International Journal of Physical Medicine & Rehabilitation

OPEN ACCESS Freely available online

Research Article

Micro Active Plus Curcumin Reduces Pain in Patients with Osteoarthritis

Christopher Topar[1], Luke Stancs[2], Janice Havansy[3], Sarika Shah[4], Lior Cohen[5], Anushka Bhat[6], Jaskomal Phagoora[7], Kaitlin Carroll[8*]

[1]Dr. Med, Ortho-Eins, Berlin, Germany; [2]BS, Yale University, USA; [3]BS, Weill Cornell Medical College, USA; [4]BS, University of Michigan, USA; [5]MSPT, Metro PT, New York; [6]Washington University Saint Louis, Missouri, USA; [7]Brooklyn College of the City University of New York, Brooklyn, NY, USA; [8]BS, Hospital for Special Surgery, New York, USA

ABSTRACT

Background: Naturally occurring anti-inflammatories, such as curcumin, have the potential to decrease pain in patients with symptomatic Osteo Arthritis (OA) and allow them to increase their physical activity without serious side effects. Despite the low bioavailability of pure curcumin, it has been shown to reduce pro-inflammatory molecules. Research has shown that Micro Active plus Curcumin has 9.7x more bioavailability than 95% pure curcumin powder.

Purpose: This current study aimed to compare the standard dose of naproxen (220 mg twice daily) to Micro Active plus Curcumin (500 mg twice daily) in the pain reduction in patients, diagnosed with symptomatic OA.

Results: There were 100 patients included in this study that were randomized into one of two groups, for a total of 50 patients per group. There were no difference in demographics between groups (p=0.741) or difference in distribution of OA grade between groups (p=0.34). Patients in the Micro Active Plus Curcumin group reports a decrease in pain after an average of 2.3 weeks. There was no difference in pain control between groups (p=0.514). In patients who took NSAIDs daily, 12% patients did not tolerate the treatment due to GI issues compared to 8% in Micro Active plus Curcumin group.

Discussion and Conclusion: In our study, Micro Active plus Curcumin was tolerated better than naproxen and shown to reduce pain in all patients. The use of Micro Active plus Curcumin should be considered as primary intervention for patients with OA pain.

Keywords: Osteoarthritis; Curcumin; Pain; Disability; Pain reduction

INTRODUCTION

Osteoarthritis (OA) is the most common musculoskeletal condition and is the primary cause of mobility disability in the elderly population in the world [1]. Globally, hip and knee Osteoarthritis (OA) as the 11th highest cause of disability, with the prevalence of knee and hip OA within the global population being 3.8% and 0.85%, respectively [2]. Within the United States, there is an increasing population living with OA and it is estimated that 30.8 million adults are afflicted [3]. OA, which is defined as the degeneration of articular cartilage within the joint, causes many symptoms: Joint pain, tenderness and stiffness, limitation of movement, joint inflammation and abnormal bone growth within the joint [4,5]. In patients with OA, it has been found that with an increased walking disability, there is an increased risk of mortality, most notably from cardiovascular disease and dementia [6]. This finding was specified by Cleveland, et al. [7], which demonstrated that there

Correspondence to: Kaitlin M. Carroll, Department of Orthopaedic Surgery, Hospital for Special Surgery, New York City, United States, E-mail: kaitlincarroll@gmail.com

Received: 26-Jan-2023, Manuscript No. JPMR-23-21567; **Editor assigned:** 30-Jan-2023, PreQC No. JPMR-23-21567 (PQ); **Reviewed:** 13-Feb-2023, QC No. JPMR-23-21567; **Revised:** 20-Feb-2023, Manuscript No. JPMR-23-21567 (R); **Published:** 27-Feb-2023, DOI: 10.35248/2329-9096.23.11.664

Citation: Topar C, Stancs L, Havansy J, Shah S, Cohen L, Bhat A, et al. (2023) Micro Active Plus Curcumin Reduces Pain in Patients with Osteoarthritis. Int J Phys Med Rehabil. 11:664.

was an increased risk of mortality among patients with symptomatic knee OA (pain). This may be brought on due to exacerbation of pain brought on by physical activity causing a sedentary lifestyle, which then promotes co-morbidities such as cardiovascular disease and diabetes [7].

The main methods of pain reduction for patients with symptomatic OA includes acetaminophen, Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) and selective Cyclooxygenase-2 (COX-2) inhibitors. All three of these pharmaceutical analgesics have dose and duration dependent gastrointestinal, hepatic, cardio and renal side effects [8]. NSAIDs, such as naproxen, work to reduce pain by inhibiting the COX-1 and COX-2 enzymes, which is responsible for the creation of prostaglandins. Unfortunately, with the non-selective inhibition of both COX-1 and COX-2 enzymes, naproxen has also been shown to have approximately three times greater relative risk for developing the gastrointestinal side effects, such as ulcers, compared to patients who did not use NSAIDs [9,10]. Due to NSAIDs potential for side effects, other methods of pain control have been utilized in patients with OA, such as physical activity (both land and aquatic based programs), acupuncture, glucosamine sulfate, and topical capsaicin cream [8].

Naturally occurring anti-inflammatories, such as curcumin, have the potential to decrease pain in patients with symptomatic OA and allow them to increase their physical activity without serious side effects. Curcumin is derived from *Curcuma longa L.* and is a lipophilic, phenolic compound that has been researched as a potent anti-inflammatory and anti-oxidant compound [11]. Despite the low bioavailability of pure curcumin, it has been shown to reduce pro-inflammatory molecules such as IL-8, TNF-α, NF-κB, IFN-γ, COX-1 and COX-2 [12-16]. Madhavi and Kagan (2014) developed MicroActive Curcumin, a medical food that is a proprietary mixture of surfactants, oil and sustained release polymers that allow curcumin to be more readily absorbed across the intestinal epithelium and distribution throughout the body. Research has shown that MicroActive Plus Curcumin has 9.7x more bioavailability than 95% pure curcumin powder. When patients had side effects to MicroActive Plus Curcumin, they were mainly less severe gastrointestinal events, such as bloating and/or gas [11]. This current study aimed to compare the standard dose of naproxen (200 mg twice daily) to MicroActive Curcumin (500 mg twice daily) in the pain reduction in patients diagnosed with symptomatic OA.

MATERIALS AND METHODS

All patients presented for persistent knee pain for OA. Patients were excluded from the study if any of the following exist:

- Allergy to MicroActive Plus Curcumin.
- Preoperative hepatic or renal dysfunction.
- History of gastrointestinal issues.
- Pregnant.
- Breastfeeding.
- Diagnosis of inflammatory arthritis.
- Younger than 18 or greater than 100 years of age.
- Grade IV OA as defined by radiographs.

Patients were randomized into one of 2 groups; Micro Active plus Curcumin (500 mg) 2 capsules daily and Naproxen twice daily (control group). Patients had an initial physical exam and baseline radiographs with documented Grade 3 or less OA according to the Kellgren-Lawrence scale. Patients were asked to rate their pain using the Numeric Pain Rating Scale (NPRS) at baseline and 6 weeks post-treatment. They were asked complete a medication diary verify medication compliance and record any medication side effects. Any GI intolerance was self-reported by the patient in the medication diary and reported to their physician. If persistent symptoms, patients were told to stop treatment.

RESULTS

After Institutional Review Board approval, patients were randomized into one of two groups MicroActive Plus Curcumin (500 mg) 2 capsules daily and Naproxen twice daily (control group). There were 100 patients included in this study for a total of 50 patients per group. There were no difference in demographics between groups (p=0.741) or difference in distribution of OA grade between groups (p=0.34) (Table 1).

	Group 1	Group 2
Age (years)	55.6 ± 8.3	54.7 ± 9.1
Sex (M/F)	14/11	15/10
Body Mass Index (kg/m^2)	32.7 ± 4.1	31.9 ± 3.7

Table 1: Patient Demographics.

Patients in the MicroActive Plus Curcumin group reported a decrease in pain after an average of 2.3 weeks. There was no difference in pain control between groups (p=0.514). In patients who took NSAIDs daily, 12% patients did not tolerate the treatment due to GI issues compared to 8% in MicroActive Plus Curcumin group.

DISCUSSION

Osteoarthritis has been linked to various health conditions and daily life limitations that affects a large portion of the population, however, the numerous treatments available all pose additional potential side effects. Recent studies have linked OA with cardiovascular disease as a result from patients treating their pain with chronic use of nonsteroidal anti-inflammatory medications. Mohammad, et al. found that the use of NSAIDs was directly correlated with cardiovascular disease [17]. In addition, two previous studies assessed the mediating role of NSAIDs on all-cause mortality in patients with OA, however the results in these studies were inconsistent. One study found the risk to be increased by 51% whereas one did not find any evidence to support risk of cardiovascular disease and NSAID use [18,19]. While many studies have analyzed the correlation between NSAIDs and cardiovascular disease, but this longitudinal study suggest that 41% of patient who used NSAIDs for OA pain were at an increased risk for developing

cardiovascular disease such as ischemic heart attack, congestive heart failure, and stroke [17]. The findings of this study and other studies reported in the literature warrant investigation on alternative treatments for OA in an effort to decrease NSAID use and the potential risk their use may cause patients.

With the risks of chronic use for NSAIDs becoming a heightened concern there is a need to find alternative treatment options for OA pain. Curcumin has been used as a traditional medicine in several cultures because its health benefits including and could have the potential to reduce OA pain. Previous studies have supported its use for anti-oxidant, anti-inflammatory and wound-healing properties as well as its role in reversal of multidrug resistance of cancer cells [20-26]. While poor bioavailability has previously limited its use, the recent advancement of curcumin products have provided a new interest in its use for various medical treatments [27-29]. There have been various developments to improve its oral bioavailability, which have acted as a vehicle for delivery to help increase its ability to penetrate inflamed tissues and disperse in the gastrointestinal tract to maximize drug absorption. In our study, we used MicroActive Plus Curcumin, which is a proprietary formula that has very high bioactivity that can reduce high sensitive CRP.

CONCLUSION

The strength of our study is that is a randomized controlled trial with a specific cohort of patients with knee osteoarthritis. This allowed for our study to look at a direct correlation in a subset of patients, however, it is also a limitation of our study as it does not have a control group of health individuals. Another limitation to our study is that we did not limit or exclude patients on duration or dose of NSAID use prior to randomizing them into groups. Lastly, all gastrointestinal issues were self-reported by the patient and we did not record severity to compare between groups. In conclusion, our study using MicroActive Plus Curcumin was formulated to increase absorbability and was well tolerated better than naproxen and shown to reduce pain in all patients. The use of MicroActive Plus Curcumin should be considered as primary intervention for patients with OA pain.

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