 1. Neuroanatomy and nerve supply of the pelvis



Pelvic pain sensations can influence any of the closely related pelvic structures due to the innervation of the pelvic organs

Figure adapted from: Origoni M, et al. Neurobiological mechanisms of pelvic pain. Biomed Res Int. 2014; 903848

Dysfunctional processing of pain and sensory information can contribute to the development of CPP resulting in a continuous and amplified pain signal being transmitted to the pelvis, often despite injury or inflammation.[7]

Central Sensitisation: Faulty pain signalling system in CPP

This may occur due to prolonged stimulation of nociceptors leading to mild stimuli being interpreted as painful (hyperalgesia). Holistic management of CPP encompasses a biopsychosocial model that understands that in many cases CPP lacks a somatic driver and may instead be generated by the brain and spinal cord (see Table 1).

Etiopathogenesis

Biological mechanisms underpinning CPP are multifaceted and include inflammatory, nociceptive, neuropathic, and psychogenic factors. Underlying pathophysiology involves a complex interplay between hormones, activated mast cells, inflammatory cytokines, neurotransmitters, endocannabinoids, as well as pro-inflammatory and nociceptive mediators such as substance P and nerve growth factor (NGF).[8]

Endocrine-Neurological-Immune interactions

Prolonged stress has been shown to worsen CPP, and women with CPP may show alterations in normal HPA axis function.[9] Disturbances in the neuroendocrine system may lead to activation of inflammatory cytokines and upregulation of corticotrophin releasing hormone expressed on mast cells with subsequent release of neuropeptides that promote central sensitisation. Approximately 50% of women with CPP report a history of sexual, physical, or emotional trauma and one-third are positive for Post Traumatic Stress Disorder (PTSD). Practitioners should be aware of applying a trauma-centred approach to care.[10]

Table 1: Endocrine-Immune-Neurological Pain Interactions in CPP

Oestrogen[8]
- May be dysregulated in CPP
- Oestrogen dominance = ⬆ activated mast cells
- Oestrogen dominance enhances production of Nerve Growth Factor (mediates pain)

Activated mast cells[8]
- Release histamine and serotonin = vasodilation and inflammation
- Stimulate afferent somatosensory fibres to promote central sensitisation and shift to chronic and neuropathic pain

Nerve growth factor[8]
- Released by mast cells
- Functions to ⬆ pain receptors
- Increases production of substance P

Substance P and Calcitonin gene-related peptide
- Neuropeptides responsible for the development of neurogenic inflammation in the pelvis[11]
- Activate mast cells[12]

SUPPLEMENTATION

Palmitoylethanolamide (PEA)

PEA appears to work on the mast cell-glial axis and has shown efficacy in several CPP based conditions (see Table 2). PEA may work for CPP via multiple mechanisms including reducing inflammation, down-regulating mast cell hyperactivity, and decreasing NGF release from nerve cells, thus reducing associated hyperalgesia and allodynia (see Table 2).

Quercetin

Quercetin has been shown to reduce CPP in men, and CPP associated with endometriosis in women. Quercetin demonstrates anti-inflammatory potential however, *in vitro* studies reveal it may also reduce neuropathic pain via its ability to stabilise mast cells[16] making it a useful option for CPP.

Table 2: PEA efficacy in a number of CPP based conditions

CONDITION	DOSAGE	OUTCOME
Interstitial Cystitis/ Bladder Pain Syndrome[13] 6 months, n= 32 Pilot, open-label study	• 400 mg m-PEA plus 40 mg polydatin twice daily for 3 months followed by once daily for 3 months	⬇ Pain intensity ⬇ Severity of symptoms ⬇ Cystitis ⬇ Decreased urinary frequency
Vestibulodynia[14] 60 days, n= 20 RCT	• 400 mg PEA + 40 mg transpolydatin or placebo, twice daily for 60 days with TENS machine support	⬇ Pain with intercourse ⬇ Overall pain
Endometriosis[15] 90 days, n=30 Pilot, open-label study	• um-PEA twice daily for 10 days followed by m(PEA/PLD) twice daily for 80 days	⬇ Pain intensity ⬇ Deep dyspareunia ⬇ Dysmenorrhea ⬇ Dyschezia

Vitamin D

While no studies have been conducted specifically for CPP, vitamin D has been shown to assist with reducing chronic pain in a range of conditions including dysmenorrhea.[17,18,19] This may be via multiple mechanisms including reducing inflammation and influencing peripheral and parasympathetic nerve function[20] highlighting its role for CPP.

Saffron (*Crocus sativus*)

Antidepressants are often prescribed for the management of CPP and may function by modifying neural mechanisms of pain. This application provides a rationale for the use of herbal medicines such as saffron which demonstrates antinociceptive, analgesic, and neuroprotective properties. While no specific studies have been undertaken in CPP, saffron has been shown to reduce pain in dysmenorrhea, fibromyalgia, rheumatoid arthritis, and peripheral neuropathy.[21] Saffron should be considered as an option for managing CPP as well as comorbid depression.

Anti-Inflammatories - Ginger (*Zingiber officinalis*), Curcumin (*Curcuma longa*), and Specialised Pro-Resolving Mediators (SPMs)

Toll-like receptor 4 activation plays a role in increasing inflammatory pain in CPP.[22] Anti-inflammatory and immune regulating therapeutics such as Ginger, Curcumin and SPMs may be considered for the management of CPP.

LIFESTYLE

Cognitive Behavioural Therapy (CBT)

Neuroimaging of women with CPP reveals that the brain undergoes changes in morphology in response to constant pelvic pain, specifically loss of grey matter volume in regions involved in pain processing.[23] Interestingly, CBT interventions have been shown to increase grey matter volume in areas associated with reducing pain catastrophising and thus may be a useful adjuvant treatment strategy for managing CPP.

Yoga

Reduction in pain severity, improvements in emotional well-being, and sexual function were observed after 6 weeks of Iyengar-based yoga therapy in women with CPP.[24] A possible mechanism of action in reducing CPP includes the ability of yoga to increase brain derived neurotrophic factor (BDNF), promoting neuroplasticity and modifying the stress response.[25]

Tens Machine

Transcutaneous electrical nerve stimulation (TENS) with a pulse duration of 50-400 µs, at a frequency of 2-120 Hz may mildly reduce CPP[26] and could be considered as an in-home strategy to manage CCP.

ACTION PLAN: CHRONIC PELVIC PAIN

- **Practitioners to view CPP** through a biopsychosocial model
- **Consider trauma history** and apply trauma informed care
- **Reduce nociceptive pain** Consider key ingredients such as saffron, PEA, and quercetin
- **Reduce inflammatory pain** SPMs, ginger, curcumin, and quercetin

PLUS:

- **TENS machine** 20 mins/day
- **Yoga** daily 1 hour/day
- **Support HPA axis:** sleep, physical activity, mindfulness, adaptogens, magnesium, and B vitamins
- **Referrals/collaborations:** Psychologist (CBT), Women's Health/ Pelvic Floor Physiotherapist

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