

A Study of Efficacy of Metformin in Rheumatoid Arthritis

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Abstract

Background: The prevalence rate of Rheumatoid arthritis (RA) is around 0.4 percent to 1.1 percent globally. In India we do not have a statistical record which can be trusted. But many studies have reported more than that of the global statistics. The treatment of Rheumatoid arthritis was mainly steroids and other anti-inflammatory substances which itself causes plethora of adverse effects. But it is also a known fact and in fact have been advocated in many studies that the treatment lines fail as the disease becomes resistant to continuous anti-inflammatory line of drugs over a period of time. The treatment of Rheumatoid arthritis has become good in the last decade after the introduction of disease modifying anti-rheumatic drugs (csDMARDs) in the treatment. Metformin drug has been shown to improve the quality of life after one year of the treatment. This calls for further studies. This study was designed to evaluate the potential benefits of metformin use as an adjuvant therapy in RA arthritis patients with moderate and high disease activity and its effect on serum C-Reactive Protein. **Aims and Objectives:** To determine the Efficacy of Metformin in Rheumatoid Arthritis. **Materials and Methods:** This study was done in the Department of General Medicine, Kanachur Institute of Medical Sciences, Mangalore. The study was done in thirty subjects who are proven cases of Rheumatoid arthritis. The study was done from Nov 2019 to Oct 2020. **Results & Conclusion:** Use of metformin in Rheumatoid Arthritis as an adjuvant is highly advisable in the practice.

Keywords: Metformin, CRP, Rheumatoid Arthritis, Adjuvant.

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Introduction

The prevalence rate of Rheumatoid arthritis (RA) is around 0.4 percent to 1.1 percent globally[1]. In India we do not have a statistical record which can be trusted. But many studies have reported more than that of the global statistics. The genetics background plays a predominant role in this disease and many studies have reported more than fifty percent chances of having this disease through genetic predisposition. Amongst all the cases around two third of the disease prevalence is contributed by females and the rest one third is contributed by males[2]. The clinical signs and symptoms include restricted joint mobility and pain. The other signs and symptoms may be due to the manifestations of the systemic inflammatory response[3]. These will directly contribute to the reduced quality of life of the patient, increased burden to the financial status of the family and in turn is responsible for the decrease socio-economic burden and less productivity to the community[4,5]. This may also contribute to the burdening of the already stretched health-care system in our country. Metformin is widely used as an anti-diabetic drug in type – 2 diabetes mellitus⁶. It is also used extensively by gynaecologists in the treatment of PCOD and gestational diabetes. Recently some even recommend it in the use of pre-diabetes and obesity. It is also known to be anti-neoplastic, cardio-protective and also anti-inflammatory[7,8]. Many clinical evaluations have shown that metformin has anti-inflammatory and anti-inflammatory effects which can be very useful for the suffering patients whose quality of life is down the drain. Many mechanisms have been studied and have been postulated and in fact have been proved to explain this wonder drug. Some are lowering the inflammatory markers, down regulation of the TNF- α , IL-1beta levels, and IL-6 gene[9-11].

This study was designed to evaluate the potential benefits of metformin use as an adjuvant therapy in RA arthritis patients with moderate and high disease activity and its effect on serum C-Reactive Protein.

Aims and objectives

To determine the efficacy of Metformin in Rheumatoid Arthritis.

Materials and methods

This study was done in the Department of General Medicine, Kanachur Institute of Medical Sciences, Mangalore.

The study was done in thirty subjects who are proven cases of Rheumatoid arthritis of mild to moderate severity. The study was done from Nov 2019 to Oct 2020.

Inclusion Criteria

- Mild to moderate cases between 20 to 60 years were taken up for the study

Exclusion criteria

- Patients who have other metabolic disorders
- Patients already on metformin

Methodology: The subjects are thoroughly examined and their detailed history was taken. Taking all necessary aseptic precautions, blood was drawn and sent to the Biochemistry lab for the base line evaluation of CRP levels. The patients were started on metformin. The other treatment was continued and metformin was added. The dose depended on the weight of the patient and other compliance factors. It was in the range of 500mg to 1500mg in divided doses. The patients were followed up after 1 month, 3 months and 6 months. Serum CRP levels were checked and the levels have been reported in this study.

Statistical Analysis: Paired t test.

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Results

Table 1: Age

Total	Mean Age	Std Deviation
30	48.87 years	± 9.76 years

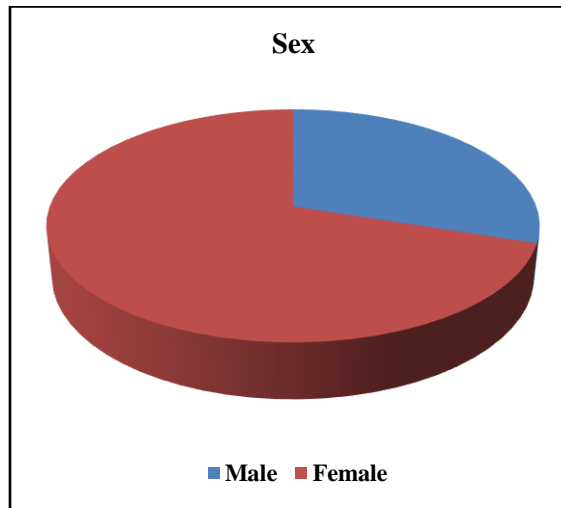


Fig 1: Sex Distribution

Table 2: Mean CRP Levels (Base line: At the start of the study)

Time	Mean CRP Levels	Std Deviation
At the start	16.73	3.18329
After one month	14.9	1.918153
After three months	12.8	1.788854
After six months	8.4	2.252967

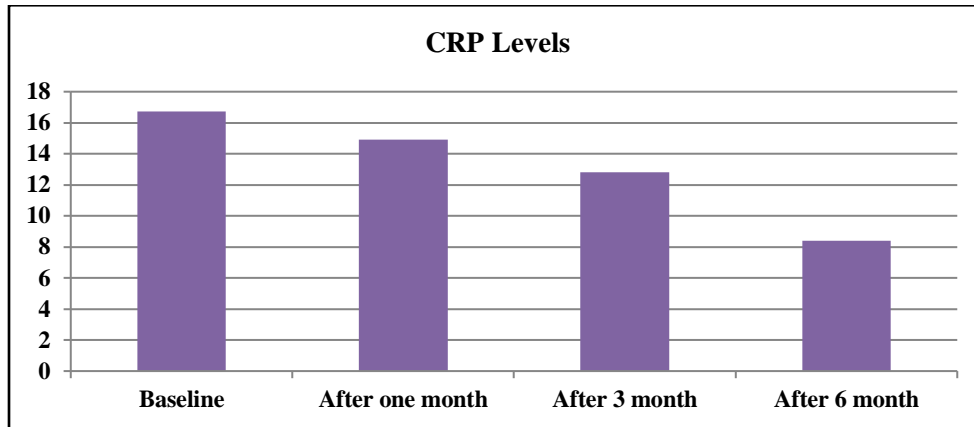


Fig 2: (CRP Levels at different times after starting)

Table 3: Paired t test

Total	Base line Mean CRP Levels	CRP Levels (After six months)	p-value	Sig
30	16.73±3.18329	8.4±2.252967	<0.001	Sig

The quality of life in these patients has drastically improved when compared to the initial quality of life.

The pain and restriction in the joints also were markedly decreased.

Discussion

The pathogenesis of Rheumatoid Arthritis includes the increase as a result of direct up regulation of T-helper cells differentiation which is followed by down regulation of regulatory T cells. This mainly causes the inflammatory condition especially in the joints[12] . This in turn is responsible for secretion of various inflammatory markers like IL-17, IL-22, IL-26, TNF-alpha and GM-CSF. These in turn stimulate the fibroblast and macrophages

which are responsible to secrete the cytokines and other inflammatory markers which is actually responsible for the widespread destruction[13]. The other effects that are notable are stimulation of osteoclasts which breaks down the bones leading to more inflammation, synovial hyperplasia, destruction of the articular cartilages and also causes notable bone erosions[14]. This actually leads to a cyclic change which again leads to more inflammatory substances in the system[15]. The treatment of

Rheumatoid arthritis was mainly steroids and other anti-inflammatory substances which itself causes plethora of adverse effects. But it is also a known fact and infact have been advocated in many studies that the treatment lines fail as the disease becomes resistant to continuous anti-inflammatory line of drugs over a period of time[16]. The treatment of Rheumatoid arthritis has become good in the last decade after the introduction of disease modifying anti-rheumatic drugs (csDMARDs) in the treatment[17]. Rheumatoid arthritis is known to respond very well for this treatment and the quality of life has actually become good after the treatment[18]. The only problem is the treatment costs which is very high and actually is unaffordable to patients and because of this many patients do not wish to continue with this treatment[19]. In this study metformin drug has been shown to improve the quality of life after one year of the treatment. This calls for further studies. Even though it was used only as an adjuvant in this study, the potential of this drug seems to be massive. The C-Reactive protein levels also is shown to drastically reduce in this treatment and thus is an eye opener for the practising physicians and rheumatologists. The drug is easily available, is very cheap compared to other drugs used in the treatment and thus opens the door for a low cost effective treatment of this dreaded condition.

Conclusion

Use of metformin in Rheumatoid Arthritis as an adjuvant is highly advisable in the practice. The action is not immediately seen but the affect was very clear after six months of continuous treatment.

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