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Improvement in Immunological and Inflammatory Markers in Patients of Rheumatoid Arthritis by Naturopathy

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Abstract: ***Rheumatoid arthritis is a severe crippling disease which affects approximately 2 to 3 percent of the world's population. The aim of the study was to evaluate the effects of Naturopathy and Yoga intervention on regression of RA. A total number of 134 patients were divided into three Groups. Group-1 included yoga, naturopathy and allopathic medicines, Group-2 was provided yoga and allopathic medicines and Group-3 was the control Group provided only allopathic medicines. A significant difference was also found with decrease in inflammatory markers CRP ($p<0.05$), TNF-alpha ($p<0.05$) and ESR ($p<0.05$), immunological markers ACCPA ($p<0.001$) within all three groups and RF ($p<0.001$) only in group 1 but the study could not find significant difference in ANA. The study is one of its kind. The study concluded that Yoga and Naturopathy when combined with modern medicines provide important additional physical and psychological health benefits for RA patients.***

Keywords: Rheumatoid Arthritis, Naturopathy, Yoga, Immunological and Inflammatory Markers

1. Introduction

Rheumatoid arthritis (RA) is a systemic inflammatory disease affecting nearly 2-3% of the adult population in world with its primary manifestation in the synovium [1]. RA occurs at the same frequency throughout the world, thereby demonstrating that neither climate nor diet alone play a role in its genesis. It affects all races worldwide at the same frequency and is associated with reduced life-expectancy [2]. Prevalence of approximately 0.75% in India [3]. About 40% diseased become work disabled within 5 years from onset of symptoms [4]. Not all individuals with genetic susceptibility develop the disease, and in such cases environmental influences do play a crucial role. Amongst the environmental factors infections, drugs and chemicals are believed to be triggers of various autoimmune diseases [5].

Rheumatoid arthritis is potentially devastating disease that often results in progressive joint destruction, deformity, disability. In rheumatoid arthritis, the immune system targets synovial membrane and attacks it. The synovial membrane secretes synovial fluid into the joint. Synovial fluid is the joint fluid that lubricates and nourishes the joints. Other tissues can also be
targeted by the immune system in rheumatoid arthritis, but the synovium, or synovial membrane, is generally the primary target. When the synovial membrane is attacked, it becomes inflamed (synovitis) and can thicken and erode. As the synovial membrane is destroyed, the synovial fluid is also and not secreted. The surrounding structures can also become involved leading to the joint deformities as can be seen in rheumatoid arthritis [6].About 90% of the people with RA suffer from irreparable joint damages and loss of function. The disease causes restriction in movement hence leads to various psychological disorders like depression. However, only pain can be decreased and the progress of joint damages and loss of function narrowed down. This is achieved by several treatments as drugs, physiotherapy, occupational therapy and adjuvants as prostheses [7] [8]. Chronic fatigue is a very life impairing factor in rheumatoid arthritis [9]. The pain is neither entirely predictable nor controllable but probably lasting a lifetime [10].The pain can lead to Rheumatoid Arthritis is often concomitant with significant levels of depression and disability [11].

Even with variety of medical treatments available, patients suffering from RA often report continued pain, distress, and mobility limitations affecting everyday activities [12] [7]. Early diagnosis and better supportive management is the only way out for curtailing this disease. Early diagnosis includes regular blood monitoring in future could provide a diagnostic window for evaluating the impact of exercises on health and also in relation to chronic disorders like RA various markers to be checked amongst which some were chosen for this study. Some of the inflammatory markers (CRP, TNF-alpha & ESR) and immunological markers (ACCPA, RF&ANA)mark the presence of RA.As RA cannot be completely cured by the use of modern medicine alone, this research study was carried out to find an alternative treatment which can control the disease and yet be economic, less toxic and more readily available. The study is another mark to prove the efficacy of Naturopathy and Yoga as adjunct to modern medicine for better management of chronic diseases like RA.

2. Material and Method

The study was conducted for three years in department of research, Bapu Nature Cure Hospital in collaboration with department of Biochemistry, GB Pant Hospital. Blood samples were collected from 134 radiologically and serologically proven RA patients. Written consent was taken from all the patients and Ethical guidelines were

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followed during the study of Rheumatoid arthritis patients satisfying the American College Of Rheumatology criteria for rheumatoid arthritis were recruited by inclusion and exclusion criteria [13].

Treatment:

1. Naturopathy Treatment [14]

a) **Massage:** Massage is the manipulating of superficial and deeper layers of muscle and connective tissue using various techniques, to enhance function, aid in the healing process, decrease muscle reflex activity, inhibit motor-neuron excitability and promote relaxation and well-being. Following are the techniques of massage:

a. Stroking
b. Friction
c. Kneading
d. Percussion
e. Vibration

Sesame oil (50 ml per sitting) was used for the massage of the patients during the therapy. It has anti-inflammatory properties and is suitable for patients of rheumatoid arthritis.Inflammatory markers (CRP, ESR and TNF-alpha) were evaluated at 0 level, 6th and 12th month out of immunological markers (RA, Anti-ccp and ANA) were evaluated at 0 level and 12th month.

b) Hot and cold fomentation was provided to every patient for 11 minutes – hot fomentation for 5 minutes and cold fomentation for 30 seconds for two rounds, followed by a heating compress using a dry cotton cloth and woolen flannel for 10 minutes. The temperature of both hot fomentation (40°- 45 °C) and cold fomentation (18°- 26 °C) was controlled well during the treatment period.

c) Yoga Therapy : The yoga therapies (20 min.), practiced for the treatment of Rheumatoid Arthritis (RA), were Pawanmuktasana part I (anti-rheumatic), Shavasana and Pranayama (Bhramari, Kapalbati, Deep breathing and Nadisodhana) [15]. The total treatment period for each patient was one year. Therapies were administered thrice a week on alternate days for first two months (1-2) then followed by twice in a week for the next four months (3-6) and in last six months (7-12) once a week.

3. Allopathic Medicines

The prescribed medicines were methotrexate, sulfasalazine, hydroxychloroquine, cipcal, folvite and altrady.

4. Statistical Methods

The statistical package was used for statistical analysis and results are expressed as mean ± standard deviation (SD). Student's paired t test (two-tailed) from baseline to 12 months was computed.

5. Results

Table 1: P value, MEAN ± SD (U/ml) of hs C reactive protein in group 1, 2, 3 at 0, 6th and 12th Months

	0th Month	*6th Month*	*12th Month*
Group1	7.10±3.79	5.67±3.12	5.51±3.80
Group 2	7.95±4.02	5.67±3.40	6.44±3.53
Group 3	5.78±4.18	4.72±3.24	5.91±3.44

High Sensitivity C-Reactive Protein (p-value)			
P- value	*Group 1*	*Group 2*	*Group 3*
Group 1	-	0.100	0.013*
Group 2	0.100	-	0.000***
Group 3	0.013*	0.000***	-

There is significant difference between Group 1 and Group 3, and Group 2 and Group 3 (P- value <0.05).

Table 2: The MEAN ± SD (mm/hr) of ESR in group 1,2,3 at 0 ,6th and 12th Months.

	0th Month	*6th Month*	*12th Month*
Group 1	47.41±25.39	38.49±19.16	35.92±18.19
Group 2	53.64±21.73	50.33±18.67	39.17±16.47
Group 3	44.92±29.11	45.06±24.53	36.61±17.01

Table 3: The P- value, MEAN ± SD (pg/ml) of Tumor Necrosis Factor- Alpha 1,2,3 at 0 ,6th and 12th Months

	0th Month	*6th Month*	*12th Month*
Group 1	17.38±9.20 (-)	26.92±18.35 (0.009)***	12.34±5.07 (0.167)
Group 2	22.69±20.06 (-)	34.69±22.28 (0.023)*	14.19±8.91 (0.107)
Group 3	19.46±15.34 (-)	21.44±14.86 (0.637)	16.06±14.79 (0.418)

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P- value	*Group 1*	*Group 2*	*Group 3*
Group 1	-	0.000***	0.270
Group 2	0.000***	-	0.005***
Group 3	0.270	0.005***	-

There is significant difference between Group 1 and Group 3, and Group 2 and Group 3 (P- value <0.05)

Table 4: The P value, MEAN ± SD (U/ml) of RA in group 1, 2 and 3 at 0 and 12th Months.

	0th Month	*12th Month*	*P- Value Paired t test*
Group 1	174.72±120.05	111.82±79.63	0.000***
Group 2	164.56±117.71	142.25±105.15	0.075
Group 3	120.94±93.99	127.06±91.79	0.598

P- value	*Group 1*	*Group 2*	*Group 3*
Group 1	-	0.548	0.253
Group 2	0.548	-	0.088
Group 3	0.253	0.088	-

Table 5: The P value, MEAN ± SD (U/ml) of Anti-Cyclic Citrullinated Peptide in group 1,2 and 3 at 0 and 12th Months

	0th Month	*12th Month*	*P- Value Paired t test*
Group 1	174.72±120.05	111.82±79.63	0.000***

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Group 2	164.56±117.71	142.25±105.15	0.075
Group 3	120.94±93.99	127.06±91.79	0.598

P- value	*Group 1*	*Group 2*	*Group 3*
Group 1	-	0.331	0.023*
Group 2	0.331	-	0.200
Group 3	0.023*	0.200	-

There is significant difference between Group 1 and Group 3 (P- value <0.05)

Table 6: The P value of Anti-Nuclear Anti-Bodies in group 1,2 and 3 at 0 and 12th Months.

	0th Month	*12th Month*	*P- Value Paired t test*
Group 1	0.33±0.21	0.36±0.22	0.246
Group 2	0.39±0.33	0.34±0.28	0.184
Group 3	0.46±0.39	0.42±0.39	0.211

P- value	*Group 1*	*Group 2*	*Group 3*
Group 1	-	0.188	0.761
Group 2	0.188	-	0.320
Group 3	0.761	0.320	-

There is no significant difference among the Groups (p-value > 0.05)

Table 7: The comparison between P value in hs-CRP, ESR, TNF-α, RA Factor, Anti-CCP and ANA.

Dependent Variables	*Type III SS*	*MS*	*F*	*p-value*
hs-CRP	263.232	131.6	8.3	0.000***
ESR	6860.555	3430.2	7.1	0.001***
TNF-α	5987.768	2993.8	8.3	0.000***
RA Factor	32178.506	16089.2	1.5	0.221
Anti-CCP	178465.58	89232.7	2.6	0.075
ANA	5.759	2.8	0.9	0.391

*Indicates significance at the 5% level, ** at 1% level and *** at 0.1% level

From the above Table we can see that hs-CRP and TNF-alpha are found to be significant (p < 0.05).

6. Discussion

Rheumatoid arthritis (RA) is accompanied by inflammatory disorder of synovial membrane that causes inflammation and deformity of the joints. It also has systemic manifestations i.e. inflammation of blood vessels (vasculitis), development of bumps (rheumatoid nodules) in various parts of the body, lung disease, blood disorders, and weakening of the bones (osteoporosis) [16]. The pathological hallmark of RA is persistent destructive inflammation in the synovial membranes of the joint, which leads to a gradual destruction of the supporting structures of the joints, such as bone and cartilage. Although the aetiology is still unknown, the inflammation resulting from the immunological reaction is quite well described [17].

A number of tests are required that can suggest the diagnosis of RA like inflammatory markers, and immunological markers. RA Symptoms are caused by increase in chemical messengers called cytokines. These pro-inflammatory cytokines such as TNF-alpha, interleukin-1 and interleukin-6 into the circulatory system may account for systematic symptoms such as fatigue [18]. These along with musculo-skeletal symptoms are the first indicator of the disease. These inflammatory cytokines have been shown to destroy joint cartilage and bone. In the present study total number of 134 RA patients were checked for Immunological and inflammatory markers.The immune system is extremely sensitive to stress and lifestyle both physiological and psychological and thus, potentially, immune variables could be used as an index of stress in relation to RA. Among all inflammatory markers studied in the patients were found to differ significantly between the three Groups. hs-CRP (0.000***), TNF-alpha (0.000***) and ESR (0.001***) (Table 1,2,3) .Immunological markers of the patients studied were Rheumatoid Arthritis Factor, Anti-Cyclic Citrullinated Peptide and Anti Nuclear Antibodies. It was concluded that Rheumatoid Arthritic Factor, Anti-Cyclic Citrullinated Peptide in Group-1 were significantly different (p<0.001) (Table 4,5), indicating that yoga and naturopathy along with allopathic medication was useful in regression of the clinical manifestations of rheumatoid arthritis compared to the Group-2 and Group-3. However, ANA was non significant between the groups (Table 6) .The RA factor was significant in Group -1 (0.000***). In previous studies it was observed that in RA patients values for anti-CCP antibodies obtained were significantly (p<0.05) higher Anti-CCP antibodies resulted positive in 85.1% patients and RF significantly (p<0.05) higher was positive in 81.4% [19]. Some studies showed Antinuclear antibody (ANA) detects antibody binding to nuclear constituents, it is extremely useful as a screening test for these diseases. Low levels of ANA are common in RA, but high levels of ANA do not indicate RA, if the anti-CCP and RF are negative.

Some of the non-steroidal anti-inflammatory drugs (NSAIDS) which patients of RA take can cause ulcers which can lead to blood loss. Modern drugs that neutralise TNF-Alpha for the treatment of RA show remarkable ability to suppress symptoms of RA and show the progression of joint damage. But these drugs are very expensive and have side effects that include increased risk of serious infections and certain types of cancer [19]. Because of their expenses and side effects researchers are looking for other ways and means which may suppress the inflammatory cascade and reduce physical disability because of arthritis [20]. Exercise, meditation, medicines and yoga are the ways that help in burning off stress and lowering of inflammatory markers in blood. The immune system is extremely sensitive to stress - both physiological and psychological and thus, potentially, immune variables could be used as an index of stress in relation to exercise training. Regular blood monitoring in future could provide a diagnostic window for evaluating the impact of exercise

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on health [21]. With regard to Naturopathy and Yoga in terms of thermal advantage, we considered if enhanced warmth resulting from massage and blood flow might contribute to improved physical outcomes, but again, the evidence for this is not available from the results of included studies and we were unable to pursue this point. Nevertheless, there is some evidence that certain supplements and natural therapies could have a role in managing the disease. Some of the mechanisms by which massage might promote improved outcomes in humans have been investigated in both animal and human populations. For example, in rodents high frequency of licking and grooming of the pups has been shown to be associated with reduced fearfulness and dampened responsiveness to stress in adulthood as a result of such stimulation on the hippocampal glucocorticoid receptors, and hypothalamic-pituitary-adrenal reactivity. Other studies have shown that higher frequency licking and grooming is associated with improved cognitive development in rats (specifically greater spatial learning and memory performance) [22]. as a result of enhanced synaptogenesis and neuronal survival in the hippocampus [23]. A number of studies have examined the potential mechanisms by which tactile stimulation could impact on human infants. For example it was found that infant massage resulted in reduced catecholamine (norepinephrine and epinephrine) and cortisol excretion, and it is now recognized that high cortisol levels have damaging effects on the developing brain, particularly in terms of the later capacity of such infants to regulate their stress levels [24] [25].

It is important to maintain a balance between sedentary life (which will reduce inflammation) and exercise (which will relieve stiffness and weakness). Yoga and naturopathy treatments are cost effective and can be used effectively as an adjunct therapy in treatment of Rheumatoid Arthritis. Including Yogic exercise in the daily routine can help control pain, inflammation and stiffness. Muscle weakness can be prevented and possibly reversed through strength training such as using hand or leg weights. The type and intensity of exercise needs to be regulated, depending on disease activity. While traditional guidelines have restricted RA patients to only gentle exercise, research suggests that more intense exercise may not only be safe, but may actually produce greater muscle strength and overall functioning. Uvnas-Moberg 1987 [26] reported that massage increase vagal activity and secretion of insulin and gastrin improving the absorption of food, and thereby suggesting a plausible biological mechanism for the impact of infant massage on growth [27]. These findings in the study will help to develop a natural regime for the management of chronic rheumatoid arthritis condition in a scientific manner. Thus, yoga and naturopathy treatments may offer the best hope of arresting arthritic condition and reversing normal health to patients.

7. Conclusion

The studies are novel and unique in nature and have addressed potential biological mechanisms for a decrease in Immunological and Inflammatory markers. An important outcome of the study was that we found patients in Group-1 (naturopathy + yoga + allopathic medicines) were more benefited as compared to other two Groups (Group-2 (yoga + allopathic medicines) and Group-3 (allopathic medicines)). The findings of the study will help to develop a natural regime for the management of chronic rheumatoid arthritis condition in a scientific manner. Naturopathy and diet improved metabolism of various organs of the body of the patients, which further improved the life style of RA patients. The main drawback here is that measures of immune function are expensive and usually limited to just one aspect of what is a multifaceted system which contains much redundancy. Non-pharmacologic measures form an important aspect of treatment of RA. Exercise is essential in maintaining joint mobility, muscle strength, and for management of fatigue. Weight loss decreases joint load in overweight patients and lessens pain. Treatment of depression is important in the overall well-being of a patient with RA [28].The study significantly proves that the reduction in Immunological and Inflammatory markers because of the modalities introduced in these patients regime. However, more carefully controlled clinical trials are must before this treatment modality will gain wide acceptance [29].

For people with inflammatory conditions, such as rheumatoid arthritis, who have tried other medications with little success, may have better relief along with yoga and naturopathy. Yoga and naturopathy therapies may offer the best hope of arresting arthritic condition and reversing normal health to RA patients [30]. Yoga and naturopathy is cost effective and can be used effectively as an adjunct therapy in treatment of Rheumatoid Arthritis. There is, however, a lack of biological plausibility in terms of some of the findings. More work in the area should be done to bring about the standards in the field for better understanding and management of chronic disease as RA.

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