ORIGINAL ARTICLE

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Pharmacological treatment and regional anesthesia techniques for pain management after completion of both conservative and surgical treatment of endometriosis and pelvic adhesions in women with chronic pelvic pain as a mandated treatment strategy

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Abstract

Introduction. Chronic pelvic pain syndrome occurs in 4–14% of women. Pain pathomechanism in this syndrome is complex, as it is common to observe the features of nociceptive, inflammatory, neuropathic and psychogenic pain. The common findings in women with pelvic pain are endometriosis and pelvic adhesions.

Objective. Aim of the study was to test the effectiveness of pharmacological treatment and regional anesthesia techniques for pain control as the next step of treatment after the lack of clinical results of surgical and pharmacological methods normally used in the management of endometriosis and pelvic adhesions.

Materials and method. 18 women were treated between January 2010 – October 2013 in the Pain Clinic of the Department of Anaesthesiology and Intensive Care at the Centre for Postgraduate Education in Warsaw due to chronic pelvic pain syndrome related to either endometriosis or pelvic adhesions. During the previous step of management, both conservative and surgical treatments were completed without achieving satisfactory results. Initial constant pain severity was 3–9 points on the Numeric Rating Scale, while the reported paroxysmal pain level was 7–10. The pharmacological treatment implemented was based on oral gabapentinoids and antidepressants, aided by neurolytic block of ganglion of Walther, pudendal nerve blocks and topical treatment (5% lidocaine, 10% amitriptyline, 10% gabapentin).

Results. In 17 women, a significant reduction of both constant and paroxysmal pain was achieved, of which complete and permanent cessation of pain occurred in 6 cases. One patient experienced no improvement in the severity of her symptoms.

Conclusions. The combination of pain management with pharmacological treatment, pudendal nerve blocks, neurolysis of ganglion impar (Walther) and topical preparations in cases of chronic pelvic pain syndrome seems to be adequate medical conduct after failed or otherwise ineffective causative therapy.

Key words

chronic pelvic pain syndrome, endometriosis, pelvic adhesions, amitriptyline, gabapentin, pudendal nerve block, ganglion of Walther

INTRODUCTION

Pelvic pain is a symptom, but when it becomes a substance of the disease, chronic pelvic pain syndrome (CPPS) becomes the appropriate nomenclature for this clinical feature. According to its definition, CPPS is a syndrome characterized by the presence of chronic pain localized in the lower abdomen and lasting for more than 6 months, which may be accompanied by pain in periumbilical, epigastric, sacral and perineal area, as well as in lower extremities [1]. Its risk factors include: age, history of physical and/or sexual abuse, pelvic inflammatory disease (PID), endometriosis, history of obstetric and gynecological interventions, gastrointestinal surgery, analgesics, alcohol abuse and depressive disorders. The common features of CPPS are: dysmenorrhea, dyspareunia, concomitant GI symptoms, depression and poor response to analgesics. [2, 3, 4]. Pain is of a continuous or intermittent character, of changeable severity, and more often than not has a detrimental effect on patients' day-to-day functioning [5, 6]. Its prevalence in women is 4–14% [7, 8]. More than 80% of women suffer for more than 12 months before they present to a doctor, and one third wait for more than five years. An additional delay in Pain Clinic referral stems from the particular areas from which the pain originates, and the devastating but very popular belief among primary care

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physicians that psychogenic factors are responsible for the great majority of symptoms. The causes and consequences of chronic pain have been an issue of interest for a number of years and consequently the pathomechanism of pelvic pain is now better understood. In the transition from acute to chronic pain, both peripheral and central mechanisms are involved. Pain amplification occurs at multiple levels, which is the reason for the variety and complexity of symptoms.

One of the prominent central nervous system (CNS) features in CPPS women with endometriosis is decreased volume and density of the grey matter in regions related to nociception, such as the thalamus, insular cortex and cingulated cortex. In CPPS women without endometriosis, similar findings are noted in the thalamus only, while in cases of painless endometriosis, no such findings are reported [9,10]. CNS regions involved in stress response, endocrine function and pain modulation (inferior and medial frontal gyri, left amygdaloid, cingular cortex and hypothalamus) are characterized by a greater density and volume in patients with CPPS. A recent meta-analysis of studies regarding the assessment of change in pain perception has concluded that alterations in brain structure and function are undoubtedly present, but it is too early to draw conclusions of clinical relevance, as data on the involvement of particular CNS structures are not only insufficient but also sometimes contradictory [11].

Establishing a diagnosis of CPPS is highly challenging. It is mostly due to a large number of probable anatomical sources of pain and the high potential for coexisting comorbidities which may result in pelvic pain. Hence, a multidisciplinary approach should be employed in the process of differential diagnosis. Nevertheless, the introduction of appropriate analgesia should not be postponed by pending diagnostic processes, as any delay in this regard would increase the risk of pain chronicity [4, 12]. Identified risk factors for CPPS are PID, irritable bowel syndrome (IBS) and interstitial cystitis, as well as endometriosis and pelvic adhesions.

OBJECTIVE

Testing the effectiveness of pharmacological treatment and interventional pain management techniques for pain control as the next step of treatment after the lack of clinical results of surgical and conservatve methods normally used in the management of endometriosis and pelvic adhesions.

MATERIALS AND METHOD

Between January 2010 – October 2013, 18 women were treated due to persistent pelvic pain in a tertiary pain centre – the Pain Clinic, Department of Anaesthesiology and Intensive Care, Teaching Hospital of the Medical Centre of Postgraduate Education in Warsaw. They were referred after diagnosis and treatment in the 1st Department of Obstetrics and Gynecology Department of the same hospital. The diagnosis consisted of CT, MRI, transvaginal ultrasound and protein markers of neoplasia. After the diagnosis, all 18 patients passed the laparoscopy. Neoplasia was definitively excluded in all cases. The endometriomas and visible endometriotic nodules were removed in 5 cases, being consistent with an endometriosis grade of no less than III in revised American Fertility Society classification (fAFS), while in the other 13 cases high-grade pelvic adhesions were identified and partially resolved. In these patients, no active endometriotic lesions were found – adhesions could have resulted from a prior inflammatory process or fibrosis related to previously active endometriosis. Patients with endometriosis also received the concomitant treatment of 2 mg of dinogest daily for 3 months. Since the control of clinical symptoms was not sufficient, a diagnosis of CPPS was proposed and all 18 patients were referred to Pain Clinic. Their ages varied from 21–77 years, pain duration from 6 months to 30 years, and 4 women reported paroxysmal pain episodes of extreme severity, of 10 points in a numeric rating scale (NRS), where a value of 0 describes no pain and 10 is the worst pain imaginable. 14 patients reported both constant and paroxysmal pain of NRS 3–9 and NRS 7–10, respectively.

Intervention. Treatment consisted of pharmacological management (oral anti-depressants and gabapentinoids), pudendal nerve blocks, diagnostic and neurolytic block of ganglion impar (Walther) and topical preparations (local anesthetics, antidepressants and gabapentinoids). The detailed pathway of the treatment implemented is presented in Figure 1.

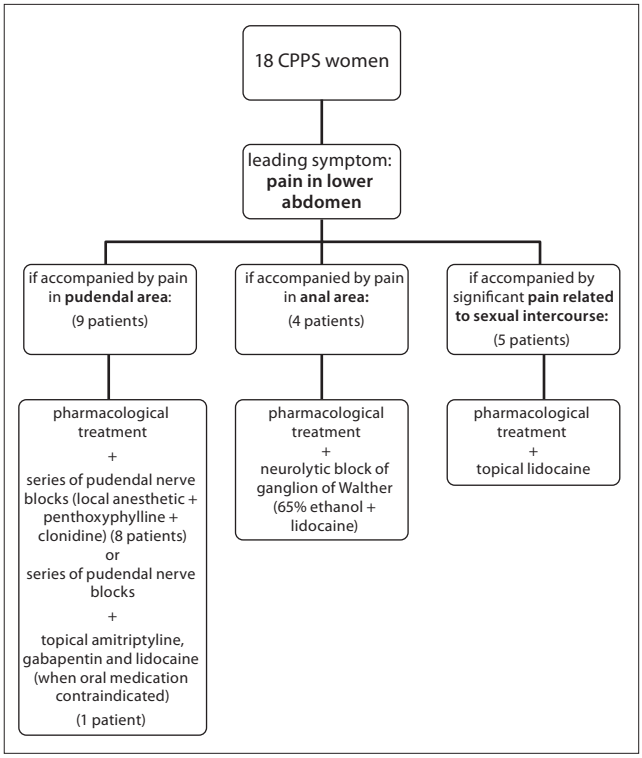

Figure 1. CPPS management strategy, as directed by the affected area

Oral medication was prescribed in 17 out of 18 patients; it was withheld in one case due to chronic renal failure with the history of renal transplant. In this case, the antidepressant amitriptyline and antiepileptic gabapentin in the form of topical preparations were prescribed and used three times daily in affected areas, as well as lidocaine gel after intercourse. The most commonly prescribed oral gabapentinoid was gabapentin at a dose of 300–1200mg/24hrs. Pregabalin (150mg/24hrs) was used in one case only. The most commonly used anti-depressant medication was

amitriptyline (25–75mg/24hrs; 13 women). Citalopram or escitalopram (10–20mg/24hrs) was used in 3 cases and mianserin (30mg/24hrs) in one. If lower abdomen pain was also localized in the perineal and sacral area, prognostic block of the ganglion impar (Walther) using local anesthetic was performed which, if successful, allowed neurolytic block to be undertaken under fluoroscopic guidance (4 patients). If lower abdomen symptoms were accompanied by pain in the area innervated by the pudendal nerve, a series of pudendal nerve blocks was performed (local anesthetic + pentoxyphillin 20mg + clonidine 75mg). The peripheral nerve stimulator technique was used to identify the targeted nerve (9 patients). A significant feature of the disorder in 5 women was pain related to sexual intercourse; in these cases 5% lidocaine gel was prescribed, to be used after intercourse.

RESULTS

The majority of patients (14) complained of both constant and paroxysmal pain, while 4 presented with purely paroxysmal pain episodes. The treatment outcomes in groups of similar management is presented in Figure 2. In 6 women, the complete resolution of both paroxysmal and constant pain occurred; they remained pain-free for sufficient time to down-titrate their medication and assure permanent improvement. A significant decrease in constant pain severity (down to NRS 1–3), with the complete cessation of severe pain episodes was achieved in 7 cases, while no constant pain and occasional pain episodes of NRS 3 was the outcome reported by 1 of the patients. None of the 4 women who suffered from solely paroxysmal pain reported no pain at the end of the follow-up, although in 3 cases the pain relief was significant. In 1 of them (patient with pain in predominantly pudendal area), the treatment undertaken could be considered a failure (NRS 10 before and no change after pharmacological treatment and a series of pudendal nerve blocks), although the frequency of pain episodes decreased, similarly to other patients in this group.

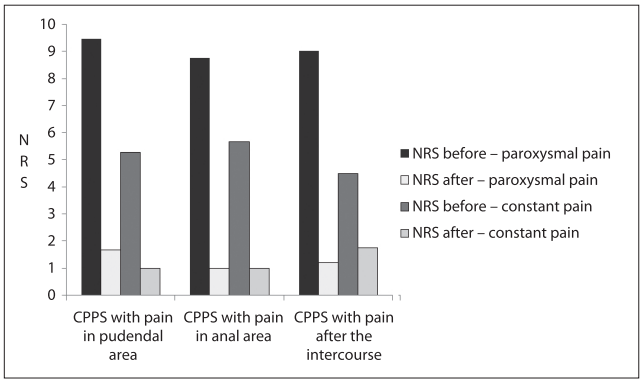

Figure 2. CPPS management outcomes. Data presented as means

DISCUSSION

Clinical trials investigating peripheral nociception in CPPS patients suggest the presence of hyperalgesia after sensory, thermal and electrical stimuli. Similarly, the subcutaneous administration of capsaicin in CPPS women results in more pronounced hyperalgesia and alodynia than in controls, which is suggestive of increased nociceptive sensitivity of the CNS [13]. On the other hand, there is insufficient evidence on touch and vibration hypersensitivity in CPPS [11]. There is also no alteration of descending pain control mechanisms, which is in contrast to significantly hypersensitive ascending pain pathways, and may provide an explanation for the positive clinical effects of peripheral nerve blockade [14].

Gynecologists are convinced that endometriosis is the leading cause of pelvic pain [15]; therefore, the most common mode of management is either invasive or pharmacological (or both) destruction of endometriotic lesions, or – alternatively – the nociceptive ascending routes (e.g. laparoscopic uterine nerve ablation – LUNA). Unfortunately, the link between endometriosis and pelvic pain is not easily identified, which is advocated by the fact that the aforementioned procedures are ineffective in a large number of cases. It was established that the recurrence of pain is not necessarily related to the presence of new implants, while the grade of endometriosis is not related to pain severity. Some women also experience no pain in spite of endometriosis being present [16, 17]. Central sensitization might be responsible for the above and would explain the pain in cases where inactive endometriotic lesions are found during the course of the diagnostic process.

An equally important risk factor of CPPS is a history of surgical intervention, although the mechanism of pain origin here is not obvious. The suggested pathomechanism in cases of pelvic adhesions is the pulling of the well-innervated peritoneum and/or the presence of nerve endings in the adhesions themselves. Surgical lysis of adhesions is known to be effective in reducing pain severity, but its efficacy is limited by the lack of effective methods which could be used to prevent their recurrence [18]. Through the analysis of available data, the conclusion was drawn that 'there is no evidence of benefit, rather than evidence of no benefit' [19]. It is therefore not surprising that these procedures are not very common.

Multiple risk factors and the failure to identify the cause in 30–40% of cases are probably the reasons for which no Evidence-Based Medicine reports on CPPS are available. Guidelines supported by good quality trials are lacking. Consequently, more attention should be directed towards possible causative therapy. In CPPS women, there are 2 leading routes: the surgical removal of endometriotic implants, especially deep infiltrating endometriosis (DIE), division of adhesions and hormonal treatment [19]. Only a few randomized controlled trials investigating the effectiveness of surgical treatment in pelvic pain are available. Their results point to a high ratio of failures, as only transient pain relief is achieved in up to 50% of women, and the outcome is highly dependent on the skills of the surgeon [17].

Hormonal treatment as a causative therapy alleviates pain related to endometriosis. It appears that gaining relative progestogens advantage over estrogens may play a role. An interesting finding is that reducing estrogen levels with the use of aromatase inhibitors has resulted in decreased nociception, which was also noted in women without endometriosis [20]. The above management, even if supported by surgical procedures, would not be successful in all cases. What is more, it is not possible to identify women in whom failures are likely [21, 22, 23]. Patients described in this report have not responded to multimodal management, which in some cases included more than one surgical procedure. In all women with endometriosis, DIE was diagnosed and

managed surgically (which meant the total destruction or significant reduction of endometriotic lesions) with subsequent progestogens. Once first line treatment options had been exhausted, patients were referred to the Pain Clinic. Here, a multimodal approach to pain therapy was implemented. The major players in this field are obviously analgesics, the use of which is guided by an analgesic ladder. Unfortunately, their efficacy in CPPS is not spectacular and no specific preparations have been indicated as being the most effective. Available sources tend to confirm a positive effect of antidepressants, especially tricyclic preparations, and mostly amitriptyline at the dose of 25–75mg/24hrs. Thus, amitriptyline was used in the majority of patients in the presented study. Modern antiepileptic drugs are being readily prescribed nowadays, of which gabapentin is used at doses ranging from 300–3,600mg/24hrs and pregabalin from 150–600mg/24hrs [1, 6]. The patients in the current study were prescribed gabapentin (300–1,200mg/24hrs in 16 women) or pregabalin (150mg/24hrs in 1 patient). Should intolerance or contraindications for any of the above drugs occur, it is possible to convert to their topical use [24]. It is also plausible to implement concomitant therapy with oral and topical preparations, which was used in 4 patients. The topical application of local anesthetics (LA) is also of clinical value. 5% lidocaine was prescribed to 5 women who complained of severe pain after intercourse. Apart from the above, some of the interventional pain management procedures may be added as adjuvant or used as a solitary treatment. Pudendal nerve block or neurolytic block of ganglion impar may be offered to patients, depending on the area affected. The effectiveness of both pudendal nerve an ganglion of Walther blocks an neurolysis has been investigated, although the reports are limited to case series and case reports. Vancaillie et al. have treated women with clinical signs of pudendal neuralgia with a single pudendal nerve block and concomitant pharmacological therapy, which was successful in providing >64 hours relief in 5–25% of women, depending on the symptom assessed [25]. Pulsed radiofrequency ablation of the pudendal nerve has recently been reported to be effective in some refractory cases of neuralgia, providing long-lasting pain relief [26]. Neurolysis of the ganglion impar (Walther) is not very common but highly effective in battling intractable pain in the perineal and anal area. The neurolysis technique used in the Pain Centre in Warsaw has been described elsewhere [27] and the results are similar to those reported worldwide [28].

The multimodal approach allows for intervention at various levels of the neurologic system: from the most peripheral nociception (LA), through ascending pain modulation (pudendal nerve and ganglion impar blocks), central modulation (analgesics) and descending pain control systems (anti-depressants and anti-epileptics).

CONCLUSIONS

Pharmacological management with oral antidepressants and gabapentinoids, aided by either pudendal nerve blocks, neurolytic blocks of the ganglion impar (Walther) or topical preparations of LA, TCA and gabapentinoids appears to be an effective treatment strategy for persistent pain related to endometriosis and pelvic adhesions, when the first-line treatment failed to provide the expected results.

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