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Treatment of Residual Pain After Total Knee Arthroplasty

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ABSTRACT

Currently, total knee arthroplasty (TKA) is a well-established surgery in medical practice, with a high degree of success. However, recent studies have reported that many patients show dissatisfaction, including residual pain and limited function, even after TKA without evident clinical or radiological findings. Understanding the causes of the residual pain by a systematic approach is essential to its treatment and, in some cases, revision surgery is mandatory. Once the eminent surgical indications were excluded, we performed the non-operative treatment. The goal of the treatment is to decrease pain and improve knee function. Periarticular injections and nerve blocks are gaining popularity for being effective, with low adverse effects. The use of pain medications should be carefully indicated as a support, and the advantages should be evaluated individually.

Abbreviations: TKA: Total Knee Arthroplasty; PCS: Pain Catastrophizing Scale; PRP: Platelet Rich Plasma; PNB: Peripheral Nerve Blocks; FNB: Femoral Nerve Block; ACB: Adductor Canal Blockage; GNB: Genicular Nerve Blocks; RCT: Randomized Controlled Trail

Introduction

Currently, Total Knee Arthroplasty (TKA) is a well-established surgery in medical practice, with a high degree of success. TKA is indicated in cases of severe knee osteoarthritis that had no success with conservative non-surgical treatment, in patients without contraindications to surgical treatment, who are aware of and agree with the risks inherent to the surgery. The literature demonstrates that TKA is capable of improving knee pain, function and deformities in the last stage of osteoarthritis [1,2], but complications are not uncommon. Rozell investigated a group of 802 patients who underwent TKA and hip arthroplasty and found that 382 patients had postoperative complications [3]. The level of satisfaction with the results of the surgery is not high, with dissatisfaction reaching levels higher than 50% [4-8]. Considering that the absolute and relative numbers of TKAs in society is increasing, and that the population is growing continuously, associated with an increase in longevity, metabolic syndrome and joint diseases, it is expected that the number of complications and unsatisfactory results in TKA tend to essential in the conduction of the patient with residual pain after TKA. A review of the surgery without the proper diagnosis, in most cases leads to persistence of pain or case worsening [9]. The diagnosis of residual pain after arthroplasty, its surgical indications, and especially indications and non-operative treatments will be discussed in this paper.

Diagnosis and Pathogenesis of Residual Pain After Total Knee Arthroplasty

There are many causes of residual pain after TKA, and the literature classifies the symptoms in several ways, mainly as: (a) articular and extra-articular and (b) infectious and non-infectious. The focus of this review is to determine which diagnoses indicate a revision surgery or other surgical procedure, and those (that appear to be the overwhelming majority) which will be treated with interventional techniques for pain and regenerative medicine. The most important for the elucidation of the cause of pain in these patients is to initially listen carefully to the complaint, the detailed history of the characteristics of the pain, the factors of worsening and improvement, the time of evolution, the treatments

already performed and, especially, how limiting the pain is. At this stage of the anamnesis, we suggest the use of a numerical pain scale for future follow-upand for measuring the importance of the pain. Personal and family history are also important, and this set of data alone often provides the clinician with a narrow picture of diagnostic hypotheses.

Static physical examination with the patient standing, if possible, will show alignment, deformities in flexion and recurvatum, edema, hyperemia, visualization of the scar, fistulas or wounds. In the dynamic examination, the knee's temperature is checked, as well as, the effusion test, palpation of painful stitches with pen-marking for ultrasonographic examination, passive and active flexion-extension, ligament stress and examination of the other joints, especially the lumbar sacral spine and hip. After physical examination, we routinely perform an ultrasound examination of the joint to diagnose bone and prosthesis prominences that may cause pain, especially points already marked with pen on physical examination, synovitis, joint effusion, patella height, patellar and quadriceps tendon integrity, cysts research, examination of the popliteal artery and vein and dynamic examination to show loosening of the tibial, femoral or patellar components.

When the Surgical Revision Is Mandatory

The failure of a TKA, especially if the surgery is recent, is usually caused by ascetic release, infection or instability. For a surgeon who is accustomed to the classical signs of this condition, the diagnosis is relatively straightforward. However, for a pain doctor, a special attention is needed, so as not to treat clinically a condition that is eminently surgical. In cases of release by infection, the prosthesis is removed and a spacer with cement and antibiotics is left as a "protector" of the knee for the healing period of the infection by cleaning and antibiotic therapy. After the identification of the pathogen, the assistance of an infectious disease doctor is always welcome. Once the infection has been cleared, the spacer is removed, and a new prosthesis is implanted [10,11].

Allergy to Metal

Hypersensitivity to metals affects approximately 10% of the population, mainly people who have daily exposure to metals [12,13]. Therefore, it is very important to investigate allergies to metals in the anamnesis. Nickel allergy is the easiest to identify. Chromium and cobalt allergies are the most difficult ones to be identified. They can be tested on specific exam, although dermal tests have high sensitivity but low specificity, and the skin response may not be the same as synovial tissue, which is especially very immunologically reactive [14]. The diagnosis of metal allergy is especially difficult. Some recent "in vitro" tests such as the lymphocyte transformation test, evaluation of cytokine concentration with ELISA and migration inhibitory factor, are still under academic discussion about the " in vivo" reproducibility [15]. In the clinical evaluation of patients suspected of metal hypersensitivity, we observed persistent and symptomatic effusion and synovitis, pruritus in different parts of the body and impaired joint function. Medicinal treatments usually have no effect, and usually revision with an antiallergic prosthesis is the solution. Currently, there are prostheses with less allergenic power such as zirconium and ceramics.

Other Synovitis

In the differential diagnosis of synovitis due to hypersensitivity to the metal, magnetic resonance and synovial fluid examination are common tools in the diagnosis of gout, chondrocalcinosis, polyethylene debris, rheumatoid arthritis and infection. Magnetic resonance imaging can show typical images with a high degree of specificity, and in case of release of the prosthesis by polyethylene debris, a frondlike image is a strong indication of the pathology [16,17]. Another common cause of synovitis after TKA is chondrocalcinosis. The incidence of deposition of calcium pyrophosphate crystals in knee prostheses reaches 60% in some series. In magnetic resonance imaging, the image will be of non-specific synovitis, however, the investigation of crystals in the aspirated liquid of the knee will be weakly positive, when birefringence is examined, and the crystals of urate will be negative [18].

Complex Regional Pain Syndrome

The complex regional pain syndrome is a sympathetic or parasympathetic imbalance that can occur after TKA. It is followed by local skin changes such as sweat, temperature, edema and vascularization. It can lead to knee stiffness and is often treated with blockage to enable kinesiotherapy [19-21].

Pseudoaneurysm

Pseudoaneurysm is a rare complication after TKA but should never be forgotten as a cause of pain. The pseudoaneurysm of the genicular arteries can produce bleeding that will lead to hemolytic synovitis. The diagnosis is made by palpation of pulsatile masses, bloody aspiration of the joint and color Doppler ultrasonography. Treatment of pseudoaneurysm can be performed with surgical repair or percutaneous embolization [22-25].

Anterior Knee Pain

Anterior knee pain is one of the most common causes of persistent problems after implantation of the prosthesis. It may occur in cases where patellar resurfacing has or have not been performed. The incidence of anterior knee pain after TKA is 8% [26]. The need of performing patellar resurfacing is still a great discussion in the literature. On the one hand, resurfacing can lead to complications such as aseptic loosening, lateral facet syndrome, patellar fracture and overstuffing. On the other hand, failure to perform resurfacing of the patella can lead to chondrolysis and progression of patellar arthrosis. In cases of anterior knee pain when resurfacing of the patella is not performed, revision surgery for resurfacing has low success rates, and extra-articular causes should always be considered [27]. Anterior knee pain has to be carefully considered in cases of recent surgeries, since the natural tendency is spontaneous pain reduction in one year [28]

and some non-modifiable predictors include female gender, severe preoperative pain, low pain threshold, young age and severe preoperative arthritis [29,30]. The modifiable predictors are anxiety, depression and problems in pain processing. Patients with increased postoperative pain tend to have an increased value on the pain catastrophizing scale (PCS) [31- 33].

Neurophysiology of Patellofemoral Pain

Different causes for anterior pain may be considered, however the main cause is the insertional pain of the extensor apparatus [34-37]. Patients with anterior knee pain have a higher density of nociceptors in the lateral retinaculum, and a higher incidence of mechanical disorders in the patellofemoral joint. These disorders are instability, increased pressure in the sagittal plane and poor alignment of the extensor apparatus. Several causes for these disorders may occur, such as component position error, valgus alignment, and instability. Valgus alignment may be caused by muscle imbalance (dynamic valgus) or poor component positioning. Patellar tenosynovitis, synovitis, inflammatory processes of the Hoffa's fat pad and bone edema may also cause anterior knee pain. Van Jonbergen demonstrated a significant improvement in pain after TKA with synovectomy [38-40]. Also, avascular necrosis and patellar fracture may cause anterior pain, as well as the advancement of patellofemoral arthritis, the "patella baja" which is a shortening of the patellar tendon, and the offset error of the femoral component, which increases the patellar femoral pressure [41]. Functional pain often occurs in patients after TKA, since osteoarthritis leads to a weakness of the quadriceps. In addition, usually these patients also have fragility of the adductor and abductor muscles of the hip, and even with a good alignment of the prosthesis, a functional valgus can occur, causing instability in the extensor apparatus. In these cases, the strategy of treating pain with ultrasound guided blockage is used, as it will be shown later, to allow the patient to begin kinesiotherapy to correct fragility and muscle imbalance [42-46].

Other Causes of Pain

Other causes of residual pain after TKA are cutaneous neuromas, tendinitis, periarticular bursitis, root compression of the sciatic nerve, and hip osteoarthritis. The diagnosis of incisional neuroma is performed by the examination of the scar, with palpation and provocation of the symptom. We usually use ultrasound-guided blockages in the treatment of neuroma [47]. Peri-articular bursitis and tendinitis are diagnosed by palpatory physical examination and ultrasonographic confirmation. Physiotherapeutic treatment is generally effective, and ultrasound-guided injections of Hyaluronic Acid and Growth Factors may assist as treatment adjuncts [48,49]. The diagnosis of residual pain after TKA should be extended to the ipsilateral hip and lumbar sacral column, which are frequent causes of knee pain.

Nonoperative Treatment

Once the eminently surgical indications are excluded, the nonoperative treatment is carried out. The goal of this treatment is to decrease pain and improve knee function. The functional causes are treated preferably with exercises. A systematic review has shown that kinesiotherapy should not only focus on strengthening the quadriceps, but also stabilizing the hip and trunk. Other evidence shows a positive effect on knee brace use that stabilizes the patella in cases of anterior pain. In conclusion, the gain of the knee arch and the improvement of the function and the stabilization of the joint for the perfect functioning of the musculature will always be the best way for the treatment of residual pain after TKA. However, for effective kinesiotherapy, adjuvant drug therapy or ultrasound-guided blockages is often necessary [50-53].

Joint and Periarticular Injections

The treatment of residual pain after TKA with joint injections, mainly with corticosteroids, has become a usual practice, mainly after the advances of this technique with the aid of ultrasound. Also, it is a common practice to use other substances, like hyaluronic acid, platelet rich plasma, ketorolac and other analgesics. In the case of an already installed prosthesis, any discussion about potential damages caused by the drug due to chondrotoxicity is lost, but it must be noted that the synovium continues to deserve attention and its homeostasis is necessary for the proper functioning of the knee. Corticoid is an inhibitor of the endogenous production of hyaluronic acid, while hyaluronic acid and platelet rich plasma have the property of decreasing synovitis and increasing the production of endogenous glycosaminoglycans to restore synovial liquid [54,55]. Patients with residual pain after TKA have high levels of P-substance in the synovial fluid. Botulinum toxin, which is a neurotoxin, has high affinity for cholinergic synapses, causing a blockage in the release of acetylcholine from these nerve terminals, without altering the electrical conduction signals and/or the synthesis and storage of acetylcholine. Jasvinder found significant improvement in pain and knee function with residual pain after TKA with botulinum toxin joint injections and found no side effects in the 6 months period of study [56]. The major concern in joint injections is infection. While studying the risk of infections in corticosteroid injections in knees with pre-existing prostheses, Mills found a risk of 1 infection per 625 injections [57]. The indication of joint injections may take place in selected cases, when the suspicion of infection already exists and the aspiration of the inflammatory fluid is programmed, or in cases of rebellious synovitis to all other proposed treatments and where there is already the indication of synovectomy. Even so, the patient should be advised of the risk of infection.

Periarticular injections are generally used to control immediate postoperative pain, so the opioid administration can be decreased [58-60]. The great advantage of periarticular injection is to reduce pain, minimizing side effects and facilitating rehabilitation, total load and improvement of joint function [61,62]. Drugs used in periarticular injection are anesthetics, non-steroidal anti-inflammatories, corticosteroids, platelet rich plasma and hyaluronic acid [62,63]. The use of corticoid is still controversial as a drug for periarticular injection, although it has a potent anti-inflammatory and antiemetic action, it may increase the chances of infection and cutaneous atrophy. Different cocktails are currently

used and tested, such as ropivacaine and epinephrine, or clonidine, ketorolac, but the differences between them are questionable. The most used cocktail is the combination of ropivacaine, morphine and ketorolac, which act synergistically, without the addition of corticosteroids [64]. Botulinum toxin is also used in periarticular injections, especially in cases of flexion contracture [65]. Muchedzi conducted a systematic review of the use of periarticular injection of Platelet Rich Plasma (PRP) in TKA and concluded that in the short and medium terms, patients who used PRP achieved benefits in terms of pain improvement. Li performed a meta-analysis with 1,316 patients who received periarticular injections after TKA and concluded that the use of PRP is associated with an increase in the short- and long-term joint movement, and also a decrease in pain, without increasing the occurrence of infections [66].

Peripheral Nerve Blocks

Peripheral Nerve Blocks (PNB) have been considered an excellent technique for postoperative analgesia, but some questions are still under discussion, such as decreased motor function, risk of falls, risk of infection and neurological complications [67]. With the use of ultrasound as a guide for PNB techniques, the success of the procedures increased considerably, and the complications were minimized [68]. The current literature is not yet consensual as to the best technique indication for PNB, but there is a general agreement that the best results occur with ultrasound-guided injections. Femoral Nerve Block (FNB) is still the gold standard technique in control of TKA postoperative pain. FNB showed to be superior to analgesia caused by protocols with opioid use. When compared to epidural analgesia, FNB is similar as far as analgesic capacity, causing less vomiting, nausea and greater patient satisfaction [68]. Continuous FNB may weaken the quadriceps, increase the risk of falls and infections. It is still debatable whether continuous block is necessary, and some studies do not demonstrate superiority of continuous block versus single block. Moreover, a recent study indicates that blockages of peripheral nerves do not necessarily increase the probability of falls [69]. In cases of FNB insufficiency, blockage of the sciatic nerve can be suggested, but this indication is still controversial, due to the risk of nerve damage and muscle weakness [70,71].

Adductor Canal Blockage (ACB) is a procedure capable of blocking the sensory branches of the knee, without the disadvantage of causing motor blockade of the quadriceps [72]. However, the literature shows some controversy as whether ACB is superior to FNB. Wang and Albrecht have shown that the complications of the two techniques are similar and rare [73,74]. Genicular Nerve Blocks (GNB) are a good alternative for the treatment of residual pain after TKA. Access to genicular nerves began for radio frequency procedures, as well as those guided by fluoroscopy. The literature is not yet consensual as whether radiofrequency is able to obtain better results than with anesthetic and corticoid blockade in terms of pain relief. However, the adverse effects of corticosteroids must be highlighted [75]. GNB can also be performed with the help of the ultrasound technique, and we do not yet know the superiority between techniques using fluoroscopy or ultrasound. However, the technique guided by ultrasound is simpler and does not use radiation [76,77].

Cryotherapy

Application of ice in the knee with residual pain after TKA is still controversial in the literature as to its ability to decrease pain. Some studies show a great deal of effectiveness in improving pain, others show a few, and others shows no effectiveness at all. The mechanism of action of cryotherapy is based on decreasing local metabolism and enzymatic activity, including COX enzymes. It reduces nerve signaling, produces direct analgesia and decreases the development of hyperalgesia, induces vasoconstriction and reduces edema. Cryotherapy should be used with care to avoid damage to the skin [78,79].

Anticonvulsants

Pregabalin acts on the calcium channel and was originally introduced in medical practice in 2004 as an anticonvulsant for the treatment of epilepsy. Engelman and Cateloy performed a meta-analysis of the efficacy and safety of Pregabalin on postoperative pain in 1,547 patients, concluding that Pregabalin is effective in improving pain, but it can cause dizziness and visual disturbances [80]. Pregabalin has been used for the treatment of chronic pain and may be used to treat residual TKA pain in patients who do not present side effects to the drug or risk of falls [81,82].

Duloxetine Hydrochloride

Duloxetine is an inhibitor of serotonin and noradrenaline reception [83]. Theoretically, these actions should make it a good pain modulating agent [84]. Serotonin modulates the pro-nociceptive and anti- nociceptive effects in the central action of the brainstem. Noradrenaline has a predominantly anti- nociceptive effect. The balance between facilitation and depression of pain pathways is important for normal function. It decreases the absorption persistence of serotonin and the neurotransmission of monoamine that potentializes serotonin and noradrenaline in pathways of the descending inhibitory spine trat. Potentiation of serotonin and noradrenaline is necessary to produce effective analgesia. The action of drugs such as duloxetine on pain is independent of its effects on depression [85]. The onset of the pain benefit starts earlier than in depression. In addition, they have similar effects on pain in depressed and non-depressed people. Common side effects include nausea, headache, dry mouth, insomnia, constipation, dizziness, fatigue, drowsiness, hyperhidrosis and diarrhea [86].

These are mainly classified as mild to moderate and in the clinical setting appear less prevalent than the side effects with tricyclic antidepressants. In a systematic review of the Cochrane Institute, Lunn studied the efficacy and side effects of duloxetine for the treatment of diabetic neuropathy, fibromyalgia and chronic pain. The study comprised 12 studies with 2,728 patients and concluded

that duloxetine at the dose of 60 mg daily has moderate quality of evidence in the treatment of pain, but not in smaller dosages. As for the side effects, Lunn qualifies them as rare and small [87]. Although we do not yet have any literature with sufficient evidence regarding the treatment of residual pain in TKA, Wang conducted a Randomized Controlled Trail (RCT) for pain to study the efficacy of duloxetine 60 mg with 407 patients who presented pain and knee or hip osteoarthritis. He concluded that at this dosage duloxetine is effective in the treatment of pain, safe and with low side effects [88-91].

Author Preferred Method of Treating

In the treatment of residual pain after TKA, it is very important to discard the causes of pain that are eminently surgical. In some cases, as in infections, the time between diagnosis and treatment should be as short as possible due to the risk of worsening local and clinics conditions of the patient. Initially, we should treat patient comorbidities that are extremely common, such as diabetes, hypothyroidism, depression, obesity and others. Once the surgical causes are ruled out, we move on to the nonoperative treatment, which aims to minimize the pain, so that the patient will be able to perform rehabilitation, which is essential for therapeutic success. The use of pain medications should be carefully indicated, and duloxetine at a dose of 60 mg daily is very effective, especially for patients with associated depression. However, even non-depressed patients may benefit from this drug. The combination with Pregabalin may be indicated in specific cases, but the patient and the family should be advised about the side effects, especially the risk of falls. In patients who cannot be monitored on the first days of use of Pregabalin, the indication of the drug is impaired and another methodology without the risk of falls should be implemented.

In skin or scarring lesions, platelet rich plasma and hyaluronic acid offer surprising results, improving the viscoelastic quality of the skin, or even in the treatment of infections, since PRP also has bactericidal properties. The applications should always be superficial or guided by ultrasound to maintain superficiality and to avoid the chance of infections [92,93]. In the case of neuromas, we can also use the technique of injection guided by ultrasound [94-96]. Joint injections should be avoided because of the increased chance of infection. Rarely, and only in very important synovitis, and that already have surgical indication, we can use ultrasound-guided joint injection techniques, and PRP and hyaluronic acid are the substances of choice. We routinely examine the hip and lumbar sacral column, and in the case of irradiated pain, we perform ultrasound-guided blockages and viscossuplementation.

Conflict of Interest

The authors declare that they have no conflict of interest.

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