Original Research Article

A comparison of efficacy of tocotrienol and turmeric (curcuma longa) in knee osteoarthritis

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Abstract

Background: Osteoarthritis (OA) is the most prevalent musculoskeletal disorder worldwide and increasingly important in public health concern. The present study was conducted to compare the efficacy of tocotrienol and turmeric (curcuma longa) in osteoarthritis.**Materials & Methods:** 72 patients with OA were divided into 4 groups. Group I-Diclofenac 50 mg (twice a day), Group II- Diclofenac 50 mg + CL 500 mg (twice a day), Group III- Diclofenac 50 mg + Tocotrienol 200mg (twice a day) and Group IV- Diclofenac 50 mg + CL 500 mg + Tocotrienol 200mg (twice a day). Parmaeter such as knee pain by VAS, WOMAC score, IL- 1β, SOD were determined.**Results:** All the patients were found to be suffering from Grade 2 and Grade 3 osteoarthritis. Out of 72 patients enrolled in the study, 39 (54.2%) were Grade 2 and rest 33 (45.8%) were Grade 3. Difference in Grade of osteoarthritis among patients of above four groups was not found to be statistically significant (p=0.581).VAS score was significant at day 120 (P< 0.05). A significant WOMAC score at 60 and 120 days (P< 0.05).IL1-β and SOD showed significant difference at day 60, 120 respectively (P< 0.05).**Conclusion:**Combination of standard drug+curcumin+tocotrienol was better at inflammation control by reduction of IL1-β expression than the remaining three. However, if we take a single drug into account then tocotrienol was better than the others at curbing the process of inflammation.

Keywords: Osteoarthritis, Curcumin, Tocotrienol

Introduction

Osteoarthritis (OA) is the most prevalent musculoskeletal disorder worldwide and increasingly important in public health concern. It is a degenerative disease with multifactorial etiology characterized by biochemical/morphological alterations in the synovial membrane and joint capsule, and defect in articular cartilage, marginal hypertrophy in bone, subchondral sclerosis[1]. Pathological changes present in the late stage of OA like softening, ulceration, and focal disintegration of the articular cartilage and synovial inflammation[2].The main clinical symptoms are pain, joint instability and stiffness may be experienced due to inactivity. It is also known as degenerative arthritis, which commonly affects the hands, feet, spine, and large joints. Mostly OA have unknown cause and are referred to as primary OA. Generally, OA is commonly related to aging and presents as localized, generalized, or as erosive OA. However, OA at secondary level is caused by another disease or clinical condition [3,4]. The common aetiological factors for OA include age, gender, prior joint injury, obesity, genetic predisposition and mechanical factors. The link between obesity and OA is multifactorial, obesity induces low-grade systemic inflammation caused by the secretion of proinflammatory adipokines and cytokines. The unregulated secretions of these marker are contribute in joint degeneration during OA. Moreover, alteration in genes which encode different interleukins like IL-1A, IL-1B, IL17A, IL6 etc have been reported their association with OA[5].Tocotrienol is a subfamily of vitamin E and known for its wide array of medicinal properties, involved in prevention and treatment of various communicable and non-communicable diseases. Curcumin is also a traditional Indian medicine used in treatment biliary digestive disorder, wounds, and rheumatic diseases. It possesses both anti-inflammatory and antioxidative activities. Curcumin exists as 2 tautomeric forms, keto and enol[5]. The present study was conducted to compared the efficacy of tocotrienol and turmeric (curcuma longa) in osteoarthritis.

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Materials & Methods

The present study comprised of 72 patients of age 45 to 80 years suffering from Osteoarthritis in period of May 2019 to October 2020 were included in this study. All the patients were recruited from the Department of Orthopaedic Surgery, King George's Medical University (KGMU), Lucknow, UP, India, after obtaining ethical approval from the Institutional Ethics Committee.Patients were selected on basis of KL (Kellgren and Lawrence) grading and randomly divided into four groups.Grade1: Doubtful narrowing of joint space and possible osteophyte lipping. Grade2: Definite osteophyte, definite narrowing of joint space. Grade3: Moderate multiple osteophytes, definite narrowing of joint space, some sclerosis and possible deformity of bone contour. Grade4: Large osteophytes, marked narrowing of joint space, severe sclerosis and definite deformity of bone contour physiology of cartilage. After allotment of groups in the study, every patient was received Curcumin extract (CL) 500 mg or Tocotrienol 200 mg or (CL 500mg + tocotrienol 200 mg) as drugs twice a day daily. All curcumin, Tocotrienol was given in form of capsules. The effect on

following groups was compared: Group I-Diclofenac 50 mg (twice a day), Group II- Diclofenac 50 mg + CL 500 mg (twice a day), Group III- Diclofenac 50 mg + Tocotrienol 200mg (twice a day) and Group IV- Diclofenac 50 mg + CL 500 mg + Tocotrienol 200mg (twice a day). Parmaeter such as knee pain by VAS, WOMAC score, IL- 1β, SOD were determined. P value<0.O5 was considered significant for data analysis.

Results

Table 1: KL grade in all groups

		Group				Total
		Group I (Control)	Group II (Curcumin)	Group III (Tocotrienol)	Group IV (Curcumin+Tocotrienol)	
KL grade	Grade II	10	12	8	9	39
		55.6%	66.7%	44.4%	50.0%	54.2%
	Grade III	8	6	10	9	33
		44.4%	33.3%	55.6%	50.0%	45.8%
Total		18	18	18	18	72
		100.0%	100.0%	100.0%	100.0%	100.0%

Table I shows that all the patients were found to be suffering from Grade 2 and Grade 3 osteoarthritis. Out of 72 patients enrolled in the study, 39 (54.2%) were Grade 2 and rest 33 (45.8%) were Grade 3. Difference in Grade of osteoarthritis among patients of above four groups was not found to be statistically significant (p=0.581).

Table 2: Intergroup comparison of pain (VAS) score at different time intervals

	Group								p-value
Pain (VAS) score	Group I (Control)		Group II (Curcumin)		Group III (Tocotrienol)		Group IV (Curcumin+Tocotrienol)		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
VAS 0	7.00	0.77	7.28	0.75	7.22	0.88	7.11	0.76	0.691
VAS 60	6.06	0.64	5.78	1.40	6.00	0.84	5.39	1.65	0.667
VAS 120	4.83	0.71	4.67	1.24	3.89	0.90	3.56	1.15	0.002

Table 2 shows that VAS score was significant at day 120 (P< 0.05).

Table 3: Comparison of WOMAC pain score at different time intervals

	Group								p-value
WOMAC pain score	Group I (Control)		Group II (Curcumin)		Group III (Tocotrienol)		Group IV (Curcumin+Tocotrienol)		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
0 days	15.06	3.10	14.94	2.62	15.22	3.14	15.11	3.18	0.996
60 days	13.89	2.95	10.39	1.38	10.78	1.90	9.11	1.57	<0.001
120 days	12.22	1.86	7.89	1.45	8.00	1.46	6.94	.94	<0.001

Table 3 shows significant WOMAC score at 60 and 120 days (P< 0.05).

Table 4: Comparison of IL1-β score at different time intervals

Biochemical	Group I (Control)		Group II (Curcumin)		Group III (Tocotrienol)		Group IV (Curcumin+Tocotrienol)		P value
IL1-β score	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
at 0 days	135.00	4.37	134.28	6.06	134.06	5.81	133.83	3.59	0.933
at 60 days	114.11	9.77	110.44	5.41	107.56	5.11	98.22	9.75	<0.001
at 120 days	86.94	5.30	67.44	13.42	64.33	5.37	30.67	16.93	<0.001
SOD levels at 0	2.608	.239	2.615	.195	2.623	.135	2.615	.195	0.997
SOD levels at 60	2.904	.271	3.212	.136	3.168	.149	3.420	.217	<0.001
SOD levels at 120	3.001	.248	3.570	.232	3.493	.224	3.636	.198	<0.001

Table 4,Fig 1 shows that IL1-β and SOD showed significant difference at day 60, 120 respectively (P< 0.05).

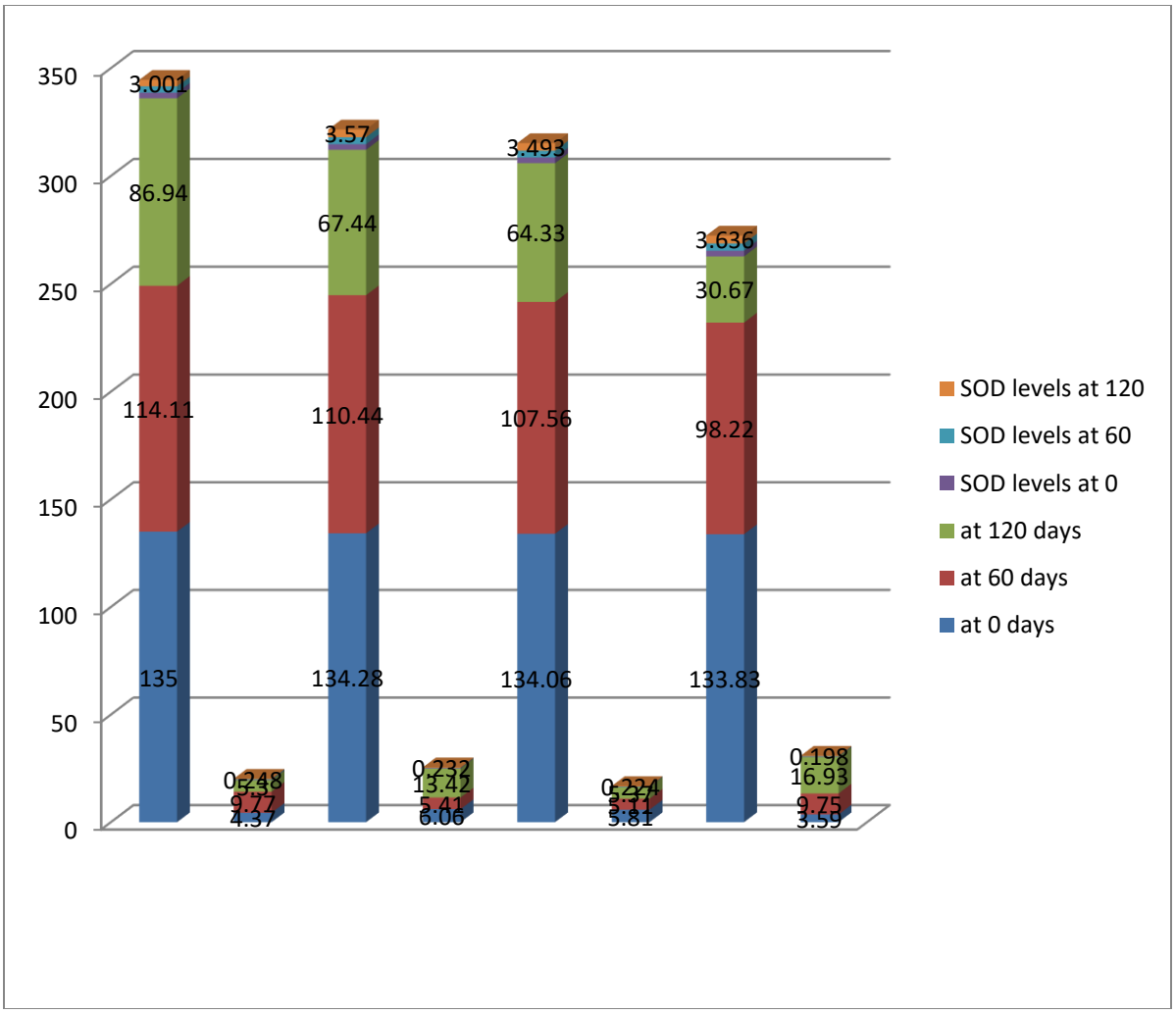

Fig 1: IL1-β and SOD showed significant difference at day 60, 120 respectively

Discussion

Curcumin inhibits IL-1β/TNF-α catabolic signalling pathway in chondrocytes and acts as an anti-inflammatory agent. Additionally, turmeric alters pro-inflammatory cytokines like interleukin production and phospholipase A2, and 5-LOX activity[6].Among the various pathways, curcumin can also reduce inflammation due to its capacity of decreasing the production of interleukin-1 (IL-1), IL-6, IL-8, IL-12.Patient education and self-management, exercises, weight reduction, walking supports (crutches), bracing, shoe and insoles modification, local cooling/heating, acupuncture, electromagnetic therapy should be tried earlier to pharmacological treatment or with it to provide maximum relief to patient[7].The present study was conducted to compared the efficacy of tocotrienol and turmeric (curcuma longa) in osteoarthritis.In present study, 72 patients were divided into 4 groups as Group I- Diclofenac 50 mg (twice a day), Group II- Diclofenac 50 mg + CL 500 mg (twice a day), Group III- Diclofenac 50 mg + Tocotrienol 200mg (twice a day) and Group IV- Diclofenac 50 mg + CL 500 mg+Tocotrienol 200mg (twice a day).Henrotin et al[8] investigated 150 patients with knee OA were followed for 90 days. They accessed PGADA and serum sColl2-1, a biomarker of cartilage degradation, as co-primary end points.

They were equally distributed grades II to IV of KL between the study groups, found 99% of grade II and III patients.We found that all the patients were found to be suffering from Grade 2 and Grade 3 osteoarthritis. Out of 72 patients enrolled in the study, 39 (54.2%) were Grade 2 and rest 33 (45.8%) were Grade 3. Difference in Grade of osteoarthritis among patients of above four groups was not found to be statistically significant (p=0.581).Pal et al[9] reported overall prevalence of knee OA was 28.7%. The associated factors were found to be female gender (31.6%), obesity, age and sedentary work. We found that VAS score was significant at day 120 (P< 0.05). A significant WOMAC score at 60 and 120 days (P< 0.05) was observed. IL1-β and SOD showed significant difference at day 60, 120 respectively (P< 0.05).In healthy cartilage, chondrocytes respond to their microenvironment to maintain a delicate balance between synthesis and degradation of the extracellular matrix (ECM). However, abnormal physiological mechanism of joint may lead to loss of ECM component, stressed cellular environment, and ultimately cause the chondrocyte apoptosis. Failure of matrix equilibrium is occurred through excessive production of pro-inflammatory mediators, including cytokines, chemokines, and matrix degradation products [9,10].Current research has demonstra-ted that inflammation is one of the key factors leading to the destruction of cartilage in OA. In the OA synovium, inflammatory cell infiltration is frequently observed[11]. The infiltrate pro-inflammatory cytokines IL-1β, IL-6, and TNF-α play the most important roles in pathogenesis of OA, while IL-15, IL-17, IL-18, IL-21, and some chemokines MCP-1,

and GRO have also been implicated. IL-1 β is produced by several cell types in joints, including chondrocytes and immune cells and induces the expression and release of proteolytic enzymes, such as matrix metalloproteinases (MMPs). These MMPs suppress the expression of ECM components. IL-1β also acts synergistically with cytokines and chemokines to further increase inflammation [12].During the late phase of OA, cartilage becomes hypocellular and the rate of apoptotic chondrocytes has been reported as high. The death of chondrocytes residing in cartilage would result in the failure to maintain the structure of articular cartilage and cause th matrix degradation within a short period of time. Chondrocyte apoptosis may lead to reduction of ECM, and decrease of ECM may in turn result in further chondrocyte apoptosis because of the loss of matrix-cell interaction[13]

Conclusion

Authors found that combination of standard drug+curcumin+ tocotrienol was better at inflammation control by reduction of IL1-β expression than the remaining three. However, if we take a single drug into account then tocotrienol was better than the others at curbing the process of inflammation.

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