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Is Curcumin Effective in Reducing Pain in Arthritis Patients?

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ABSTRACT

OBJECTIVE: The objective of the selective EBM review is to determine whether or not, "Is curcumin effective at reducing pain in arthritis patients?"

STUDY DESIGN: Review of three, double blind, randomized controlled trials (RCTs), published between 2012 and 2014, all in English language. The articles compared oral curcumin to visually matched placebo or accepted standard treatment.

DATA SOURCES: Three RCTs were found using PubMed. All articles were published in peer-reviewed journals and selected based on correlation to topic choice, date of publication, and evaluating POEMs.

OUTCOMES MEASURED: Patient reported pain level, as measured by visual analog scale (VAS) score.

RESULTS: All three studied demonstrated a statistically significant reduction in patients' pain levels in the curcumin group versus the control group. Chandran et al reported a mean change in baseline pain of 59.9% in the curcumin group, as compared to 49.94% in control group. Nakagawa et al also demonstrated a statistically significant change in mean from baseline between curcumin treatment and placebo. Panahi et al similarly found a post-treatment reduction in VAS to be statistically significant between curcumin and placebo.

CONCLUSION: Based off the data collected from the three RCTs, curcumin is effective in reducing arthritis pain in patients.

KEY WORDS: curcumin, arthritis

INTRODUCTION

Osteoarthritis is a chronic degenerative condition of the joints that can cause disability and loss of function. Hallmarks of the condition include cartilage degeneration, increased subchondral thickness, osteophyte formation, and mild joint inflammation. The most common joints affected are knees, hips, interphalangeal joints and lumbosacral spine[5]. Rheumatoid arthritis is a systemic inflammatory disease characterized by synovitis in multiple joints[9]. This paper evaluates three randomized controlled trials (RCTs) comparing the efficacy of oral curcumin to placebo at reducing arthritis patients' pain.

Currently 54.4 million United States adults have been diagnosed with a form of arthritis by a doctor. This represents 22.7% of the adult population of the country. The incidence is predicted to increase to 26% and by 2040 an estimated 78 million US adults will have a diagnosis of arthritis[3]. In 2003 arthritis accounted for $128 billion of health care costs[4]. Arthritis visits are extremely common in primary care and physician assistants are frequently responsible for management of the condition. Arthritis-related complaints account for over 100 million office visits each year[1].

Risk factors for developing arthritis include joint injury, overuse, increased age, female gender, obesity, family history and race[2]. As the population ages and obesity affects more individuals the incidence of arthritis will continue to increase. Treatment for osteoarthritis includes non-pharmacologic measures such as physical therapy, exercise, joint unloading and weight loss. Pharmacologic therapies available are acetaminophen, oral or topical NSAIDs, topical capsaicin, intra-articular steroid injections or opioids. For advanced cases, surgical treatment such as joint replacement is indicated[5]. Rheumatoid arthritis treatments may include oral or intra-articular steroids and DMARDs such as methotrexate or TNF inhibitors[9]. A

concerning factor for treatment of arthritis is long term use of anti-inflammatory agents. Both osteoarthritis and rheumatoid arthritis have inflammatory components of the disease that contribute to pain. Risks of long term NSAID use include cardiovascular complications and gastrointestinal ulcers, while long term corticosteroid use carries significant complications of bone loss, cataracts and neurological changes. Due to the chronic nature of arthritis it is important to seek safer alternatives to current treatments, as well as evaluate add-on therapies.

OBJECTIVE

The objective of this selective EBM review is to determine whether or not curcumin is effecting in reducing pain in arthritis patients.

METHODS

Three randomized controlled trials were used in this review. Adults (over age 18) with osteoarthritis or rheumatoid arthritis comprise the population of the studies utilized. The experimental intervention was oral curcumin. Studies varied in dose of curcumin from 180 mg/day to 1500 mg/day. The control group in Chandran et al study was given diclofenac sodium 50 mg[6]. The control group in Nakagawa et al and Panahi et al received a visually-matched placebo pill[6,7]. The outcome evaluated in all three studies was a reduction in pain level, as demonstrated by VAS score.

All RCTs reviewed were published in peer-reviewed articles, written in English and found on the PubMed database. The keywords used in searches were "curcumin" and "arthritis." The articles were chosen based on relevance to the objective and whether the outcome evaluated was a POEM. The inclusion criteria were randomized, controlled studies published within the last ten years. Exclusion criteria included patients under 18 years of age and disease-oriented

evidence. Reported statistics were mean change from baseline, p-value and independent samples t-test.

Table 1: Demographics and Characteristics of Included Studies

Study	Type	# Pts	Age (yrs)	Inclusion Criteria	Exclusion Criteria	W/D	Interventions
Chandran, 2012	RCT	45	18-65	RA diagnosis, RA functional class I/II, Disease activity score>5.1	Concurrent treatment with NSAID/DMARD/anti-TNF; Hgb <6.2, creatinine >1.4 mg/dL; bone/joint surgery within 8 weeks of screening or planned <12 weeks after randomization; fibromyalgia dx; hx TB, uncontrolled DM, severe allergic reaction to medications; pregnant or nursing; hx of alcohol or drug abuse	7	Curcumin BCM-95 500mg
Nakagawa, 2014	RCT	50	>40	Primary medial knee OA, Kellgren-Lawrence grades II/III via xray	Previous knee surgeries; knee injection during study; knee injection within 2 months of study; other steroids within 4 weeks of study	9	Theracurmin containing 180 mg/day of curcumin
Panahi, 2014	RCT	53	<80	Degenerative primary knee OA mild-moderate severity; bilateral OA	Allergy to curcuminoids; candidate for joint replacement; OA secondary to trauma; malabsorption disorders; ESR>20; heart/renal/liver failure; corticosteroid use above 10 mg/day in last 3 months; history psych disorders; intra-articular injections within last 3 months	13	C3complex® 1500mg/day with 5-mg Bioperine®

OUTCOMES MEASURED

The primary outcome measured in all three studies was change in visual activity scale score. The patient-oriented outcome addressed in all three studies is patients' pain levels indicated by patient marking a line on a scale of 0 (no pain) to 100 (severe pain). Each study collected initial VAS scores prior to intervention and again after the trial.

RESULTS

Two studies compared oral curcumin with placebo and one with oral curcumin vs. diclofenac (standard treatment)[5,6,7]. Panahi et al evaluated the intervention over 6 weeks, while both Chandran et al and Nakagawa et al evaluated over 8 weeks[5,6,7]. Chandran et al was a single-blinded study, while both Nakagawa et al and Panahi et al were double-blinded[5,6,7].

The Chandran et al study was conducted in Karala, India and included patients age 18-65 who have been diagnosed with rheumatoid arthritis and disease activity score greater than 5.1[6]. Exclusion criteria for the study included recent treatment for RA, low hemoglobin, elevated liver enzymes, recent surgery, other significant rheumatologic disease, history of tuberculosis, pregnancy, and history of alcohol or drug abuse[6]. Chandran et al evaluated 45 patients randomly divided into three groups[6]. The first group received oral curcumin (500mg), the second received diclofenac sodium (50 mg) and the third received a combination over a period of 8 weeks[6]. Only the first two groups will be discussed in this review[6]. Of the initial 45 patients, 38 completed the study and the author did not report reasons for leaving the trial[6]. At the end of the trial patients reported their assessment of disease activity by visual analog scale (VAS) with 0 being no pain and 100 being severe pain. Chandran et al also evaluated patients' vital signs and laboratory values bi-weekly for safety[6]. Results were calculated by change from baseline to endpoint and the curcumin group was found to have the highest reduction in VAS score[6]. An ANOVA test

was used to assess primary outcome of the trial between groups[6]. Within the groups an

independent t-test was used to evaluate significance of change from baseline[6]. A significant p-

value of <.05 was calculated for change from baseline for this group[6]. There was not a significant

difference between curcumin and diclofenac pain reduction percentages, however this

demonstrates similar efficacy to conventional NSAID treatment for rheumatoid arthritis[6]. The

diclofenac group had the most adverse events, with three patients reporting side effects, while

curcumin patients reported two adverse events (minor fever and throat infection)[6].

Table 2: Patient Outcomes as Evaluated by Mean Change in VAS in Chandran et al

	Baseline	End of Treatment	p-value
Curcumin	68.57±17.14	27.5±9.45	<.05
Diclofenac	78.25±11.25	39.17±20.1	<.05

Nakagara et al conducted their study in Japan and included 50 patients with primary

medial knee osteoarthritis[7]. Exclusion criteria included previous knee surgeries, recent knee

injections or recent steroid treatment[7]. Patients were randomly divided into two groups, the first

of which received 180 mg of oral curcumin per day and the control received a visually-matched

placebo[7]. Three subjects in total were lost to follow-up during the study (two from the curcumin

group and one from the control) and three patients dropped out due to adverse effects[7]. Two

patients in the curcumin group withdrew due to hypertension and redness of the tongue, while

one in the control group felt unwell[7]. Patients were seen at weeks 2, 4, 6 and 8 for compliance

checks. Patients gave an initial knee pain visual analog scale score and were re-evaluated at the

8-week mark[7]. 41 patients in total were evaluated and those treated with curcumin had

significantly decreases in their VAS scores from baseline versus the placebo group (p=.023)[7].

The authors opted to exclude patients with low initial VAS scores (<.15) when evaluating the efficacy of the curcumin, as their pain level was already so low no significant change could be reported[7]. The authors were also able to verify the safety of the supplement by evaluating laboratory values on the patients throughout the study[7].

Panahi et al conducted a study in Tehran, Iran including 53 patients with primary degenerative knee osteoarthritis[8]. Exclusion criteria included allergy to curcuminoids, OA secondary to trauma, active inflammatory conditions, and heart, renal or liver failure[8]. Patients were randomly assigned to two groups where one group received curcuminoids 1500 mg/day and the other received a visually matched placebo[8]. 40 subjects completed the 6-week trial[8]. The remaining 13 patients were lost to follow up[8]. Patients were evaluated by change in VAS from baseline to end of treatment[8]. Panahi et al used paired samples t-tests to compare baseline versus end-trial values for each parameter[8]. The two groups were compared using independent samples t-test[8]. The authors found significant ($p<.001$) reduction in VAS score from baseline in the curcumin group, as well as in comparison to the placebo group[8]. There were no serious adverse events reported, only minor gastrointestinal symptoms with 7 patients in the curcumin group reporting these and 4 in the placebo cases (no significant difference between the groups)[8].

Table 3: Efficacy of Oral Curcumin in Treating Arthritis Pain

	Comparison	p-value
Chandran et al	Change from baseline	<.05
Nakgawa et al	Placebo	.023
Panahi et al	Placebo	<.001

DISCUSSION

Rheumatoid arthritis and osteoarthritis are both chronic degenerative conditions for which patients must be on long term treatments to control pain. The current trouble is that accepted treatments do not have safe profiles. Acetaminophen can cause liver toxicity, chronic

NSAID use is associated with ulcers and cardiovascular complications and steroids are associated with osteoporosis[5].

Curcumin is a polyphenol extracted from turmeric. Turmeric has been used as a spice in food preparations for centuries and thus is recognized as safe[7]. The anti-inflammatory botanical inhibits mediators of the inflammatory response including cytokines, chemokines, adhesion molecules, COX-2 and tissue factor[6].

Curcumin in available widely in the United States as a supplement. There is no insurance coverage and it has not been evaluated by the FDA for use as a treatment for arthritis. For highly concentrated curcumin formulas there is a significant cost to the patient. As it has not been evaluated in the United States, it is likely that medical practitioners in the country are not familiar with the treatment and thus are not likely to recommend curcumin to their arthritis patients.

The three studies considered in this review all indicate that curcumin is an effective treatment for arthritis pain, as evidenced by patient's reported VAS score. Chandran et al demonstrates similar efficacy between curcumin and diclofenac in rheumatoid arthritis patients, which is encouraging since diclofenac is an accepted treatment for pain[5]. Both Nakagara et al and Panahi et al relay information compared to placebo and note clinically significant improvement in osteoarthritis symptoms[6,7].

While all three studies evaluated the effect of curcumin on a patient's VAS score, Chandran et al only evaluated mean change from baseline. They evaluated curcumin and diclofenac separately and found similar reduction in pain levels between the groups but did not do a statistical analysis for the comparison[5]. Chandran et al was also the only study that was single-blinded[5]. Nakagawa et al and Panahi et al evaluated mean change and compared the two

groups to find a significant benefit in treatment with curcumin versus placebo[6,7]. Also, it should be noted that all three studies took place in Asia, so there warrants further testing in other countries. There are genetic components of both arthritis and metabolism of medications and supplements that could affect the efficacy of curcumin as a treatment. The duration of the three studies ranged from 6-8 weeks which is an acceptable length of time to evaluate how curcumin affects pain levels in arthritis patients, however it is not a significant amount of time to determine disease progression and long term effects of curcumin.

CONCLUSION

The results of this review suggest that curcumin is a safe and effective treatment for arthritis. While all three studies reported a significant (p<.05) reduction in arthritis pain in patients treated with oral curcumin, the sample sizes were small[5,6,7]. It is also important to note that all took place in Asia, so there should be trials on other ethnicities to determine if the treatment is effective for the general population of the United States. The trials were of a short duration so longer studies would be important to conduct in the future that include radiologic evidence of changes in disease progression, as well as long term side effects of curcumin. In conclusion, the three trials evaluated in this review indicate curcumin is an effective treatment, but further evaluation with a larger sample size and longer duration trial is needed to fully determine the effectiveness of curcumin.

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