STUDY THE EFFECTS OF ANTI-INFLAMMATORY CURCUMEX CAPSULES CONTAINING THREE PLANTS (GINGER, CURCUMIN AND BLACK PEPPER) IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS

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ABSTRACT

Background: *RA is an autoimmune disease that presented with chronic inflammation due to synovial hyperplasia, this disease progress through joint destruction. DMARD s is the most usual drug for treating this disease that accompanies with various adverse effects and complications. Aim of this study is to evaluate anti-inflammatory effect of a compound herbaceous drug consist of (ginger, Curcumin and black pepper) in rheumatoid patients so that decreasing dosage of DMARD s.* ***Method:*** *60 patients with Rheumatoid Arthritis upon ACR2010 criteria, enrolled study and divided to two groups consist of 30 patients. Both group received routine treatment of anti-rheumatoid agent consist of Methotrexate as DMARD, prednisolon and* Hydroxychloroquine *(HCQ) , one group received compound herbal drug named Curcumex consist of (ginger, Curcumin and black pepper) and control group received placebo as a same dose. Before and after 8 weeks DAS 28 score, TJC, SJC, ESR and CRP was calculated and compared in two groups.* ***Result:s:*** *Curcumex reduces TJC AND SJC significantly rather than placebo in patients with rheumatoid arthritis. Also DAS Score 28 decreased in Curcumex group rather than placebo (p-value<0.001). Laboratory markers such as ESR decreased in patients group, but there were no differences between two groups in CRP scales. (Value=0.322)*

KEY WORDS
ginger, Curcumin, black pepper, Rheumatoid Arthritis,DAS28,Curcume

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INTRODUCTION

Rheumatoid arthritis (RA) is the most common systemic autoimmune disease and is a chronic illness related to joint inflammation, progressive disability and complications in patients which have adverse impacts on their quality of life [1]. Rheumatoid arthritis affecting approximately 1% of the population. Women are three times more likely to be affected than men, with 80% of patients developing the disease between the ages of 35 and 50 [2]. RA is a systemic disease; therefore, many patients exhibit extra-articular manifestations [3,4]. Despite exhaustive research, the precise cause of RA remains unknown. Although a variety of cells play a role in RA disease, macrophages may be of particular significance in the disease process. Proinflammatory cytokines secreted by macrophages, such as tumor necrosis factor-alpha (TNF-α), interleukin 1 (IL-1), and interleukin 6 (IL-6), are believed to have a critically important role in the induction and propagation of chronic inflammation [4]. Rheumatoid arthritis (RA) causes premature death, disability, and lowers the quality of life in the industrialized and developing world [5]. The contemporary recommended approach to treating RA is very aggressive [6]. Non-biologic disease-modifying antirheumatic drugs (DMARDs), which reduce disease activity and prevent joint deformity, are prescribed within three months of diagnosis. Previously most people started with corticosteroids/non-steroidal anti-inflammatory drugs (NSAIDs), then fewer people slowly progressed to non-biologic DMARDs and even fewer people received biologic DMARDs if they did not respond to the previous drugs. Treatment guidelines have also changed with the increased biologic DMARDs available. In 2012, the American College of Rheumatology updated RA medical management guidelines [7]. These guidelines describe which biologic DMARDs to use for specific RA disease profiles (e.g., features such as disease activity, signs and symptoms, and prognosis) [7]. Recently, the beneficial anti-inflammatory properties of statins have been investigated among humans in diseases with high levels of inflammation such as RA, sepsis, organ transplantation and multiple sclerosis. The current clinical trial has been done to determine the anti-inflammatory impact of statin in rheumatoid arthritis because the clinical trials in this matter are not sufficient.

Nowadays, Due to the antioxidant properties And High anti-inflammatory, Extracts and derivative of plants is widely used [1]. DMARD s is the most usual drug for treating this disease that accompanies with various adverse effects and complications. Aim of this study is to evaluate anti-inflammatory effect of a compound herbaceous drug consist of (ginger, Curcumin and black pepper) in rheumatoid patients so that decreasing dosage of DMARD s.

MATERIALS AND METHODS

This trial was randomized double blind that so that patients and researcher was not informed from type of intervention ,All participant were 18 years old or more, and met ACR2010 criteria for diagnosis of rheumatoid arthritis. All of them affected to moderate or severe stages of disease that their symptoms was not controlled with DMARD s and other routine treatments. They divided into two groups consist of 30 patients. Exclusion criteria were consisting of pregnancy, kidney or liver failure, and using other drugs that may be affected disease activity. Both group received metothroxate with a dose of 0.2 mg /kg administrated 2 last days of week, prednisolone with a dose of 5 mg twice daily in divided dose and HCQ with a dose of 200 mg daily. Otherwise this treatment a group received Curcumex daily and control group received placebo with a same dose. Before intervention and 8 weeks later DAS28 Score in two groups calculated and mean differences were compared.

Statistical analysis

For description of data we used from median and standard deviation in quantitative data and from percentage and abundance in qualitative data ,at first invariable analysis was used , after multivariate analysis done for correlation between independent and dependent variables.in this step all independent variable entered in regression model. We used chi – square and Fisher's exact test for correlation between two qualitative variable and from independent T test and Mann–Whitney U test for comparison of median in two groups for assessment of coincidental of qualitative and independent variables used Generalized Estimating Equation. And covariance for independent and quantitative variables. P values between 0.05 and 0.1 were supposed borderline. And a P value less than 0.05 was significant. All analysis was done with SPSS software version 20.

RESULTS

Curcumex administration in case group reduced tender joint count (TJC) significantly in patients rather than control group (P Value < 0.001).
Otherwise patients that received Curcumex have less swelling joint count at the end of study (P value < 0.009).
Patients had less DAS28 score at the end of study versus control group. (P value < 0.001)
Erythrocyte sedimentation rate (ESR) diminished in Curcumex group rather than placebo, but there was no differences in CRP scale in case and control group at the end of study (P value = 0.322).summaries of results shown in [Table 1, 2].

Table 1: Mean differences between placebo and Curcumex group

Variable	Curcumex (Mean±SD)	Placebo (Mean±SD)	P-value
TJC	2.27±1.96	10.33±3.66	<0.001
SJC	1.07±1.17	7.13±3.84	<0.001
DAS28 Score	3.29±0.89	5.51±0.72	<0.001
ESR	21.50±12.67	38.47±18.92	<0.001

Table 2 : CRP scale changes before and after intervention

Variables (CRP)	OR	95%CI	P-value
Placebo After to Before	2.361	(0.652,8.546)	0.191
Curcumex After to Before	57.606	(15.917,208.48)	<0.001
Before			
Curcumex to Placebo	0.08	(0.023,0.282)	<0.001
After			
Curcumex to Placebo	1.953	(0.520,7.338)	0.322
Age	0.924	(0.895,0.954)	<0.001

DISCUSSION

In this trial, we evaluated effect of compound drug named Curcumex consist of (ginger, Curcumin and black pepper) and found that this drug significantly reduces inflamation both cilinically and paraclinicaly in RA patients.

Rheumatoid arthritis and chronic inflammation that accompanied with this disease obligated patients using long term chemical drugs with enormous complications. New investigations try new drugs and policies with less complication and more beneficial [8]. In this trial struggle to use herbaceous drugs for treatment of rheumatoid arthritis. Proved before this trial that, Additives such as curcumin inhibit inflammatory mediators such as leukoterians and prostaglandins.They role this effect through antioxidant property [9].

At first time Binu Chandran1 and ET al in 2012 in a pilot study showed that using Curcumin in RA patients have better outcome for control of disease activity rather than NSAID such diclofenac. And cucrumin patients have less disease activity scores rather than diclofenac group. Results of this study was Favourable with our study, but this trial was a pilot with small sample size , otherwise we tested a compound drug that one of its components were curcumin and cannot tell this curative effect in our study was related directly to curcumin or other gradients [10].

Abdel-Motaal M. Found in 2008 showed that Zingier with a dose of 50 mg/kg/day in rheumatoid patients other than reduction in DAS28 Score, also reduces inflammatory markers such as IL-1, IL-6, however in our study other clinical items such as tender joint count and swellings joint count was assessed, otherwise laboratorial markers of our study consist of Erythrocyte sedimentation rate and C reactive protein that was differ from this study [11].

Ludwig Boltzmann and ET al in 2013 showed that curcumin in vitro environments induce apoptosis in human fibroblasts and increases cell damage that all of this lead to anti-inflammatory effects that is useful for RA treatment. Also this finding was compatible with our study in confirming of anti-inflammation, but this study mentioned was in vitro, while our study was done in vivo environment and this was our superiority feature of our study [12].

Our study has some limitation and *strength*. One of this limitations is that we evaluated a compound drug consists of 3 various herbal, that cannot exactly say that anti-inflammatory and anti-ache effect of this drug in RA patients is contributed to each component of drug. from its strength of this study should say that this trial was done on human model while other studies done up to now, was performed on animal model or in vitro environments [13-15] or animal model [16] .otherwise in our study both anti-pain and anti-inflammatory effect of drug was evaluated while other studies usually studied only anti pain or anti inflammation alone [17].

At last, regarding various complications of routine anti rheumatoid drugs, and intending that these patients usually use non steroid anti-inflammatory agents for pain relief that have so many complications, and regarding of minimum complication of herbaceous drugs, using of such drugs for relief of pain and inflammation reduces complications of DMARDS drugs with various complications.

CONCLUSION

Administration of Curcumex with a dose of daily during 8 weeks reduce disease activity score (DAS28 Score), TJC, SJC and ESR in rheumatoid patients. Using Curcumex herbal drug in patients affected rheumatoid disease reduces inflammation and pain with minimum of side effects and lead to reducing dose of other chemical and routine DMARD s with too complications[18].

CONFLICT OF INTEREST
There is no conflict of interest.

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FINANCIAL DISCLOSURE
None

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