ORIGINAL ARTICLE

"Effect Of Mycobacterium Tuberculosis Infection And Anti Tuberculosis Treatment On Serum Magnesium Level."

Jemil S Makadia[1*], Anju Jain[2]

[1]Md Biochemistry, Assistant Professor, Smt Nhl Mmc, Ahmedabad, [2]Md Biochemistry, Director Professor, LHMC, New Delhi

ABSTRACT

BACKGROUND: Study was conducted to observe effect of mycobacterium tuberculosis infection and anti tuberculosis treatment on serum magnesium level. **MATERIAL & METHODS:** It was a longitudinal case control study. 50 diagnosed cases of pulmonary tuberculosis before starting treatment (group PTB-1) were followed after 2 months of treatment (group PTB-2). 50 diagnosed case of multi drug resistant tuberculosis (group MDR-TB). 50 age and sex matched healthy controls were taken and every candidate was examined for serum magnesium. **RESULTS:** In our study, serum magnesium level in pulmonary tuberculosis (PTB) and multi drug resistance tuberculosis patients were significantly lower compared to control (p value <0.001). In follow up cases of PTB after 2 months of treatment, though levels showed an increase compared to pre-treatment value (p value 0.001), still the levels were significantly lower than control group (p value <0.001). The magnesium levels were also found to be significantly lower in MDR patients as compared to PTB patients (p=0.004). **CONCLUSION:** Magnesium ion concentration of blood is inversely proportional to the type and extent of the disease which could possibly be due to chronic malnutrition and the amount and destruction of lung tissue in cases of pulmonary tuberculosis and it can also be used to measure the response to treatment.

Key words: Pulmonary Tuberculosis, MDR-TB, Nutrition

INTRODUCTION

Tuberculosis is an infectious disease caused mainly by *M.tuberculosis*. Primarily it affects the lungs causing pulmonary tuberculosis which is the most common manifestation of tuberculosis affecting man. TB has remained a worldwide public health problem despite the availability of highly effective drug therapy and vaccine. The global TB epidemic like situation is further aggravated by HIV infection and emergence of drug-resistant tuberculosis[1]. A particularly dangerous form of drug-resistant TB is multidrug-resistant TB (MDR-TB), which is defined by WHO as the disease caused by TB bacilli resistant to at least isoniazid and rifampicin, the two most prescribed anti-TB drugs[2,3]. It is a serious threat to TB control programme and requires new guidelines for its management[2]. Malnutrition and tuberculosis are both problems of considerable magnitude in most of the underdeveloped regions of the world. It is important to consider, how these two problems tend to interact with each other. Malnutrition may predispose people to the development of clinical disease and tuberculosis can contribute to malnutrition[4]. Substantial experimental evidence suggests that malnutrition can lead to secondary immunodeficiency that increases the host's susceptibility to infection. Diagnosis of tuberculosis in Revised National Tuberculosis Control program (RNTCP) is still based on sputum AFB microscopy and Culture is considered as gold standard[3]. To improve the diagnosis of TB, more rapid diagnostic techniques have been investigated in recent years. Magnesium is an essential component of body in man and other mammals. Next to potassium it is the most abundant cation of the body. Changes in the level of serum magnesium have been

Corresponding Author:
Dr. Jemil S Makadia
3rd floor, Biochemistry department
Smt NHL Medical College & VS Hospital
Ahmedabad-380006
Email: jemil_sjm@yahoo.com
Contact No: 9409526787

reported by various workers. Hypermagnesemia has been reported in cases of uncontrolled diabetes, adrenocortical insufficiency, hypothyroidism, advanced renal failure, schizophrenia, infective hepatitis and pneumonia. Hypomagnesaemia has been reported in malabsorption syndromes, portal cirrhosis, renal diseases without azotemia, postparathyroidectomy, prolonged use of diuretics, chronic alcoholism, ischaemic heart diseases, epilepsy, recovery phase of diabetic acidosis, primary aldosteronism, prolonged gastric suction, hyperthyroidism, bronchial asthma, and familial hereditary hypomagnesaemia. This study was conducted to observe how magnesium respond to PTB, MDR-TB and treatment in pulmonary tuberculosis patients and how this help in early detection of treatment failure which may be due to MDR TB.

MATERIALS AND METHODS:

Study subjects: The study was conducted jointly in the Departments of Biochemistry and Microbiology, Lady Hardinge Medical College and Associated Hospitals, New Delhi and Department of Chest clinic, Lok Nayak Hospital, New Delhi, India after getting approval from the Institutional Ethical Committee of Lady Hardinge Medical College, Delhi University, New Delhi, India. This study was done after obtaining written informed consent from the enrolled subjects included in our study. A total of 150 subjects were enrolled in our study and they were divided into three groups. 50 patients of newly diagnosed pulmonary TB (PTB group), 50 patients of newly diagnosed MDR TB (MDR TB group) and 50 age and sex matched healthy control after excluding inflammatory diseases (Control group).

Study design: This study was a longitudinal case control study. Blood sample were collected from healthy control (after excluding TB and other inflammatory disease), MDR-TB patients before starting treatment and PTB patients twice, first before starting treatment (PTB-1) and at the end of intensive phase of treatment that is after 2 months of treatment (PTB-2). Blood sample were processed and serum samples were separated and stored.

Methods of measurements: All patients and healthy control were subjected to detailed history and clinical examination. The blood sample in plain evacuated tube was allowed to clot at room temperature. It was then centrifuged at 3000 rpm for 10 minutes to separate serum samples were stored at -20^{o}C for further batch analysis for serum magnesium level. Tests were carried out in fully automated clinical chemistry analyzer, Beckman Coulter (SYNCHRON CX9) using standard reagents/kits. For serum magnesium (mg/dl) analysis xylidylblue method was used.

Statistical evaluation: The data obtained were analysed by using statistical tests ANOVA, independent t-test and paired t-test for comparison between groups and p value was calculated, p value < 0.05 was taken as a significant using Statistical Package of Social Sciences (SPSS) version 17.

RESULT

Demographic and clinical profile: In our study the maximum numbers of patients (70%) were in the age group of 20-40 years and it was more common in male (56.66%) than female (43.33%). Most of the patients presented with complain of cough with sputum, weight loss, fever and haemoptysis.

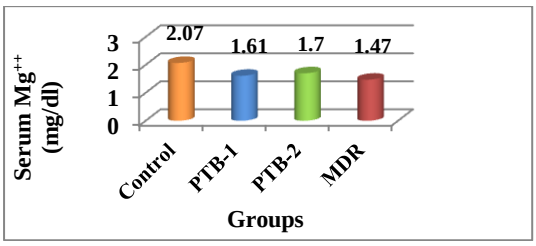
Serum analysis: In our study we estimated serum magnesium for all the subjects and results is shown in table-1 and graphical presentation in figure-1. We applied statistical test ANOVA between all the groups and we found difference in mean of magnesium in all the groups to be statistically significant with p value < 0.001. It was observed that Mg^{++} levels were significantly decreases in PTB and MDR cases as compared to control group. The Mg^{++} levels were also found to be significantly lower in MDR patients as compared to PTB patients (p=0.004). Independent t-test was applied to compare the difference in mean of magnesium between the Control group and the Study groups (PTB-1, PTB-2 and MDR), which

was found to be statistically significant (p<0.001). Paired t-test was used to analyse treatment response in PTB patients the difference in mean of magnesium before (PTB-1) and after (PTB-2) starting treatment was observed to be statistically significant (p=0.001). After 2 months of anti tuberculosis treatment (ATT) magnesium levels were found to increase significantly, but were still lower as compared to the control group.

Table-1: Serum Magnesium (Mg^{++}) in Control and Study groups.

Groups	No.	Mean ± SD (mg/dl)	SE of mean	p value compared to Control	p value compared to PTB-1
Control	50	2.07 ± 0.23	0.032	-	-
PTB-1	50	1.61 ± 0.24	0.034	**<0.001***	-
PTB-2	50	1.70 ± 0.25	0.035	**<0.001***	**0.001***
MDR	50	1.47 ± 0.23	0.032	**<0.001***	**0.004***

Fig-1: Serum Magnesium (Mg^{++}) in Control and Study groups



DISCUSSION

According to Revised National Tuberculosis Control Programme (RNTCP), TB is diagnosed based on sputum microscopy and chest X-ray. For the treatment, patients are divided into two categories base on site and extent of disease, Category-I (New cases of pulmonary and extra pulmonary tuberculosis), Category-II (Sputum smear-positive Relapse, Failure and Default). First time diagnosed patients; treatment is given according to category I. Patients who come after treatment failure, relapse or default of category I are given treatment according to category II. Patients who fail to respond even to category II are suspected to have MDR-TB. So MDR-TB is not a clinical diagnosis. At present the common protocol for diagnosis of MDR-TB has been subjecting the culture isolates to antibiotic sensitivity test which may take 3-8 weeks time depending on the direct or indirect diagnostic approach. Thus, these techniques have a major limitation with respect to time taken in arriving at a diagnosis which is a huge drawback in MDR-TB patients as it has a very rapid course and may be fatal[5,6]. So there is requirement of techniques which diagnose MDR TB early and it should be less complex and easily available as other techniques like PCR based Line Probe Assay and DNA sequencing which diagnosed MDR TB early but the techniques are more complex and costly which makes it's unavailability at primary and secondary health care centres. Magnesium (Mg^{++}) is an essential metal playing an important role in various reactions in our body. In our study serum Mg^{++} levels in study groups were found to be significantly lower compared to control group. Mg^{++} (mg/dl) was 2.07 ± 0.23 in controls, 1.61 ± 0.24 in PTB-1 (p value <0.001), 1.70 ± 0.25 in PTB-2 (p value <0.001) and 1.47 ± 0.23 in MDR (p value <0.001). Difference in Mg^{++} levels between PTB-1 and MDR group was found to be statistically significant (p value 0.004), these suggest that Mg^{++} level has some relation with severity of disease. This study is comparable with study by Jain et al[7] 1976 that shows Mg^{++} level in minimal, moderately and far advanced tuberculosis were 1.90, 1.78 ± 0.177 and 1.608 ± 0.242 respectively. In follow up cases of PTB after 2 months of ATT, though serum Mg^{++} levels showed an increase compared to pre-treatment value (p value 0.001), still the levels were significantly lower than control group (p value <0.001). Thus it shows that Mg^{++} decreases in TB and gradually comes to normal level after starting ATT. Magnesium ion concentration of blood is inversely proportional to the type and extent of the disease which could possibly be due to chronic malnutrition and the amount and destruction of lung tissue in cases of pulmonary tuberculosis[7]. General debility in PTB patients can be suggested by hypomagnesaemia. It has been observed that Mg^{++} level was lower in MDR compared to PTB that can be explained by extent of damage and it can also be used to measure the response to treatment.

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