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Physiopathology and Treatment

Edited by Vicente Vanaclocha and Nieves Saiz-Sapena

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Meet the editors

Professor Dr. Vicente Vanaclocha received his medical degree from the University of Valencia and did his training as a neurosurgeon in the hospital affiliated with it. From the beginning of his professional career, he put great effort into continuous training, resulting in 15 long-term residencies in hospitals around the world, and the completion of 188 courses of medical training. He is always eager to learn and is devoted to teaching. He has published 80 articles in peer-reviewed journals with close to 3000 citations, written 15 book chapters, and served as the editor of 2 books. He has also been involved in humanitarian work in Syria and Egypt. He is a devoted husband and the father of three lovely daughters.

Nieves Saiz-Sapena is a Doctor of Medicine and Surgery at the University of Valencia and obtained her Ph.D. from the University of Navarra, both in Spain. She has over 25 years of professional experience, with an emphasis in neurosurgical anesthesia, anesthesia in a hostile environment, bariatric anesthesia, and occluded airway anesthesia. After a short stay at the Groote Schuur Hospital in Cape Town (South Africa), she specialized in Anaesthesia and Critical Care at Clinica Universidad de Navarra (Spain). She was an associate professor at the University of Navarra, the head of the Department of Anaesthesiology at Hospital San Jaime (Torrevieja, Alicante), and an associate professor at Universidad Católica San Vicente Martir, Valencia. Currently, she is an active member of several scientific societies including ESA, ASA, SOBA, and SEDAR, with a role in Neurosciences and in Safety and Quality Sections. She also serves as a reviewer for a number of national and international scientific journals and combines her job at the General University Hospital in Valencia (Spain) with her participation in professional books, education, and basic and specialist training in Anesthesia and Critical Care.

Contents

Preface **XIII**

Acknowledgements **XVII**

Section 1
Introduction **1**

Chapter 1 **3**
Where We Come From and Are We Aware of Where We Are Going To?
by Vicente Vanaclocha, Nieves Saiz-Sapena, José María Ortiz-Criado and Leyre Vanaclocha

Section 2 **17**
Physiopathology Chronic Pain

Chapter 2 **19**
Chronic Pain, Dopamine and Depression: Insights from Research on Fibromyalgia
by Katharina Ledermann and Chantal Martin-Sölch

Section 3 **31**
Radiofrecuency Treatment of Chronic Pain

Chapter 3 **33**
Radio Frequency in the Treatment of Lumbar Facet Joint Arthropathy: Indications and Technical Notes
by Antonios El Helou, Charbel Fawaz, Robert Adams and Dhany Charest

Chapter 4 **45**
Chronic Pain Associated with Lateral Epicondylitis: Treatment with Radiofrequency
by Vicente Vanaclocha, Nieves Saiz-Sapena, José María Ortiz-Criado and Leyre Vanaclocha

Chapter 5 **57**
Percutaneous Radiofrequency Hip Joint Denervation
by Nieves Saiz-Sapena, Vicente Vanaclocha, José María Ortiz-Criado and Leyre Vanaclocha

Chapter 6 **79**
Uterosacral Nerve Ablation and Presacral Neurectomy in the Treatment of Chronic Pelvic Pain in Women
by Funda Gungor Ugurlucan and Cenk Yasa

Preface

Pain is a primary defensive mechanism existing in all living animals. As such, it helps to prevent or abort any harmful activity or stimulus, thereby stopping and avoiding further damage. But it can also be a source of immense trouble. Once the pain becomes chronic, it can lose this defensive aspect and transform itself into a new problem. Controlling chronic pain is the aim and purpose of many of our currently existing treatment strategies, significantly when the pain's original cause cannot be corrected any longer. How this chronic pain can be controlled is another source of concern.

People often take over-the-counter drugs, opioids, and other pain-management medications without in-depth knowledge of their long-term consequences. Examples include kidney damage that can be induced by NSAIDs or the strong addictive properties of opioids. As a result, our developed societies currently face an opioid epidemic, yet we often see many of these drugs being advertised on the TV as if they were a commodity to be used ad libitum.

Drugs have a significant advantage in that their use can be stopped if side effects appear, but chronic pain is not like other diseases. Once patients start with pain killers, particularly with opioids, all that can be expected is a progressive escalation in the dose and the drugs' analgesic power. In case of adverse effects, it is possible to change the drug but, in general, not to stop them altogether.

Over the years, many invasive procedures have been devised, aimed at controlling chronic pain. They can be broadly divided into reversible and disruptive. Generally, reversible treatments are preferred as no bridge is burnt, allowing other possibilities to be explored in case of failure. Among these reversible procedures, a wide array of neurostimulation options are available to control pain by inhibiting the chronic pain pathways. By modifying stimulation parameters or the location where stimulation is applied, different options can be explored. Ultimately, if there is no success, the equipment can always be disconnected and something else attempted.

In comparison, disruptive procedures are not reversible, but they are beneficial in treating some forms of chronic pain (i.e., DREZ procedure for brachial plexus avulsion pain), but these procedures are not devoid of problems and complications.

Unfortunately, at times, the economic cost of these procedures comes into play. For example, reversible stimulation procedures require very costly electronic equipment that is not always affordable, particularly in low-income countries. Conversely, disruptive procedures (i.e., cordotomy, DREZ, and zygapophyseal joint rhizotomy) are not that expensive and are available to a more significant range of economies. Unfortunately, not all pain-treating physicians have expertise with all of these techniques. Some are clinicians with a better understanding of drugs and their management, some are anesthetists that can perform certain invasive procedures (particularly neurostimulation), and others can fully perform disruptive operations. Today's pain clinics coordinate all of these players into a single treating group;

without them, patients must often go from one clinic to the next until they find a solution to their case at a price their pockets can afford.

This book attempts to illustrate some of the aforementioned disruptive procedures that can be of particular help to certain patients. It is also important to keep in mind that due to their very reasonable cost, these procedures can be utilized in almost any country, provided the treating physician masters them.

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Dedication

To the memory of my parents, my eternal support and inspiration.

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Section 1

Introduction

Chapter 1

Where We Come From and Are We Aware of Where We Are Going To?

Vicente Vanaclocha, Nieves Saiz-Sapena, José María Ortiz-Criado and Leyre Vanaclocha

Abstract

Chronic pain is a pathological condition that requests specific medical attention. Its treatment has been imperative since the origin of our species, taking advantage of herbs and natural remedies available in the primitive environment. Morphine has stood the test of time as has been continuously used for the past 8 millennia. The anatomical knowledge of the nociceptive sensation pathways led to the introduction of some surgical techniques directed to stop this pain transmission. Due to their aggressiveness and to the fact that they are irreversible, these techniques were soon replaced by neurostimulation procedures. Being reversible and allowing a change in stimulation parameters soon became the preferred treatment strategy. Over the years a small subset of patients continues to suffer from chronic pain refractory to the usual neurostimulation and pain-controlling medications. These patients can perhaps benefit from one of the surgical ablative procedures. Some of these techniques have been proven particularly effective throughout the years. For some limited income patients in underdeveloped countries, these techniques may be their only accessible option. Doctors have to keep in mind these surgical techniques to put them at the service of our patients in the very few cases in which they are needed. Letting these ablative techniques to die in oblivion would be a disservice to our patients.

Keywords: chronic pain, chronic pain management, surgical techniques for chronic pain management, pain clinic

1. Introduction

Pain is a defensive mechanism essential for normal life [1]. It helps us to prevent, avoid or stop any potential or real damage to us [2]. Yet, it becomes a disease in itself once it transforms into a chronic condition, oftentimes when the disease that originated the pain is no longer present [3].

The word pain itself is a matter of interest. In Arabic there are hundreds of words to express it, while in European languages, this wealth of vocabulary does not exist, and different types of pain have to be expressed through a much limited number of words [4]. As a rule a language develops more words when it has to describe a bigger amount of details of single entity. This is the case for the word snow in Eskimo-Aleut languages [5]. In fact it is known that the verbalization of pain can somehow change its same perception [6–8].

From the very beginning, humanity has looked for means to control pain using several vegetal preparations [9–13]. The use of morphine for pain control can be dated in Mesopotamia back to the sixth millennium before Christ [14, 15]. In the Roman times, it was commonly used [16], and Galen described the use of a morphine-based ointment for the treatment of a variety of medical conditions, including chronic pain [17]. This is probably the first description of transdermal morphine use and the first known antecedent of opioid transdermal patches. Apart from the treatment of pain, morphine was used for many other medical conditions due to its antitussive, antidiarrheal and hypnotic properties [15].

In Europe during the Middle Ages, morphine became an expensive item as it had to be brought from distant places in Asia, so few people could afford it [4, 18], and yet opium (vegetal preparation containing morphine) was part of several pharmaceutical preparations [19].

Addiction to morphine was already known in Roman times [16], but it became commonplace in the Renaissance, particularly among upper class individuals [14], as they were the ones who could afford it?

In 1680, Thomas Sydenham introduced the laudanum, a mixture of opium in sherry wine [4]. This made the administration of this drug much easier and its popularity rose. Consequently, opium became a lucrative product, and its trade led to conflict, escalating to wars such as those between China and Great Britain [20, 21].

In 1803, Sertürner isolated morphine crystals and paved the way to the use of this alkaloid instead of vegetal-derived products [4, 22]. This allowed its chemical characterisation and the creation of new drugs that improved specifically the antitussive, antidiarrheal and hypnotic properties of morphine [10]. Sertürner's work also allowed a more precise control of morphine doses being administered and thus a better control of side effects and overdose.

In the nineteenth century the first non-steroidal anti-inflammatory medications were discovered [10], and local and general anaesthesia were introduced [23]. These made morphine less important as it was no longer the only analgesic medication available.

Surgical treatment of chronic pain emerged after the anatomical pathways involved in pain transmission were discovered. Cordotomy, a procedure to lesion the pathways that transmit nociceptive sensation at the spinal cord level, was introduced in 1912 by Spiller and Martin [24] and was used until the mid-twentieth century [25–27]. It was performed initially as an open procedure but was later done percutaneously [28, 29]. Another pain control surgical technique was commissural myelotomy, but it was used much more sparingly [30, 31]. These ablative procedures were also attempted at higher levels like the brainstem and the thalamus [32].

The dorsal root entry zone (DREZ) lesion was introduced by Sindou [33] and Nashold [34] in the 1960s, and ever since it has been used in brachial plexus avulsion pain. DREZ is particularly successful for this specific medical condition and is still in use up to today [35–38].

Initially mostly surgeons [39] dealt with chronic pain, but subsequently the anaesthetists became involved [40], and the first pain clinics were created [41]. The idea was to integrate in a single unit all the specialities involved in the treatment of chronic pain [42, 43].

The introduction of the posterior spinal column stimulation in the 1970s [44] and the implanted morphine infusion systems in the 1980s [45] were revolutionary, and myelotomies, cordotomies and peripheral neurectomies were soon put aside [46, 47], as reversible procedures are often preferred above ablative lesions. With posterior spinal cord stimulation, if there is any trouble to the patient or unsatisfactory results, the stimulation parameters could be modified, the stimulation stopped altogether, or the morphine dose increased. In case of failure, other management approaches could be considered [48]. In case of the implantable morphine infusion systems, they could be implanted with ease so that physicians other than surgeons could use them.

2. Current situation

Over the years, surgeons have lost interest and importance in most pain clinics [49]. The anaesthetists have taken over [50] and provided a large selection of minimally invasive techniques and revolutionised the percutaneous and oral management of chronic pain [51]. The surgical techniques of pain management have been slowly obliterated [52] in favour of those that involve peripheral or central nervous system stimulation [53, 54] and intrathecal or epidural drug administration [55–57]. In posterior spinal cord stimulation procedures, it has been proven that the surgically implanted pad electrodes provide better results than the needle-inserted ones [58]. This has strong implications on which specialty should implant the definitive posterior spinal column electrodes.

Opioids have become a common treatment strategy, available to the patients by means apart from doctor's prescriptions [59–61]. As a result, the morphine consumption per person has been increasing in the latest years [62] to reach what has been named an opioid epidemic [46, 63–67]. Sometimes the process starts after the prescription of opioids to treat acute pain, for example, after a surgical procedure, but patients get addicted to the drug, and then it becomes difficult to make them abandon their use [68–72]. Opioids are nowadays so widespread that they can be acquired in the illegal market [61, 73]. This means that patients can use them with little or no physician control [59, 60] suffering from unwanted serious side effects and even death [74–77].

3. Future trends

Some have urged the creation of new analgesics with stronger actions and less addictive effects [78]. Ziconotide is one of them but has the disadvantage that it can only be administered intrathecally [79–81]. Some toxin-derived peptide drugs have been analysed, but the results are not consistent [82], while drugs that interact with the cellular membrane potassium channels are also being investigated [83]. Some recombinant proteins have been studied in the experimental setting, but they have not yet reached the clinical study phase [84].

In the latest years, there seems to be a renewed interest in old surgical procedures to treat chronic pain, particularly for oncological patients [85]. Under this category are the cordotomy [24], the block of the *plexus coeliacus* [86], the *nervus splacnicus* [87] or the *hypogastric nerve* [87] and the *vidian nerve* radiofrequency neurotomy [88], to mention a just few. It is currently used as a last resource for patients whose pain has not been controlled with other more conservative measures [85, 87, 89, 90]. Other procedures like the DREZ [38, 91], the zygapophyseal joint percutaneous rhizotomy [92] or the radiofrequency sacroiliac joint denervation [93] are still commonly used nowadays. Some old techniques have been improved and adapted to be minimally invasive, such as the radiofrequency thalamotomy [94, 95]. There are also new interesting additions, like the genicular nerve cooled radiofrequency neurotomy to treat chronic knee pain [96, 97], the obturator and femoral nerve sensory percutaneous neurotomy to deal with hip problems [98, 99], the shoulder pulsed radiofrequency of the suprascapular and axillary nerve to treat chronic pain shoulder [100, 101] or the epicondyle radiofrequency treatment for chronic elbow pain [102, 103]. All these and other less common surgical procedures are there to be considered and used in selected cases [87, 104]. However the lack of interest of the surgeons in an area mostly controlled these days by the anaesthetists [49] has led to the oblivion of surgical techniques that could be of potential help to some patients, particularly in refractory cases in which all had previously failed [87]. We need to keep the knowledge of these surgical techniques that can be of potential interest to particularly refractory cases.

On the other hand, not all patients worldwide have access to the same options [105–108]. Economic issues can make some neurostimulative or implantable pump techniques unaffordable that might be advisable in a patient [109–111]. Nevertheless, some of the old surgical ablative procedures might be affordable [87, 112] as they have a much lower monetary cost [110] and may be beneficial for these patients. Hence, surgical control of pain has to remain a known alternative, sometimes preferable to long-term opioid use and its associated side effects [113].

The continuation of the study of the basic mechanisms of pain production, transmission, perception and induced suffering is imperative [114–117], as is the investigation of new treatment strategies. A very promising area is fibromyalgia [118, 119], a condition for which pathological studies are negative [120] in the affected individuals and yet they claim to be in constant pain. This also happens in other medical conditions such as schizophrenia, and nobody will dare to state that schizophrenia does not exist because it lacks a previse pathological correlate [121]. Recent studies have highlighted neurotransmitter changes in chronic pain that need to be thoroughly analysed and studied [122–124].

4. Situation in each hospital

Each country, each area and even each hospital pose a particular scenario. Over the years many neurosurgeons have lost interest in the chronic pain treatment and retreated from the pain clinics [49]. We need to change this trend and get more involved in this area [52], so that our capabilities can be requested when they could be of particular help, benefitting patients which lack viable alternatives.

This book is a plea to awaken physicians in some ablative procedures that should have never been forgotten.

5. Conclusions

Treatment of chronic pain demands a multidisciplinary approach. Everybody is welcomed and needed. In the latest years, anaesthetists have taken a big role in this arena, but surgeons need to keep ready for those uncommon cases in which everything fails. In some low-income countries or patients with refractory pain, some ablative procedures might be an option that their pockets can afford. Surgical techniques of chronic pain management should not fall into the oblivion. Continuous research is needed to better understand the chronic pain condition and to find new remedies against it.

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Section 2

Physiopathology Chronic Pain

Chapter 2

Chronic Pain, Dopamine and Depression: Insights from Research on Fibromyalgia

Katharina Ledermann and Chantal Martin-Sölch

Abstract

There have been several indications that pain and reward are partly mediated by similar neural pathways in the central nervous system, and that these common pathways are related to both the dopamine (DA) and the opioid systems. Several studies have demonstrated the analgesic effects of rewarding stimuli or activities on positive affective states. On the other hand, chronic pain was shown to impair several aspects of reward processing by possibly altering pain-reward interactions. However, the precise mechanisms of the mutual pain-reward interaction are unclear and few studies have investigated the influence of pain on rewards and vice versa in humans. Therefore, we aim to summarize recent findings on the neuroanatomical and molecular chances associated with chronic pain conditions, particularly fibromyalgia syndrome (FMS) with a focus on the dopamine system. Recent findings on the mechanisms involved in the alterations of the brain reward circuit in chronic pain and FMS as well as the role of DA in the pathophysiology of FMS and other chronic pain conditions will be discussed. Furthermore, we aim to discuss the interplay between the dopaminergic reward system and depression in chronic pain, as the prevalence of co-morbid depression in chronic pain is quite high.

Keywords: chronic pain, dopamine, fibromyalgia, depression

1. Introduction (Chronic pain and fibromyalgia)

1.1 The burden associated with chronic pain

Chronic pain is defined as "a pain that persists past the normal time of healing" ([1], p. 4). In practice, chronic pain is defined as a pain that lasts for more than 3–6 months [1, 2]. With an estimated prevalence up to 40%, chronic pain is regarded as a major health problem with approximated direct and indirect costs reaching to 5% of the gross national product in western European countries [3]. Also in term of prevalence, chronic pain represents an important public health issue. A recent epidemiological survey indicated that almost one in five Europeans report having experienced moderate to severe pain in the last month and at least twice a week [3]. Chronic pain significantly decreases individuals' health status and quality of life [4] and is linked with a wide range of physical and mental problems such as sleep disorders, depression, anxiety disorders, and alcohol or substance abuse, either as antecedent conditions or as consequences of the development of pain [5]. The fact that the number of people suffering from a chronic pain condition is steadily rising [6], in spite of the overall improving standards of health care, emphasizes the urgent need for novel insights informing better diagnosis, prevention and treatment of patients with chronic pain.

1.2 The specific case of Fibromyalgia

Fibromyalgia syndrome (FMS) is a chronic, painful musculoskeletal disorder characterized by widespread pain, accompanied by a broad spectrum of associated somatic and psychological manifestations, including fatigue, sleep disturbances, stiffness, anxiety and cognitive dysfunction [7, 8]. The current diagnostic criteria of FMS emphasize the behavioral and psychological aspects of the disease and are based on self-reported evaluation of symptoms [9]. This is an important change compared to the previous diagnostic criteria that required tender point examination [8], while the new criteria are essentially based on self-reported symptoms. The development of new diagnostic criteria for FMS is related to the evolution of the understanding of the underlying pathophysiology of this disorder [10]. While the old criteria conceptualized FMS as peripheral musculoskeletal condition, the new criteria account better for the role of the central nervous system (CNS) in the etiology of FMS. In addition, they simplify the diagnosis in primary care and integrate the diversity of symptoms (somatic and behavioral) associated with FMS [10] better.

The population prevalence of FMS in industrialized countries has been reported to range from 0.5 to 4% [11], with a ratio of 3.5% in women to 0.5% in men [12]. FMS is one of the most prevalent chronic pain conditions [12]. Like other chronic pain conditions, FMS often leads to disability, affective disturbance and poor quality of life and is also associated with high direct and indirect disease related costs [13]. The etiology of FMS is widely unknown; and this disorder remains very difficult to treat. However, accumulated evidence over the past years suggests that a wide range of factors that could potentially underlie the disorder, including dysfunctions of the central CNS and autonomic nervous systems, neurotransmitters, hormones, immune system, external stressors, psychiatric aspects and others [14]. Although there is increasing evidence for changes in the CNS, FMS is differentiated from neuropathic pain as there is no evidence for a primary lesion or disease of the somatosensory system in FMS [15]. It has been hypothesized however that FMS and neuropathic pain phenomena may be variations of the same condition [16, 17] with many common features such as precipitation or aggravation by stress, as well as complaining about similar symptoms such as tingling, numbness, cutaneous hyperalgesia or pain attacks [18]. Finally, the recent evidence for impaired small fiber function in FMS patients also points towards a neuropathic nature of pain in FMS [19].

1.3 Challenges for the treatment of FMS

Despite this high clinical significance, the neural correlates and the interaction between psychological and neurobiological processes in the pathophysiology of FMS are still poorly understood, which in turn makes the development of treatment strategies difficult. At pharmacological level, three medications have been approved by the FDA for the treatment of fibromyalgia [20]: one anti-epileptic drug (pregabalin) and two antidepressive drugs (duloxetine and milnacipran). Interestingly, all of them directly act on the CNS. However, recent research indicates that current pharmacological treatments are not really effective in the reduction of pain or improvement in function in patients with FMS, and there is still a lack of effective drugs for the treatment of FMS over time [21]. Furthermore, the current evidence-based guidelines for the treatment of patients with FMS are inconsistent [22]. Finally, recent meta-analyses conclude that optimal treatment interventions should include components aimed at enhancing adaptive cognitive and behavioral responses [23, 24], and large improvements have been observed with treatment plans that include non-pharmacologic interventions [25]. This is in line with the current international guidelines that recommend aerobic exercise, cognitive-behavioral therapy (CBT), and multicomponent treatment as first choice for the care of FMS patients [22]. These conclusions are also in agreement with the current state of research concerning the treatment of chronic pain in general. For chronic pain also, most of the available medications show poor efficacy, are accompanied by severe side effects with chronic use, or, in the case of opioids, may lead to dependence or addiction [26]. In addition, chronic pain is commonly associated with comorbid affective disorders (e.g. anxiety, depression) and cognitive deficits (e.g. memory impairment), suggesting on one hand critical involvement of higher order neural brain processing [27], and on the other hand the necessity to develop specific interventions targeting the comorbid mental disorder the mood and cognitive dysfunctions as well (see for instance [28].

This chapter will therefore focus on specific neural changes associated with chronic pain in general, and with FMS in particular, that could bring new advances in the development of efficient treatment strategies for these conditions. These neural factors concern the changes in the dopamine function observed in chronic pain and their implication for responses to rewarding stimuli.

2. The dopamine function in chronic pain and in fibromyalgia

2.1 Changes in dopamine function in chronic pain disorders and in FMS

Among the neural changes observed in chronic pain, there is increasing evidence for alterations in the dopamine (DA) system. These changes seem to be related with a reduction of the DA function in chronic pain conditions. Evidence supporting a hypodopaminergic state in chronic pain comes from both preclinical [29] and clinical data [30, 31]. For instance, alterations in the DA function were described in burning mouth syndrome and atypical facial pain [32, 33]. The high incidence of central pain (including neuropathic pain) in patients suffering from Parkinson's disease suggests that pain is a common symptom in patients with hypofunctional nigrostriatal dopaminergic pathways [34], and that low DA may contribute to increased pain [35]. Similar changes were observed in FMS. For instance, two PET-studies showed that self-reported pain induced by hypertonic saline injection in healthy volunteers correlated with the amount of DA released in the basal ganglia [32, 33]. These findings suggest an involvement of DA activity in endogenous analgesia [36, 37]. In contrast to healthy subjects, FMS patients did not show DA release in response to noxious stimulation [36]. Furthermore, activity of the ventral tegmental area was decreased during both pain perception and expectation of pain relief in FMS patients in an fMRI (functional Magnetic Resonance Imaging) study [30] suggesting a dysregulation of DA signaling in these patients. A previous study by our group added evidence of a reduced DA function in FMS patients, and indicated a role of depression in the relation between pain perception and DA changes [38]. Our main results yielded that investigation of the DA function allows differentiating between FMS patients with and without depression, as well as between FMS patients and healthy subjects and that the neurobiological mechanisms underlying depressive symptoms in FMS patients with depression are different from the ones reported in depressed patients without pain.

Even among healthy individuals, low DA receptor availability has been associated with enhanced pain responses [39]; and DA depletion has been shown to influence pain affect and not the sensory aspects of acute painful stimuli [40]. This could suggest that in chronic pain, a low DA function could lead to changes in affective states [41]. Additionally, recent studies using animal models of neuropathic pain link changes in DA receptor signal transduction, the amount of released DA and other neurochemical adaptations in the midbrain DA circuit with depression-like behaviors and reduced motivation [42–44]. This is in line with findings showing that aberrant dopaminergic transmission in the mesolimbic DA network underlay several mood disorders [45]. On the other hand, accumulating evidence suggests that the mesolimbic DA system modulates the perception of nociceptive information, and the affective symptoms of chronic pain [46]. Notably, several diseases associated with dysfunctional DA transmission are comorbid with chronic pain, including Parkinson's disease, drug addiction and major depression [41].

Taken together, there are now multiple lines of evidence showing that chronic pain, including FMS, leads to a hypodopaminergic state that results in enhanced pain sensitivity and might impair motivated behavior [47]. In addition, DA is involved in descending inhibitory modulation of pain transmission, which is an additional link between hypodopaminergia and chronic pain [48]. Strategies to restore dopamine signaling may therefore represent a novel approach to manage pain symptoms in FMS.

2.2 Alterations of the brain reward circuit in chronic pain and FMS

It is well documented that the mesocorticolimbic and mesostriatal DA systems play a role in the processing of reward information [49–51], even if other neurotransmitter systems, such as the opiate system, are also important in the mediation of reward [52]. Recent studies indicating that alterations of the mesolimbic reward pathway contribute to the pathology of chronic pain [53, 54] suggest a neurobiological overlap between pain processing and the reward circuitry. Pain and reward can be regarded as opponent processes that interact and influence each other [55]. Several studies demonstrated that rewards, including pleasurable stimuli and activities and positive affective states have an analgesic effect and decrease pain sensitivity [55–58]. Finally, some findings suggest that pain and reward are mediated by similar neural pathways in the central nervous system and that these pathways are related to both the DA and the opioid systems [55, 58]. At a neurochemical level, several preclinical and clinical findings suggest that chronic pain leads to a hypodopaminergic condition in the reward circuitry, resulting in the diminution of the hedonic tone (see Section 2.1). This suggests that the brain reward center might play a key role in the modulation of nociception, and that adaptions in dopaminergic circuitry may affect several sensory and affective components of chronic pain syndromes. These adaptations involve changes in the levels of released DA, as well as postsynaptic changes in the levels of receptors and signal transduction molecules [59].

After having established that pain and reward might influence each other through the implication of the DA system, the next subsections will provide an overview of the findings reporting changes in the responses to reward in chronic pain first, and then secondly specifically in FMS.

2.2.1 Changes in the brain reward circuitry in chronic pain

Findings from functional neuroimaging studies indicate that a network of brain regions, including the orbitofrontal cortex, the ventral (specifically the nucleus accumbens, Nacc) and dorsal striatum, the amygdala and the anterior cingulate gyrus, specifically interact to process reward information [60] and form the so-called cerebral reward system. In chronic pain, alterations in brain structural features, functional connectivity, or activity of these regions have been reported [37, 46, 61]. Additional evidence from clinical studies links chronic pain conditions to aberrant functioning of circuits involved in mood and motivation, including the dopamine brain reward center [62, 63]. The neural changes observed in regions associated with the cerebral reward system could provide a possible explanation for the high incidence of comorbid affective disorders in chronic pain patients [59]. In summary, the reported empirical evidence suggests that pain, in particular chronic pain, impairs several aspects of reward processing: (1) chronic pain is associated with anhedonia, that is, the inability to enjoy pleasurable activities [44, 64]; (2) decreased reward sensitivity and/or decreased motivation was observed in rats with neuropathic pain [65]; (3) impaired operant learning of pain sensitization and habituation was found in FMS patients [66]; and (4) impaired decision making based on reward and punishment was reported in patients with chronic back pain and complex regional pain syndrome (CPRS) [67]. Decreased reward responsivity may therefore underlie a key system mediating anhedonia and depression common with chronic pain [41, 68, 69]. This is highly relevant since the prevalence of depression in chronic pain exceeds 20% [70] and often includes anhedonia [44, 64]. Anhedonia is also one of the cardinal symptoms of depression, and has been hypothesized to be associated with an hypofunction of the DA system, what in turn could affect the neural processing of rewarding information [51]. As a matter of fact, a large body of research has evidenced reduced neural activation as well as reduced DA transmission in response to reward information in patients with major depressive disorder (MDD) (see for instance [71–73]). Recent evidence from animal studies suggest that suppression of dopaminergic neurotransmission in the mesolimbic reward circuit may be a common neuroplastic change underlying chronic pain and depression that develops in a time-dependent manner [74].

2.2.2 Changes in the brain reward circuitry in FMS

To our knowledge, there is so far only one study that has directly investigated the DA responses to reward in vivo in FMS patients [59]. In this research of our group, we used the [^{11}C]Raclopride positron emission tomography (PET), a radiotracer that is sensitive to changes in intrasynaptic DA concentrations while participants were performing a slot machine compared FMS participants with and without depression with healthy controls (all women). We expected the patients' groups to have reduced DA responses to reward, expressed as a larger Raclopride binding in the FMS groups of participants than in the group of healthy controls. In addition, we expected this alteration to be stronger in FMS patients with than in FMS patients without depression. However, our results showed, at the contrary of our hypothesis, the greatest [^{11}C]Raclopride displacement in response to rewards in the group of FMS participants with depression [59], which is thought to reflect the largest increase in DA transmission. This can be explained by a greater increase of synaptic DA transmission or by adaptative receptor changes in this group, but necessitate further investigation to be more clearly understood. Our results also indicated that the depression associated with FMS has different neurochemical correlates as primary major depressive disorder. More specifically, a previous study by our group [71] using the same methodology found no [^{11}C]Raclopride displacement in response to rewards in a group of MDD patients without pain symptoms, suggesting reduced DA responses in the brain of depressive patients at the contrary of our group of FMS patients with depression. In conclusion, there is first evidence for a hypodopaminergic state in FMS and an alteration of the neural reactions to reward mediated by the DA system. Even if the exact mechanisms by which the brain reward center modulates chronic pain resp. FMS are not completely established yet, this opens new treatment avenues. Certainly, pharmacological interventions targeting the DA system could be an option. However, we will focus here on psychological interventions that might directly work on the behavioral responses to reward and in turn might be able to restore the DA function.

3. Implications for the treatment of FMS

The current international guidelines for the treatment of FMS all recommend psychological interventions, more specifically cognitive behavioral therapy (CBT), as one of the treatments of choice for the care of FMS patients [22]. According to a recent meta-analysis, CBT is significantly better than the other psychological interventions for which randomized controlled trials exist [75]. The effects of CBT are relatively small but robust and similar to those reported for other pain and drug treatments [75], but have limited success in ameliorating affective and social complaints in FMS patients [25, 75, 76]. There is therefore a need for the development of new CBT methods targeting specific behavioral, emotional or cognitive processes in the treatment of chronic pain. Recently, the so-called "third wave" cognitive-behavior therapies [77] have integrated mindfulness-based cognitive therapy as additional intervention. Mindfulness is defined as "a process of bringing a certain quality of attention to moment-by-moment experience" [78]. Mindfulness capacity can be developed using various meditation techniques that originate from Buddhist spiritual practices [78]. A growing body of research has demonstrated that mindfulness-based interventions are clinically effective for a wide range of problematic conditions (for a review see Grossmann et al. [78]) and have gained increasingly wide use for the treatment of chronic pain conditions including FMS, showing promising results [79, 80]. A recent systematic review indicates a moderate significant effect for mindfulness on the amelioration of mood-related outcomes in FMS [81]. Among these new interventions, Mindfulness-Oriented Recovery Enhancement (MORE) is a mental training program that unites complementary aspects of mindfulness training, CBT and positive psychological principles into an integrative treatment strategy [82]. MORE was originally designed as a behavioral medical intervention for addictive behaviors [83, 84], but was more recently adapted to address chronic pain among individuals receiving long-term opioid analgesic therapy [82]. A randomized clinical trial showed that MORE significantly reduces pain symptoms [82] in chronic pain patients. First empirical evidence suggests that MORE is also associated with behavioral and neurophysiological changes in reward processing [85, 86], suggesting that interventions working on the reward system might be efficient for pain reduction.

4. Conclusion

In conclusion, CBT-based treatments specifically working on the awareness of pleasant experiences, such as MORE, seem to be effective in restoring the behavioral and neural responses to reward and also to diminish pain symptoms in chronic pain patients. Although not yet tested in FMS patients, this could be a promising new treatment alternative for this group of patients, in which changes in the DA function and in the responses to reward have been evidenced, but for whom no efficient treatment is available so far.

Conflicts of interest

There are no conflicts of interests.

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Section 3

Radiofrecuency Treatment of Chronic Pain

Chapter 3

Radio Frequency in the Treatment of Lumbar Facet Joint Arthropathy: Indications and Technical Notes

Antonios El Helou, Charbel Fawaz, Robert Adams and Dhany Charest

Abstract

Low back pain is one of the most reported symptoms in adult life. Different etiologies have been evoked. Degenerative disease of the spine is the most common cause. Facet joint arthropathy is the second leading cause of low back pain in degenerative disease. Failure of medical treatment will lead to more invasive therapeutic option. Radio frequency is a well-known therapeutic option for refractory low back pain related to facet arthropathy. We present our results analyzed retrospectively between January 2015 and March 2018. In addition, we describe our workflow, our procedure technique, and our results. According to our findings, 73% improved their VAS pain score by at least 50% over 3 months. Twenty-seven percent failed to improve with this procedure. There was a 20-point improvement on the SF-36 QOL; the overall satisfaction was high. When patients are selected carefully, radio-frequency ablation technique is a safe and efficient procedure. Its complication rate and cost are low. We recommend it as one of the therapeutic tools in the management of low back pain related to facet joint disease.

Keywords: low back pain, facet joint arthropathy, neurolysis, radio-frequency ablation, denervation

1. Introduction

Low back pain is one of the most reported symptoms in adult life [1]. Eighty percent of the population has experienced at least one episode in their life. It results in major disability for patients when it becomes chronic [2].

Different etiologies were described, but in more than 75% of cases, a nonspecific cause is evoked. Several factors were implicated: age, work, smoking, obesity, and psychological.

Pure low back pain is generally related to degenerative changes in one or more structures of the spine. The most common cause is discogenic followed by facet joint arthropathy [1, 3].

Facet joint disease is a multifactorial problem implicating mechanical and inflammatory damages, and the most common underlying etiology is arthritis [2–4].

Radio frequency is a well-known therapeutic option for refractory low back pain related to facet arthropathy [3]. It is still a very controversial procedure in terms of efficiency. Some studies showed its superiority to placebo or conservative treatment where others were not conclusive [4–6]. We consider it as a safe, minimally invasive, inexpensive procedure. It is successful in well-selected patients.

2. Anatomy of the facet joint

The spine is a complex structure in which its integrity depends on multiple anatomical elements that are functionally and structurally related to each other. The spine is a multi-articular system. Its function is to maintain axial stability. Spinal stability is based on three connected systems: the columns, the muscles, and the spinal cord with its nerve roots [7].

The columns contain mechanical receptors that send proprioceptive information on the load, motion, and postures through the spinal nerves to the central nervous system.

Facet or zygoapophysial joints are part of the columns. They are bilateral on each level and contain synovial fluid lined with hyaline cartilage. Their role is to control the direction and the amplitude of the movements in addition to share the loads. In the physiological condition, a balanced action exists between the three columns. The posterior facets support up to the third of the load depending on the posture [3, 7].

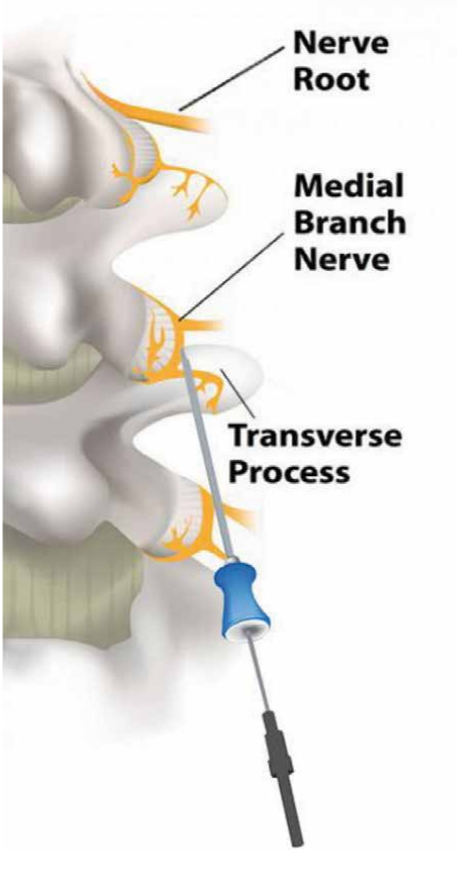

Figure 1.
Anatomy of the medial branch at the level of the facet joint with schematic representation of the needle in addition to the radio-frequency probe.

Facet joints are symmetrical which maintain the correct function in mobility. Any changes in the symmetry predispose to instability and lead to degeneration of the joint. Degenerative disease of the facet joints is accompanied by an inflammatory reaction leading to nervous irritation and low back pain.

There are two types of innervation in the lumbar spine, the somatic and the sympathetic.

The L1–L4 dorsal rami are different from the L5. They are shorter and go backward into intertransverse spaces, whereas the L5 goes over the top of all of the sacrum. L1–L4 are divided into three branches; L5 has two branches: the medial and the intermediate [8]. The medial branch at all levels is responsible for the innervation of the facet joint. It runs on the top of the transverse process toward the articular process (**Figure 1**). Each medial branch covers two levels though each articular facet joint gets its innervation from the level itself and the level above [7, 8].

3. Clinical and para-clinical evaluation

Patients suffering from low back pain are initially assessed by their family physician. The majority are referred to low back pain clinic developed in our hospital. If there is a failure of conservative medical treatment for 12 weeks in the absence of red flags, patients are referred to neurosurgical evaluation. MRI or CT scan of the lumbosacral spine is always done before their first visit, in addition to the dynamic lumbosacral spine X-rays and laboratory workup. Initial findings on MRI or CT scan of the lumbosacral spine are related to facet joint arthropathy. There is a joint space narrowing with intra-articular fluid leading to T2 hypersignal on MRI [3, 9]. Osteophyte formation at the level of the superior articular facet of the lower vertebra, ligamentum flavum with recess stenosis is frequently observed. They are evaluated clinically by a multidisciplinary team (neurosurgeon, anesthesiologist pain specialist, neuropsychologist, physiotherapist, occupational therapist) after being referred from their primary care physician.

The initial evaluation is done by a neurosurgeon. Patients answer three questionnaires before their initial consultation: the visual analog scale, the McGill pain questionnaire, and the Sf-36 quality-of-life questionnaire. Those questionnaires are evaluated before the patient is seen at the office. In the absence of red flags, we developed a workflow for the management of chronic low back pain (**Figure 2**).

Patient undergoes a complete neurological examination. Facet joint inflammation is suspected when there is an increase in pain on palpation of the joint or in hyperextension position and lateral torsion of the low back. Pain is induced by position changes from supine to sitting and from sitting to standing. In some patients, we may observe some radiating pain mainly to the hip and thigh. Without discogenic disease, straight leg rising is non-painful usually. Motor and sensory examination of the lower limbs is normal.

In the absence of any surgical condition but evident facet hypertrophy of the MRI or the CT, patients are referred for SPECT CT scan (single photon emission computed tomography) [9] and neuropsychological evaluation. SPECT CT scan usually shows an increase uptake at the level of facet joint and eliminates other inflammatory process mainly at the disc level. The mean waiting time between the initial evaluation and the follow-up is 6–8 weeks.

If the SPECT CT scan is normal or if there is a severe psychological problem, conservative treatment is considered. Otherwise, in case where the SPECT CT confirms the presence of facet arthropathy (**Figure 3**), patients are referred for facet

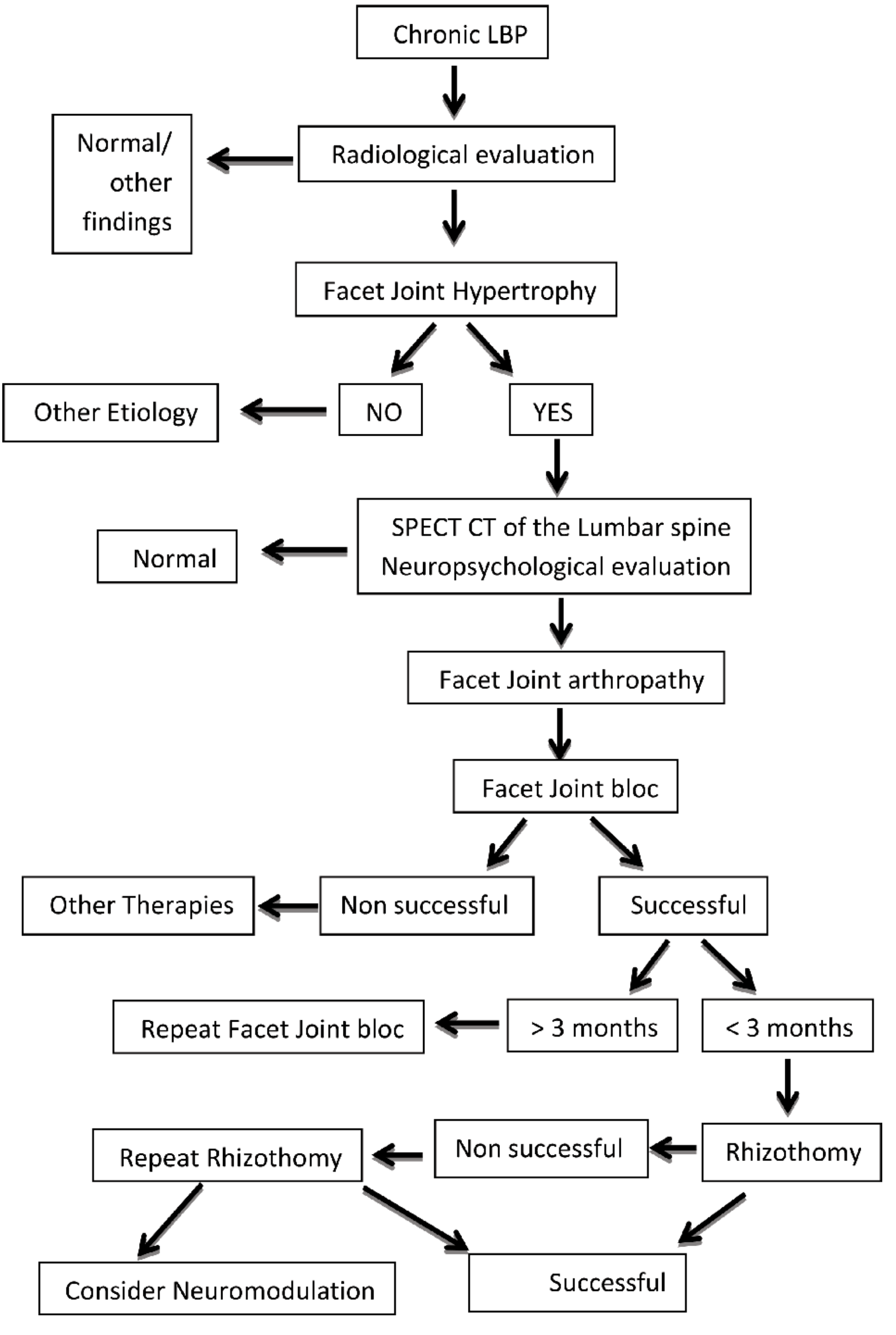

Figure 2.
The Moncton workflow for facet radio-frequency ablation treatment.

block under fluoroscopy at the pain clinic. In case of improvement that lasts more than 3 months, reevaluation and second facet block are offered to the patient.

In case of improvement for more than 48 h but less than 3 months, patients are considered candidates for radio-frequency ablation.

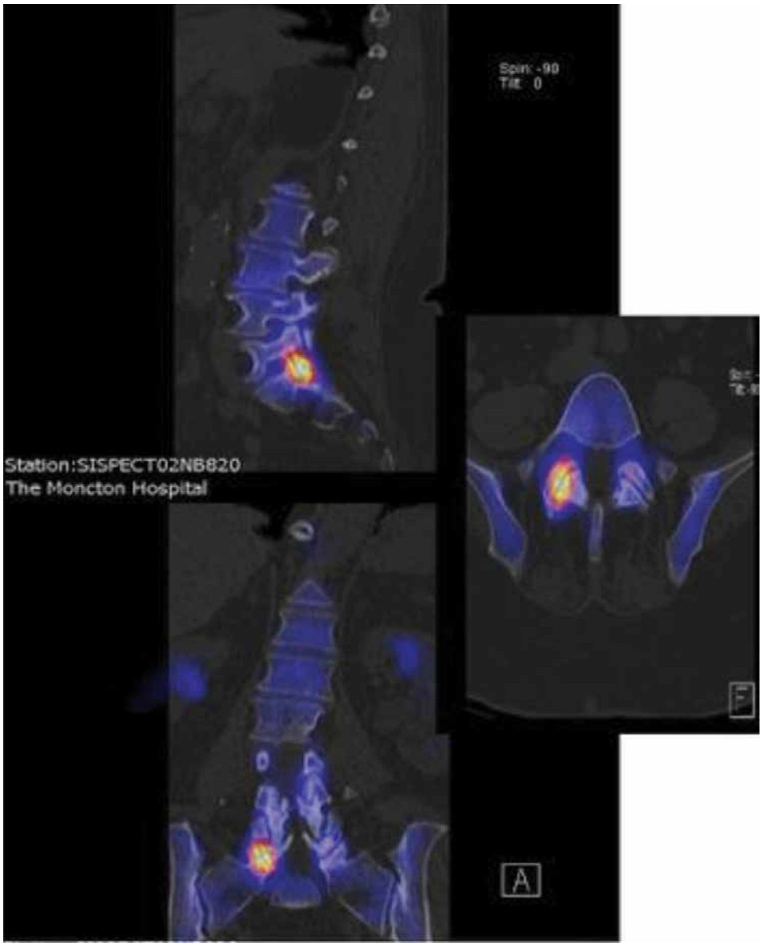

Figure 3.
SPECT CT of the lumbosacral spine showing increase uptake of the right L5–S1 facet joint in favor of facet arthropathy.

4. Surgical technique

Rhizotomy is an outpatient procedure performed under local-assisted anesthesia [10]. Patients are evaluated at the office few weeks prior to the procedure; surgical consent and laboratory workup with a complete blood count in addition to PT are signed; PTT tests are done.

Patients are asked to fast 6 h prior to the procedure. All anticoagulant and anti-aggregant are stopped according to guidelines.

The procedure is done in the operating room. The anesthesiologist proceeds by inserting an intravenous access on the arrival of the patient to the OR. The patient is positioned prone on a radiolucent table with pillow under the head; the arms are above the head in a comfortable position.

Fluoroscopy is used for anteroposterior and lateral views (**Figure 4**). Aseptic technique is used. Once level is verified, local anesthesia using xylocaine 2% is infiltrated from the skin to the muscle aponeurosis. Under fluoroscopy, we insert a 20 gauge needle percutaneously targeting the junction of the transverse process and superior articulating facet, where the medial branch of the Luschka nerve runs innervating the facet joint. The needle is advanced until bone contact is made. Once position is verified, the patient is assessed for motor and sensory manifestations in the lower limb.

Figure 4.
Anteroposterior and lateral per operative views for L4–L5 rhizotomy.

Using Baylis radio-frequency machine (Baylis medical), we start by a stimulation until reproducing patients pain and paraspinal lumbar muscle contraction. Radio frequency is started at 80°C for 90 s. Once 80° is reached (10–15 s), the needle is rotated progressively every 15 s to reach 360° coverage. The patient is then reassessed for motor or sensory manifestations in the lower limb.

A new stimulation trial is performed. In case there is a need to increase the stimulation two times compared to prior or there is no pain reported by the patient, the procedure is considered successful, and the needle is removed. The entry point is covered by a small dressing. If the patient still feels the pain or the pain was reproduced with the same stimulation level, the procedure is repeated for 60 s at 80°. After the second trial, when needed, the needle is removed and a dressing is applied. Patients are turned to their back and transferred to the same day care facility.

5. Postoperative care

Patients are discharged the same day, 30–60 min after the procedure. They are followed at 2 and 4 weeks post procedure. Pain is reevaluated by visual analog scale and quality-of-life scale at the office (questionnaire is administered to the patient before their appointment).

In case of recurrence of pain after 2 weeks of relief, patients are rescheduled for a second radio-frequency treatment. During the second procedure, we target the same level as the first in addition to the superior level trying to cover the largest area and ablating the two medial branches innervating that facet. In case of failure at 1 month, we offer other neuromodulation procedures for the patient.

6. Complications

The overall complication rate is very low in radio-frequency procedure in the treatment of facet joint arthropathy [3, 10]. The main complication is injury to the nerve root at its exit if the needle is advanced beyond the bony anatomical landmark inferior to the transverse process.

Infectious rate is very low in purely aseptic technique done in the neurosurgical operating room. Dural puncture may occur if the needle is advanced medially or if the technique is not done under fluoroscopy.

7. Methods

The radio-frequency treatment is a minimally invasive cost-effective procedure. Although it is still very controversial, we found it as a safe and efficacious procedure to be offered for chronic low back pain patients refractory to conservative treatment. Selection criteria for the patients are very important to benefit from the procedure.

7.1 Selection criteria

Patient's age is 18 years and older.

Refractory low back pain to at least 3 months of conservative treatment.

Positive SPECT CT for facet joint arthropathy. Absent MRI/CT scan finding for other spinal disease.

Improvement for at least 48 h after facet joint block and absent neurocognitive diseases.

7.2 Study design

All charts of patients that benefited from the procedure were analyzed retrospectively. The procedure was done by the same neurosurgeon, but the clinical evaluation and the indication were decided at the practice of all the neurosurgical team included in this study.

7.3 Outcomes

The primary outcome was the pain intensity evaluated by the visual analog scale (VAS), 11 points of evaluation of the pain where 0 indicates the absence of pain and 10 is the worst pain ever.

The McGill pain questionnaire score between 20 and 30 points indicates the presence of chronic low back pain.

The SF-36 QOL questionnaire, with a score of 0, indicates severe or absent activities and worse QOL, whereas a score of 100 shows an excellent QOL.

Patients' response to the procedure was considered by an improvement of 50% or more on the VAS and a change of 20 or more points on the SF-36 QOL score. An improvement of 25–50% on the VAS leads us to suggest a second rhizotomy procedure to increase the area of coverage and try to have a better outcome.

8. Results

In total, 63 patients were treated by radio-frequency ablation of the medial branch of the facet joint in the lumbar spine between 2015 and March 2018.

All included patients had long history of low back pain refractory to medical treatment with short-term response to facet joint steroid injection block. Patients didn't have any major psychological disease.

All included patients were adults. The mean age was 57 years (21–84 years). Forty-one patients were male, and 22 patients were females.

The mean pretreatment VAS was 8.4, the McGill pain score was between 20 and 30, and the SF-36 score was 58.6.

The post-procedure mean VAS was 3.8. Forty-four patients had an improvement of more than 50% of their pain; eight patient had an improvement of 25% of their pain, and 11 patients did not notice any changes at 2 weeks.

All the eight patients that reported 25% of improvement were scheduled for a second procedure. Six of eight reported an improvement of more than 50%, one did not notice any difference, and one returned to his previous VAS.

At 3 months, 40 patients were maintaining a VAS score of 50% or more than their initial pain score. Five patients had their pain score between 25 and 50%. And, seven patients returned to their baseline score. From all seven, four had already two radio-frequency treatments and were redirected to a neuromodulation procedure, and three had a second rhizotomy. One improved and was considered successful.

The overall patients that improved were 73%. Sixty-five percent had a major improvement, 8% moderate improvement, and 27% failed to improve after one or two trials.

In the 65% of patients, the overall SF-36 score improvement was to a mean of 77.9.

Three patients reported lower limb paresthesia post-procedure. Two of them had a complete remission of their symptoms at 2 weeks of follow-up, and the third improved after 6 weeks. No infection, no CSF leak, and no injury to the motor nerve root were observed.

9. Discussion

Our result on low back improvement is similar to different studies at 2 and 4 weeks of the procedure [2, 11, 13].

At 3 months, we had a better outcome compared to other studies [11, 12]. All studies used the VAS for pain evaluation.

We consider the selection criteria specifically the positive SPECT CT findings in addition to the response to facet block as a major contributor in the prediction of the success of the procedure. No previous study used both criteria in conjunction. Van Wijk et al. showed the importance of the diagnostic test block, although their result was the same compared to sham at 3 months [12].

We followed the patients for 3 months, which is an intermediate time follow up as in other studies that showed the same results [11–14]. We found that improving pain score and QOL for 3 months was a sufficient time to consider the procedure as efficient. The subjective satisfaction rate and the reported improvement on VAS and SF-36 score, respectively, were good indicators to maintain the procedure as one of the armamentarium in the treatment of chronic low back pain related to facet joint arthropathy; this finding is against Juch et al. findings that have a statistically positive finding without any clinical improvement [4]. Although, in their study published in JAMA, they suggested to improve the selection criteria to improve the outcome related to that procedure, our workflow chart improved the results dramatically.

10. Conclusion

Radio-frequency ablation technique is a safe and efficient procedure. Its complication rate and cost are low. It is a reproducible procedure. Careful patient selection increases its success rate.

The use of this technique for the treatment of other etiologies has been described. Its use in the management of metastatic vertebral bone disease is promising and becoming a very useful tool as a pain management procedure.

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Conflict of interest

All four authors have no conflict of interest.

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Chapter 4

Chronic Pain Associated with Lateral Epicondylitis: Treatment with Radiofrequency

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Abstract

Lateral epicondylitis is a painful condition that impairs the quality of life and the working capacities of many middle-aged people. Conservative treatments offer an opportunity for improvement in the majority of cases. Surgical alternatives can be considered in those patients with persisting pain. Open, arthroscopic and percutaneous extensor tendon procedures offer similar results with 10–20% failure rates. Radiofrequency microtenotomies have been introduced with comparable results to traditional surgical procedures. Although both thermal and pulsed radiofrequency techniques have been applied, there is more experience with the thermal. In the past, thermal radiofrequency has been applied through a 3–5 cm skin incision, but now some researchers have reported its percutaneous application with radiofrequency cannulas. The results are similar to former techniques but with significantly reduced surgical aggressiveness that correlates with less postoperative discomfort and a faster recovery.

Keywords: lateral epicondylitis, radiofrequency, pulsed radiofrequency, radiofrequency microtenotomy, tennis elbow, elbow joint

1. Introduction

Lateral epicondylitis relates to pain in the humeral insertion of the hand extensor tendons, loss of hand grip strength and aggravation of the pain on grasping objects like turning the doorknob or handshaking [1, 2]. The name lateral epicondylitis is a misnomer in itself as it is not an inflammatory process but rather a tendinosis of the humeral insertion of the hand extensor muscles, usually the extensor carpi radialis brevis [3]. Despite its popular name—tennis elbow—only 5–10% of those suffering from it play tennis [4]. This condition arises from repetitive gripping with wrist extension, radial deviation and/or forearm supination [3, 5, 6], and its incidence is 1–3 per 1000 inhabitants/year [7–10]. Lateral epicondylitis can be diagnosed clinically, as direct pressure to the lateral epicondyle reproduces the pain [11], and confirmed with the Thomsen test, in which resisted wrist extension with the elbow in an extended position aggravates the pain [12, 13]. It affects people aged 40–50 years with similar distribution between men and women [7] and can lead to work absenteeism and permanent work incapacities [2, 14].

In about 80% of cases of lateral epicondylitis, symptoms improve over a year [15, 16] often after the offending activity is stopped [17], but in the remaining 20%, it becomes a chronic condition [18].

Physical therapy is a first-line treatment [11, 18–21], which can be supplemented with wrist orthoses [20].

Local steroid injections in the painful areas are commonly used in the treatment of lateral epicondylitis [16, 22] despite being associated with iatrogenic soft tissue calfication [23] and long-term poor outcomes in some cases [24–26].

Botulinum toxin injections weaken temporarily the hand extensor muscles facilitating the healing of the extensor tendon injury [27–29] but can induce weakness in wrist and finger extension, impairing hand grip [28].

Newer treatment modalities include injection in the lateral epicondyle of platelet-rich plasma [30–34], autologous whole blood [35, 36] and stem cell therapy [37, 38]. These are as effective as some more invasive techniques and thus are becoming increasingly popular [31].

Surgical treatment is indicated when all conservative treatments have failed, which occurs in 5–10% of the patients [39–42]. Open surgical resection of the extensor carpi radialis brevis tendon was traditionally the gold standard [43, 44], but recently it is being reevaluated [45]. Some surgeons recommend more extensive procedures with simultaneous posterior interosseous nerve decompression and intra-articular pathology resolution [46], and others prefer collateral ligament repair [47]. To reduce the surgical aggressiveness, several arthroscopic extensor tendon release techniques have been introduced [48–50] finding that they render equivalent clinical results to the open surgical resection of the same anatomical structures [51, 52]. Further refinements are performing the extensor tendon release with an 18-gauge needle [53] or with ultrasound equipment [54]. On comparing open, arthroscopic and percutaneous procedures, no significant differences in clinical outcomes were observed [55], all of them rendering 10–20% of cases with persistent pain and functional incapacity [56–59].

Moreover, lateral epicondyle innervation is provided by sensory branches coming mostly from the radial nerve [60, 61]. Open surgical removal of those branches was attempted [62–64], but it is an aggressive technique and yielded poor clinical results. Other nearby nerves also contribute to the lateral epicondyle pain perception such as the musculocutaneous, the median and the ulnar nerves [60, 65, 66]. Considering that the removal of the sensory branches from all of them was not feasible, other alternatives have been tried.

One of these alternatives is radiofrequency. Radiofrequency—both thermal and pulsed—is a well-stablished technique for chronic pain treatment [67, 68], but its application to recalcitrant cases of lateral epicondylitis is a relatively new procedure [69, 70]. The rationale was that the pulse radiofrequency modulates the nerve function and alters the pain transmission [71], while the thermal radiofrequency destroys the sensory nerve terminals and induces collagen fibre reorganization [72].

1.1 Lateral epicondylitis radiofrequency treatment: historical background

In 2005, Tasto et al. [70] were the first to report radiofrequency microtenotomy in the treatment of chronic lateral epicondyle pain that persisted after 6 months of conservative treatment. The procedure was performed with a Topaz Microdebrider device (ArthroCare, Sunnyvale, CA) through a 3 cm skin incision. In 13 patients and with a 24-month follow-up, they reported pain amelioration but did not quantify it. No complications were reported. It was Meknas et al. [69] in 2008 using the same equipment and 3 cm skin incision who compared the radiofrequency microtenotomy with the open surgical extensor tendon release and repair. At 18 months, both groups had similar pain relief rates, but hand grip strength improved only in the radiofrequency group. No side effects were reported. Further studies with more patients and longer follow-ups (7 [13] and 9 [73] years) confirmed these results [74, 75]. The reduced surgical aggressiveness correlated with a shorter operating time [13], lower rates of post-operative discomfort [76] and faster recoveries [75]. The percentage of patients with residual pain was 10% [75], similar to the reported for the open and arthroscopic procedures [57].

The next step was taken by Lin et al. [77] in 2011, where they investigated the applications of percutaneous radiofrequency. With a Radionics RFG-3C Generator (Radionics Inc., Burlington, Massachusetts, USA), special cannulas and under ultrasound guidance, they applied the radiofrequency with no skin incision in 34 patients that had been symptomatic for lateral epicondylitis for over 6 months and had exhausted all conservative treatment options. With an average follow-up of 14.3 months (range 12–21 months), Lin et al. [77] found an improvement of 78% in pain and 20.6–27.0 kg in hand grip strength. No complications were reported.

Subsequently, Weber and Kabelka [78] in 2012 reported the administration of radiofrequency directly on the skin to the lateral epicondyle without needles. The procedure—known as monopolar capacitive-coupled radiofrequency (mcRF)—was applied with the Alpha Orthopaedics' AT2 System (Hayward, CA, USA). This equipment provides a maximum local temperature increase of 50°C [79], damaging selectively the unmyelinated fibres, while the myelinated axons are mostly spared [80]. This study involved 39 patients with an average 14-month follow-up, reporting an 81% successful outcome and an 89% patient satisfaction with no adverse effects.

Another possibility is pulsed radiofrequency, which can be applied without an irreversible neural damage [81] and has been used in many areas of chronic pain management. Oh et al. [82] in 2016 reported its use on elbow pain, aiming at the radial nerve as it crosses the elbow joint. The procedure was performed with a radiofrequency 22G cannula with a 5 mm active tip (SL-S505-2, Neuro-Them, Wilmington, DE, USA). Only two patients were treated this way but showed significant pain relief for 12 months. No long-term results were reported but no statistically significant data can be extracted from two isolated cases.

2. Indications for radiofrequency lateral epicondyle treatment

Patients must have confirmed lateral epicondyle chronic pain that has not been controlled after at least 6 months of conservative treatment [39, 43].

Exclusion criteria: elbow instability, rheumatic arthritis, cervical radiculopathy, severe cervical osteoarthritis and higher-grade extensor tendon damage [69, 74].

3. Surgical techniques for radiofrequency lateral epicondyle treatment

The techniques reported to apply the radiofrequency in the treatment of lateral epicondylitis are the radiofrequency-based microtenotomy, the monopolar capacitive-coupled radiofrequency, the monopolar thermal radiofrequency and the bipolar thermal radiofrequency. To these, we could add the pulsed radiofrequency, but as its used has only been described in two patients and there are no long-term results, we will not describe it.

The technique for radiofrequency-based microtenotomy as performed by several groups [13, 69, 70, 73–75] will be described first. Under general anaesthesia and in the supine position, a tourniquet is applied to the affected arm. The humeral insertion of the extensor tendons is exposed through a 3–5 cm skin incision.

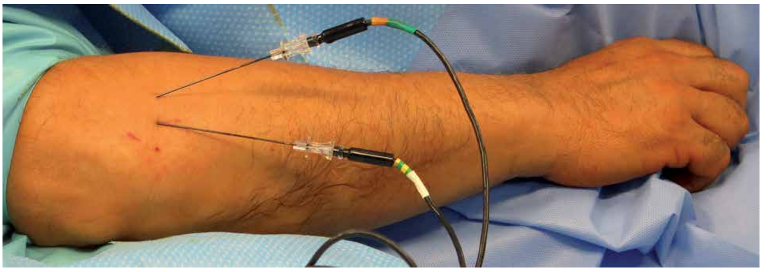

Figure 1.
Bipolar radiofrequency treatment of lateral epicondyle chronic pain.

The tendons from the extensor carpi radialis brevis, the extensor carpi radialis longus and the extensor digitorum communis are identified. The radiofrequency-based microtenotomy is performed with the Topaz Microdebrider electrode. The electrode is inserted 3–5 mm deep inside the extensor carpi radialis brevis tendon at 5 mm intervals in a grid-like pattern. Usually 3–6 lesions are required [13]. Once the procedure is over, the wound is closed by layers. After the procedure, patients are discouraged from heavy work for 6 weeks.

The monopolar capacitive-coupled radiofrequency is performed with the Alpha Orthopaedics' AT2 System and applied directly to the skin without any anaesthetic agent [78, 83]. The painful points are marked and a grid depicted on the skin to guide the treatment's application. A grounding pad is placed on the forearm volar side. The energy pulses are delivered applying the equipment hand piece directly on the skin and concentrated on the most painful points. Patients are advised not to apply ice or NSAIDs over the treated area and to return the next morning to normal daily activities with no restrictions at all [78].

Another alternative is thermal radiofrequency, applied with a Radionics RFG-3C Generator (Radionics Inc., Burlington, Massachusetts, USA) [77]. The procedure is guided and controlled with ultrasound imaging. With the patient in the supine position, the painful lateral epicondyle areas are identified by manual palpation and marked with a pen. After local anaesthetic agent is injected, a 22-gauge cannula is inserted through the skin with a 30–45° angle and advanced to the painful spots parallel to the extensor carpi radialis brevis tendon. To confirm the painful spots, sensory stimulation is applied at 50H frequency and 0.5 V. Muscle stimulation is also performed to rule out proximity of any motor nerve or that the active electrode tip lies inside muscular tissue. Another 0.3 mL of local anaesthetic is injected though the lesioning cannula and the radiofrequency applied to achieve a temperature of 80° for 120 s. For optimal results, the lesion should be performed at the extensor muscle humeral insertion [77]. Patients are allowed to regain normal working activities by 6 weeks after the procedure.

To improve the results, we do a variation of this procedure. The thermal radiofrequency is applied not monopolar but bipolar. This increases the size of the lesion and covers the painful areas better. To do it, two radiofrequency cannulas are used (22 gauge, 100 mm length, 5 mm active tip, Halyard, Alpharetta, GA, USA) and the energy provided by a generator (Coolief Cooled Radiofrequency Pain Management Generator, Halyard Alpharetta, GA, USA) (**Figure 1**).

4. Conclusions

Lateral epicondylitis is a painful condition that often resolves spontaneously. The recalcitrant cases in which the pain persists can be treated with a vast array of options. Physiotherapy and local steroid injections are commonly used. Further conservative treatment modalities include local injection of botulinum toxin, platelet-enriched plasma, autologous blood or stem cells. The traditional open surgery has been subsided by other less invasive procedures like arthroscopic or percutaneous tenotomies. Radiofrequency, particularly thermal, has been proven as an adequate alternative to the surgical procedures and after failure of conservative treatments. Although in the past the radiofrequency was applied through a 3–5 cm skin incision, it is now possible to apply it through a cannula, minimising the surgical aggressiveness, reducing the patients' discomfort and speeding up the recovery.

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Chapter 5

Percutaneous Radiofrequency Hip Joint Denervation

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Abstract

With an aging population, chronic osteoarthritic hip joint pain is becoming a major issue. Most patients with hip pain can control their pain with conservative measures but with a gradual reduction in their quality of life. When gradually reduced ambulation and pain become recalcitrant, total hip arthroplasty is the next step. For most patients, this is a good way to improve pain control and to recover some quality of life, but for a few this aggressive surgical procedure is not possible. Sometimes co-morbidities make total hip arthroplasties undesirable. At other times, the age of the patients recommends to wait for a while. In these cases, other options have to be explored. Percutaneous partial hip joint sensory denervation has become a notable option as it can provide acceptable rates of pain relief with minimal surgical aggressiveness. There are three modalities to perform it: thermal, cooled and pulsed radiofrequency.

Keywords: chronic hip joint pain, hip osteoarthritis, hip joint denervation, treatment of chronic hip pain, radiofrequency hip joint denervation, interventional pain management, obturator nerve, femoral nerve, radiofrequency ablation, post-total hip arthroplasty pain

1. Introduction

Hip joint osteoarthritis - the most frequent cause of chronic hip pain (CHP) [1, 2] - induces pain, rigidity, muscular atrophy, and walking and sleeping difficulties [3–7]. Its prevalence in people over 45 years old is 9.2% [8]–11% [9] (men 7%–8.7%, women 9.3–10% [1, 8, 10]), reaching 25% by 85 years of age [11]. Not all cases with radiological changes are symptomatic [1, 12]. Other less common causes of CHP are osteonecrosis, rheumatoid arthritis, chronic infectious or post-traumatic arthritis and persistent pain after a total hip arthroplasty (THA) [13, 14].

Conservative measures are the first line of treatment [9, 15, 16]. These include physiotherapy and anti-inflammatory medication [17]. Intraarticular steroid or hyaluronic acid injections are helpful but only on a short term basis [17–20]. THA is indicated when the pain is chronic and the reduced mobility persists despite all conservative measures [21]. This surgical procedure is undertaken in hip joints damaged due to osteoarthritis, rheumatoid or inflammatory arthritis and avascular femoral head osteonecrosis [22–24]. THA is a very common surgical procedure world-wide [25], with more than 500000 cases/year in the USA [22] and 400 cases/year/100000 inhabitants in Sweden [26] (1.4 million THA/year in the whole European Union).

At times, THA is not recommendable due to concomitant severe co-morbidities that increase the risk of severe post-operative complications [27] or because the doctor, the patient or both of them think that it is better to wait before undertaking such a radical surgical procedure. Another reason to delay THA is its failure rate - 5-15% [28–31] - with 7–28% of patients left with post-operative CHP [32–34]. As THA implants have a life expectancy ranging from 10 to 25 years [30, 35–37] many surgeons consider that under 50 years of age it is wiser to delay this surgical procedure as much as possible [38–41]. When THAs are not advisable, hip joint denervation is an option that has been performed for over one hundred years. Continuous refinement in the surgical technique to achieve the denervation of this joint has ameliorated results and reduced complications and side effects.

2. Anatomy of the hip joint capsule nerve supply

The sensory nerve supply for the hip joint is provided by the obturator, femoral and sciatic nerves [42–53] as well as by the lumbar sympathetic plexus [42, 45]. The antero-lateral aspect of this joint is innervated by branches from the femoral nerve, the antero-medial by the accessory obturator and obturator nerves, and the posterior from the sciatic nerve though the *quadratus femoris* nerve branch and the superior gluteal nerve [42, 44, 46, 54–56]. The largest sensory nerve contribution for the hip joint comes from the obturator nerve and the *quadratus femoris* nerve branch [42, 44, 57], while the hip capsule areas with the highest articular nerve coverage are the superior, the anterior and the antero-medial [55, 58].

The articular branches coming from the femoral and obturator nerves can be reached with ease and limited risk of side effects [42, 46, 55, 59], but the hip sensory branches coming from the sciatic nerve are too close to its main trunk to cut them safely [60]. The femoral nerve articular branches pass by close to the periosteum between the inferior iliac spine and the ilio-pubic eminence [44], to lie below the ilio-psoas tendon above the anterior and lateral aspects of the HJ [55, 59]. The obturator nerve's articular branches travel between the pectineus and obturator externus muscles entering the medial joint capsule at the pubo-femoral ligament close by the infero-medial acetabulum in the area known as the "pelvic teardrop" [44, 55, 59]. The accessory obturator nerve can be found at the ilio-pubic eminence just before giving off its hip articular branches [44, 61–63].

Just as the obturator nerve goes out of the obturator canal it divides into two main branches [45]. The anterior branch innervates the adductor *longus*, *pectineus* and *gracillis* muscles and provides sensory branches for the hip joint capsule [46, 55, 59] and runs in the interfascial plane between the pectineus and adductor brevis muscles [64]. The posterior branch innervates the obturator externus, adductor *magnus* and brevis muscles and provides a sensory branch to the knee joint [42, 46, 65].

Referred groin area pain from the hip joint is conveyed by the articular branches of the obturator nerve, while trochanteric area pain comes from the articular branches of the femoral nerve [27, 42, 54]. In a damaged hip joint, the biggest discomfort comes from hip flexion (putting trousers on, climbing stairs) and from hip abduction (genital area hygiene) [66]. The sensation for both movements are mostly covered by the articular branches of the obturator and femoral nerves [42].

3. Historical background hip joint denervation

Selig [67] in 1912 was the first to report obturator nerve trunk intra-pelvic open surgical resection to control chronic osteoarthritic hip joint pain. To alleviate the pain coming from hip extension, other surgeons added the section of the *quadratus femoris* nerve branch [68]. This combined surgical technique was adopted widely [65, 69–71], but gradually abandoned because it induced hip adductor weakness and numbness at the inner thigh [57, 72]. Adding the section of the articular branches of the femoral nerve to the previous combined technique of obturator nerve trunk and quadratus femoris nerve branch resection was reported in 1975, showing improvement in hip pain control [73]. The inconsistent results of all these open surgical procedures were attributed to the wide anatomical variation of the hip joint articular branches [74].

Attempting to avoid the side effects induced by intra-pelvic obturator nerve trunk resection, some researchers attempted local anesthetic agent infiltration at the obturator nerve outside the obturator canal and at the *quadratus femoris* nerve branch and reported that it also provided good short term pain relief [43, 57, 72, 75–82]. This pain improvement lasted usually one to four days [27, 81] but in some exceptional cases up to three months [80, 81]. This extended effect has been attributed to the rupture of the pain vicious cycle [17, 81]. The next supplement was steroids, added to the local anesthetic agent in hip joint infiltration. Steroids are useful short-term [17] but repeated injections can lead to an increase in the infection rate if THA is attempted [83] and to articular cartilage damage [84]. Alcohol injected at the hip joint capsule has been used to treat acute hip fracture pain in people in their nineties [85]. Nowadays, local anesthetic blocks are used exclusively for diagnostic purposes [86].

Moreover, Okada et al. [87] in 1993 introduced the use of thermal radiofrequency to control hip pain. They found it advantageous because it could be applied percutaneously with specially designed cannulas, the size and shape of the lesion could be controlled through the intensity and time of the applied electrical current, and the lesion could be repeated if necessary [88]. Okada et al. lesioned the obturator, femoral and *quadratus femoris* nerves [87]. The obturator nerve trunk was lesioned at its exit from the obturator canal, inducing the same weakness in the hip adductor muscles and sensory loss in the inner aspect of the thigh [87] as with intra-pelvic resection of this nerve.

Hence, over the years several groups of researchers have attempted to improve thermal radiofrequency hip joint partial denervation to maintain pain control effectiveness whilst reducing its side effects [27, 54, 75, 77, 89–93]. Others researchers have also investigated other methods which might yield better results, such as pulsed radiofrequency [94, 95] which avoids damage to the treated nerves because the local temperature does not rise over 42°C [96].

4. Diagnosis, inclusion and exclusion criteria

The clinical diagnosis of chronic osteoarthritis is based on pain in the hip area aggravated by activity (walking, putting trousers on, genital area hygiene, etc.). At times patients find difficult to sleep on the affected side. On clinical examination, there must be pain on hip abduction and flexion. The radiological evaluation of the hip osteoarthritic changes is based on the Kellgren-Lawrence classification [97, 98].

To confirm that the pain is coming from the hip joint and to try to predict the results of a partial hip joint denervation, a diagnostic block of the articular branches is performed [27, 54, 75, 77, 87, 89, 90, 92, 99–102]. Patients are contacted the next day or the following week after the anesthetic block and at least 50% pain improvement is required to proceed with a partial hip joint sensory neurotomy [95, 103], although some researchers request two positive results to diagnostic blocks [103]. These blocks have a good predictive value as there is good correlation between anesthetic block pain relief and the results of articular branch thermal radiofrequency neurotomy [103].

4.1 Inclusion criteria

Moderate to severe CHP for more than 3 months duration with ambulation impairment, unresponsive to conservative treatments [86], radiographic Tönnis grades I and II [40] and refusal of the Orthopedic Surgeons to perform a THA.

4.2 Exclusion criteria

Lumbar radiculopathy, Paget's disease, neurological disorders, hip bony fracture and local infection

4.3 Indications

Hip osteoarthritis [27, 54, 75, 77, 87, 92, 94, 104, 105], rheumatoid arthritis [87], osteonecrosis [87], avascular necrosis [90, 92, 99, 100], chronic infectious coxarthrosis [77, 87], metastasis [54, 92, 101] and persistent pain after THA [27, 87, 90, 102] or after hip dislocation [54, 91].

In most reported series, patients are older than 47 years [75, 77, 87, 89, 90, 92, 94, 104], with only a few cases in the group of 26 to 46 years of age [54].

5. Surgical technique

The first step is to perform an anesthetic block to rule out other causes of buttock/groin pain [82, 100]. This is performed following the technique described by Locher [55]. The patient is placed supine on a radiolucent table and sedated with Propofol (0.5 mg/kg/h). A 22-gauge 80–100 mm long spinal needle can be used. A radiofrequency cannula is preferred (Neurotherm, KC, Cosman® 20G 145mm long needle with a 10 mm un-isolated tip, Burlington, Massachusetts, USA) because it allows electrical stimulation before injecting the local anesthetic agent. Electrical stimulation is performed with a Cosman® Radiofrequency Generator (Burlington, Massachusetts, USA) at 0.4–0.6 V at 50 Hz, 1 msec (sensory testing) and less than 0.9 V at 2 Hz, 1 msec (motor testing). This reduces the chance of anesthetic agent injection close to the main nerve trunks instead of near the articular branches [27, 77, 89–91, 94, 99–102].

The pubic tubercle and femoral vessels must be localized by manual palpation (**Figure 1**) but if the location is not fully clear (e.g. obese patients) ultrasound guidance is advisable [85, 91, 101–103].

For the obturator nerve articular branches, the needle is inserted two centimeters medial to the femoral vessels and two centimeters below the inguinal ligament. The needle is advanced under radiological guidance in the AP projection towards the bottom of the *incisura acetabuli* until the bony "teardrop shape" is reached (outer upper quarter of the junction point between the superior pubic and the ischia-iliac rami, at 2 or 10 o'clock position depending on the side). Bone contact should be felt at the tip of the needle. Electrical stimulation with the above mentioned parameters is performed to rule out proximity to the obturator nerve trunk.

For the femoral nerve articular branches, the needle is inserted 2 cm lateral to the femoral vessels and the needle is advanced again under radiological guidance. The needle's tip is positioned at the antero-lateral margin of the hip joint, below the anterior inferior iliac spine. Again, electrical stimulation with the same parameters is performed.

Figure 1.
Local anesthetic block, palpating the femoral vessels.

Needle aspiration must be performed before injecting any local anesthetic agent to prevent accidental intravascular administration. No intra-articular anesthetic agent injection is performed. Once both needles are in place (one for the obturator and one for the femoral nerve articular branches) 1-2 ml of local anesthetic - lidocaine [75, 77, 90, 99, 101], mepivacaine [89], bupivacaine [92, 100, 103] or ropivacaine [95] - are injected through each needle. No more than 1-2 ml of local anesthetic agent must be used to avoid false positives induced by its spread to nearby major nerves (femoral and obturator) or inside the hip joint itself [95, 103]. Some researchers have added steroids (e.g. triamcinolone) to the anesthetic block [101] aiming to prolong the beneficial effects.

Patients are interviewed the following day [86] or the following week [89]. Only those reporting in a VAS scale (Visual Analogue Scale) ≥ 50% pain reduction for the time of action of the local anesthetic agent are considered for percutaneous radiofrequency hip joint neurotomy. It is important to record not only the degree of pain control but also its duration, as the duration of action varies between the different anesthetic agents from two hours for lidocaine [106], two to four hours for mepivacaine [107] and ropivacaine [108] and four to eight hours for bupivacaine [109] – making bupivacaine the preferred anesthetic agent for this type of blocks [92, 100, 102].

Patients showing no improvement with the anesthetic block are referred back to Orthopedic Surgery and to the Physiotherapy Department for further treatments.

5.1 Description of the thermal radiofrequency partial hip joint denervation

The patient is placed supine on a radiolucent table. X-ray, ultrasound or both can be used for guidance during the procedure. A light sedation with propofol is provided.

First, the femoral nerve articular branches are reached with the aid of an 18 gauge, 100 mm length, 10 mm active tip cannula (Halyard, Alpharetta, GA, USA) or a 20G 145mm long needle with a 10 mm un-isolated tip (Neurotherm, KC, Cosman®). The location of skin puncture can be antero-medial (two centimeters lateral to the femoral vessels) [54, 77, 87, 89, 92, 101] or antero-lateral (ten centimeters lateral to the same anatomical structure) [27, 55, 89, 91, 104, 110] (**Figure 2**). Some surgeons are reluctant to use the antero-medial approach as there were three cases of post-operative local hematoma due to femoral artery incidental puncture [27], although other researchers avoid this by using ultrasound guidance [91, 101–103]. Furthermore, Stone and Matchett use ultrasound to navigate the needle in the antero-posterior direction passing between the femoral artery and vein to reach the obturator nerve articular branches [101].

In the lateral approach to the femoral nerve articular branches, the cannula is inserted in the lateral side of the thigh about 10 cm below the anterior iliac spine close to the antero-lateral border of the hip joint. The cannula crosses the *rectus femoris* tendon and the *iliacus* muscle with final position in the area between the ilio-femoral ligament just above the femoral head. This is the place where the articular branches of the femoral nerve travel over the pubic bone before reaching the hip joint [85].

Next, the obturator nerve's articular branches are approached from the thigh medial side, medial to the femoral vessels (**Figure 3**) or from a lateral approach (**Figure 4**). The same type of cannula is used as for the femoral nerve articular branches. The target area is deep to the *pectineus* muscle, adjacent to the pubo-femoral ligament at the junction of the pubic and ischia-iliac rami [59, 85]. As the obturator nerve branches have a big area of distribution [55], the needle tip must be placed as parallel as possible to the ischia-iliac ramus to increase the probability of lesioning all of them [102].

Just as in the anesthetic block performed earlier, electrical stimulation with a Halyard (Alpharetta, GA, USA) or a Cosman® Radiofrequency Generator (Burlington, Massachusetts, USA) should be done at 0.4–0.6 V at 50 Hz, 1 msec

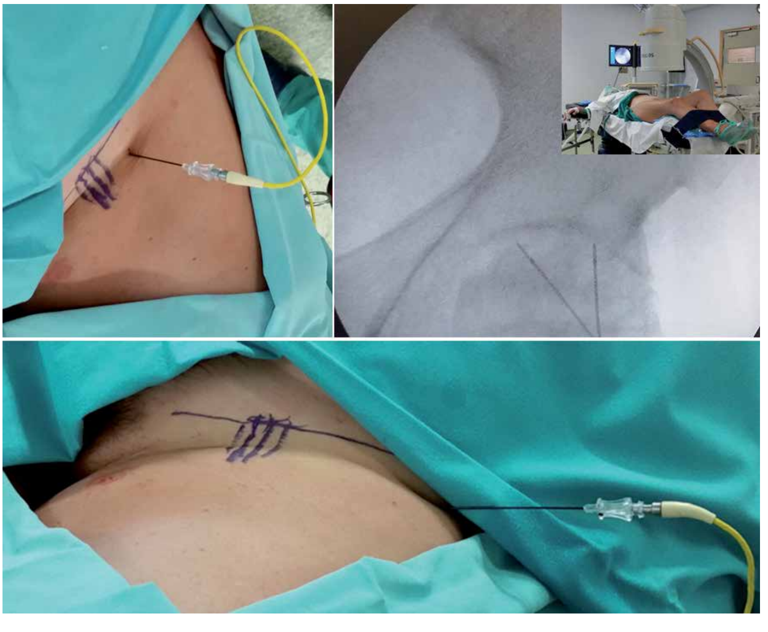

Figure 2.
Monopolar antero-medial versus antero-lateral femora nerve articular branches radiofrequency neurotomy.

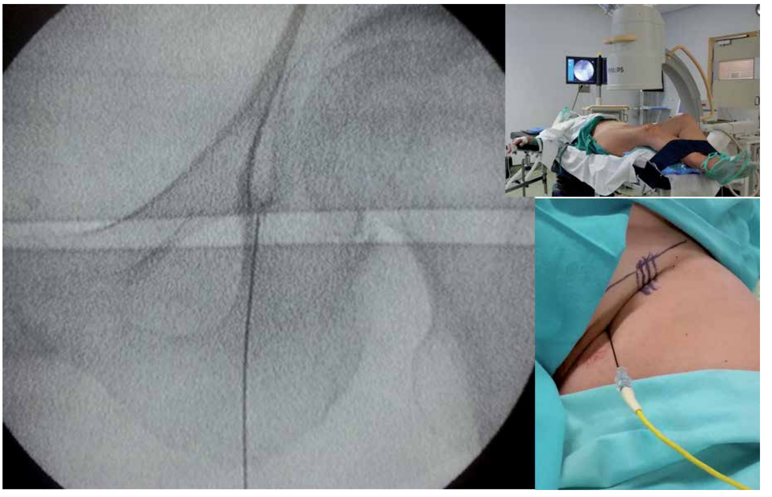

Figure 3.
Monopolar antero-medial obturator nerve articular branches radiofrequency neurotomy.

(sensory testing) and less than 0.9 V at 2 Hz, 1 msec (motor testing) to rule out proximity to the obturator or femoral nerve trunks. This step is essential to avoid sensory anesthesia, neuropathic deafferentation pain or motor nerve damage that could induce weakness of the adductor and/or hip flexor muscles. If any abnormal motor or sensory response is seen, the tip of the cannula has to be repositioned and the electrostimulation repeated. Once in a safe position, two consecutive thermal radiofrequency lesions for each of the femoral and obturator nerve articular branches are made at 90°C for 120 seconds, varying the position of the needle. Patients are continuously monitored for any signs of discomfort. Then, 20 mg of methylprednisolone are injected through the lesioning cannula to reduce local swelling and to prevent a possible neuritis of the lesioned nerves [95]. After the I.V. Propofol effect weans off, patients are discharged home with monitoring.

5.2 Intraoperative guidance

Most clinical studies use only radiological guidance. In the AP X-ray projection, the "teardrop" for the obturator nerve articular branches [27, 54, 89, 91–93, 100, 101, 104] and the antero-inferior iliac spine and the supero-lateral aspect of the acetabular margin for femoral nerve articular branches [27, 54, 91, 92, 100, 104] have been found as reliable landmarks. Adding electrical stimulation [111] or ultrasound guidance [80, 91, 101, 103, 112, 113] to the fluoroscopy increases the accuracy of nerve and great vessel localization, but does not improve the pain relief [27], meaning that they increase the safety of the procedure but do not affect the concluding results [27].

5.3 Nerve targets

Almost all reported studies aim to lesion the articular branches of both femoral and obturator nerves [27, 54, 77, 87, 90–92, 94, 99–101, 100, 104]. The two exceptions are a group of researchers – Akatov and Dreval and Vanaclocha et al. - that only lesioned the obturator nerve articular branches [75, 89] and Kim et al. that applied radiofrequency only to the femoral nerve articular branches in a single case of hip pain after a revision THA. The articular nerves supplying the posterior hip

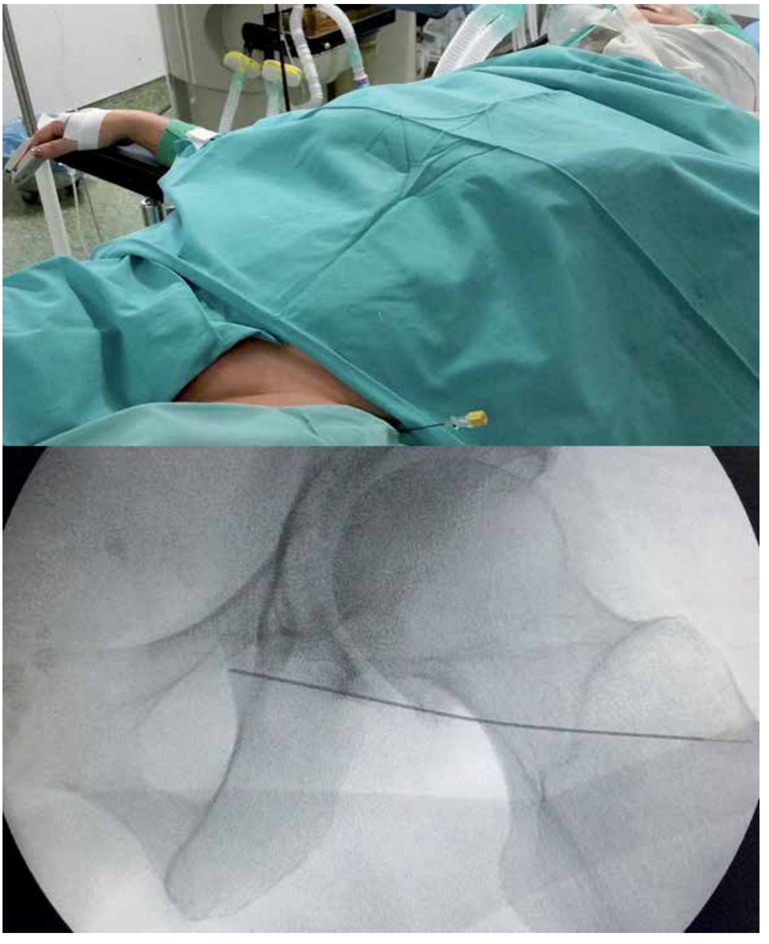

Figure 4.
Monopolar lateral obturator nerve articular branches radiofrequency neurotomy.

joint capsule coming from the superior gluteal and sciatic nerves were lesioned in a single patient, but no details on how the surgical procedure was performed were provided [87].

5.4 Type of radiofrequency: thermal, pulsed or cooled

Thermal radiofrequency with temperatures ≥80°C are the most commonly used [27, 75, 87, 89, 104]. For a maximal effect, the lesioning cannula has to be placed parallel to the nerve branch to be lesioned [114] and as close as possible to it [115]. This is important to remember when inserting the needle, as a completely vertical approach will diminish the damage to the target articular nerve branch [88].

The precise anatomical distribution and number of the articular branches vary widely between individuals and even between sides of the same patient [55]. Thus, a bigger lesion has a bigger chance of lesioning all or at least most of them [103, 116, 117]. This is the reason why some researchers use cooled radiofrequency [102, 103], as it creates lesions much larger than regular thermal radiofrequency [116, 118–120]. Another advantage is that cooled radiofrequency lesions project forwards from the needle tip, so that an articular nerve branch placed perpendicular to the needle can be lesioned [116, 117, 119]. Nevertheless, a lesion too big has also the risk of painful post-operative neuritis as described in a case of cooled radiofrequency [103]. The advantage of cooled radiofrequency is that it allows a single big enough lesion [102, 103] instead of having to repeat the procedure at least twice as in the case of thermal radiofrequency [116–118]. Another possibility is to use bipolar thermal radiofrequency, which we previously explored [89] (**Figures 5** and **6**). This can increase the shape and size of the lesion. Nevertheless, the higher the number of needle passes the higher the chance of incidental femoral vessel puncture with local hematoma formation [103].

Radiofrequency with temperatures over 55°C induces indiscriminate nerve fiber damage due to protein denaturation [121] and possible neuropathic pain [122, 123]. This is the case of both thermal and cooled radiofrequency (60°C) [102]. Thus, some researchers have used pulsed radiofrequency [90, 94, 95] because the temperature does not increase over 42°C and there is no irreversible neural tissue damage [96, 122]. However the effects are not long-lasting, about 3–4 [90] months to a year [94, 95].

5.5 Gauge of the lesioning cannulas

Their size varies among different doctors with 25 [103], 22 [27, 77, 85, 90, 91, 94, 99, 100], 21 [101], 18 [89, 95] or even 17 [110]. Although a bigger diameter increases the size of the final lesion it also increases intraoperative pain and the chance of post-operative local hematoma formation. Contrariwise, too thin cannulas are difficult to navigate inside the muscle bulk to reach a deep location. The choice is probably a compromise for each individual doctor.

Figure 5.
Bipolar antero-medial obturator nerve articular branches radiofrequency neurotomy.

Figure 6.
Bipolar antero-lateral femoral nerve articular branches radiofrequency neurotomy.

5.6 Lesioning cannula tip size

The exposed electrode tip varies from 4mm [77] to 5mm [27, 91] and 10mm [89, 90, 94, 95, 104]. A 10 mm exposed tip is better as the location of the obturator and femoral articular nerve branches has a big anatomical variation between patients and between sides of the same patient [55]. Thus, a bigger lesion has a higher chance of success.

5.7 Temperature of the radiofrequency lesion

In thermal radiofrequency it varies from 60°C [102] to 75–80°C [54, 75, 87, 91, 92, 99, 104] or even 90°C [27, 77, 89, 100]. To allow for the wide anatomical variability it is recommended to increase the temperature over 80°C to induce a lesion of sufficient size that includes all articular branches [88]. In pulsed radiofrequency, the temperature is raised to 42 [94]-45°C [90].

5.8 Time to create the lesion

Duration matters, as lesion size increases 11–20% from 1 to 2 minutes and 20 to 23% from 2 to 3 minutes [88]. The times used have varied from 60 [91] to 80 [101], 90 [27, 27, 54, 92, 99, 100],, 150 [102] and 180 seconds [94]. Again, a larger lesion is advisable provided it does not damage the nearby 120” [75, 77, 87, 90, 104] femoral and obturator nerve trunks. Most groups of researchers report using 90” [27, 27, 54, 92, 99, 100] or 120 seconds [75, 77, 87, 90, 104] per lesion.

5.9 Number of lesions

The majority of researchers only do two lesions (one for the femoral and one for the obturator articular nerve branches) [27, 54, 75, 87, 91, 92, 100, 101]. Only three studies report two adjacent lesions per treated nerve to improve the lesion size to account for the anatomical variability in the number and distribution of the articular branches [89, 99, 104]. This was already recommended by Locher et al. [55] after a cadaveric anatomical study and confirmed recently by Short et al. [44].

6. Results

The open intrapelvic surgical section of the obturator nerve trunk introduced by Selig [67] provided 83% pain relief at six months [71] and 18% at three years [124]. Okada et al. [87] report pain relief in 14 out of 15 patients with no further details. Akatov and Dreval [75] lesioning the obturator nerve trunk at its exit from the obturator canal reported pain relief in 12 out of 13 patients with an increase in the range of hip motion in 9 patients and 80% 'excellent' results at 3 years follow-up. Fukui and Nosaka [77] reported 80% pain relief and improvement in walking at 6 months with gradual return of pain by 2 years without reaching baseline pain levels. Kawaguchi et al. [54] reported 60% pain reduction in 11 out of 14 patients with a failure rate of 22%. Malik et al. [92] reported 30–70% pain reduction with improvement in function in 3 out of 4 patients and decrease in pain medication use in 2 out of 4 patients. Rivera et al. [27] reported 33% pain reduction with ≥50% pain improvement in 8 out of 18 patients, 16% reduction in WOMAC and 34% in Harris Hip Score. Gupta et al. [104] reported 90% pain improvement with return to baseline function and stopping analgesic consumption for 6 months. Kim et al. [102] reported a single case with excellent pain control at two years follow-up.

Moreover, the reduction in analgesic use was demonstrated by some researchers but no details were provided about the reduction in the amount or follow-up [27, 92, 94, 100, 101]. Some researchers have reported that in spite of good post-procedural hip pain control, patients continue taking similar amounts of opioids [103]. This observation can be attributed to the fact that these patients often have other chronic pain conditions, i.e. chronic lumbar, cervical or knee pain [103].

The initial favorable results decline over time [77, 104] but long term data is limited. Vanaclocha et al. [89] in a follow-up ranging from 24 months to 8 yrs. (mean 3.91 ± 1.67SD yrs.) reported a marked improvement in 72 out of 131 patients (69.19%). This is the longest and most detailed study: VAS preop 8.2 ± 0.84SD; postop 2.53 ± 0.76SD 1 month, 2.40 ± 0.78SD 6 months, 3.82 ± 1.27SD 12 months and 5.07 ± 1.61SD 24 months. WOMAC pain 16.10 ± 2.15SD pre-op, post-op 3.72 ± 1.44SD 1 month, 3.56 ± 1.2SD 6 months, 5.1 ± 2.12SD 12 months and 8.36 ± 4.54SD 24 months. NSAID'S consumption, pre-op 2.78 ± 0.41SD; postop 1.67 ± 0.74 1 month, 1.44 ± 0.95 6 months, 1.55 ± 0.86SD 12 months and 1.78 ± 0.74 24 months. Opioid consumption pre-op 20.74 ± 30.23SD, post-op 9.34 ± 17.28 1 month, 8.60 ± 23.23SD 6 months, 6.63 ± 16.59SD 12 months and 12.50 ± 32.83SD 24 months. No changes in the pain control were seen after two years post-thermal radiofrequency obturator and femoral articular nerve branches neurolysis. No complications were reported.

With pulsed radiofrequency, the results are not as good. Initially, there is a ≥ 50–80% [90, 94] pain reduction with improvement in walking and reduction in analgesic medication. However pain recurs by three months and mostly within a year [3, 67, 68], not improving much on thermal radiofrequency results.

6.1 Results on repeating the procedure a second time

It has only been reported by Fukui et al. [77], Gupta et al. [104] and Vanaclocha et al. [89]. Fukui et al. [77] reported a single case with limited pain improvement but no details were provided. Gupta et al. [125] on repeating the procedure a second time found a 20–50% pain improvement, moderate limitations in function and pain medication cessation for 4 months after this second treatment. Vanaclocha et al. [89] reported that the procedure was repeated a second time in 27 out of 131 patients, and in 12 a third time. The duration of pain relief for the second-time thermal radiofrequency obturator and femoral articular nerve branches was 3–4 years (mean 3.2 ± 1.09SD years) and for the third time 2.5–3 years (mean 2.8 ± 0.7SD years). The results of the second and third procedures are evidently worse than for first one, but pain improved in a significant amount of patients.

7. Follow-up

It ranges from 3 months [90–92, 94], 4 months [90], 6 months [27, 77, 99, 100], 11 [54] months, 12 months [87], 2 years [77, 102], 3 years [75] and 8 years [89]. Longer follow-ups provide more data on the real effect of these pain controlling procedures but are limited to a single publication [89].

8. Side effects

Local hematoma formation after percutaneous radiofrequency procedure occurs sometimes when the procedure is done only under radiological guidance. Some researchers have reported three such cases [27] due to femoral vessel puncture. Ever since they changed the needle insertion point from the midline thigh area to a more lateral approach [27]. To minimize this risk, some have recommended the use of ultrasound guidance [103]. Adductor and hip muscle weakness and sensory disturbances were described in the old reports when the procedure involved lesioning the nerve trunks [67, 68, 75, 87] but not since the aim of the treatment is only the articular branches. No major complications have been described except allergy to the local anesthetic agent [27, 54, 73, 92]. Malik et al. [92] in 2003 reported a case that complained post-operatively of numbness in the inner aspect of the thigh. Cortiñas-Saénz et al. [100] reported a case of permanent anesthesia over the hip joint but no details were provided on the nerve distribution.

9. Long term consequences

A major concern is that hip joint denervation might accelerate the progression of hip osteoarthritis or induce a Charcot arthropathy. Obletz in 1949 [125] reported no radiological changes at 20 months follow-up after open partial sensory denervation of the hip, but Kaiser [65] in the same year and with the same surgical technique reported Charcot joint changes in some of his cases. Fernandes et al. [111] showed no radiological deterioration in a 5 to 14 month follow-up after anesthetic block. Only Kang and Bulstrode [126] saw radiological deterioration after repeated hip anesthetic and cortisone blocks, perhaps attributable to the cortisone being injected inside the hip joint. No cases of hip joint degeneration attributable to the technique have been observed with hip radiofrequency - thermal, pulsed or cooled - articular nerve branch neurotomy. In a study with eight years follow-up, Vanaclocha et al. [89] did not see any radiographic changes suggestive of acceleration of natural degenerative progression.

10. Conclusions

Aging population may suffer from significant co-morbidities that may impede hip arthroplasty. Percutaneous radiofrequency denervation of the femoral and obturator sensory branches to the hip offers an alternative for those patients with severe hip pain who are not surgical candidates. The relative simplicity of this technique is worthwhile for these patients, often confined to wheelchairs and with no prospect of surgical relief. They are often pleased even with a partial pain improvement. This procedure had no major complications and could be applied to patients who had a very poor general status. The results are satisfactory in the majority of cases with a good long term control reported for the thermal radiofrequency. With cooled radiofrequency there are no long term follow-up [102, 103] reports and with the pulsed radiofrequency the pain is back in less than a year.

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Chapter 6

Uterosacral Nerve Ablation and Presacral Neurectomy in the Treatment of Chronic Pelvic Pain in Women

Funda Gungor Ugurlucan and Cenk Yasa

Abstract

Chronic pelvic pain affects 2–24% of women in the reproductive period. There are various causes of chronic pelvic pain in women including gynecologic, urologic, gastrointestinal, and musculoskeletal problems. The treatment of pain is directed toward the underlying pathology. However, in some cases, no pathology can be found, and sometimes, more than one underlying pathology may be found in the same patient. Surgical denervation methods may be used in the treatment of chronic pelvic pain in women including uterosacral nerve ablation and presacral neurectomy. Uterosacral nerve ablation has been used as a treatment method for uterine causes of pelvic pain. It has been used widely in the treatment of dysmenorrhea- and endometriosis-related pain. But recent randomized studies and meta-analysis have questioned the effect of uterosacral nerve ablation in the treatment of chronic pelvic pain. Presacral neurectomy involves damage of the uterine sympathetic innervation at the level of superior hypogastric plexus. It is effective in the treatment of midline pelvic pain. It has been found to be more effective than laparoscopic uterosacral nerve ablation in a randomized study. The method, effect, and studies evaluating uterosacral nerve ablation and presacral neurectomy will be discussed in this chapter.

Keywords: uterosacral nerve ablation, presacral neurectomy, LUNA, chronic pelvic pain, dysmenorrhea

1. Introduction

Chronic pelvic pain (CPP) is a constant or recurrent pain and generally defined as lasting for more than 6 months, and clinically carries significant physical, functional, and psychological impacts that have an adverse effect on quality of life. This pain frequently localized to the pelvis, the anterior abdominal wall at or below the umbilicus, lumbosacral back, and the buttocks. Its prevalence ranges from 6.4 to 25.4% in different countries, and about 18% of women take 1 day of sick leave annually due to CPP [1].

The etiology of CPP has not been clearly defined and explained. This disorder has multifactorial overlapping etiology, and more than 70 causes are associated with CPP [2]. Acute pain is a result of tissue damage and reveals simultaneously with healing, but chronic pain persists long after the tissue has healed or remains stable in the absence of etiological factors. In chronic pain, some lesions affect the central and peripheral nervous system. Sometimes immunologic factors like cytokines and chemokines activate normally inactive fibers and cause peripheral nervous system dysfunction. Also, long-term pain could increase pain stimulus which is called visceral hyperalgesia.

Etiological factors of CPP can be divided into gynecological or non-gynecological causes. Endometriosis, adenomyosis, leiomyomas, ovarian tumors, pelvic inflammatory disease, surgery related adhesions, and pelvic congestion syndrome are mostly encountered gynecologic causes. Also, surgical, urological, gastrointestinal, musculoskeletal, psychosomatic, and neurological problems could be causative factors of CPP.

The etiology of CPP is complex and multifactorial; therefore, extensive diagnostic procedures are required. The first but maybe the most important step consists of history-taking and physical examination. In history-taking, the factors that induce or aggravate pain should be clarified. Also, effects of pain on the quality of life should be assessed. With the results of this initial step, imaging studies such as transvaginal ultrasound of the pelvis, computerized tomography (CT), magnetic resonance imaging (MRI), and venography could direct diagnosis and management. Blood tests, bacteriological tests, and cystoscopy also may be useful in the differential diagnosis [3]. Last of all, diagnostic laparoscopy may be performed keeping in mind that in 1/3 of the patients etiologic factors cannot be identified by laparoscopy.

The aim of therapy in CPP is to improve quality of life and overall function. Treatment is focused mainly on symptomatic relief. In the presence of obvious etiological factors, it should be treated. But even in these patients, targeted therapy may not result in resolution of pain. Because pain generators involve multiple mechanisms, treatment should include physical, behavioral, psychological, and sexual components. In the first-line management, if the underlying disease process is known, treatment should be directed according to specific management of this cause. If treatment is inadequate or the cause of pain is not known, with the pharmacological therapy, symptomatic relief should be targeted. To do this, analgesics, hormonal therapy (e.g., oral contraceptive, progesterone, levonorgestrel-releasing intrauterine system, gonadotropin-releasing hormone agonist), tricyclic antidepressants, serotonin-norepinephrine reuptake inhibitors, anticonvulsants, and opioids are potentially useful medications. Surgical interventions, sometimes may be diagnostic, should be guided by the underlying diagnosis. Diagnostic laparoscopy, conscious laparoscopic mapping, adhesiolysis, surgical excision of ovarian remnant, and hysterectomy are the among the most common surgical procedures in the management of chronic pelvic pain [4].

For the patients with CPP who desire to retain their reproductive potential, surgical pelvic denervation procedures may be useful. First, presacral neurectomy was described by Jourboulay and Ruggi in 1899 [5]. These procedures showed decrement after the increase in the use of analgesics and hormonal contraceptives. With the introduction of minimal invasive surgical techniques, pelvic denervation procedures had become popularized especially in the medical treatment-resistant patients.

Superior and inferior hypogastric nerve plexuses carry pelvic visceral pain through the sympathetic nervous system [6]. These afferent fibers that carry pain signals from the upper vagina, cervix, and uterus should be targeted for pelvic denervation. The sacrouterine ligament is the point that inferior hypogastric nerve plexus exits the uterus. At the sacral promontory in the interiliac triangle bilateral inferior, hypogastric nerves come together to form the superior hypogastric plexus which return to the spinal cord through lumbar splanchnic nerves. Especially, the pain fibers from the ovary and distal fallopian tubes go through the ovarian plexus to the vagus nerve. Because these fibers join with the superior hypogastric plexus, pelvic denervation procedures are only indicated for patients with midline pelvic pain.

Pelvic denervation procedures are indicated in women with chronic pelvic pain with a predominant midline component who desire to maintain their reproductive potential and fail or have contraindications to medical management [7]. Patients with endometriosis who have midline chronic pelvic pain, pelvic denervation interventions also improve pain when combined with surgical excision of endometriosis [8].

2. Presacral neurectomy

Presacral neurectomy is the surgical procedure that transects the superior hypogastric plexus to denervate the sensorial communication of the pelvic viscera and abdominal wall in order to treat refractory pelvic pain [9].

In this surgical procedure, experienced surgeons in the presacral space are essential. Due to known benefits of minimally invasive surgery and the advantage of identify potential etiologies of pelvic pain, conventional or robot-assisted laparoscopy is the preferred route for presacral neurectomy. Presacral space has close proximity to major vascular structures such as aortic bifurcation, common iliac arteries, left common iliac vein, and inferior mesenteric artery and ureters (**Figure 1**). The parietal peritoneum overlying the sacral promontory is incised transversely. Original opening is extended proximally to the point just above aortic bifurcation and distally to the sacral promontory. Especially, complete removal of fibrous and adipose tissue located between the iliac vessels is crucial because modification of procedure leads to lower than expected success rates [10]. Visualization of vasculature and ureters all during procedure prevents major complications.

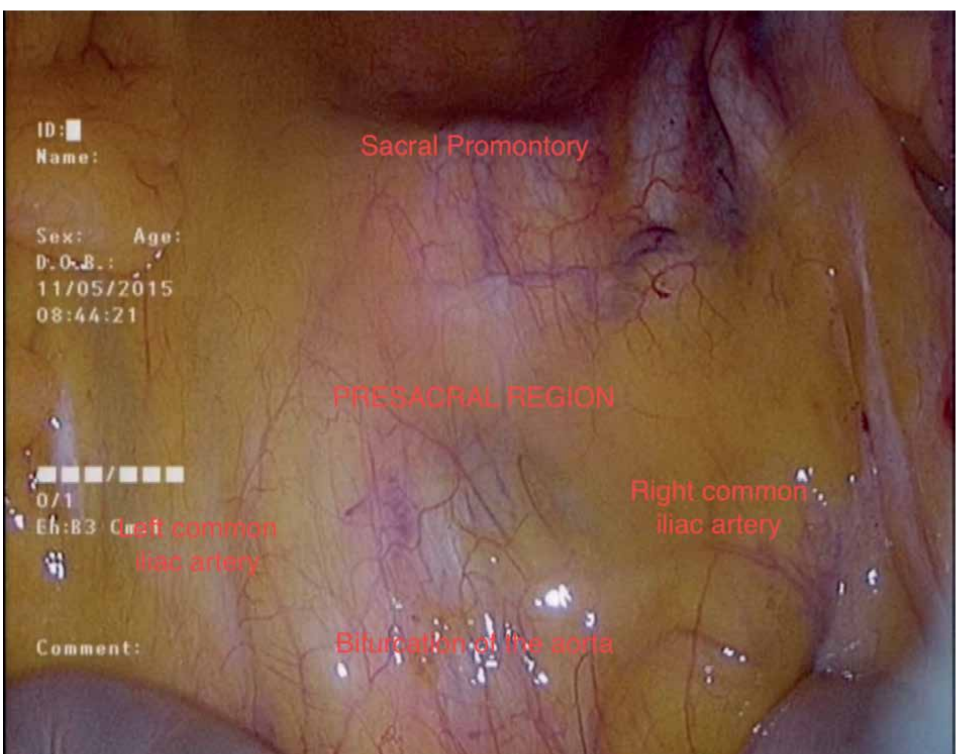

Figure 1.
The appearance of the presacral space.

Cadaveric studies have revealed numerous anatomic variations of the localization and morphology of the superior hypogastric plexus [11]. Ripperda et al. found that the superior hypogastric plexus was located inferior to the aortic bifurcation in 83% of the cases and it was located superiorly in the rest [12]. Correia et al. reported six different morphologies of the superior hypogastric plexus [13]. These anatomic variations are a challenge for surgeons during presacral neurectomy.

There are no randomized controlled trials regarding presacral neurectomy in the treatment of CPP. Retrospective studies report success rates of 62–73% with this intervention, especially in patients with CPP unresponsive to other treatments [14, 15]. Regardless of pathologic features, improvement in midline pelvic pain is observed more than lateral pelvic pain [16].

Presacral neurectomy is also used in combination with endometriosis surgery. In these patients, additional midline pain relief related with menses but not dyspareunia or nonmenstrual pain was demonstrated [17, 18]. In one randomized controlled trial, addition of presacral neurectomy to conservative laparoscopic surgery in endometriosis patients reported improvement in dysmenorrhea, dyspareunia, and quality of life of patients than endometriosis surgery alone [19]. Patients with midline pelvic pain associated with endometriosis have greater improvement in pain if presacral neurectomy is added to surgical treatment of endometriosis.

Middle sacral vessels and left common iliac veins are major vascular structures more prone to injury. In order to prevent ureteral injury, identification of the ureter prior to nerve dissection is important. With the careless transection of lymphatic vessels, chylous ascites may be encountered. This complication could be prevented with sealing of the lymphatic vessels. There have been limited reports about bowel and bladder dysfunction with respect to this procedure. Among them constipation is very well known [20].

Hagg et al. evaluated the sexual functions of women who underwent anterior fusion and denervation of the superior hypogastric plexus [21]. The authors found disturbance in orgasm and genital sensation of 20% women who underwent surgery. Martin-Alguacil et al. studied the neuronal tracing from the clitoris to the spinal tracts in female mice and found that pudendal and hypogastric nerves had a major role in the innervation of the external genitalia and neuronal pathologies, and trauma may lead to sexual dysfunction [22]. The possible effect of presacral neurectomy on sexual functions should be evaluated in randomized studies.

3. Uterosacral nerve ablation

The presence of nerve fibers and ganglia in the uterosacral ligaments has been described in the nineteenth century [23]. Sympathetic fibers originating from T10 to L1 spinal roots run through the superior hypogastric plexus which is at the level of the aortic bifurcation in the presacral space. Nerve fibers from the superior hypogastric plexus split into two hypogastric nerves that course along the internal iliac vessels on each side and connect to the inferior hypogastric plexus.

The parasympathetic innervation derives from S1 to S4 via the pelvic splanchnic nerves and travels through the lateral pelvic wall to join the inferior hypogastric plexus and form the Frankenhauser ganglia lateral to the cervix. The inferior hypogastric plexus consists of three areas: the vesical plexus, the uterovaginal plexus, and the middle rectal plexus.

The uterovaginal plexus receives sympathetic fibers from T10 to L1 and parasympathetic fibers from S1 to S4 and lies on the medial side of the uterine vessels, lateral to the attachment of uterosacral ligaments (**Figure 2**). Therefore, division of the uterosacral ligaments may interrupt many sensory fibers that carry painful stimuli of the cervix and uterine corpus.

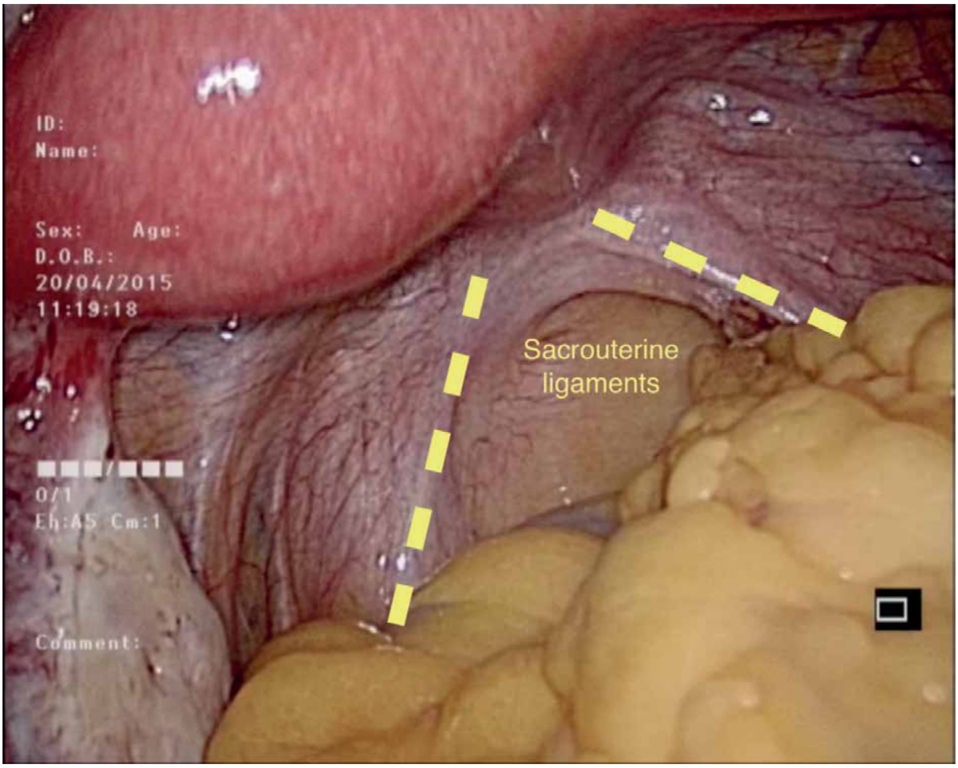

Figure 2.
The uterosacral ligaments located on the inferoposterior part of the uterus contain the nerve fibers of the inferior hypogastric plexus.

The technique of uterosacral nerve ablation was first described by Ruggi in 1899 [24]. Later, Doyle evolved the technique proposed by Ruggi [5]. Doyle suggested that the transection of the cervical division of the Frankenhauser uterovaginal plexus lying in, around, and under the terminal 2.5 cm of the uterosacral ligaments permitted sensory denervation of the cervix and uterine fundus and the proximal parts of the uterine tubes. Transection of the nerve fibers did not result in autonomic imbalance because both sympathetic and parasympathetic pathways were interrupted and the rectal and bladder functions were not affected. In Doyle's series, dysmenorrhea was relieved in 69 of 73 cases (94.5%). Relief was partial in six cases (8.2%), and there were four failures (5.5%) [5].

Uterosacral nerve ablation may be performed through abdominal, vaginal, or laparoscopic routes. Laparoscopic route is called laparoscopic uterosacral nerve ablation (LUNA). There are huge variations in the technique of LUNA without clear evidence on which technique is superior to the other [25]. It has been suggested that division of the uterosacral ligaments approximately 1.5 cm distal to the cervix should interrupt many sensory nerve fibers of the cervix and uterine corpus, and Doyle suggested that this was possible even through the vaginal route [5]. However, anatomical studies showed that the majority of uterosacral nerve fibers were found at a distance of 6.5–33 mm and at a depth of 3–5 mm distal to the attachment site of the uterosacral ligaments to the cervix [26]. There are widespread variations in the technique performed, including the route of surgery, the site of nerve ablation, and the method used for nerve ablation such as laser, electrodiathermy, scissors cutting, or harmonic scalpel [27].

Uterine nerve ablation is performed under general anesthesia. At the beginning of the procedure, attention should be given to the course of the ureters and the neighboring vessels in order to prevent inadvertent damage. A uterine manipulator may aid in the visualization of the uterosacral ligaments by permitting anteflexion of the uterus. First, incision is made on the medial aspect of the ligament at its insertion to the uterus, and the second incision is made lateral to the uterosacral ligament and medial to the ureter. The ligament may be grasped with a forceps and stretched toward the lateral pelvic wall to aid in the ablation process. One or both of the ligaments may be transected. Full or partial transection of the ligaments may be done bilaterally with laser or electrodiathermy, according to the surgeons' preference. Laser usage may result in less thermal damage to the neighboring structures. The posterior part of the cervix between the insertions of the uterosacral ligaments may be ablated to interrupt the sensory fibers that cross to the contralateral uterosacral ligament. A small portion of the ligament may be transected and examined histologically to confirm the presence of the nerves fibers in the specimen [28].

Uterine nerve ablation may be classified as a safe operation with few complications reported in the literature; the complications such as constipation, postoperative bleeding, and urinary urgency were more common with presacral neurectomy when compared with LUNA [29]. Potential adverse events that may be observed after uterosacral nerve ablation include vascular, bowel or ureteric injury, bleeding, the need for conversion to open surgery, and pelvic organ prolapse.

Latthe et al. evaluated the variations in the indications and surgical technique of LUNA among the members of the UK Royal College of Obstetrics and Gynecologists and European Society of Gynecological Endoscopy [30]. The most common indication for LUNA was chronic pelvic pain (68%) followed by dysmenorrhea (66%), endometriosis (60%), and dyspareunia (39%). The authors stated that the European group was more likely to perform LUNA (62 versus 21%), and the technique differed between the two groups. The European group completely transected the uterosacral ligaments (56 versus 36%) and at a distance of more than 2 cm from its cervical insertion (50 versus 21%) when compared to the UK group. The authors concluded that there was variation in the LUNA technique in Europe according to operator experience. In addition to variations in the technique and indications, gynecologists' opinions regarding surgery for CPP may differ. Latthe et al. evaluated the gynecologists' beliefs about the effectiveness of laparoscopic uterosacral nerve ablation using a structured survey [31]. Twenty-five gynecologists responded to the questionnaire; none stated that LUNA would increase pain, while two gynecologists stated that the intervention would worsen the pain. However, most of the respondents believed that LUNA would have a small beneficial effect on pain.

There are studies evaluating the efficacy of uterosacral nerve ablation in the treatment of primary or secondary dysmenorrhea, CPP related to endometriosis, and dyspareunia. Feste reported significant improvement in the symptoms of primary dysmenorrhea or dysmenorrhea associated with endometriosis in 71% of the patients who underwent uterosacral nerve ablation [32]. Donnez et al. reported complete relief in 50% and mild to moderate relief in 41% of the patients [33]. Davis reported significant improvement in dysmenorrhea and dyspareunia in 92 and 94% of the patients with endometriosis who underwent uterine nerve ablation and vaporization of endometriosis, respectively [34]. Yen et al., in their randomized study, evaluated the effect of LUNA on secondary dysmenorrhea associated with myoma and concluded that LUNA had a beneficial effect on alleviating pain related to dysmenorrhea [35]. Lichten and Bombard in their randomized, prospective, double-blind study of the effect of LUNA on treatment-resistant dysmenorrhea showed complete relief in almost half of the patients 1 year after surgery [36].

Johnson et al., in their randomized study included 123 patients with chronic pelvic pain. There was significant reduction in dysmenorrhea, but there was no benefit in nonmenstrual chronic pelvic pain in patients with or without endometriosis [37].

No improvement was observed on dyspareunia and dysmenorrhea. Vercellini et al., in their randomized study on the effect of LUNA on endometriosis-related dysmenorrhea, showed no reduction in the frequency and severity of dysmenorrhea [38]. LUNA had no additional effect on health-related quality of life, psychiatric profile, and sexual satisfaction. Shawki, in his randomized controlled trial, evaluated the efficacy and satisfaction related to LUNA in patients suffering from CPP associated with either no or mild endometriosis [39]. The authors found no significant difference between the groups that underwent diagnostic laparoscopy and LUNA and diagnostic laparoscopy only in the treatment of primary and secondary dysmenorrhea, but there was a significant difference regarding dyspareunia. Daniels et al., in their randomized controlled trial, showed that there was no significant difference regarding pain scores and quality of life between the LUNA group and no LUNA in the treatment of CPP [40].

There is only one randomized trial comparing the effect of presacral neurectomy and LUNA. Chen et al. compared the effect of presacral neurectomy and LUNA on primary dysmenorrhea [41]. Laparoscopic presacral neurectomy was more effective than LUNA in the long-term follow-up. In a systematic review of nine randomized trials on the surgical interruption of the pelvic nerve pathways, five trials investigated the effect of LUNA, two trials laparoscopic presacral neurectomy, and two trials open presacral neurectomy [42]. For the treatment of primary dysmenorrhea, LUNA had a small beneficial effect when compared to control group. There was no significant difference between LUNA and presacral neurectomy in the treatment of dysmenorrhea in the short-term follow-up; however, laparoscopic presacral neurectomy was more effective than LUNA in the long term. LUNA was not found effective in the treatment of secondary dysmenorrhea.

Therefore, although initial case series have shown promising results, both prospective and randomized controlled studies have shown that LUNA had no significant effect in the cure of CPP, but it may have a beneficial effect in some patients with pelvic pain and primary dysmenorrhea. The European Society of Human Reproduction and Embryology (ESHRE) guideline on management of women with endometriosis has suggested that clinicians should not perform LUNA as an additional procedure to conservative surgery to reduce endometriosis-associated pain and presacral neurectomy was effective as an additional procedure to conservative surgery to reduce endometriosis-associated midline pain with significant potential complications [43].

4. Conclusions

Pelvic denervation procedures such as presacral neurectomy and uterosacral nerve ablation have been evaluated in the treatment of chronic pelvic pain with or without endometriosis with varying results. Recent randomized trials regarding uterosacral nerve ablation have shown no significant benefit of uterosacral nerve ablation. Presacral neurectomy may be used as an adjunct in the treatment of CPP with or without endometriosis; however, the surgery may not have the desired effect due to variations in the anatomy. In addition, the beneficial effect may diminish over time due to regeneration of the nerve fibers.

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Chronic pain is a part of the human condition, despite immense advancements in pain treatment and management. In many societies, easy access to opioids has created a drug abuse crisis. Unfortunately, we seem to have forgotten many techniques that have been used in the past with great success. Some of these techniques continue to be useful, particularly in areas of the globe where resources are limited. This book attempts to remind those of us in the medical profession about the existence of some of these techniques and their ongoing utility. We need to master them or keep them in our armamentarium for the good of our patients.

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