

Feature article

Tackling Osteoarthritic Knee Pain with Electroacupuncture*

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ABSTRACT Electroacupuncture (EA) has been widely used in pain relief. Clinical evidence has revealed its unique advantages and effectiveness in alleviating pain. Studies on EA and pain relief have revealed that EA displays greater analgesic effects for different types of pain in comparison to manual acupuncture. Here, we reviewed the clinical application and mechanism of EA in treating osteoarthritic knee pain and its influence factors in curative effect.

KEYWORDS electroacupuncture, osteoarthritic knee pain, clinical application, mechanism of action

Acupuncture therapy for pain relief⁽¹⁾ is excellent in terms of its affordability,⁽²⁾ and safety⁽³⁾ and is applied for different types of musculoskeletal pain disorders. Acupuncture is conditionally recommended according to the American College of Rheumatology guidelines on knee osteoarthritis (KOA),⁽⁴⁾ and some systematic review studies have verified the effects of acupuncture on pain control in KOA patients.⁽⁵⁾ Electroacupuncture (EA) is a relatively new approach in Chinese medicine. It is like regular acupuncture with needles inserted into acupuncture points but with a small crocodile clips attached to the ends of needles and connected to an EA device with wire. EA is widely used in the clinical treatment of pain, which has unique advantages and effectiveness in alleviating pain.⁽⁶⁾ Instead of manual manipulation of acupuncture needle, EA provides extra stimulation for a longer duration of time. Therefore, EA displays greater analgesic effects for different types of pain than manual acupuncture. In order to give full play to the use of EA in the treatment of osteoarthritic knee pain, we reviewed clinical application and the mechanism in treating osteoarthritic knee pain, along with its influence factors in curative effect.

Clinical Application and Its Mechanism

Pain is one of the major symptoms of KOA. Clinical studies have revealed that EA displayed remarkable clinical effects in alleviating the pain in KOA patients with a low risk of adverse reactions,⁽⁷⁾ reversing chronification of acute pain,⁽⁸⁾ and the capability to be used as an alternative pain relief

strategy in patients with osteoarthritis.⁽⁹⁾

The mechanism of EA administered pain relief is complicated. Previous studies have proved that the analgesic effect resulting from the stimulation of the acupuncture point occurred through inhibition of the neural activity of the dorsal periaqueductal gray region and the reticular formation of the brainstem. The acupuncture needle insertion stimulates the pain receptors (nerve endings) and causes the secretion of endogenous opioids, which was proved very effective in pain control. The activating of pain controlling system causes the neurons that originate from mesencephalon, periaqueductal gray substance in the periventricular region deliver the stimuli to the nuclei of *reticulospinalis* and *nucleus reticularis parvocellularis*. These stimuli go to the dorsolateral column of the medulla spinalis and the pain suppressing complex. There are neurotransmitters like endorphin, enkephalin, and serotonin in the analgesia system.⁽¹⁰⁾ EA was used to activate serotonergic neurons in the nucleus raphe magnus that project to the spinal cord, induce spinal serotonin release and stimulate serotonin (5-HT)_{2A/2c} receptor activities at the

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spinal cord to suppress osteoarthritis-induced pain.⁽¹¹⁾ *In vitro* results further proved that electroacupuncture serum (EAS) could inhibit tumor necrosis factor (TNF) α -mediated chondrocyte inflammation via the Ras Raf MEK1/2 ERK1/2 signaling pathway *in vitro*.⁽¹²⁾ In addition, EA reduce the protein expression of Bax and Caspase-3 and increase the proportion of Bcl-2/Bax protein, suggesting that EA can inhibit cell apoptosis of KOA rabbits.⁽¹³⁾ Remarkable progress has obtained in the study of therapeutic mechanisms of EA treatment on osteoarthritic knee pain, and further studies are required for characterizations.

Influence Factors of Curative Effect

Previous studies revealed that there are many influence factors such as acupoints selection, electric pulse frequencies, which are the major factors affecting the curative effect. The selection of acupoints represent a key effector which may largely determin EA effect. Taechaarpornkul, et al⁽¹⁴⁾ found no difference between the effectiveness of EA in treating KOA using two points at ST 35 (Dubi) and EX-LE4 (Neixiyan) alone, and 6 points, viz. ST 35 and EX-LE4 together with ST 36 (Zusanli), SP 9 (Yinlinquan), SP 10 (Xuehai) and ST 34 (Liangqiu).⁽¹⁴⁾ Another study conducted by Qi, et al, on the other hand, revealed that three kinds of EA treatments including two-point group (including ST 35 and EX-LE4), four-point group (including ST 34, SP 10, ST 35 and EX-LE5) and six-point group (including ST 34, SP 10, SP 9, ST 36, ST 35 and EX-LE4) were all of significant clinical effects on KOA patients with down-regulated scores of Visual Analog Scale (VAS) and McMaster Universities Osteoarthritis Index (WOMAC).⁽¹⁵⁾ Regarding post-treatment efficacy, the six-point group exhibited lower VAS score and higher WOMAC score compared with the other two groups. For patients with different KOA grades, patients with higher KOA grades were associated with lower grade of treatment efficacy.⁽¹⁵⁾

Selection of electric pulse frequencies is another major factor which may determine the therapeutic effect. It is shown that lower frequency EA (2 Hz) stimulated the release of β -endorphin, enkephalin, and endomorphin followed by the activating of the M- and δ -opioid receptors, whereas higher-frequency EA (100 Hz) stimulated dynorphin, activated the κ -opioid receptor.⁽¹⁶⁾

Different frequencies of EA had different

curative effect. Seo, et al⁽¹⁷⁾ reported that EA on ST 36 could attenuate the osteoarthritic pain in collagenase-induced arthritis, and 2 Hz EA resulted in a significantly greater analgesic effect than 100 Hz EA. The analgesic effect of 2 Hz EA was reduced by pretreatment of 5-HT1 receptor, 5-HT3 receptor and muscarinic cholinergic receptor antagonists.⁽¹⁸⁾ Both high- and low-intensity EA treatments reduced the levels of TNF- α and apelin in serum obviously. Plasma level of interleukin-6 was significantly decreased only after high-intensity EA treatment, suggesting that EA could regulate the imbalance of inflammatory factors.⁽¹⁹⁾

Expectation

It was noted that the incidence or prevalence of KOA had increased quite significantly in recent years, and the age of diagnosis tends to be younger. EA treatment has the advantages in definite curative effects, little risk, low cost and little side effects evidently. However, application of EA on KOA pain lacks an standardized, optimized program owing to the following reasons: most of the clinical studies only focused on the short-term efficacy; a unified standard of the clinical efficacy assessment was absent,⁽²⁰⁾ the clinical designs was not perfect, including small sample and lack of specific objective indicators; the selection of acupoints was insufficiently specific; effective assessment of the degree of pain in patients was absent, etc. Therefore, in order to improve the clinical application of EA, multi-center and large-sample randomized controlled trials should be carried out, focusing on the observation of long-term efficacy. To resolve the issue that there were no systematic and normative study on the quantity of stimuli and the selection of acupoints during the course of EA treatment, a strict control group and the objective control on the quantity of stimulation should be established, basing on previous clinical experience and the standardized operation of clinical research, and the acupoints selection should be standardized according to the rules of clinical acupoints selection. Furthermore, in order to verify the curative effects of EA on KOA pain, the objective indicators and instruments should be explored to evaluate KOA pain objectively.

Interdisciplinary, multi-channel, multi-level research of EA treatment on KOA pain is needed by using the biochips and other modern scientific techniques in order to clarify the mechanism of action as well as provide theoretical basis for further clinical

diagnosis, evaluation and treatment standardization.

REFERENCES

1. Leung L. Neurophysiological basis of acupuncture-induced analgesia—an updated review. *J Acupunct Merid Stud* 2012;5:261-270.
2. Kim SY, Lee H, Chae Y, Park HJ, Lee H. A systematic review of cost-effectiveness analyses alongside randomised controlled trials of acupuncture. *Acupunct Med* 2012;30:273-285.
3. Manheimer E, Cheng K, Linde K, Lao L, Yoo J, Wieland S, et al. Acupuncture for peripheral joint osteoarthritis. *Cochrane Database Syst Rev* 2010. doi: 10.1002/14651858.CD001977.
4. Hochberg MC, Altman RD, April KT, Benkhalti M, Guyatt G, McGowan J, et al. American College of Rheumatology 2012 recommendations for the use of nonpharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip, and knee. *Arthritis Care Res* 2012;64:465-474.
5. Cao L, Zhang XL, Gao YS, Jiang Y. Needle acupuncture for osteoarthritis of the knee. A systematic review and updated meta-analysis. *Saudi Med J* 2012;33:526-532.
6. Plaster R, Vieira WB, Alencar FA, Nakano EY, Liebano RE. Immediate effects of electroacupuncture and manual acupuncture on pain, mobility and muscle strength in patients with knee osteoarthritis. *Acupunct Med* 2014;32:236-241.
7. Chen N, Wang J, Mucelli A, Xu ZX, Wang C. Electroacupuncture is beneficial for knee osteoarthritis: the evidence from meta-analysis of randomized controlled trials. *Am J Chin Med* 2017;45:965-985.
8. Shen LL, Huang GF, Tian W, Yu LL, Yuan XC, Zhang ZQ, et al. Electroacupuncture inhibits chronification of the acute pain of knee osteoarthritis: study protocol for a randomized controlled trial. *Trials* 2015;16:131.
9. Manyanga T, Froese M, Zarychanski R, Abou-Setta A, Friesen C, Tennenhouse M, et al. Pain management with acupuncture in osteoarthritis: a systematic review and meta-analysis. *BMC Complement Altern Med* 2014;14:312.
10. Cabýoglu MT, Ergene N, Tan U. The mechanism of acupuncture and clinical applications. *Int J Neurosci* 2006;116:115-125.
11. Li A, Zhang Y, Lao L, Xin J, Ren K, Berman BM, et al. Serotonin receptor 2A/C is involved in electroacupuncture inhibition of pain in an osteoarthritis rat model. *Evid Based Complement Alternat Med* 2011;2011:619650.
12. Chen H, Shao X, Li L, Zheng C, Xu X, Hong X, et al. Electroacupuncture serum inhibits TNF α mediated chondrocyte inflammation via the Ras Raf MEK1/2 ERK1/2 signaling pathway. *Mol Med Rep* 2017;16:5807-5814.
13. Huang YR, Jin YL, Li N, Lei LD, Yu F, Li YB, et al. Effects of acupotomy, electroacupuncture or round-sharp acupuncture needle interventions on expression of Bcl-2, Bax, Caspase-3 proteins of rectus femoris in rabbits with knee osteoarthritis. *Acupunct Res* 2014;39:100-105, 123.
14. Taechaarpornkul W, Suvapan D, Theppanom C, Chanthipwaree C, Chirawatkul A. Comparison of the effectiveness of six and two acupuncture point regimens in osteoarthritis of the knee: a randomised trial. *Acupunct Med* 2009;27:3-8.
15. Qi L, Tang Y, You Y, Qin F, Zhai L, Peng H, et al. Comparing the effectiveness of electroacupuncture with different grades of knee osteoarthritis: a prospective study. *Cell Physiol Biochem* 2016;39:2331-2340.
16. Lin JG, Chen WL. Acupuncture analgesia: a review of its mechanisms of actions. *Am J Chin Med* 2008;36:635-645.
17. Seo BK, Park DS, Baek YH. The analgesic effect of electroacupuncture on inflammatory pain in the rat model of collagenase-induced arthritis: mediation by opioidergic receptors. *Rheumatol Int* 2013;33:1177-1183.
18. Seo BK, Sung WS, Park YC, Baek YH. The electroacupuncture-induced analgesic effect mediated by 5-HT₁, 5-HT₃ receptor and muscarinic cholinergic receptors in rat model of collagenase-induced osteoarthritis. *BMC Complement Altern Med* 2016;16:212.
19. Ju Z, Guo X, Jiang X, Wang X, Liu S, He J, et al. Electroacupuncture with different current intensities to treat knee osteoarthritis: a single-blinded controlled study. *Int J Clin Exp Med* 2015;8:18981-18989.
20. Egorova N, Gollub RL, Kong J. Repeated verum but not placebo acupuncture normalizes connectivity in brain regions dysregulated in chronic pain. *Neuroimage Clin* 2015;9:430-435.

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