

Withania somnifera L. Dunal A potential herb for the treatment of rheumatoid arthritis

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Abstract

Rheumatoid arthritis (RA) is an autoimmune disorder in which various joints of the body are inflamed, leading to swelling, pain, stiffness and possibly loss of function. The goals of management of patients with RA are to control pain and swelling, delay disease progression, minimize disability, and improve quality of life. The growing interest in traditional medicines for RA, there exists a need for investigate their safety and efficacy on scientific basis. The purpose of this randomized clinical trial (RCT) was to evaluate the safety and efficacy of the traditional herb, *Withania somnifera* L. Dunal in case of rheumatoid arthritis with sample size of 60 cases (between the age group 20 to 40 years), divided into Group A (test group) and Group B (placebo group) equally. The final outcome of the trial was satisfactory and highly promoted for treatment of rheumatoid arthritis, although advance research is needed to examine its efficacy, safety and potential drug interactions.

Key words: *Withania somnifera* L. Dunal, rheumatoid arthritis, traditional medicine

1. Introduction

The word Rheumatoid is derived from the Greek Word “Rheuma” or “Rheumatoid” for “Flow”, applied to watery humours which was tough to flow in joints and causes pain (Kelly *et al.*, 2013). Rheumatoid arthritis (RA) is a chronic progressive disease in which various joints of the body are inflamed, leading to swelling, pain, stiffness and possibly loss of function. It usually begins in the small joints of the hands and the feet, spreading later to the larger joints. The inflamed synovium extends and then erodes the articular cartilage and bone, causing joint deformity and progressive physical disability (Aletaha *et al.*, 2010). The prevalence and incidence of RA are higher in women than men (Anderson *et al.*, 2012). It increases with age and peaks at about age 70 then declines. RA tends to run in families, little is known about the environmental triggers for RA, smoking, obesity and infection may play a part in some individuals (Carlens *et al.*, 2010). One of the genetic components of sero positive RA has been mapped to a short gene sequence now, known as the shared epitope. This appears to be the marker for RA disease severity rather than susceptibility (Barton and Worthington, 2009). There are complex interactions between the female sex hormones and RA. The oral contraceptive pill, or some other factor associated with its use, appears to protect against the development of the severe RA (Areskoug-Josefsson *et al.*, 2009). In those with an onset before the age of 50, men have a worse prognosis than women, while in those over the age of 50, women far worse. This may in part, explain the different patterns of RA, seen around the globe (Katchamart *et al.*, 2010).

In spite of all the causes and its treatment, only symptomatic and conservative drugs like corticosteroids and immune suppressive agents are available for the management in modern system of medicine, causing so many adverse effects on long term use (Daha and Toes, 2011; Van Venrooij *et al.*, 2011).

Alternative system of medicine is popular among individuals for natural support to manage rheumatoid arthritis. Numerous safe and therapeutically efficient single or compound formulations are exist in the indigenous systems of medicine, but have not been evaluate on scientific parameter so far. Hence, the present clinical trial conducted to estimate safety and clinical efficacy of single drug, *Withania somnifera* for the management of rheumatoid arthritis.

1.1 Research studies supported for selection of research drug *Withania somnifera* L. Dunal

Withania somnifera L. Dunal commonly known as *Ashwagandha* or Indian ginseng, is the major Indian medicinal plant, used in Ayurveda, Siddha and Unani systems of medicine. It belongs to family Solanaceae. It has been used as an antioxidant, antistress, adaptogenic, neurotonic, aphrodisiac, anxiolytic, anti-inflammatory agent, hypolipidemic, liver tonic and more recently as antibacterial agent (Singh and Gilca, 2010; Singh, 2008; Kuboyam *et al.*, 2006; Abbas and Singh, 2006; Sumanran *et al.*, 2007; Harikrishna *et al.*, 2008; Pujari and Gandhi, 2012; Shanthi and Swaminathan, 2011). Several reports have demonstrated the immunomodulator and antitumour activity of root extract of *Withania somnifera* (Devis and Kuttan, 2002; Gupta *et al.*, 2010). Alcoholism, parkinsonism, neuropathy, paralysis and uterine tumours (Fibroids and other tumours) including cutaneous endodermal diseases treated successfully through various preparation of *Withania somnifera* (Abdel Magied *et al.*, 2001; Abbas *et al.*, 2004).

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1.2 Objectives

- To assess the safety and efficacy of *Withania somnifera* in management of rheumatoid arthritis.
- To assess the analgesic and anti-inflammatory effect of *Withania somnifera* in management of rheumatoid arthritis.
- Improvement in cardinal signs and symptoms and quality of life of rheumatoid arthritis patients.

2. Materials and Methods

- **Study design:** A randomized single blind, placebo controlled study conducted at ZVMUMC, Pune, India.
- **Duration of study:** 90 days with fortnight follow up.
- **Sample size:** 60 patients of RA were randomly divided equally into Group A (test group) and Group B (placebo group).
- **Drug and doses scheduled:** Group A (test group): Powder of *Withania somnifera* 7gm twice a day.
- **Group B (placebo group):** Powder of coded drug (SWM-2) 7 gm twice a day.

2.1 Criteria for selection of cases

60 cases were selected on the basis of history taking, physical examination, RA factor and C-reactive protein. After getting the approval from the Ethical Committee, the subject between the age group 20 to 40 years fulfilling the revised ARA criteria and having complaint of pain, morning stiffness, restricted joint movement and swelling were included in while pregnant and lactating women, osteoarthritis or gout, systemic illness (related to heart, kidney, liver, brain etc.), diabetes and other metabolic diseases, patients had history of alcohol and drug abuse, epilepsy and other neurological disorders were excluded from the study. All patients have to be strict to avoid any experimental drugs, NSAID's etc. within 30 days prior to the trial. No concomitant medication allowed. The objective assessments for all the signs and symptoms of RA was done by the patient on a scale of 0 to 10, using visual analogue scale (VAS) score at base line and end of the treatment.

2.2 Biochemical parameters before and after treatment

The following investigations were carried out in each patient before commencing the therapy and after completion:

- Complete haemogramme with E.S.R
- Routine urine examination
- R-A factor and C reactive protein
- Liver function tests
- X-ray of the affected

3. Results and Discussion

The present clinical trial conducted on 60 patients, to estimate safety and clinical efficacy of single drug, *Withania somnifera* L. Dunal for the management of rheumatoid arthritis.

The highest incidence 33.33% of RA was noted in the age group of 56 to 60 years, followed by 30 % in the age group of 45 to 50 years, according to gender 56.67% were males and 48.33% were females

(Figure 1). This shows that this disease increase with the increasing age, supported by Helmick *et al.* (2008).

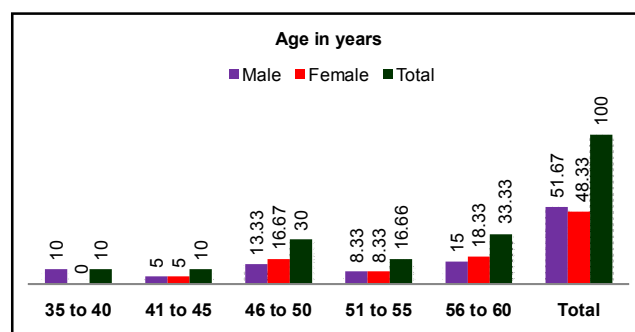


Figure 1: Age and sex wise distribution

It was also evident (Figure 2) that maximum number of cases (48.33%) were recorded in chronicity of 1<2 years, indicating that joint damage in RA occurs early, often within the first two years of the disease (El-Miedany, 2002).

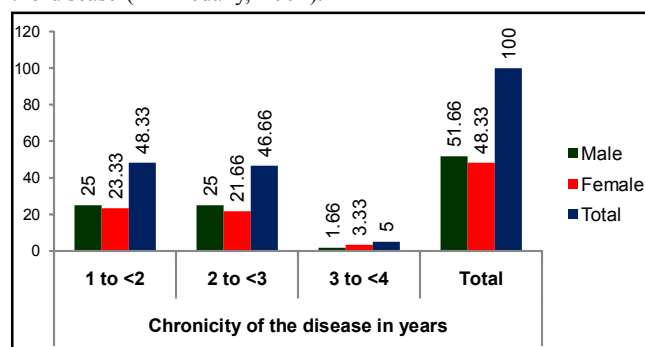


Figure 2: Chronicity of the disease

It was also observed (Figure 3) in present study that highest number of cases were belongs to lower middle class, i.e., income group where there is stress and excessive joint usage resulting in early wear and tear of the cartilage. These findings also supported by CDC at a Glance in 2007.

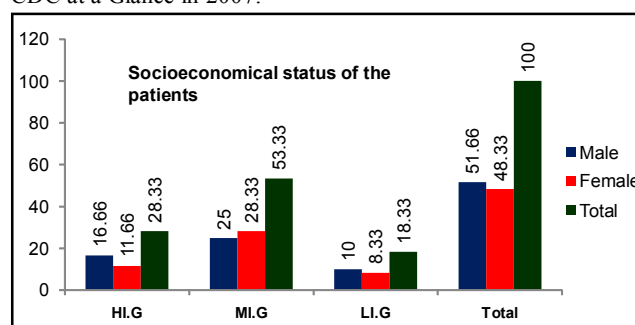


Figure 3: Socioeconomic status of the patients

On analyzing the dietary habits of the patients (Figure 4), it was found that maximum patients (55%) were obese (BMI d" 30) with non vegetarian dietary habit, suggesting that diet, obesity and sedentary lifestyle can predisposes or can acts as risk factors for the development of rheumatoid arthritis. However, there is no evidence available for the same but the National Center for Complementary and Alternative Medicine (NCCAM) within the National Institutes of Health (NIH), have concluded that evidence

for the use of fish oil (or other omega-3 supplements) for the treatment of RA is promising. Some effect has been noted for symptoms such as tender joints, morning stiffness *etc.*, which indicate that changes in lifestyle with dietary manipulation provides a means by which patients can a regain a sense of control the disease.

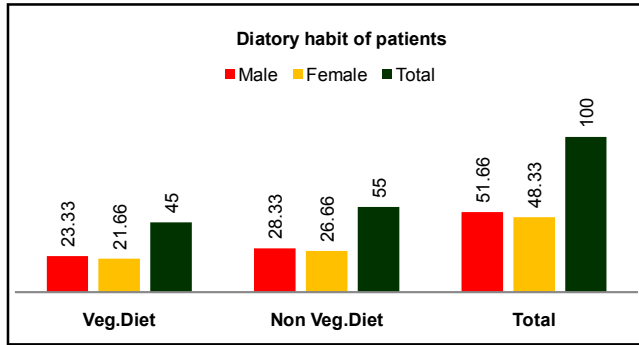


Figure 4: Dilatory habit of the patients

Hereditary factor was also plays an important role in this disease. Out of 60 patients, with various occupations, the majority was the working male and female, specially the housewives and labourers were shows more problem. This prevalence may be due to excessive use and overloading of the joints during the hard work, producing an adverse biochemical effects on the joints that are in repetitive use.

After completion of trial, it was also observed that maximum cases 43 (71.66%) had the insidious onset while 17 (28.33%) cases had sudden onset, which shows that the disease mostly occur insidiously (Figure 5).

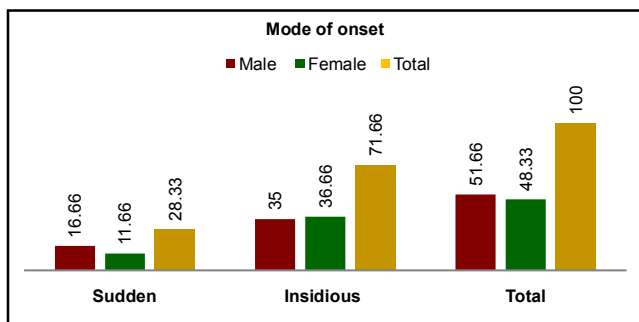


Figure 5: Mode of onset of disease

The final outcome for mean reduction in morning stiffness was highly significant ($p < 0.0001$) in test group (Figure 6). After using this formulation in Group A, patients showed a considerable relief in symptoms and decrease in functional lequesne score as compared to Group B. After completion of the study, raised leucocytes count and ESR value also decreased significantly ($p < 0.0001$) in Group A as compared to Group B (Figures 7 and 8). Power, pinch and tripod grip strength measurements were made using an MIE digital pinch grip analyzer. These strength data were correlated with specific local forearm anthropometric measurements: forearm circumference, forearm length, forearm volume, hand circumference, hand length, hand volume, hand and forearm volume, and various general anthropometric parameters (weight, height and age) and difference was significant for mean changes in grip strength between both groups. Rise in grip strength (by 54) was observed in test

group (Figure 9). No relapse or recurrence of symptoms was noted in treated cases in one month's time.

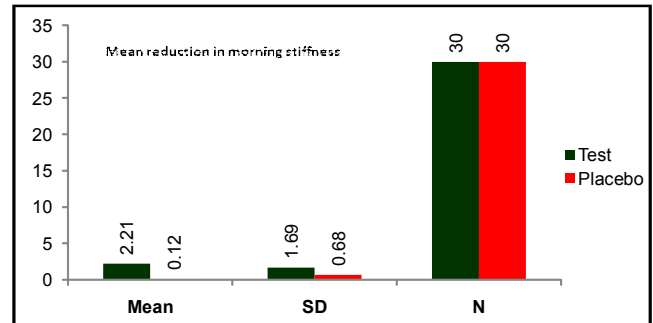


Figure 6: Mean reduction in morning stiffness between group A and B

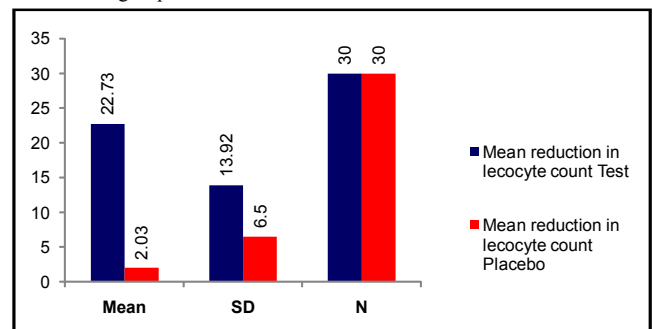


Figure 7: Mean reduction in differential leucocytes count between group A and B

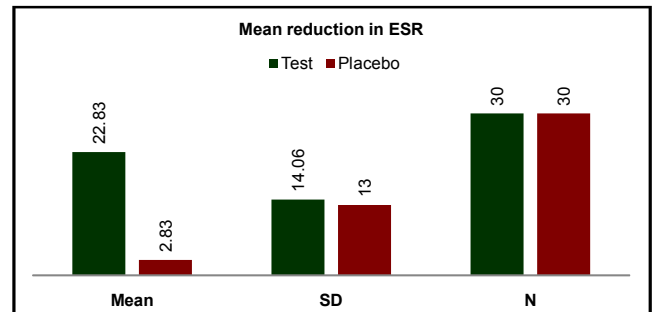


Figure 8: Mean reduction in ESR between group A and B

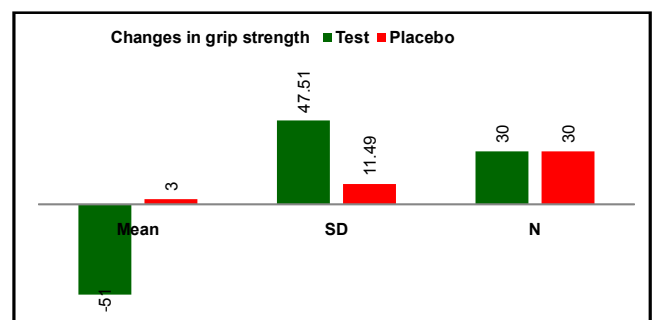


Figure 9: Mean changes in grip strength between group A and B

In present study, due to its anti-inflammatory and analgesic effect, it reduces the pain, stiffness, swelling and, thus, results in feasibility to do day-to-day work, ultimately result in improving the quality of life. These findings also supported by many research studies

(clinical / preclinical trials) which showed that the sequential role of inflammatory mediators in anti-inflammatory activity of *W. somnifera* is proposed through inhibition of histamine, 5-hydroxytryptamine and prostaglandins as the antagonists of these inflammatory mediators (Sahni and Srivastava, 1993). A case study revealed that *Withania somnifera* has direct effects on human cartilage which may help protect against inflammation and cartilage damage associated with osteoarthritis. It contains constituents like cuseohygrine, anahygrine, tropine, and anaferine, glycosides, withanolide with starches and amino acid. Withanolide consists of steroidal molecules which is said to fight inflammation (Umadevi *et al.*, 2012).

It has been in use for over 2500 years to treat all kind of diseases and human ailments. The species name *somnifera* means “sleep-bearing” in Latin, indicating it was considered a sedative or calming effect. In Unani and Ayurveda classical text, the fresh roots are sometimes boiled in milk, prior to drying, in order to enhance the memory, aphrodisiac and for general health of a person (Veena *et al.*, 2011).

Thus, the above findings clearly support the conclusion that *Withania somnifera* is a real potent traditional herb with multiple pharmacological actions like anti-inflammatory, analgesic, antiarthritic, antistress, neuroprotective and regenerative tonic.

4. Conclusion

Withania somnifera L. Dunal has been proved an effective remedy in management of rheumatoid arthritis. However, in depth clinical studies with advanced investigations (C T Scan and immunoglobulin tests) on large numbers of population should be explored. Data on different types of arthritis, such as infectious arthritis, gout and undifferentiated arthritis, which are more relevant in developing countries, should be also collected to validate the direct effect of this traditional herb.

Conflict of interest

We declare that we have no conflict of interest.

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