A Randomized, Pilot Study to Assess the Efficacy and Safety of Curcumin in Patients with Active Rheumatoid Arthritis

Binu Chandran1 and Ajay Goel2*
1Nirmala Medical Centre, Muvattupuzha, Kerala, India
2Baylor Research Institute and Sammons Cancer Center, Baylor University Medical Center, Dallas, TX, USA

Curcumin is known to possess potent antiinflammatory and antiarthritic properties. This pilot clinical study evaluated the safety and effectiveness of curcumin alone, and in combination with diclofenac sodium in patients with active rheumatoid arthritis (RA). Forty-five patients diagnosed with RA were randomized into three groups with patients receiving curcumin (500 mg) and diclofenac sodium (50 mg) alone or their combination. The primary endpoints were reduction in Disease Activity Score (DAS) 28. The secondary endpoints included American College of Rheumatology (ACR) criteria for reduction in tenderness and swelling of joint scores. Patients in all three treatment groups showed statistically significant changes in their DAS scores. Interestingly, the curcumin group showed the highest percentage of improvement in overall DAS and ACR scores (ACR 20, 50 and 70) and these scores were significantly better than the patients in the diclofenac sodium group. More importantly, curcumin treatment was found to be safe and did not relate any adverse events. Our study provides the first evidence for the safety and superiority of curcumin treatment in patients with active RA, and highlights the need for future large-scale trials to validate these findings in patients with RA and other arthritic conditions.

Copyright © 2012 John Wiley & Sons, Ltd.

Keywords: curcumin; diclofenac sodium; Disease Activity Score; American College of Rheumatology criteria.

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic systemic inflammatory disorder that primarily affects various body joints and causes progressive destruction of articular structures, particularly, the cartilage and bone. Notably, the joint destruction is a prominent feature of the disease that not only differentiates RA from other arthritic diseases but also determines its outcome in the majority of individuals affected (Shiozawa and Tsumiyama, 2009). The long-term prognosis of RA is poor with as much as 80% of patients affected becoming disabled after 20 yr and a concomitant reduction in life expectancy by an average of 3–18 yr. If the disease remains untreated, 20–30% of patients may become permanently work-disabled within 2–3 yr of diagnosis. Predictors of poor outcome for RA include relatively low functional disease activity scores early in the disease progression, lower socio-economic status and education level, strong family history of the disease, and early involvement of many joints (Rindfleisch and Muller, 2005; Schmajuk et al., 2011). Thirty per cent of the patients with severe forms of the disease typically remain unresponsive to any classic treatment intervention. Nonetheless, patients with milder forms of the disease may derive some level of benefit from early diagnosis and treatment (Breedveld, 2011).

Pharmacotherapy for rheumatoid arthritis generally involves treatment regimens including non-steroidal antiinflammatory drugs (NSAIDs) for the pain management, low-dose therapy using oral or intraarticular glucocorticoids, disease-modifying antirheumatic drugs (DMARD) and the newer biological treatments (Rindfleisch and Muller, 2005; Marks, 2011). Unfortunately, the majority of these drugs typically associate with severe side effects including gastrointestinal bleeding, increased blood pressure, accelerated osteoporosis, myelosuppression, hepatotoxicity, ocular toxicity, hypersensitivity and allergic reactions, as well as increased risk of infections (Lipsky et al., 2000; Newsome, 2002; Rahme and Bernatsky, 2010). Diclofenac belongs to the NSAID class of drugs and is used to relieve pain, tenderness, swelling and stiffness caused by osteoarthritis, rheumatoid arthritis and ankylosing spondylitis (Altman et al., 2009; Ruff et al., 2011). Since this drug constitutes the current standard of care for managing patients with RA, we selected diclofenac sodium as a reference drug for evaluating and comparing its efficacy with curcumin in RA patients in this study (Ruff et al., 2011).

Curcumin is the active component of the common spice turmeric, and exerts a wide spectrum of biological activities by modulating several transcription factors and signalling pathways (Aggarwal et al., 2007; Goel et al., 2008a,b). It possesses several functional groups that exhibit antioxidant activity (Goel et al., 2008a; Goel and Aggarwal, 2010), which permits curcumin to modulate redox-signalling pathways in cells. Curcumin can also activate the intracellular antioxidant defence system through stimulation of nuclear factor-erythroid-2-
related factor 2 (Nrf2), a transcription factor which binds to the antioxidant response element (ARE) in the regulatory region of several genes that code for intracellular antioxidants, cytoprotective and detoxification proteins (Scapagnini et al., 2011). Curcumin is a potent and established antiinflammatory dietary botanical component that inhibits all mediators of the inflammatory response such as cytokines, chemokines, adhesion molecules and growth factors, as well as other mediators such as cyclooxygenase-2, inducible nitric oxide, tissue factor and epigenetic alterations (Goel et al., 2001, 2008b; Reuter et al., 2011). These effects of curcumin are due to its ability to inhibit the NF-κB pathway and other proinflammatory signalling pathways including COX-2, AP-1, Egr-1, STAT (signal transducers and activators of transcription) members and mitogen-activated protein (MAP) kinases. Curcumin is both a chemopreventive and an anticancer agent (Aggarwal and Shishodia, 2006; Aggarwal et al., 2007). It inhibits cell proliferation, induces apoptosis and growth arrest in different phases of the cell cycle (depending on the cell type) and inhibits angiogenesis (Shishodia et al., 2007). Curcumin is able to exert such effects due to its ability to act on multiple targets and at multiple levels invoking several mechanisms, including activation of peroxisomal proliferator activated receptor gamma (PPARγ), degradation of p53, activation of proapoptotic genes (including caspases, Bax and Bak family members), down-regulating survival genes (e.g. Bcl-2) (Bhattacharyya et al., 2007; Shankar and Srivastava, 2007; Goel et al., 2008a,b). Owing to such multiple activities curcumin is currently being evaluated in several human clinical trials for several diseases, including cardiovascular diseases, type 2 diabetes, Alzheimer’s disease, rheumatoid arthritis, multiple sclerosis and a variety of human cancers. In view of the overwhelming literature and promise for the potential benefits of curcumin-induced chemoprevention and treatment of several human diseases, the current study was a pilot effort to assess the efficacy and safety of curcumin compared with diclofenac sodium, and curcumin in combination with diclofenac sodium for 8 weeks in patients with mild to moderate rheumatoid arthritis.

MATERIALS AND METHODS

Patient characteristics: inclusion and exclusion criteria. The present study was conducted at Nirmala Medical Centre in Muvattupuzha, Kerala, India. Forty-five patients (38 female, 7 male; mean age 47.88 yr) with active RA were prospectively enrolled in this clinical trial. The clinical trial registration number is BCM HS 01–2008. Eligible patients were of 18–65 yr of age, and were diagnosed to have RA according to the revised 1987 American College of Rheumatology (ACR) criteria (with RA functional class I or II) and Disease Activity Score (DAS) > 5.1.

The exclusion criteria included patients with any of the several conditions listed as follows: concurrent treatment with any NSAID, DMARD or any anti-TNF-α therapy or other antiarthritic therapy, treatment with any investigational agent within 4 weeks of screening and intraarticular or parenteral corticosteroids within 4 weeks prior to the screening visit. Other criteria for exclusion were as follows: haemoglobin < 6.2 mmol/L (9.9 g/dL); neutrophil count < 2 × 10^9/L; serum creatinine > 1.4 mg/dL for women or 1.6 mg/dL for men; aspartate transaminase (AST) or alanine transaminase (ALT) > 2.5 times the upper limit of normal; platelet count < 100000/μL; bone/joint surgery within 8 weeks prior to screening (including joint fusion), or joint surgery planned within 12 weeks of randomization; rheumatic autoimmune disease other than RA, or significant systemic involvement of secondary RA (e.g. vasculitis, pulmonary fibrosis or Felty’s syndrome), past or current inflammatory joint disease other than RA (e.g. gout, reactive arthritis, psoriatic arthritis, sero-negative spondyloarthropathy, Lyme disease) or other systemic rheumatic disorders (e.g. systemic lupus erythematosus, inflammatory bowel disease, scleroderma, inflammatory myopathy, overlap syndrome); diagnosis of fibromyalgia or other chronic pain syndrome requiring daily narcotic treatment; patients having a secondary, non-inflammatory type of arthritis (e.g. osteoarthritis or fibromyalgia); a history of tuberculosis or positive chest X-ray for tuberculosis; uncontrolled diabetes mellitus or hypertension; history of severe allergic reactions to the type of drugs used in the study, uncontrolled diseases (such as asthma, psoriasis, or inflammatory bowel disease where flares are commonly treated with corticosteroids); evidence of significant comorbid diseases (such as cardiovascular disease, nervous system, pulmonary, renal, hepatic, endocrine, cerebrovascular disease or gastrointestinal disorders); history of recurrent significant infection requiring hospitalization or treatment with antibiotics within 4 weeks of screening or oral antibiotics within 2 weeks prior to screening; history of or features of cancer (including solid tumours and haematologic malignancies and primary or secondary immunodeficiency); pregnant women or nursing (breast feeding) mothers; and history of alcohol, drug or chemical abuse within 6 months prior to screening.

Any antiinflammatory, antiarthromatoid, analgesics, steroids or other drugs that in the opinion of the investigators would interfere with the study were not permitted for 4 weeks in the case of parenteral or intraarticular drugs and 2 weeks in the case of oral drugs before study enrolment and during the study period. This study was conducted in accordance with the International Conference on Harmonization guidelines (ICHG) for good clinical practice and the Declaration of Helsinki. Independent Ethics Committee, Aluva, Kerala, India approved the study protocol. Patients gave written informed consent before participating in the study.

Study design. The present study was a randomized, single-blinded, pilot study designed to determine the safety and effectiveness of twice daily oral therapy of curcumin 500 mg capsule and diclofenac sodium 50 mg tablet individually and in combination for 8 weeks in patients with active rheumatoid arthritis. Forty-five patients were randomized in 1:1:1 ratio using Random Allocation Software, to receive curcumin 500 mg (Group I) or curcumin 500 mg + diclofenac sodium 50 mg (Group II), or diclofenac sodium 50 mg (Group III) over a period of 8 weeks. Curcumin, in the form of BCM-95® (a patented and registered formulation of curcumin with enhanced bioavailability) for these studies was kindly provided by Arjuna Natural Extracts, Kochi, Kerala, India.

Copyright © 2012 John Wiley & Sons, Ltd.

(Antony et al., 2008). The purity of BCM-95® was assessed by HPLC analysis, in which the chromatograms from BCM-95® samples were compared with those of commercially available pure standards for different curcuminoids. The sample purity was determined by comparing the peak areas of individual peaks present in the standards versus BCM-95® samples. As shown in Fig. 1, HPLC analysis not only revealed absence of any impurities in the BCM-95® curcumin, but the ratios and retention times of various peaks in BCM-95® were parallel to those of the curcuminoid standards.

Eligible subjects were assigned a three-digit, unique randomization number. Data on demographic characteristics, medical history and prior and concomitant medications were also collected. Body weight and height were measured, physical examination was performed, and vital signs including blood pressure and heart rate were recorded. Laboratory examinations including haematology, blood chemistry, C-reactive protein (CRP), antistreptolysin-O (ASO), blood sugar and pregnancy test in women were performed. A 28 joint assessment was performed for a tender joint count, swollen joint count and duration of morning stiffness. Each patient underwent X-ray AP view of chest/hands/wrist/foot and 12-lead electrocardiography.

Efficacy and safety evaluation. The primary end point of the study was to determine the frequencies of the patients with good or moderate DAS28 response, as defined by the European League Against Rheumatism (EULAR) criteria, at week 8. The EULAR response criteria are based on the change from baseline in disease activity as assessed by the DAS28 (a composite index based on assessment of 28 joints), the erythrocyte sedimentation rate (ESR) and visual analog scales (VAS) on which the patient scored his/her global assessment of disease activity. The secondary end point was the proportion of patients achieving an ACR response of 20%, 50% or 70% (ACR20, ACR50, ACR70) at week 8 and an assessment of the severity of inflammation as judged by CRP values.

The ACR criteria measure improvement in tenderness or swollen joint counts and improvement in three of the following five parameters: patient global assessment – global assessment of disease activity on a 0–100 scale (0, best; 100, worst); physician assessment – global assessment of disease activity on a 0–100 scale (0, best; 100, worst); pain scale disability – visual analogue scale for pain (VAS; 0, no pain and 100, severe pain); functional questionnaire – HAQ (Health Assessment Questionnaire) includes four categories: dressing and grooming, arising, eating and walking, on a 0–3 scale (0, best; 3, worst); acute phase reactant (such as erythrocyte sedimentation rate, ESR). The ACR20 category is defined as a reduction in tender and swollen joint counts by 20%, ACR50 by 50% and ACR70 by 70%, from baseline. Efficacy evaluations were performed at bi-weekly intervals.

Monitoring of vital signs, physical examinations, laboratory parameters (haematology, blood chemistry,
CRP, ASO, rheumatoid factor, blood sugar) were performed bi-weekly for safety evaluation. The occurrence of adverse events was the primary safety variable.

Statistical analysis. Thirty-eight subjects completed all visits in accordance with protocol and were selected for efficacy analysis. Primary and secondary endpoint measurements were analysed by calculating the change and percentage change from baseline to endpoint. All statistical tests were two-sided with a significance level of $\alpha = 0.05$. Data were summarized using descriptive statistics (number of subjects [$n$], means, standard deviation [SD]) for continuous variables, and using frequency and percentage (i.e. number and proportion of subjects – $n$, %) for discrete/categorical variables, unless specified otherwise. The ANOVA test was used to assess primary outcome of the trial between groups. Within the groups analysis for all parameters was carried out using an independent $t$-test. SPSS 10.0 was used for all analysis. The statistical power was calculated using a post hoc statistical power calculator for Student’s $t$-test and the study had 95% power to detect a 37% change within the group.

The safety analysis was performed on all 45 patients. This included the collection of both adverse and serious adverse event data. Serious adverse events were defined as those presenting a significant hazard or side effect (e.g. any event that was fatal, life-threatening, required hospitalization, or resulted in persistent or significant disability).

RESULTS

Demographics and baseline characteristics

Forty-five patients who were enrolled into the study were randomized into three groups (15 in curcumin, 15 in curcumin + diclofenac sodium and 15 in diclofenac sodium alone). The mean age was 47.8 yr in the curcumin group; 47 in the curcumin + diclofenac sodium group; and 48.87 in the diclofenac sodium group. All RA patients had an active disease (with mean DAS scores in the curcumin group = 6.40, curcumin + diclofenac sodium group = 6.44 and diclofenac sodium group = 6.72). There was no significant difference in baseline characteristics including values for body mass index (BMI), disability index of the HAQ, positive rate of serum rheumatoid factor and baseline chemistry values (Tables 1 and 2).

Efficacy assessment: DAS28

All three treatments showed significant improvement in DAS28 scores, although the changes between individual groups were not statistically significant. However, among the three groups, the curcumin group showed the highest percentage of improvement. Among the components of DAS, ESR in all three groups showed similar mean baseline values (Table 3), while the percentage change from baseline was highest in the curcumin + diclofenac sodium group (13.3%). Mean VAS scores for pain in all groups were comparable at baseline, but the curcumin group showed the highest reduction in VAS score from baseline (59.9%). Percentage changes in VAS scores in all three groups were statistically significant. The results are summarized in Tables 4 and 5.

Efficacy assessment: ACR20, ACR50 and ACR70 response

A summary of ACR20, ACR50 and ACR70 at week 8 (end of study) shows that the highest percentage of ACR20 (93%), ACR50 (73%) and ACR70 (33%) was achieved by the curcumin alone group. Although the difference between treatment groups in the proportion of ACR20 responders was not significant, there was a marked trend towards ACR20 response rate in the curcumin group compared with the other two groups. The components of ACR response criteria showed significant changes from baseline to end of study in all three groups. However, CRP showed a statistically significant change only in the curcumin group. The results are summarized in Tables 6 and 7.

ECG, haematology and chemistry

There were no significant changes in ECG, haematology and chemistry parameters. However, serum glutamic oxaloacetic transaminase (SGOT) showed a 33.94% increase in the diclofenac sodium group.

Safety

Adverse events were reported more frequently in the diclofenac sodium group than in the curcumin and curcumin + diclofenac sodium groups. Three adverse events were reported in the diclofenac sodium group, namely: itching and swelling around the eyes, dimness of vision; worsening of condition; serum glutamic pyruvic transaminase (SGPT) and SGOT values increased, which were probably related to the drug. One adverse event, fever, was not related to the drug. Adverse events reported in the curcumin group were mild fever and throat infection. There was one case of worsening of condition in the curcumin + diclofenac sodium group.

Table 1. Demographics and baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>Curcumin ($n = 15$)</th>
<th>Curcumin + diclofenac sodium ($n = 15$)</th>
<th>Diclofenac sodium ($n = 15$)</th>
<th>Overall ($n = 15$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>47.8 ± 8.60</td>
<td>47 ± 16.22</td>
<td>48.87 ± 10.78</td>
<td>47.88 ± 12.03</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.52 ± 3.75</td>
<td>22.73 ± 3.65</td>
<td>21.99 ± 3.75</td>
<td>23.08 ± 3.79</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>2</td>
<td>4</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>Female</td>
<td>13</td>
<td>11</td>
<td>14</td>
<td>38</td>
</tr>
</tbody>
</table>
**DISCUSSION**

The primary objective of this study was to undertake a pilot clinical study to ascertain the efficacy of curcumin alone, or in combination with diclofenac sodium in patients with rheumatoid arthritis. Since the study was a proof-of-principle and a pilot one, it had the limitations of being an open labelled study. The results from this 8-week randomized study in patients with active RA provide evidence that curcumin is safe, and has a significant efficacy in improving the DAS and ACR scores in patients with mild or moderate RA, when given alone or in combination with diclofenac sodium. In fact, patients who received curcumin achieved higher ACR response rates than the other two groups. For all three-treatment groups, the ACR response was significant. All components of ACR, namely total number of painful joints, total swollen joints, patient’s GA, physician’s GA, disability index and HAQ showed significant changes in all three groups. It is noteworthy that the acute phase reactant, CRP, showed significant improvement only in the curcumin group. Consistent with this, this group showed the most significant improvement in the DAS scores.

The findings of this study are significant, as these demonstrate that curcumin was not only safe and effective, but was surprisingly more effective in alleviating pain compared with diclofenac. Our findings are consistent with a previously published report by Kuptniratsaikul and colleagues in which they demonstrated the safety and efficacy of *Curcuma domestica* for the treatment of patients with knee osteoarthritis (Kuptniratsaikul et al., 2009). These investigators reported not only that both curcumin and ibuprofen had comparable efficacy in mitigating the clinical symptoms for osteoarthritis, but also that the rate of adverse events with curcumin was lower than that of ibuprofen (33.3% in curcumin group versus 44.2% with ibuprofen), an observation that has been independently validated in our present study in patients with rheumatoid arthritis. Although the molecular mechanisms for such efficacy of curcumin are unclear, it is reasonable to speculate that curcumin may differentially regulate molecular targets that control chronic pain versus the ones that mediate acute pain. Curcumin has been reported to be effective in alleviating chronic pain in different experimental models (Sharma et al., 2006, 2007; Maes et al., 2007; Tajik et al., 2007, 2008; Mittal et al., 2009), including neuropathic pain (Sharma et al., 2006, 2007), one of the most difficult forms of pain to treat. In an animal model of formalin-induced orofacial pain (Mittal et al., 2009), curcumin was found to potentiate a subanaalgia dose (0.2 mg/kg) of diclofenac. In the present study, however, curcumin + diclofenac...
The combination was slightly less efficacious than curcumin alone, even though the curcumin dose remained unchanged. On the contrary, the diclofenac sodium group experienced several adverse events that were probably a direct consequence of the use of this drug. Supplementation of curcumin alone provided significant overall improvement in patients with active RA, and this efficacy was better than that provided by diclofenac sodium, and was not associated with any adverse events. Our findings are of further interest considering that although curcumin has long been known to possess a wide spectrum of activities including antioxidant, antiinflammatory and anticancer properties in different preclinical and clinical models, poor absorption and bioavailability of this phytonutrient has severely limited its application to various diseases. In this study, we were able to overcome this shortcoming by using a proprietary preparation of curcumin, BCM-95®, which is not only all natural, but has six- to eight-fold enhanced bioavailability as reported previously (Antony et al., 2008). Our observations that curcumin alone was able to alleviate symptoms of rheumatoid arthritis in this study are quite encouraging, and these results provide an ideal springboard for investigating the potential of curcumin in other chronic diseases arising in the setting of dysregulated chronic inflammation.

The study was designed as a 2-month trial, which is probably not long enough to detect radiographic changes. However, since both DAS and ACR are the indicators of the physical functioning in RA, the significant improvement in both parameters would suggest that radiographic progression was likely inhibited in these patients. The study shows that curcumin can provide significant improvement in treatment efficacy in active RA. The reported findings are especially relevant in view of recent reports of monotherapy failure in RA (Combe et al., 2009; van der Heijde et al., 2006; Zintzaras et al., 2008; Breedveld et al., 2006).

In conclusion, curcumin was generally safe and well-tolerated in most subjects when given up to 8 weeks. Although our present data are very encouraging they are a platform only for future planning of long-term studies with the drug in combination with existing standard therapies in RA, which will provide a complete picture of the utility of curcumin. Curcumin has activities similar to the anti-TNF drugs, but without their serious side-effects and a study comparing these two drugs is warranted.

Table 5. Treatment efficacy results – visual analog scale (VAS)

<table>
<thead>
<tr>
<th>Group</th>
<th>Baseline (n = 45)</th>
<th>End of treatment (n = 38)</th>
<th>% change</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Curcumin (n = 14)</td>
<td>68.57 ± 17.14</td>
<td>27.5 ± 9.35</td>
<td>59.9</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Curcumin + diclofenac sodium</td>
<td>77.25 ± 9.65</td>
<td>34.29 ± 26.75</td>
<td>56.62</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Diclofenac sodium (n = 12)</td>
<td>78.25 ± 11.25</td>
<td>39.17 ± 20.1</td>
<td>49.94</td>
<td>&lt; 0.05</td>
</tr>
</tbody>
</table>

*Analysis was within the group. Independent t-test was used.

Table 6. Components of American College of Rheumatology (ACR) responses*

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Curcumin (n = 14)</th>
<th>Curcumin + diclofenac sodium (n = 12)</th>
<th>Diclofenac sodium (n = 12)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline EOT</td>
<td>p valueb</td>
<td>Baseline EOT</td>
</tr>
<tr>
<td>Total painful joints</td>
<td>18.64 3.14</td>
<td>&lt; 0.05</td>
<td>16.67 2.75</td>
</tr>
<tr>
<td>Total swollen joints</td>
<td>12.15 0.36</td>
<td>&lt; 0.05</td>
<td>11.5 0.42</td>
</tr>
<tr>
<td>Patient’s GA&lt;sup&gt;g&lt;/sup&gt;</td>
<td>83.93 30.7</td>
<td>&lt; 0.05</td>
<td>78.75 40.83</td>
</tr>
<tr>
<td>Physician’s GA&lt;sup&gt;c&lt;/sup&gt;</td>
<td>79.64 28.21</td>
<td>&lt; 0.05</td>
<td>74.58 36.25</td>
</tr>
<tr>
<td>Disability index, HAQ&lt;sup&gt;d&lt;/sup&gt;</td>
<td>4.41 1.06</td>
<td>&lt; 0.05</td>
<td>3.95 1.53</td>
</tr>
</tbody>
</table>

*Data presented as mean based on change from baseline; EOT, end of treatment.

Table 7. Treatment efficacy results – C-reactive protein (CRP)

<table>
<thead>
<tr>
<th>Group</th>
<th>Baseline (n = 45)</th>
<th>End of treatment (n = 38)</th>
<th>% change</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Curcumin (n = 14)</td>
<td>5.34 ± 4.12</td>
<td>2.56 ± 1.8</td>
<td>52</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Curcumin + diclofenac sodium</td>
<td>9.11 ± 9.93</td>
<td>6.66 ± 6.87</td>
<td>26.9</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Diclofenac sodium (n = 12)</td>
<td>3.3 ± 2.4</td>
<td>3.35 ± 2.5</td>
<td>-1.5</td>
<td>&gt; 0.05</td>
</tr>
</tbody>
</table>

*Analysis was within the group. Independent t-test was used.
CURCUMIN IN RHEUMATOID ARTHRITIS

and effective application of curcumin alone in clinical settings for the management of rheumatoid arthritis, and other proinflammatory diseases including cancer in the future.

Acknowledgements
The authors deeply acknowledge Dr T. N. B Kaimal for his valuable suggestions and Arjuna Natural Extracts Limited for providing curcumin capsules (BCM-95®). The study was supported by a pilot project grant from the Nirmala Medical Center, Kerala, India.

Conflict of Interest
The authors have declared that there is no conflict of interest, financial or otherwise.

REFERENCES


The authors deeply acknowledge Dr T. N. B Kaimal for his valuable other proinflammatory diseases including cancer in the future.

Acknowledgements
The authors deeply acknowledge Dr T. N. B Kaimal for his valuable suggestions and Arjuna Natural Extracts Limited for providing curcumin capsules (BCM-95®). The study was supported by a pilot project grant from the Nirmala Medical Center, Kerala, India.

Conflict of Interest
The authors have declared that there is no conflict of interest, financial or otherwise.

REFERENCES


Copyright © 2012 John Wiley & Sons, Ltd.