



IONTOPHORESIS WITH NOVEL HERBAL GEL FOR KNEE OSTEOARTHRITIS: A CASE REPORT

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Abstract

The most prevalent musculoskeletal disease is osteoarthritis (OA), which impairs daily functioning, particularly in the elderly. According to the WHO, it is one of the most common causes of disability in developed countries. Even though it often affects the knee joints, osteoarthritis (OA) can affect any joint. Over the course of OA, pathological lesions are caused by an imbalance between the processes of cartilage tissue injury and healing. The illness advances over time and is influenced by both personal characteristics and outside circumstances. Long-term effects include decreased physical activity and condition, weariness, sadness, and disability, as well as a decline in sleep quality. Despite this, no treatment has been able to adequately stop or slow the progression of osteoarthritis (OA), provide long-lasting clinical relief, effectively stop the structural degeneration of bone and cartilage, or properly correct any structural flaws that already exist. The primary objective of this study was to assess the effects of new iontophoretic herbal gel (containing *Symphytum officinale*) with exercise therapy on the pain, function, sleep quality, and gait patterns of participants with osteoarthritis in the knee. This case report describes a fifty-year-old man who experienced an unintentional injury to his right leg and was experiencing abrupt onset pain and stiffness in his right knee. This case study covered evaluation, patient history, and treatment plan. This case study discovered that the patient's discomfort, function, sleep quality, and gait patterns are significantly impacted by the therapeutic intervention that was given.

Keywords: Novel, Iontophoresis, Herbal Gel, Knee osteoarthritis.

INTRODUCTION

Degenerative joint disease, also referred to as knee osteoarthritis (OA), is often caused by articular cartilage loss and wear and tear over time. It usually affects older people. Primary and secondary knee osteoarthritis are distinguished by the underlying etiology. Unknown causes of articular

cartilage deterioration lead to primary knee osteoarthritis. Typically, this is seen as deterioration brought on by aging and general wear and tear. A recognized cause of the deterioration of the articular cartilage that leads to secondary knee osteoarthritis.^{1,2} Combining pharmaceutical and non-pharmacological therapies is one of the OA therapeutic techniques.^{3,4} Along with reducing pain, the treatment aims to enhance joint functionality and stimulate cartilage healing. The patient's participation in creating a unique therapy plan is given a lot of consideration. This includes educating the patient and others around him or her, providing orthopedic equipment, and engaging in rehabilitation. The first step of therapy should include the implementation of physiotherapeutic treatment as soon as practicable.

Combining pharmaceutical and non-pharmacological treatments is one of the OA therapy options. Apart from managing pain, the therapy aims to enhance joint functionality and initiate the cartilage regeneration mechanisms. Much attention is paid to the role of the patient in establishing an individual therapy plan, including education of both the patient and his or her immediate environment, providing orthopedic equipment, and rehabilitation.⁵

According to recent studies, oxidative stress, apoptosis, inflammation, and energy metabolism are all directly linked to the mechanism of osteoarthritis (OA), and they can interact with one another. However, further research is still required as the pathophysiology of OA remains incompletely understood. No OA medication that modifies the illness has been approved by the FDA as of yet. Thus, research into safer and more effective treatments is necessary. Herbs or herbal products have a long history in treating OA and show great potential to generate less adverse events than pharmaceutical drugs.⁶

Given the various potentialities of the *Symphytum* species and their widespread use worldwide, data synthesizing the existing literature to identify the main gaps and areas of focused inquiry is essential to organizing future studies. The numerous medical properties linked to comfrey are caused by a few main substances that are present in the plant's root, leaves, and flowering tips. As medicinal properties, they are anti-exudative, granulation-promoting, analgesic, and anti-inflammatory. A few of the important bioactive substances discovered in comfrey are allantoin, RA, triterpenesaponins, tannins, alkaloids, amino acids, flavonoids, triterpenes, terpenoids, tannins, saponins, sterols, mucopolysaccharides, and several hydroxycinnamic acid derivatives. Using iontophoresis to produce synthetic phytofixin has been shown to have anti-inflammatory and anti-arthritis benefits in rat and human models; however, a review of the literature reveals no such research. As of right now, most people agree that comfrey root preparations provide medicinal benefits⁷. Iontophoresis is a therapy with potent analgesic, anti-inflammatory, and anti-swelling effects because it introduces therapeutic ions of specific chemical compounds that are electrolytically dissociating under the influence of an electric field and reach deeper tissues through the skin or mucosa. The active electrode selection process requires caution. The cathode ("-") is the active electrode beneath which the drug should be inserted when the active component is an anion; when the active component is a cation, the medication is introduced from the anode ("+"). The points of least resistance, or the sweat glands, allow the substance's ions to penetrate the skin.

The benefit of iontophoresis, it should be underlined, is that a high concentration of the medication may be delivered directly to the target tissue without the requirement for oral administration, lowering the likelihood of overdose and adverse effects.^{8,9,10}

The success of the iontophoresis treatment depends on a number of variables. These include, among other things, the compound's physicochemical characteristics, such as the size and charge of its particles, its concentration, and/or the preparation's inclusion of additional ions. Important factors include the tools utilized, the current flow's strength and type, the electrodes used, and the length of the process. The impact of the therapy is also influenced by biological elements such regional blood flow, skin surface area, and temperature. In summary, due to its unique properties, Novel Herbal Iontophoretic Gel is a safe and efficient alternative to topically administered non-steroidal anti-inflammatory drugs (NSAIDs).

Patient information

A 50-year-old male patient, who is predominantly right-handed and works as a tailor, was sent to the physiotherapy department. The patient's information indicates that in the early hours of March 20, 2023, the patient was performing a variety of household chores. During the same, he bent down to elevate the water pipe and felt a twist in his right knee. Following the event, he was immobile. He was transported to the hospital and mobilized with the help of his family; the same day, the orthopedic department consulted with him. In this orthopedic department, x-ray investigations and detailed evaluations were completed. The patient was recommended to get an MRI inquiry to rule out any further difficulties because the x-ray showed no measure findings. Degenerative alterations and reduced joint space were observed in the MRI report, leading to the diagnosis of right knee osteoarthritis in the patient. The patient was instructed to undergo physical therapy and was supplied analgesic medication. The patient has been receiving physiotherapy treatment ever since. Upon inspection, the right knee's anterior and medial aspects showed edema. The patient reported pain, giving it a 7 on a visual analog scale. Upon examination, the medial aspect of the knee showed grade 2 discomfort. When the right knee was bent, there was swelling and deformity, and the Clark test result was positive. It was discovered that the knee joint's ranges and muscular strength had decreased. The tables below provide the ranges and MMT prior to beginning therapy.

Table 1. Ranges of knee joint before and after treatment

Knee Range of motion	Before treatment	After treatment
Flexion	00-850	00-1100
Extension	850-00	1100-00

Table 2. Muscle Strength Before and After Treatment

Knee Muscles	Pre-treatment MMT	Resistive Isometric Grading	Post Treatment MMT	Resistive Isometric Grading
Flexors	3-	Painful and Weak	4	Painless and Strong
Extensors	3-	Painful and Weak	4	Painless and Strong

Table 3. VAS and WOMAC score before and after treatment

	Before treatment	After treatment
VAS Score	7	3
WOMAC Score	45%	21%
Pittsburg Sleep Quality Index	10	18

Table 4. Rehabilitation table

1st week	Iontophoresis, or the application of a new herbal gel with 1 mA transcutaneous electrical nerve stimulation on the medial area of the knee, occurs four days a week. Exercises began on the third day and included seven minutes of stationary cycling followed by Warm-up for five minutes, then cool-down for five minutes. Exercises that target the terminal knee extension, SLR, isometric hip adduction, and isometric quadriceps. Every day, do two sets of 10 reps.
2nd week	Iontophoresis: four times a week, a new herbal gel is applied to the medial aspect of the knee and transcutaneous electrical nerve stimulation is used at a 1.5 mA rate for eight minutes. Ten minutes of retro-walking and cycling, interspersed with five minutes of warm-up and Warm-up for five minutes, then cool-down for five minutes. Exercises that target the terminal knee extension, SLR, isometric hip adduction, and isometric quadriceps. Every day, do two sets of 10 reps.
3rd week	Iontophoresis: 4 days a week, a new herbal gel is applied to the medial aspect of the knee and transcutaneous electrical nerve stimulation is used at a 2 mA rate for 8 minutes. 15 minutes of retro-walking and cycling, followed by Warm-up for five minutes, then cool-down for five minutes. Exercises that target the terminal knee extension, SLR, isometric hip adduction, and isometric quadriceps. Every day, do two sets of 10 reps.

4th week	Iontophoresis: four times a week, a new herbal gel is applied to the medial aspect of the knee and transcutaneous electrical nerve stimulation is used at a 2.5 mA rate for eight minutes. 15 minutes of retro-walking interspersed with a Warm-up for five minutes, then cool-down for five minutes. Exercises that target the terminal knee extension, SLR, isometric hip adduction, and isometric quadriceps. Every day, do two sets of 10 reps.
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RESULT

Following a month of consistent care, the patient's symptoms significantly improved. The knee ranges and muscle strength of the patients improved, as shown in tables 1 and 2. After receiving consistent treatment for a month, the pain also decreased, resulting in a reduction in the VAS rating from 7 before treatments to 3. Table 3 displays the WOMAC score, which similarly showed improvement. No signs of a neurological involvement were present. After obtaining the patient's written agreement, the therapeutic interventions began on the first day.

In 1st week –Iontophoresis (Herbal gel applied with Transcutaneous electrical nerve stimulation on medial aspect of knee) with 1mA for 8 minutes (4 days a week). Exercises began on the third day and included seven minutes of stationary cycling followed by Warm-up for five minutes, then cool-down for five minutes. Exercises that target the terminal knee extension, SLR, isometric hip adduction, and isometric quadriceps. Every day, do two sets of 10 reps.

In 2nd week - Iontophoresis (Herbal gel applied with Transcutaneous electrical nerve stimulation on medial aspect of knee) with 1.5mA for 8 minutes (4 days a week). Ten minutes of retro-walking and cycling, interspersed with Warm-up for five minutes, then cool-down for five minutes. Exercises that target the terminal knee extension, SLR, isometric hip adduction, and isometric quadriceps. Every day, do two sets of 10 reps.

In 3rd week - Iontophoresis (Herbal gel applied with Transcutaneous electrical nerve stimulation on medial aspect of knee) with 2mA for 8 minutes (4 days a week). Fifteen minutes of retro-walking and cycling, followed by Warm-up for five minutes, then cool-down for five minutes. Exercises that target the terminal knee extension, SLR, isometric hip adduction, and isometric quadriceps. Every day, do two sets of 10 reps.

In 4th week - Iontophoresis (Herbal gel applied with Transcutaneous electrical nerve stimulation on medial aspect of knee) with 2.5mA for 8 minutes (4 days a week). 15 minutes of retro-walking interspersed with a Warm-up for five minutes, then cool-down for five minutes. Exercises that target the terminal knee extension, SLR, isometric hip adduction, and isometric quadriceps. Every day, do two sets of 10 reps.

DISCUSSION

The fundamental tenet of therapy for OA, as recommended by current guidelines for conservative (non-surgical) care, is the concurrent use of pharmaceutical and non-pharmacological interventions. More focus is being placed on non-pharmacological treatment approaches that guarantee the safety and efficacy of the medication due to the many drawbacks and adverse effects connected with pharmaceutical treatment. Natural herbal and botanical remedies have also been studied as an alternative to synthetic medication therapies for the treatment of osteoarthritis. We were unable to locate any research examining the effects of iontophoresis using gel containing *symphytumofficinale* on knee OA patients' pain, function, sleep quality, and gait patterns in the literature. The current study evaluated the effects of iontophoresis using a newly created gel that contained *symphytumofficinale* on walking patterns, pain, physical function, and sleep quality. Consequently, it was deduced that the patient's walking habits, quality of sleep, and reduction of pain were all related to their osteoarthritis of the knee.

FAVOURABLE STUDIES

Agnieszka Dakowicz, Zofia Dzięcioł-Anikiej, et al. (2022) state as much. In a research specifically on OA, 220 individuals with diagnosed knee OA were treated with comfrey cream applications every day or a placebo for an average of 6.5 years. When comfrey cream was used in place of a placebo, the patients' quality of life and mobility increased and their pain significantly decreased. Furthermore, research indicates that iontophoresis, which applies direct current, improves vascular flow and reduces neuromuscular excitability. Furthermore, iontophoresis adds therapeutic ions to the treatment's non-invasive character and the ability to achieve the intended result with even a low concentration of the preparation are two more advantages.¹¹

Topical treatment with 4 Joints is a safe and effective treatment for the symptoms of knee OA in individuals with moderate knee pain on most days and clinical OA, according to L.L. Laslett, S.J. Quinn et al. (2012). Specifically, after a 12-week course of treatment, it decreases pain and strengthens muscles without affecting systemic inflammation or cartilage degradation. Studies conducted in the past with comfrey have all indicated that the herb is useful in reducing OA pain and edema. According to earlier research, using comfrey cream on a regular basis reduced OA knee pain by 46% to 54.7 percent, while a placebo group only saw a 10.7% improvement in the same discomfort.¹²

Elaheh Mahmoudzadeh, Hossein Nazemiyeh et al. (2022) state that *S. officinale* L. possesses anti-inflammatory qualities that may be mostly attributable to its suppression of IL-1 β secretion. Allantoin is a uric acid oxidation metabolic product that promotes cell proliferation and enhances tissue regeneration. The leaves of *S. officinale* L. were employed in a study by Thibane et al. to promote healing, lower inflammation, alleviate joint and muscle diseases, and increase the facilitation of functional improvements.¹³

According to Agnieszka Dakowicz, Zofia Dzięcioł-Anikiej, Anna Hryniewicz, et al. (2022), there are studies in the literature that discuss the use of iontophoresis in combination with NSAIDs and steroid medicines to treat patients with osteoarthritis. The primary goal of a previous study was to determine which current polarization is suitable for injecting ketoprofen into the rat knee joint. Following iontophoresis with 5% Ibuprofen, studies on the use of NSAIDs in the treatment of knee osteopenia have shown improvements in walking speed, pain, and active range of motion. Furthermore, it has been demonstrated that iontophoresis using Piroxicam gel greatly reduces pain, improves functional capacity, and strengthens the knee extensor muscles. Furthermore, in an osteoarthritic rat model, an assessment of the iontophoretic administration of a cationic ketoprofen choline chloride shown a marked decrease in knee inflammation and pain. When iontophoresis with Perskindol gel was used on individuals with osteoarthritis of the knee, the best results were obtained.¹⁴ The importance of duration of sleep in OA and pain has been emphasized in a number of other research in addition to this one, according to Yongkyu Cho (2020). Profound correlations have been documented between the amount of sleep and the frequency of OA, and sleep disturbances are present in more than 70% of cases with KOA. Sanchez et al. discovered that interleukin (IL)-6 increases caused by inadequate sleep quantity may either cause or exacerbate discomfort. According to Quartana et al., sleep disturbance is becoming more widely acknowledged as a direct cause of hyperalgesia and poor endogenous pain regulation. Furthermore, it was discovered that CBT concentrating on sleep length helped KOA patients' pain, highlighting the significance of sleep in treatment. When working or exercising, those with radiographic OA experience synovitis and excessive mechanical strain, which impairs their quality of sleep by causing knee pain at night.¹⁵ Cigdem Kuralay (2018) reports that a correlation was found between a lower quality of life and poor sleep quality in a study including Taiwanese patients (Chen et al., 2014). It is believed that better physical and mental health translates into greater treatment for patients with poor quality of life when assessing sleep in patients with knee OA.¹⁶

Conclusion:

The patients who received symphytumofficinale gel iontophoresis showed improvement over the placebo group in terms of no significant side effects and were successful in reducing pain, function, sleep quality, and walking speed.

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Conflicts of Interests: NIL

Ethical Considerations: Approval from Biomedical Research Human Ethics Committee (DPSRU-BREC), DPSRU & Institutional Animal Ethics Committee, DPSRU has been taken. This study has been registered in clinical trial registry and got trial acknowledgement number (CTRI/2022/06/043155).

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Informed Consent: After informing the patient about the trial, their informed consent was obtained.

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