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Role of Magnesium Sulfate in Rheumatoid Arthritis patients

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ABSTRACT: ***Background:*** Rheumatoid arthritis (RA) is a systemic inflammatory disease that causes joint destruction. It has long been recognized as a clinical illness associated with organ damage that is not limited to the musculoskeletal system. Malondialdehyde (MDA) is an oxidative stress biomarker. Conventional medications used to treat RA include methotrexate (MTX), sulfasalazine, hydroxychloroquine, and nonsteroidal anti-inflammatory drugs (NSAIDs). The aim of the study was to determine to oxidative stress and find out the role of magnesium in the management of RA. ***Materials and Methods:*** Cross-Sectional experimental type of study was carried out in the Department of Pharmacology and therapeutics, Rajshahi Medical College, Rajshahi from July 2021 to July 2022. Clinically diagnosed rheumatoid arthritis patients in the age group of 40-50 years and Rheumatoid arthritis patients treated with conventional medicine (Methotrexate, sulfasalazine, NSAIDs & Hydroxychloroquine) were included in this study. Total sample size was divided into 2 groups: 15 patients treated with conventional medicine act as a control group and 15 patients treated with conventional medicine plus magnesium sulfate act as an experimental group. The study revealed that after 2 months of drug administration the MDA level decreased in experimental the group than the control group. ***Results:*** Data were collected in 2 different age groups. The mean age of experimental group was 48.47± 12.09 years, and the control group was 45.13± 9.59 years. After 2 months of drug administration, MDA level decreased in experimental group than in the control group. So, Epsom salt may be used in RA patients. ***Conclusion:*** According to the study, the combination of Epsom salt and methotrexate was considerably more effective than methotrexate alone for RA patients.

Keywords: Rheumatoid arthritis, Epsom salt, Malondialdehyde, Methotrexate.

Article at a glance:
Study Purpose: *The purpose of this study was the combination of Epsom salt and methotrexate was more effective than methotrexate alone for RA patients.*
Key findings: *Combination of Epsom salt and methotrexate reduced oxidative stress significantly in RA patients, but Methotrexate did not reduce oxidative stress significantly alone.*
Newer findings: *Epsom salt (MgSO4.7H20) might be used as an antioxidant which reduces oxidative stress in rheumatoid arthritis patients.*
Abbreviations: *RH: Rheumatoid arthritis, MgSO4.7H20: Epsom salt, MDA: Malondialdehyde, MTX: Methotrexate, NSAIDs: non-steroidal anti-inflammatory drug.*

INTRODUCTION

Systemic rheumatoid arthritis (RA) is inflammatory illness that destroys joints in a certain fashion, is well known as a medical condition connected to organ damage that affects not only the musculoskeletal system but also other organs.[1, 2] Reduced antioxidant levels, increased oxidative stress and poor anti-oxidant defenses are all linked to the a etiology of RA.[3] When RNS and ROS are two examples of reactive substances (ROS) surpass physiological amounts, they have been linked to the development of RA, particularly via means of destruction of lipids in proteins, nucleic acids, and plasmatic membranes.[4] In actuality, there was a fivefold rise in mitochondrial ROS generation has been discovered in the monocytes and whole blood of RA patients indicating that oxidative stress is a pathogenic feature in RA.[5] T cell cytokine production causes oxidative stress, hence, antioxidants like glutathione are vital for lowering oxidative state.[6] Uric acid oxidation amounts have also been found to be greater in RA patients.[7] Protein oxidation has also

been observed in RA patients. The buildup of advanced oxidation protein products is caused by oxidative stress.[8] Protein oxidation markers were detected in higher amounts in RA patients' synovial fluid and plasma fluid were linked to disease progression and improvement.[9, 10] Epsom salt, or MgSo4, 7H2O, has a higher concentration of Mg-ions in the form of MgSO4. Magnesium, sulphur, and oxygen make the form of crystal-like substance known as Epson salt (MgSo4, 7H2O). It is found in natural springs and has a straightforward chemical composition that is comparable to salts. The body's detoxification pathways are stimulated by the combination of the two ingredients. Magnesium is a natural mineral that supports several bodily processes, including the elimination of pollutants. Epsom salt which includes magnesium, may aid in the body's elimination of toxins that worsen inflammation while also easing stiffness and discomfort in arthritis sufferers. Magnesium is absorbed via the skin and into the body when Salt of Epsom is dissolved in water, forming magnesium and sulphate. As a result, there may be less pain and swelling in the muscles. Epsom salt is inexpensive, widely accessible, and has a number of health advantages in addition to its high concentration of sulphate and magnesium and sulphate. MgSo4 may also contain skin care items like lotion or body oil. As a result, it is considered important that using a MagSo4 bath in addition to a traditional treatment plan would show its beneficial effects. Since MagSo4 has no such side effects, this study was conducted to compare the treatment of RA with traditional medications alone and in combination with a MgSO4 hot bath therapy.

METHODOLOGY

The Cross-Sectional experimental type of study was carried out at the Department of Pharmacology and Therapeutics, Rajshahi Medical College, Rajshahi during July 26, 2021, to July 25, 2022. The American College of Rheumatology's (ACR) classification criteria for rheumatoid arthritis were used to select patients (RA). The patients of R.A attending RMCH at the time of data collection period were study population. Then the study population was divided into 2 groups 15 patients treated with conventional medicine and 15 patients treated with conventional medicine plus magnesium sulfate. Patients with clinically confirmed rheumatoid arthritis aged 40-50 years. Rheumatoid arthritis patients treated with conventional medicine (Methotrexate, sulfasalazine, NSAIDs & Hydroxychloroquine and both genders were included in this study. Patents with serious comorbid disease (stroke, myocardial infarction, major surgery) and patients with liver and kidney dysfunction & magnesium contraindicated were excluded in this study. This study included patients with rheumatoid arthritis who met the inclusion criteria. Following informed agreement, a comprehensive history and physical examination were performed and recorded on a prepared data sheet. Patients who met the American College of Rheumatology criteria, were given 4 mL of blood in a test tube containing the anticoagulant tri-potassium EDTA (Ethylene di-amine tetra acetic acid). After centrifuging the plasma for 15 minutes at 300rpm, the MDA level in the plasma was determined. The Thio barbituric acid (TBA) reaction is the most often used test for measuring MDA. TBA interacts with MD to generate a pink 2:1 TBA: MDA adduct, which is extracted by n-butanol and absorbs most efficiently at 532 nm. This colored complex can be measured with a spectrophotometer (SEQUOIA) TURNER CORP. model 340. Plasma oxidative stress was estimated by measuring MDA was described by Das *et al*.[6] After waiting 10 minutes, 0.5 ml plasma was combined with 0.5 ml distilled water and 1 ml of 20% trichloroacetic acid. After that, 2 mL of sulfuric acid (0.5 mol/L) and 2 mL of Thio barbituric acid (TBA) reagent (2.0 mg TBA/L in 2 mol sodium sulfate/liter) were added to the mixture. After 30 minutes in the boiling water, the test tube was cooled under running tap water. The TBA reactive material was vortexed, then mixed with 2 mL n-butanol and centrifuged for 10 minutes. An MDA standard was treated similarly. The optical density (0.0) of a plasma and MDA standard n-butanol extract was measured at 532rm in comparison to a butanol blank. The outcome was given as mol MDA/L of plasma. Prior to the start of the investigation, the ethics committee of the Institute of Biological Sciences, University of Rajshahi, Bangladesh, authorized the research protocol. The purpose and objectives of the study, as well as its protocol, risks, and advantages, were given to the responders in clearly comprehensible language, and then each participant provided informed consent. Using IBM SPSS, the data were analyzed according to the study's objectives (Version-25).

RESULT

Table 1: Distribution of The Patients by Age and Gender (N = 15 In Each Group).

Variables	Group	
	Control group	Experimental group
Mean age (Years)	45.13±9.59	48.47±12.09
Gender		
Male	2 (13.3%)	2 (13.3%)
Female	13 (86.7%)	13 (86.7%)

Table 01 displayed the distribution of age and gender of patients. The experimental group's mean age was 48.47±12.09 years, while the control groups was 45.13± 9.59 years. Male and female patients were equal in both experimental and control group and they were 13.3% and 86.7%, respectively.

Table 2: Measurement of MDA Level at Different Time Interval (N=15 In Each Group)

Time of evaluation	Control group	Experimental group	t, P-value#
At baseline	3.36±0.93	3.89±2.07	0.91, > 0.05
After 1 month	2.85±0.78	2.85±1.85	< 0.001, > 0.05
After 2 months	2.67±0.77	2.16±1.43	1.21, > 0.05

Data was analyzed using independent t statistics and were presented as mean ± SD.

In experimental group, the mean MDA level at baseline was 3.89±2.07 µmol/L which decreased to 2.85 µmol/L after 1 month and then to 2.16 µmol/L after 2 months of Epsom salt intervention with methotrexate. In the control group, the mean MDA level at baseline was 3.36±0.93 µmol/L which decreased to 2.85 µmol/L after 1 month and then to 2.67 µmol/L after 2 months of methotrexate treatment. Though the overall reduction of MDA from baseline to 2 months of intervention is not statistically significant between the two groups (p > 0.05) but intergroup reduction was relatively higher in experimental group than the control group (Table 02).

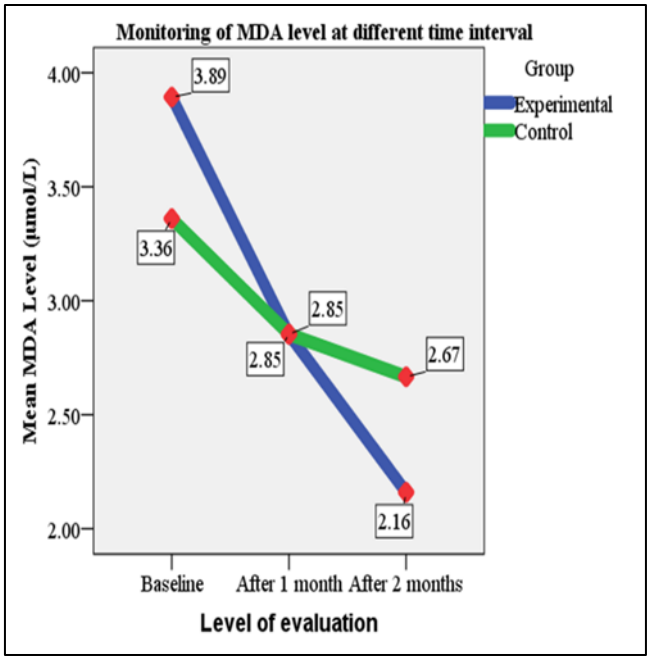

Figure 1: Monitoring of MDA Level at Different Time Interval (N=15 In Each Group)

Figure 1 showed the monitoring of MDA level at different time intervals. It revealed that after 2

months of drug administration MDA level was more decreased in the experimental group than in the control group.

Table 03: Determination of Oxidative Stress in RA Patients by Measurement of MDA Level (N=15 In Each Group)

MDA level	Control group Frequency (%)	Experimental group	Oxidative stress
≥ 3.5 µmol/L	8 (53.3)	8 (53.3)	Present
< 3.5 µmol/L	7 (46.7)	7 (46.7)	Absent

Table 03 showed the oxidative stress in RA patients by measurement of MDA level. By measuring baseline MDA, it revealed that in both experimental and control group 8 (53.3%) patients had oxidative stress, and 7 (46.7%) patients had no oxidative stress.

DISCUSSION

The study's findings revealed that the patients' age group. The experimental group's mean age was 48.47±12.09 years, while the control groups was 45.13±9.59 years. According to Wyparo-Wszelaki *et al.* the mean age was 40.9 ±9.77 years in the group with low magnesium levels and 42.3±9.58 years in the group with high magnesium levels.[11] There was no statistically significant difference between the two groups (p>0.05). The present study observed, in experimental group, the mean MDA level at baseline was 3.89±2.07 µmol/L which decreased to 2.85 µmol/L after 1 month and then to 2.16 µmol/L after 2 months of Epsom salt intervention along with methotrexate. In the control group, the mean MDA level at baseline was 3.36±0.93 µmol/L which decreased to 2.85 µmol/L after 1 month and then to 2.67 µmol/L after 2 months of methotrexate treatment alone. Though overall reduction of MDA from baseline to 2 months of intervention is not statistically significant between the two groups (p >0.05) but intergroup reduction was relatively higher in experimental group than the control group (Table 02). Nourmohammadi *er al.*, also reported in their study, in pre-treatment, mean MDA was found 3.15±0.602 nmol/mL in group I and 3.27±0.75 nmol/mL in group II.[12] In post-treatment, mean MDA was found 1.92±0.65 nmol/mL in group I and 2.75±0.681 nmol/mL in group II. Mean change of MDA was found -1.23±0.46 nmol/mL in group I and -0.525±0.28 nmol/mL in group II. There was a statistically significant decrease in the concentration of MDA in group I and group II after intervention (p<0.0001).

Jaswal et al.[13] reported that the concentrations of MDA estimated before treatment in the two study groups were observed to be significantly higher than those of the normal controls. This extensive lipid peroxidation may be the cause of inflammatory arthropathy in RA. In a study conducted by Kalavacherla *et al*., the concentrations of plasma MDA in cases of RA were significantly higher than the concentrations estimated in controls.[14] Gambhir *et al.* also reported markedly increased concentrations of MDA in patients as compared to controls.[15] Similar results have been observed by others.[16, 17] In this study, the amount of MDA was used to quantify the oxidative stress in RA patients. Baseline MDA measurements showed that both the experimental and control groups (53.3%) experienced oxidative stress, while 7 (46.7%) patients did not. Wyparo-Wszelaki *et al.* detected differences of 6%, 3% and 27%, respectively, in the serum levels of thiol groups, TAC, and bilirubin that were substantially lower in the low magnesium group compared to the high magnesium group.[11] It is clear that RA patients experience oxidative stress and have a higher risk of developing lipid peroxidation.[18] In RA, the oxidative stress caused by an inflamed joint can destroy connective tissue, resulting in joint and periarticular abnormalities.[19, 20]

CONCLUSION

The experimental group's mean MDA level reduced after 1 month and then again after 2 months of Epsom salt intervention with methotrexate. After two months of drug delivery, MDA concentrations were lower in the experimental group when compared to the control group. Magnesium sulphate can therefore be used to reduce oxidative stress in patients with RA. The study found that methotrexate alone was not as effective for treating RA patients as methotrexate combined with Epsom salt.

Limitation

It was a cross-sectional experimental type of study with small sample size. So, the study findings might not reflect the actual scenario of the whole population in the country.

Recommendation

Further research activities are recommended with large number of sample sizes for the beneficial effect of the drug.

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Conflict of Interest

There is no conflict of interest (COI) between the authors in terms of their relationships, professions, finances, or other circumstances.

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