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Review Article

Non-Manual Pain Therapy in the Lumbo-Pelvic Hip Region

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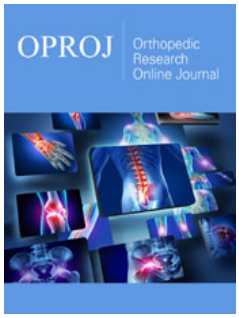

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Abstract

The goal of manual medicine / chirotherapy is to relieve patients of their pain. However, some types of pain cannot be treated by manual therapeutic methods. Therefore, the current article reviews non-manual forms of pain therapy and their mechanisms of action. A distinction must be made here between nociceptive and neuropathic pain. On one hand, these are pharmacological approaches based on world health organization (WHO) recommended treatment techniques and their current guidelines, whilst on the other hand they represent invasive treatments such as neuromodulation. For the benefit of all patients, this article aims to span a division between the two mentioned approaches to pain therapy.

Keywords: Neuropathic pain; Nociceptive pain; Pharmacotherapy; Denervation; Neuromodulation

Introduction

Manual medicine / chirotherapy may be the most people-centered method against pain of the skeleton system and inner organs [1]. Aim of this method is to relieve patients of their symptoms, mostly therapy-resistant pain [2]. Nevertheless, due to different reasons there is pain that cannot be treated just by manual medicine. Hence, we are reviewing pharmacological and invasive treatment options focusing on the lumbo-pelvic hip region. It is required to differentiate between different types of pain.

History

Tooth extractions, wound management, amputations and trepanations were performed about five millions of years ago. Mechanic, thermic, chemical, and electric pain therapies were performed ever since. These include massages, rubbing with nettles, alcohol, cold water compresses, passive stretching, Sulphur baths, diets, prayers, meditation and much more. Chewing willow bark was well known as an anti-inflammatory therapy, and thereby acetylsalicylic acid was found and in 1897 first-time synthesized. The production of opium out of opium poppy was found in 4000 bc. Scribonius [3] was a roman medical doctor, who described electric shocks from Torpedinidae as pain therapy including migraine [3]. In 1804 morphine was extracted out of Opium and 1772 nitrous oxide, also known as laughing gas, was found.

Propaedeutics, pain process, therapeutic option

Pain is an unpleasant sensory and emotional feeling associated with an actual or potential tissue damage. Pain that is caused by a usually not painful stimulation is called allodynia. Hyperalgesia is known as an increased sensitivity through irritation due to touch or not painful temperature. A painful state as a result of intensified reaction on a stimulus, or repeated stimuli with an increased threshold of pain, is called hyperpathias. And lastly, dysesthesia is an unpleasant and abnormal perception, spontaneous or as a result of irritation.

Besides the sensorial sense and psychological feeling, chronical pain includes various other factors: anxiety, depression, frustration, immobility, anorexia, sleep disorder, decline in quality of life and many more. The world health organization (WHO) developed treatment guidelines on pain: A Three-step strategy. The first step comprises mild to moderate pain, which can be treated with nonsteroidal anti-inflammatory drugs (NSAID), selective

cyclooxygenase-2-inhibitors (COX-2-inhibitors) and non-acidic non-opioid analgesics.

If there is further pain, step two adds mild opioids, with the option to add anticonvulsants and antidepressants.

The last step, step three suggests using strong opioids, if necessary, in combination with medication that is used in step one and/or adjuvants [4]. According to this step strategy a pain free stadium is ought to achieve, which clearly is not the case. Additionally, local anaesthetics, physiotherapy and physical therapies are used. Furthermore, options such as anaesthesia or a neurosurgical intervention to reduce pain can be explored.

Physiology of pain

Pain can be caused by mechanic, thermic or chemical destruction of the tissue, subdivided in nociceptive, neuropathic and functional pain [5]. Anatomical and physiological basics of pain perception are shortly revised since pain therapy is based on them.

Nociceptive pain

Nociceptive pain can be caused by mechanic, thermic or chemic tissue damage. All perceptions and reactions are conveyed by sensory cells. Series-connected sensory cells convert an impulse into an electric discharge and conduct it to the brain, where a translation takes place. The Brain can react to this pleasant or unpleasant information with either grant or flight. An irritative vertebra leads to an unpleasant sensorial and emotional perception, which concludes in motoric (restriction of motion), verbal (shouts), and emotional (crying) reactions.

Pain matrix

The substantia gelatinosa in the back horn of the spinal cord form the nociceptive afferents of the peripheric synapses with ascending spinal cord neurons, which transmit the pain signal through the tractus spinothalamic us and tractus spinoreticularis to the brainstem [6]. After one more synapse in the thalamus the signal reaches the cerebral cortex and thus the conscience. Functional Imaging studies [Positron-Emission-Tomography (PET)] show following anatomical structures for pain processing [7]:

Thalamus, basal ganglia, midbrain, periaqueductal grey, anterior cingulate cortex, insular cortex, primary sensory cortex (s1), secondary sensory cortex (s2), motor cortex, supplementary motor cortex, prefrontal cortex, posterior parietal cortex, and cerebellum. A distinction is made between

a) the lateral pain signal conduction, which is mainly responsible for the sensorial discrimination and

b) the medial pain signal conduction, which is mainly responsible for the motivational-affective and cognitive-evaluative and furthermore seems to be responsible for the "pain memory" as well as for autonomic and endocrine pain.

The lateral system transfers the impulse through the tractus spinothalamics via the ventrobasal thalamus to the primary (s1) and secondary (s2) sensory cortex and to the parietal operculum and insular cortex. The medial system passes the impulse from the tractus spinothalamicus through the intralaminar and medial thalamic nuclei to the anterior cingular cortex, amygdala, hippocampus, as well as via the spinoreticular projections through nucleus parabrachialis and locus coeruleus and through the spinomesencephalic procetions to the periaqueductal grey.

Neuropathic pain

In comparison to nociceptive pain, neuropathic pain occurs due to injury of neural structure itself (caused by trauma or of originating in trauma, inflammation, toxic, plexus avulsion or injury, neural root injury or by damage and injury of the central nervous system). Usually neuropathic pain is a loss of information in the central nervous system with an area of hypesthesia and an area of burning pain. In neuropathic pain peripheric information is lacking. A damage or dysfunction of nociceptive fibers leads to an abnormal generation or even a loss of impulse. Consequently, there are neuropathic changes of axons, glial tissue, surrounding tissue.

A decrease in the concentration of substance P and "calcitonin gene-related peptide" and a gain of galanine and neuropeptide Y in structures of primary afferent neurons may lead to a hyperexcitability and ectope pacemaker with an uncontrolled burst of neurons. Additionally, membrane characteristics may be changed. Information, in form of bursts, is forwarded from the periphery via sensorial and/or nociceptive neurons to the brain. If these are missing, the patient feels a sensible deficiency, a hypoesthesia, in this region. A pain perception dysfunction can be associated with hyperpathia or even anesthesia. The Brain replaces the lack of information with dysesthesia and usually burning pain or allodynia.

Prevalence: Neuropathic pain remains one of the most common neurological diseases. In Europe, the prevalence is 7-8%) prevalence of chronic pain with neuropathic characteristics in the general population [8,9].

Reasons: The most frequent causes of neuropathic pain in Europe include diabetes mellitus, alcohol-related polyneuropathy, vitamin b deficiency, uremia, pollutants, toxins, drugs, chemotherapeutics, autoimmune response, zoster, borreliosis and other infections, aids, trigeminal neuralgia, impingement-syndrom, backpain, phantom pain, complex regional pain syndorm (CRPS), bone fractures, bruises, sprain, malnutrition, diseases of stomach and small intestine as well as diseases of eyes and teeth [10].

Pathophysiology: The main pathological principle of neuropathic pain was issued in a few reviews during the last couple of years [11-13]. It is to be noted, that neuropathic pain is often therapy resistant and might deteriorate and intensify over time and is commonly not respected by insurances and legal trails. It can emerge on every part of the conducting or processing pathway of pain. If pathological changes occur in neurons or spinal ganglions, then that can lead to ectopic, unusual activity and sensibilization of nociceptive C- and A (delta) fibers. Augmented neurogenic inflammation is one of the reasons, e.g. in complex regional pain syndrome a modified expression of ion channels or in Waller-degeneration an increased release of pain and inflammatory

substances such as prostaglandins and proinflammatory cytokines. After peripheral lesions of nerves, spinal neurons can be sensitized too. In that case arriving signals are enhanced to higher centers. Excitatory neurotransmitter glutamate, a reduced inhibition of Gamma-Aminobutyric Acid (GABA), cholecystokinin, and the purinergic system have a major function as receptors in the central sensibilization. Also, proinflammatory, probably released out of glial cell, cytokines can lead to an alteration of spinal neurons after cell damage. Not least, spinal excitability is under the control of descending paths [14]. In some diseases e.g. acute inflammatory myelitis or radiculitis causal, therapy exists, but most of times therapies are needed to reduce severe pain states.

Key information

It is mandatory to be aware of that pain (like all perceptions) is generated in the brain not at the site of alleged perception. Nociceptive pain nerves are stimulated peripherical and the signal is the sum of action potential "bursts", which is forwarded to the brain. The pain is perceived in the cortical level, to prevent further harm. In neuropathic pain the "bursts" are caused by a damage or disease of the pain conducting sensory pathway, because of which the signals are not reaching the brain. Other previous suppressed neurons are starting ectopic oscillation resulting in burning painful states within sensory deficient areas.

Treatment of different pain modality

Nociceptive pain is mostly drug-treated. Neuropathic pain rarely responds to standard analgesics. Therefore, there are other opportunities ranging from conservative pharmacological to surgical invasive therapies.

Pharmacological therapies

The approach in pharmacological therapies in Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) is the prostaglandin biosynthesis. 1-series of prostaglandins act highly anti-inflammatory and influence blood clotting. The 2-series of prostaglandin has the exact opposite effect. They trigger wound healing. The use of Acetylsalicylic acid is attempted to suppress this effect. 3-series of prostaglandins decrease the genesis of 2- series prostaglandins and are therefore described as anti-inflammatory.

Endorphins are endogenous opioid neuropeptides, built in the diencephalon, hypothalamus, and pituitary gland out of proenkephalin and proopiomelanocortin. In vegetative synapses and other areas of the brain, like grey matter of the spinal cord opioid receptors were found. An excitation of endorphin receptors resulting in a suppression of pain stimuli. This can be achieved by medicine or physical activity. An increase of the excitation threshold by calcium- and/or sodium channels-dependent membrane potential is gained by anticonvulsants. The synaptic transmission is achieved by serotonin reuptake inhibitors and muscle relaxants. Cortical neurons are blocked by barbiturates and benzodiazepines. Aim of pharmacological therapies is to get to a pain free stadium or at least nearly pain free stadium.

According to the guidelines of the German society of neurology [15] neuropathic pain reduction between 30-50% is to strive for. Quality of life and sleep is attempted to be improved. We are taking the acute joint pain, a nociceptive pain, as a sample. Caused due to an acute irritation, without inflammation. The pharmacological therapy is listed in the national guidelines NVL "not specific lumbar pain" [16].

Aim of that NVL program includes:

A. Recommendations on interdisciplinary approach according to the best knowledge of medicine, regarding the criteria of evidence-based medicine.

B. Recommendations concerning reconciliation and coordination within different disciplines of healthcare

C. Auditing all disciplines, organizations, and patients for a more effective implementation of the recommendations.

D. To consider NVL-guidelines in medical education and further training, in quality management systems as well as in treatment programs

E. High quality patient information and decision-making tools for a common decision between doctors and patients.

Before initiating medical treatment, following principles, based on expert consensus, may be taken into account:

A. To inform that medical therapy is a supporting option in backpain only.

B. To determine a realistic and relevant aim of therapy, considering the body function e.g. to improve walking distance, resilience, or relevant reduction of pain (>30% or >50%)

C. Individual medicines respecting comorbidity, comedication, allergies, patients' preferences.

D. Stepwise titration of medication to reach the best effect with the lowest dose.

E. Regular examinations to verify the effect and to avoid side effects

F. In case of acute pain to wean as soon as possible after recovery

G. To continue with the therapy just in case of a good response

H. To quit the therapy in case of inefficacy

NSAIDs: Basically, the use of NSAIDs in the treatment of not specific back pain is recommended in the lowest effective dose for a short time period and no parenteral use. In case of risk of gastrointestinal complications, additional use of proton-pump inhibitors (PPIs). Due to the high risk of side-effects and interactions it is recommended to weigh the individual risk-benefit ratio. If NSAIDs are incompatible or contraindicated, COX-2 inhibitors can be used for unspecific back pain.

Opioids: The following is recommended for the use of opioids in acute unspecific back pain:

Opioids can be used in the case of lack of response to nonopioid analgesics or in presence of contraindications. The use is limited from 4 to 12 weeks in case of chronical unspecific back pain. Regular evaluation of this therapy should be after latest 4 weeks, in case of acute unspecific back pain and after 3 months, in case of chronic back pain. In chronical not specific backpain the time period of the use of the therapy can be expanded, if a clinically relevant reduction of pain can be obtained and no or only few side-effects occur. In case of nonresponse, the therapy must be interrupted. Transdermal opioids are not intended to be used in acute or subacute pain. A detailed information regarding the side-effects is obligatory.

A maximum dose of 120mg per day of an oral morphine equivalent may be exceeded just in exceptional cases. In the setting of a long-term therapy, it is to be noted that in the case of pain exacerbation it is not right to initially increase the opioids, but to start the NSAID therapy. The prevention of abuse is another important issue. After 6 months of therapy response a dose reduction or weaning (always stepwise) is to be considered. Furthermore, the indication has to be reevaluated in case of therapy continuation.

Muscle relaxants

The use of muscle relaxants is not recommended for acute or chronical unspecific backpain. A short time effect is seen in comparison to placebo for only two weeks. There are no benefits of using it in combination with NSAIDs compared to using NSAIDs alone. There are more frequently gastrointestinal and central nervous side-effects.

Antidepressants: There are no recommendations for antidepressants in not specific backpain. A comorbid depression or sleep disorder justify an additional use. Tricyclic antidepressants are used up to 80%-90%. Comparing to placebo no advantage has been proven.

Anticonvulsants: An anticonvulsant therapy with gabapentin, pregabalin, topiramate and carbamazepine is not recommended. The side-effects outweigh the antinociceptive effect.

Analysis of posture and patient activation

Compared to the medical treatment, the neurosurgical treatment is attempted to eliminate the source of the pain. In case of nerve compression due to a slipped disc, an operation may be a solution against pain, but first the sedation of the concerning segment is attempted. This can be reached by putting the pelvis into an upright position, posture training, and mobilization. Laying with knees raised is ought to suspend nociceptive stimulus. Medical treatment alone is contraindicated and supports misconducting of hyper lordotic lumbar spine, resulting in a flat os-sacrum-angle appearing like a "Donald Duck tale". This is affecting the main axis of the gait. The femur is in a wrong angle to the acetabulum. Subsequently the lower leg is in a malposition to the femur and that results in an unequal load of the knees. This, in turn, results in unequal load of the ankle joints. In the forefoot area that may cause a Morton´s neuroma, due to unequal load. Most important pain therapy is the education of patients.

Lesional treatment

Cryo- thermodenervation: Mundinger and Cosman implemented thermo-controlled lesions. Hence many painful facet joints were treated. 1976 the cry denervation was implemented as a pain treatment therapy. Both methods are effectively used in nociceptive pain of vertebral joints, facet joints and sacroiliac joints. Hereby a partial denervation is administered in the dorsal ramus, so the transmission of impulses to the dorsal roots is inhibited. Generally, this leasons keep one to up to two years. A repetition of this treatment is feasible anytime. A sprouting of nerve fibers is possible, and further thermo lesions may be ineffective. There cry denervation has an advantage over thermodenervation. This treatment mode freezes the nerve and a sprouting can be avoided, though the duration is shorter.

Pulsed radiofrequency lesion: This method is used to cause a temporary damage of nerves through an impulse without developing heat. Maximal temperature during an operation is 41 °C. This technique can avoid a sprouting too. Indications for pulsed radiofrequency lesions are cervical and lumbar facet joint syndrome, treatment in the gasserian ganglion, stellate ganglion, lumbar ganglia. With this method chronical pain, traumatic or degenerative genesis can be treated.

Neuromodulation

Neuromodulative methods were invented 50 years ago, thereby a transient or permanent reversible electric manipulation of neuronal structures, is performed [17]. Nowadays there is a wide spectrum of treatment of chronical pain conditions [18]. Distinction between neurostimulation and intrathecal administration of pharmaceutical therapy is made. In 1967 Shealey et al. [17] introduced the first chronic spinal cord stimulation. Initially subdural, later on epidural, using thin platinum electrodes. Chronic electric impulses resulted in an overlap of tingle paresthesia in neuropathic burning pain. Due to an activation of contact fibers (Aβ-fibres), pain conducting fibers (C-fibers) in the gelatinous substance of the posterior horn of spinal cord are inhibited [19]. In the 1960s Reynold showed an analgesia in animals, by stimulating the periaqueductal gray. Hosobuchi, Richardson [20] achieved good results in human pain therapy by stimulating the periaqueductal gray, maybe due to release of endorphins. These days many lesional methods can be replaced by neuromodulated methods, with a massive reduction of side- effects [21-23].

The main field of use is neuropathic pain. Neurosurgical techniques are seen as the last stage of treatment, because of their invasiveness. Stimulation can take place in different levels as spinal cord stimulation, nerve root stimulation, dorsal root ganglion stimulation, peripheral nerve, peripheral ganglion stimulation [24,25], subcutaneous stimulation [26]. Deep brain stimulation [27,28] and motor cortex stimulation [29-32] were invented later.

Epidural Spinal Cord Stimulation (SCS): SCS is a method used in not oncological, chronical, non-responsive to pharmacological treatment, neuropathic pain. The mechanism is based on the stimulation of afferent Aβ fibers and the inhibition of Aδ and

C fibers in the gelatinous substance. This technique is used in radicular neuropathic or composite neuropathic pain, nociceptive pain in the upper and lower limbs as failed back surgery syndrome, complex regional pain syndrome, phantom limb pain, peripheral neuropathy, vascular pain, incomplete cross section syndromes. This method is reversible. Depending on the type of electrodes this operation is done in local anesthesia. Target is the epidural area of the spinal cord. After the surgical part, a trial period of some days is added, to discover the best modulation. If the stimulation is successful, the pacemaker is implanted in full anesthesia. The pacemaker can be adjusted by the doctor and patient. State of the art SCS include high frequency stimulators, new configurations of electrodes, integrated acceleration sensors for auto adjustment in case of position change of patients., compatible systems with MRI, wireless systems etc. Yearly almost 14.000 people receive SCS.

Deep brain stimulation: In 1980s deep brain stimulation developed to a highly effective treatment option in pharmacological not treatable Parkinson's disease and essential tremor. Furthermore, it can be used in nearly all types of dystonia, Huntington's disease, Tourette syndrome, heavy alcohol and drug addiction, major depression, obsessive-compulsive disorders. During the last years, this technique improved also in the treatment of nociceptive and neuropathic pain. This method can be modified at any time of the treatment and can also deactivated. For deep brain stimulation platinum electrodes are used with a diameter from 1.2-1.5mm with 4 or 8 electrode contacts. The author has developed a method with 2 electrodes per hemisphere. One is placed in the sensory thalamus accessing from frontal, and the second in the posterior capsula interna accessing from parietal.

After the surgical part, here too a trial period of some days up to some weeks is added, to discover the best modulation through percutaneous programming of intensity, frequency, pulse width, continuous or cyclic stimulation, low or high frequency. If the stimulation is successful for the purpose of a pain reduction of more than 60%, the pacemaker is implanted. In case of disease progress or increasement in pain the parameters of stimulation intensity, frequency, penetration depth, can be adjusted. The number of impulses per second determines the effect of the current. Low frequency stimulation with 1-80Hz cause an activation or rather an irritation. High frequency stimulation with more than 100Hz leads to an inhibitive effect [33-37].

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