



Review Article

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Osteoarthritis of the Knee: Recent Advances and Management During COVID-19 Era

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Abstract

Osteoarthritis is a debilitating joint disorder that causes progressive weakening of the articular cartilage and the synovium leading to a stiff joint. It is a very common inflammatory disorder that has been closely related to aging, obesity, genetics, mechanical stress, medications, and injury. Osteoarthritis has a multifactorial etiology including constitutional and mechanical factors, biochemical processes, cellular processes, mechanical forces, local inflammation, genetic predisposition, and joint integrity. Older and newer therapies are continuously under investigation, and some have shown promising preliminary results in many studies. This review aims to give an overview of the current knowledge of therapies available for knee osteoarthritis with a focus on non-surgical intervention, especially in the COVID-19 era. COVID-19 has imposed a challenge to the usage of traditional methods and techniques for providing proper patient management. Thus, it is crucial to provide guidelines for patients with knee osteoarthritis during the COVID-19 pandemic.

Keywords: Knee osteoarthritis; Non-surgical interventions; COVID-19; Telehealth; Arthroscopy; Transcutaneous nerve stimulation; Laser therapy

Introduction

Osteoarthritis (OA) is a common inflammatory disorder that has been closely related to aging, obesity, mechanical stress, medications, and injury. Known to be caused as a result of mechanical wear and tear, it progresses slowly over the years. Hence, it is referred to as a degenerative joint disease. A key symptom of OA is pain and stiffness related to the inflammation associated with the disease. Regular activities such as walking and climbing up the stairs pose more challenges and discomfort in OA compared to other diseases [1]. OA is one of the most common reasons for total knee and hip replacement. It has a multifactorial etiology including constitutional and mechanical factors, biochemical processes, cellular processes, mechanical forces, local inflammation, genetic predisposition, and joint integrity [2]. Nevertheless, age still seems to be one of the most crucial factors involved in its pathology given the notion that it is an old age disease [2-4].

OA has multiple mechanisms and associations that are not understood well but it has been reported that the prevalence of OA is higher in elderly women [5,6]. As women age, they lose the protective effect of estrogen on the bone and this might be one of the reasons behind the sharp decline in bone strength after menopause. Estrogen plays a protective role via apoptosis of the osteoclasts that are responsible for the breakdown of the bone. Hence, age is a crucial factor involved in its pathogenicity [7]. Obesity is another interrelated factor since it has been known to cause increased stress on the weight-bearing joints of the body like the hips and the knees. Thus, over time it could also lead to deterioration of the articular cartilage leading to a weak joint [2,8]. The prevalence of knee OA in adults 60 years or older is around 10 percent in men and 13 percent in women [9,10]. Additionally, the number of people affected with the disease is likely to increase because of increasing

obesity and higher prevalence of more age-related complications [11]. Thus, OA could have an impact on the public health system and health care in the future [12]. Therapies for Knee OA have been under investigation for many years and several of them have shown promising preliminary results. However, COVID-19 has imposed a serious challenge to the usage of traditional methods and techniques for providing proper patient management. Due to the uncertainty of the COVID-19 pandemic in the upcoming months, patients with knee OA might be affected due to the precautionary measures taken during the pandemic. This review will discuss the overview of the current knowledge on knee osteoarthritis therapies with a special focus on recent developments and management during the COVID-19 pandemic.

Management of Knee OA during COVID-19

The novel coronavirus, COVID-19, presented an exceptional challenge for both personal and professional lives of healthcare providers as well as lead to some serious socioeconomic consequences all over the world [13]. To decrease the spread of the virus, hospitals had to pause many activities not related to COVID and postpone all surgeries until the pandemic is under control. Knee arthroplasty is an example of one such procedure [14-16]. Knee surgeries could expose older patients to COVID-19 since they are at high risk to develop more complications [13]. However, delaying surgeries for patients with severe knee OA could lead to an increase in joint pain, functional limitation and disability. Moreover, due to the unbearable pain, patients might misuse painkillers which could affect their health in the long run. Guidelines of OA during the pandemic should focus mainly on the available non-pharmacological options to reduce pain, enhance their joint function, and avoidance of further complications.

Exercises and Knee OA

Exercise is considered as a major non-pharmacological option of treatments for knee OA [17,18]. Several studies have shown positive outcomes with exercise in the management of pain, enhancement of function, delaying of disease progression, increases in blood flow, and boosting of joint lubrication [19-21]. Three meta-analyses, including 128 RCTs combined, showed a favorable effect of aerobic and resistance exercise on knee OA [21-23]. The frequently used types of exercises for knee OA are low-impact aerobic like walking or cycling as well as strength training in combination with proprioceptive and variant motion activities [24,25]. The 2019 guidelines of the American College of Rheumatology/Arthritis Foundation for management of hand, hip and knee osteoarthritis highly recommended exercise and weight loss, especially in overweight patients with OA [26]. In addition, balance exercises, Tai chi, yoga to enhance joint function and proprioception are recommended for OA patients [26]. Combined programs are preferred when it comes to certain types of exercises [17]. The regimen of each exercise should be based on the pain and

the mobility of the joint. Aerobic exercises and strength training for the hip or lower limb such as quadriceps strength training have favorable effects regarding pain and knee function [20,27]. A variety of motion exercise reduces the incidence of contractures while periarticular muscle strengthening alleviates symptoms [19,28]. On the other hand, some exercises should be limited, such as running on hard surfaces, jumping, stair climbing, and squatting [29]. Exercise therapy, which is the primary non-pharmacological treatment, is an effective, safe, and convenient method for treating knee OA. Exercise interventions are usually performed under the supervision of physiotherapists and may involve professional rehabilitation equipment [30,31]. Physiotherapists and researchers are increasingly supporting home-based exercise, which is a time-saving and convenient treatment modality for patients with chronic conditions such as knee OA, especially during the COVID-19 pandemic [32].

Weight Loss and Physical Therapy

Weight gain and a decrease in the strength of the muscles that support the knee leads to an increase of load on the knee joint [33]. Particularly during the pandemic, patients with knee OA are more prone to stay at home, which could lead to increased weight, weakening of a joint and decreased muscle strength if they stay inactive. Studies has shown that the weight loss is an effective method in the management of Knee osteoarthritis [18,34]. Teichtahl et al. (2015) showed that patients with OA who managed to lose only 1% of their body weight; experienced a reduction in medial femorotibial cartilage volume loss [35]. Personalized diet regimens together with exercise has been correlated with pain and functional improvements in overweight patients with severe knee OA [34,36]. A broader approach to reduce the incidence of disease should focus on reducing risk factors, such as vitamin D deficiency, smoking, joint injury, and obesity. Moreover, interventions that slow down the progression of disease are recommended.

Despite there are few studies that support the use of thermal packs and ice packs for pain management in knee OA, they are included in the treatment guidelines of OA. This is because they are more accessible as well as affordable for all patients [18]. However, ice packs application during acute episodes of inflammation and pain does not show favorable effects on OA pain [37]. A few data suggest alternation between heat and cold therapies by applying the hot pack first and then switch to the cold pack is beneficial [37].

Osteoarthritis Drugs and Viral Infections

Different OA drugs, such as NSAIDs, paracetamol, corticosteroids, and opioids have a wide range of iatrogenic effects, which may increase the incidence of COVID-19 secondary to infections or complications. NSAIDs may cause renal, gastrointestinal, and cardiovascular complications, as well as increase instances of bronchoconstriction [38-40]. Therefore, physicians should consider

monitoring NSAIDs use and its related complications if they are being used as a first-line method for managing OA symptoms pertaining special focus to their respiratory and cardiovascular complications. NSAIDs are safer for patients with knee OA patients who are not positive for COVID-19, On the other hand, OA patients with the COVID-19 infection under NSAID treatment should be monitored carefully and the use of NSAID should be considered only in the case of absolute necessity [41].

Paracetamol may cause cardiovascular, liver, and kidney complications if given at high doses [42,43] and has no adverse effects on respiratory tract infections [40]. Iatrogenic complications caused by corticosteroids are diabetes, immunosuppression and cardiovascular problems [44] whereas their effects on respiratory tract are controversial [45]. Opioids are beneficial for severe knee OA when other analgesics are insufficient to control pain or contradicted such as in allergic patients or patients with GI issues [41]. However, opioids could weaken both innate and acquired immunity and is highly linked to causing respiratory depression in cases of overdose. Hence, opioids could potentially increase the incidence and gravity of respiratory tract infections such as pneumonia [46]. Only the weaker opioids with no immunosuppressive activity are preferred during COVID-19. Nonetheless, there is no current conclusive evidence in favor or against the use of NSAIDs, paracetamol, corticosteroids and opioids during the treatment of COVID-19 patients [41].

Telehealth and Knee OA

Telehealth played an important role during COVID-19 pandemic in delivering health care remotely to patients and allowed them to interact without meeting face to face, which slowed down the spread of the virus among healthcare staff and the patients [47]. The history of telehealth goes back to the 1960s when Nebraska Psychiatric Institute and the Norfolk State Hospital used an "interactive video link" to provide care to their patients. However, people were not ready to fully adapt to it at that time [48]. Nonetheless, during the past decade, telehealth has evolved in a way that experts believe that it could actually transform how health care services will be delivered in the future. This is because it provides better accessibility, convenience, lower cost and outcomes, which all benefit the health care system and might make for a valuable care system [49].

Many changes have been introduced to the healthcare system as a result of the stay-at-home orders in many countries due to COVID-19. For example, procedures like limiting the number of patients that can be seen at one time, other infection control procedures, as well as the shortage of PPE in many countries. As a result, many physical therapy and exercise programs were offered remotely. Telephysiotherapy is a type of telemonitoring systems to provide independent rehabilitations of patients at

the convenience of their homes [50]. Telephysiotherapy involves the use of telecommunications technology as a means to provide physiotherapy services [51]. This delivery system might make for a more convenient and accessible method for patients in order to avoid close contacts and maintain social distancing. However, this approach has its limitations for both the healthcare staff and the patients in terms of applying the exercises properly, as well as the ability of the medical staff to assess the performance of the patient according to many studies.

Telephysiotherapy applications have been previously reported in some conditions such as stroke rehabilitation and patients with total knee replacement [50,52]. A study was done by Russell et al. (2011) aimed to evaluate the effectiveness of an internet-based telerehabilitation program in comparison with traditional physical therapy for patients who have undergone a total knee arthroplasty. At the end of the study, patients were highly satisfied with the new technology. The authors concluded that telerehabilitation achieved outcomes equivalent to traditional rehabilitation programs in patients with total knee arthroplasty [53]. Similar results were conducted by Tousignant et al. (2011) on patients' satisfaction regarding telerehabilitation and physiotherapists' satisfaction toward technology for post-knee arthroplasty [54]. Likewise, in a study done in a chronic pain population, the authors reported participants' satisfaction in terms of perceived usefulness, ease of use, and intent to use [55].

A recent study conducted by Sadiq et al. (2020) they did a quasi-experimental study on 50 post total knee replacement patients for a duration of 6 months at Ghurki hospital. The current study evaluated the outcomes of strength, range and functional status after knee replacement and concluded that utilization of telerehabilitation is equally effective as compared to conventional rehabilitation among total knee replacement patients. Favorable outcomes have been achieved by several studies that evaluated in-home telerehabilitation programs in terms of both technical feasibility and efficacy in different patient populations [56-61]. Other studies have been carried out on the use of telephysiotherapy programs for patients with knee OA in particular. Another study was designed to evaluate the impact of a 6-week telephysiotherapy program on quality of life of patients with knee OA using telephone medium. They confirmed that telephone-based physiotherapy is effective in the management of patients with Knee OA and it produces favorable outcomes in terms of quality of life [52]. It can be improved if patients are being contacted regularly by phone or participate in live virtual sessions with their physician or physical therapist [18,24,61]. Patients can even alternate between telerehabilitation and in-person visits. This model of health care delivery might change the future of traditional doctors' visits after the pandemic.

Recent Treatment Modalities of OA

The goals of osteoarthritis treatment and management include alleviation of pain and improvement of functional status. Examples of interventions for to control knee pain and inflammation in OA include:

Transcutaneous Nerve Stimulation (TENS)

Nerve stimulation, also known as neuromodulation, which uses electricity for decreasing the sensations of pain [62]. Few patients may experience a minimal risk of neuromodulation but it offers an alternative medication for treatment of arthritis pain. The devices used for the procedure are generally safe and involve sending electrical impulses through the body [63]. However, it is often contradicted for patient with heart problems, pregnant, and a pacemaker or other implanted devices.

TENS uses sticky electrode patches, which are attached to battery-operated devices that override the pain signals by sending electric current to the nerves. TENS helps with both acute and chronic pain and has been shown to relieve osteoarthritis pain while reducing the need for pain medications, thereby eliminating their unwanted side effects. TENS also triggers the release of naturally produced analgesic hormones like endorphins, which produces tremendous relief for pain [64]. TENS can be delivered at either high or low frequency [65]. There is tentative evidence that TENS reduces the intensity of pain over and above what is seen with placebo. In addition, there is around 50 percent reduction of pain in more than half the people who try TENS [66].

Platelet Rich Plasma and Stem Cell Therapy

Platelet rich plasma is a concentrate of autologous blood growth factor that is used for symptomatic relief in early osteoarthritis of the knee [67,68]. The therapy is simple, feasible to deliver primary care, minimally invasive intervention and relatively inexpensive to treat degenerative disorders of the articular cartilage of the knee [69,70]. The therapy has been shown to be associated with minimal adverse events with beneficial outcomes in terms of goals, patient satisfaction, health utility and pain [71].

Stem cell therapy has shown to heal various types of arthritis. Stem cells, besides healing damaged tissue, has a unique ability to modulate the immune system while shutting off the pathological response to preserve the ability to fight off the disease. The adult stem cells used to treat osteoarthritis originates from human umbilical cord (allogenic mesenchymal) tissue [72]. The stem cells are recovered from donated umbilical cords following delivery.

Genicular Artery Embolization and Arthroscopy of the Knee

Genicular artery embolization is particularly efficient and safe for the treatment of osteoarthritis. It reduces inflammation and

pain secondary to knee osteoarthritis. The minimally invasive procedure is currently available for clinical trial for the treatment of extended knee pain in patients with osteoarthritis. The procedure is performed through a small puncture in the groin and the blood flow is blocked in areas around the knee that are inflamed [73].

Moreover, arthroscopy is a simple surgical technique that can diagnose and treat knee injuries as well. Arthroscopy is a minimally invasive surgical procedure, which can be used to eliminate crystals and debris causing pain and inflammation. It is performed by creating a small incision and inserting an arthroscope that has a tiny camera. It is done by washing the joint with saline, removal of fragments of menisci and debridement of torn menisci or of other structures such as torn ligaments, resection of proliferative synovium, smoothing over of cartilage lesion, excision and removal of loose fragments of articular cartilage, grinding down or removal of osteophytes blocking the full extension of the joint, and drilling of osteochondral lesions [74].

Low-level Laser Therapy (LLLT)

Low-level laser therapy (LLLT) has recently been used to relieve pain and decrease inflammation in variant musculoskeletal disorders such as cervical spondylosis, epicondylitis, low-back pain and currently on knee OA [75-77]. It has stimulatory effects on tissue metabolism, and a great ability to modulate the inflammatory process following injuries. It is characterized by high healing efficacy, non-invasiveness and almost no adverse side effects. Furthermore, it enhances cellular oxygenation, neurotransmitter release in response to pain and release of anti-inflammatory mediators [78]. Recently there has been many randomized controlled trials (RCTs) evaluating the effectiveness of LLLT in patients with knee OA. However, patients with knee OA have showed significant variations in their response to LLLT. As some studies demonstrated non-significant results in some disorders [79-81].

Despite some other studies [81-83] that showed a significant benefit in response to LLLT, reported clinical efficacy is still controversial. However, there were variations in the studies in terms of application methods, duration of treatment, dosage and application site [81-84]. Youssef et al. (2016) concluded that LLLT together with exercise program is more effective than doing exercise alone in older patient with chronic knee OA. As a consequence of these conflicting results between clinical trials, three recent systematic reviews and meta-analysis has been carried out to conclude the matter. Two of them showed positive results referring to that effectiveness of LLLT and is varied based on many factors including laser wavelength, density, treatment duration, numbers of sessions, severity of the disease and site of application [9,85]. Stausholm MB et al. (2019) concluded that LLLT at 4–8 J with 785–860 nm wavelength and at 1–3 J with 904 nm wavelength managed to reduce pain and joint disability [86].

Conclusion

Osteoarthritis is a chronic joint disease, and the treatment should be based on reducing comorbidities and risk factors. Management should focus on conservative non-drug interventions, for example, weight loss among overweight patients with regular exercise regimes. Educating patients on behavioral modifications such as information on diet and habits linked to lowering the rates of inflammation should be provided. Interventions with high-risk procedures that outweigh benefits should be avoided unless needed. It is vital to give patients a proper education about the management of Knee Osteoarthritis, especially during the COVID-19 pandemic since different OA drugs have a wide range of iatrogenic effects that may increase the incidence of COVID-19 complications. Lastly, educating patients on these ideas and strategies through video conferences such as telemedicine and laying out a patient-focused regime is absolutely essential during the COVID-19 pandemic, which has been proven to be beneficial according to many studies.

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