

## Research Progress on Analgesic Effect of Acupuncture Knee Osteoarthritis

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Received: October 22, 2019; Published: October 31, 2019

### Abstract

Knee osteoarthritis is a chronic degenerative disease characterized by pain and joint dyskinesia that is common in middle-aged and older adults. Many methods are used for the clinical treatment of KOA. However, none of the existing treatment methods can change the natural course of KOA; the main purpose of treatment is to alleviate pain and improve joint function. Western medicine mainly focuses on medical treatments including oral medication, intra-articular injection therapy and arthroscopic treatment. Traditional Chinese medicine therapy mainly consists of the administration of Chinese herbs, acupuncture, acupotomy and other non-drug treatments. In particular, acupuncture achieves a marked analgesic effect. Although the course of acupuncture treatment is relatively long, it is generally easily accepted by patients because of its moderate cost and minimal adverse effects. Nowadays, an increasing number of people are choosing to undergo acupuncture as a clinical treatment for KOA. In the present article, we analyze the present situation of acupuncture-mediated analgesia in KOA, discuss the basic theory of acupuncture-mediated analgesia in KOA and compare the clinical analgesic effects of different therapies to aid in the development of an effective treatment plan for KOA.

**Keywords:** Acupuncture; Knee Osteoarthritis; Pain Management; Acupoint; Characteristic Therapy

### Abbreviations

KOA: Knee Osteoarthritis; GRO- $\alpha$ : Growth-Regulated Oncogene  $\alpha$ ; VEGF: Vascular Endothelial Growth Factor; IL-10: Interleukin-10; TNF- $\alpha$ : Tumor Necrosis Factor- $\alpha$ ; MMP-3: Matrix Metalloproteinase 3; TIMP-1: Tissues Inhibitors of Metalloproteinases-1

### Theoretical basis of traditional Chinese Medicine for acupuncture-mediated analgesia in knee osteoarthritis

Knee osteoarthritis (KOA) is a chronic degenerative disease characterized by pain and joint dysfunction that is common in middle-aged and older adults. The early symptoms of KOA are knee joint ache and limping, while the late symptoms include joint movement limitation, muscle atrophy, knee varus and other diseases [1].

Modern medicine has proposed many hypotheses regarding the pathogenesis of KOA, such as increased cytokine production, changed immune response and protease expression, intraosseous hypertension, decreased muscle strength of the quadriceps femoris, disorders of the sex hormones, cell apoptosis, increased concentrations of nitric oxide in plasma and synovial fluid and the oxygen free radical theory [2].

There is no clear record of the term “knee osteoarthritis” in Chinese historical documents. However, the clinical symptoms and pathogenesis of KOA suggest that this condition belongs to the traditional Chinese medicine condition referred to as “Bi (obstruction) syndrome”. KOA can be further classified into specific traditional Chinese medicine syndromes in accordance with the clinical symptoms. Liu., *et al.* [3] divided KOA into liver-kidney deficiency syndrome, phlegm and blood stasis syndrome, dampness and cold syndrome,

dampness and heat syndrome and Qi and blood deficiency syndrome in accordance with the tongue coating, pulse condition and clinical manifestations of the patients. Ge., *et al.* [4] classified KOA as Bi syndrome caused by cold and dampness, liver-kidney Yin deficiency syndrome and Qi stagnation and blood stasis syndrome. Administering treatment measures that correspond to the different syndromes achieves a more marked analgesic and therapeutic effect.

Acupuncture improves the blood supply of soft tissues and alleviates local inflammation; it has the functions of warming the meridians, expelling cold and dampness and promoting blood circulation. Acupuncture stimulation at specific points relieves Qi stagnation and blood stasis symptoms in the middle and late stages of KOA by accelerating the metabolism of local tissues and increasing the absorption rate of inflammation in the knee joint to relieve pain and reduce joint dysfunction [5].

### Acupoints used to achieve analgesia in knee osteoarthritis

Most of the acupoints used for the treatment of KOA are located in the proximal region of the knee joint. The first record of local acupoint stimulation in the proximal knee region is found in Huang Di's Inner Classic, which refers to the collection of acupoints around the diseased limbs, tissues, viscera and organs [6]. The acupoints used in the treatment of KOA are mainly selected from the acupoints of the 14 meridians. The Yangming stomach channel of the foot is most commonly used and the Taiyin spleen channel of the foot is also commonly stimulated in acupuncture treatment of KOA. The traditional Chinese medicine textbook named the Lingshu Jing states that the "stomach, the origin of the Yangming stomach channel of the foot, indicates swelling and pain of the patella in patients with diseases mainly caused by blood. The Yangming stomach channel of the foot starts from the nose; it belongs to the stomach and is connected with the spleen. The Taiyin spleen channel of the foot begins at the end of the thumb and follows the inner white flesh of the finger... into the abdomen; it belongs to the spleen and is connected with the stomach." An analysis of the routes followed by these two meridians shows that they are closely related to the knee joint. In addition, the points most commonly stimulated in the acupuncture treatment of KOA are Dubi (ST 35), Neixiyan (EX-LE 4), Ashi points, Yanglingquan (GB 34) and Xuehai (SP 10) [7].

Acupuncture at Dubi effectively treats knee pain and lower extremity paralysis and slows the degenerative changes of articular cartilage. Neixiyan is located at the medial recess of the patellar ligament when the knees are bent. Anatomically, Neixiyan includes the skin, subcutaneous fascia and deep fascia of the leg, the patellar medial retinaculum, the genicular fat body and the knee bursa. The superficial layer of the knee joint contains the subpatellar branch of the saphenous nerve and the anterior cutaneous branch of the femoral nerve, while the arteriovenous network is located in the deep layer [8]. Treating KOA with deep acupuncture stimulation of Dubi and Neixiyan achieves a rapid analgesic effect [9].

Ashi points are a temporary acupoint phenomenon. When the disease occurs, the corresponding parts of the body experience corresponding local increases in Qi and blood and then produces sore, hemp, distension, pain, a feeling of heaviness, color change, increased firmness, swelling and other reactions. KOA causes local pain and inflammation in the knee joint and the development of Ashi points. Acupuncture at Ashi points accelerates the metabolism and inflammatory absorption of affected tissues, relieves Qi and blood stagnation and alleviates pain and dysfunction [10].

Yanglingquan is known as the meeting point of the tendons. Acupuncture at Yanglingquan has the effect of strengthening muscles and bones. For example, the song of the twelve star points of Ma Danyang mentions "knee swelling and numbness due to cold arthralgia and partial wind", which provides the basis for the treatment of KOA via acupuncture at Yanglingquan.

Xuehai is the main point for the production and activation of blood. Acupuncture at Xuehai achieves a good analgesic effect in patients with KOA by relieving the blood circulation and local inflammation of the soft tissue around the knee joint. In addition, the Jia Yi Classic of Acupuncture and Moxibustion states that Xuehai has the function of invigorating the spleen and transforming dampness, relieving the pain of distension due to blood stasis, regulating the meridians and regulating the blood. The spleen plays an important role in the functional activity of the limbs. Therefore, performing acupuncture at Xuehai affects the homeostasis of the whole body [11].

The performance of acupuncture at multiple compatible acupoints increases the efficacy of acupuncture at individual acupoints and is very important in traditional Chinese medicine. A recent analysis of acupuncture points and their compatibility has found that Dubi is one of the most commonly used acupoints in the treatment of KOA. Furthermore, the two-acupoint combination most commonly used to treat KOA is Dubi and Xuehai [12]. Commonly used three-acupoint combinations include: 1) Dubi, Neixiyan and Xuehai, 2) Dubi, Neixiyan and Yanglingquan and 3) Dubi, Liangqiu and Xuehai [12]. Acupuncture at Dubi and Neixiyan effectively improves local blood flow, accelerates tissue metabolism and relieves swelling and pain [13]. Acupuncture at Dubi and Neixiyan in combination with massage therapy achieves a significant analgesic effect in patients with KOA [13].

### Treatment of knee osteoarthritis with various types of acupuncture

#### Electroacupuncture

The main symptom of KOA is pain. Clinically, electroacupuncture is widely used to relieve pain [14] and acupuncture therapy is safe and effective with minimal adverse effects [15,16]. In recent years, many clinical studies have confirmed that electroacupuncture has a significant effect in the treatment of KOA, but the mechanism remains unclear. Currently, most scholars believe that the analgesic effect of electroacupuncture may be achieved via the inhibition of the release of inflammatory factors such as GRO- $\alpha$  and VEGF and regulation of the concentration of anti-inflammatory cytokines such as IL-10. One study of 112 patients with KOA showed that the effect of electroacupuncture significantly differed in accordance with the stage of disease and that the serum VEGF concentration was significantly decreased after treatment, indicating that electroacupuncture may regulate the serum VEGF concentration [17]. Another study of 78 patients with KOA found that electroacupuncture significantly decreased the plasma GRO- $\alpha$  and VEGF concentrations and achieved significantly greater improvements in the symptoms of KOA than routine western medicine treatment [18]. In addition, a clinical study 39 patients with KOA treated with electroacupuncture therapy for 12 days suggested that electroacupuncture improves the symptoms of KOA by upregulating the serum expression of the anti-inflammatory cytokine IL-10 and decreasing the serum concentration of the inflammatory cytokine TNF- $\alpha$  [19].

Researchers have also studied the expression of various proteins in articular cartilage after electroacupuncture stimulation, which has led to the proposal of another possible mechanism. A study of KOA in a rabbit model suggested that electroacupuncture inhibits the formation of osteophytes by downregulating the expression of bone morphogenetic protein-2 and Smad1 in cartilage in early KOA, thus delaying the pathological process of KOA [20]. Another animal study performed using 40 rats suggested that the abnormal expression of MMP-3 and TIMP-1 in the synovial tissue may also be one of the mechanisms of electroacupuncture in the treatment of KOA [21].

The combination of electroacupuncture with other therapies (drugs and manipulations) effectively alleviates joint pain and stiffness in the treatment of KOA. For example, electroacupuncture has been used in combination with a traditional Chinese medicine hot compress [22], Wei's manipulation [23], Qizheng analgesic paste [24], the external application of Zhitong Powder and a TDP lamp [25], skin traction [26] and intra-articular injection of Weiling Xian [27]. Compared with electroacupuncture therapy alone, the use of electroacupuncture in combination with other therapies achieves a more marked clinical effect.

#### Warm acupuncture and moxibustion

A large amount of clinical evidence shows that warm-needle therapy achieves good results in the treatment of arthritis [28]. The mechanism of warm acupuncture in treating KOA is thought to be the regulation of the concentrations of inflammatory factors and anti-inflammatory cytokines. A study of 60 patients with KOA showed that warm acupuncture significantly decreased the concentrations of both IL-1 beta and TNF- $\alpha$  in synovial fluid [29].

Warm acupuncture is more effective than electroacupuncture in expelling cold, clearing the collaterals, warming Qi and blood, promoting local microcirculation of the affected area, relieving pain and improving blood stasis of the knee joint [29]. Many studies

have evaluated the therapeutic effects of warm acupuncture and electroacupuncture in KOA, with conflicting results. One clinical study found that warm acupuncture is more effective than electroacupuncture in treating KOA [30]. In contrast, two other studies concluded that electroacupuncture was superior to warm acupuncture in reducing inflammation, swelling and pain in patients with the kidney deficiency and marrow deficiency type of KOA, while warm acupuncture was superior to electroacupuncture in relieving joint stiffness [31,32]; electroacupuncture achieved a better overall efficacy than warm acupuncture [31,32]. Another study evaluating the kidney deficiency and pulp deficiency in marrow types of KOA found that electroacupuncture took a longer time to achieve analgesia than warm acupuncture, while warm acupuncture was more effective than electroacupuncture in relieving joint stiffness [33]; the overall effect of electroacupuncture was better than that of warm acupuncture [33].

The cause of KOA is multifactorial and complicated and its course is also regulated by the internal and external environment. Future studies should aim to strengthen the dialectical classification of KOA and then compare the effects of treatment between the different classifications.

### Accupotome therapy

The accupotome evolved from the improvements of the needle and scalpel and relieves pain by loosening the adhesive tissue to restore the function of the affected area. Acupotomy has a marked effect on KOA and reportedly achieved an overall effective rate of 100% in 31 patients with KOA [34]. Furthermore, the therapeutic effect of acupotomy is relatively stable, especially when combined with massage and acupuncture and the satisfaction level of patients is generally high.

Acupotomy and acupuncture achieve a good analgesic effect and are commonly used in the treatment of KOA. A meta-analysis showed that acupotomy achieves a better short-term total effective rate and cure rate than acupuncture in the treatment of KOA [35]. However, further verification is needed due to the low quality of included studies [35].

### Treatment of knee osteoarthritis with western medicine

#### Oral medication

There is no specific drug for the treatment of KOA. The most commonly used type of quick-acting drug is non-steroidal anti-inflammatory drugs (NSAIDs), which improve the patient's life quality via the treatment of pain but cannot achieve a complete cure. However, long-term use of NSAIDs can produce serious adverse reactions, such as gastrointestinal reactions, cardiovascular events and renal damage. Therefore, to reduce the incidence of adverse reactions, some recent guidelines recommend the use of NSAIDs externally rather than orally [36]. Many studies have investigated drug combinations to enhance the efficacy of treatment while minimizing the adverse effects. For example, Davishnia, *et al.* [37] evaluated the local external application of glucosamine hydrochloride and ketoprofen cream in a rat model of osteoarthritis and found that the combination of the two drugs achieves a better effect than the use of a single drug.

Many studies have reported that the administration of oral western medicine in combination with acupuncture and moxibustion therapy achieves a good therapeutic effect. The combination of acupuncture and moxibustion therapy is often compared with slow-acting symptomatic relief drugs like glucosamine; the results of such comparisons show that acupuncture and moxibustion therapy achieve a significantly better clinical effect than drug administration [36].

#### Intra-articular injection

Intra-articular drug therapy includes the injection of the cartilage protector glucosamine sulfate, the viscoelastic supplement hyaluronic acid, the analgesic and anti-inflammatory agent Celecoxib and a combination of several drugs. The main purpose of intra-articular drug therapy is to improve the function of the bones and the joint and relieve pain; however, it cannot change the natural course of the disease. Studies have shown that some patients with KOA do not achieve an ideal effect after sodium hyaluronate treatment due to individual

differences. The research on intra-articular injection for the treatment of KOA is focused on the identification of more effective drugs and active substances [38]. One study of 86 patients with KOA who received a combined injection of sodium hyaluronate and ozone combined with warm acupuncture showed that the curative effect of warm acupuncture was better than that of the injection alone [39].

### Conclusion

KOA is one of the most common diseases that seriously decreases quality of life. With the advent of the aging society in China, the incidence of KOA is expected to increase. As a traditional Chinese medicine therapy, acupuncture has a mature theoretical system and has proven efficacy in the clinical treatment of KOA. However, acupuncture has not been widely accepted due to the lack of clarity regarding its mechanism in modern medicine and the lack of uniform standardizations in the evaluation of its curative effects.

Many clinical studies have confirmed that acupuncture has a significant analgesic effect in patients with KOA. As acupuncture therapy has only a moderate cost and a small risk of toxicity or adverse effects, this treatment is generally well accepted by patients. Thus, acupuncture is worth popularizing in the clinical treatment of KOA.

Acupuncture plays a positive regulatory role by arousing the physiological potential of the body. However, there are certain limits to this regulatory effect and so there are problems such as the slow onset of the analgesic effect and incomplete analgesia. In addition, the quality of the existing experimental studies is variable. Much of the evidence for the efficacy of acupuncture is only of moderate quality [36], as no adverse events are reported or there is no clear evaluation system for the curative effect, which needs verification in higher quality studies. Furthermore, the long-term effect of acupuncture and moxibustion has not been assessed. Acupuncture combined with other traditional Chinese or western medicine therapies in the treatment of KOA has achieved good results [34]; however, the specific mechanism of the combination treatment remains unclear. Further research is required to determine how best to combine these therapies and establish a more effective comprehensive treatment system. Numerous studies have shown that the combination of acupuncture and western medicine achieves effective analgesia, but not all drugs enhance the effect of acupuncture. Further research is warranted into the selection of drugs to enhance the efficacy of acupuncture and avoid the occurrence of combined adverse reactions.

### Acknowledgements

Wang KY drafted and revised the manuscript. Yang QH and Jiang GX participated in its edit; Zhu XY contributed to the main structure of the manuscript and provided most of the references; All authors have read and approved the final version of the manuscript and agree with the order of presentation of the authors.

We thank Kelly Zammit, BVSc, from Liwen Bianji, Edanz Editing China ([www.liwenbianji.cn/ac](http://www.liwenbianji.cn/ac)), for editing the English text of a draft of this manuscript.

### Conflict of Interest

The authors declare that they have no competing interests.

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**Volume 8 Issue 11 November 2019**

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