ROLE OF ZINC IN PULMONARY TUBERCULOSIS

Vandana Jaiprakash Baraskar[1], Pradeep Parashuram Shinde[2]

[1]Assistant Professor, Department of Medicine, NKP Salve Institute of Medical Sciences, Nagpur, Maharashtra.
[2]Associate Professor, Department of Community Medicine, Institute of Medical Sciences and Research, Satara, Mayani, Maharashtra.

ABSTRACT

BACKGROUND

Tuberculosis remains a worldwide public health problem, despite the fact that the causative organisms were discovered more than ten decades ago and highly effective medicines are available. Zinc is an important factor for cell mediated immunity. The objectives of this study were to evaluate the status of zinc as a micronutrient in pulmonary TB in study population and to see the effectiveness of zinc therapy.

MATERIALS AND METHODS

The study participants included 40 (20 males and 20 females) sputum positive Pulmonary TB cases as per the DOTS guidelines and 40 control subjects (20 males & 20 females of same age groups).

RESULTS

Study subjects had significantly low plasma zinc levels. Estimation of plasma zinc level in pulmonary T.B. is an important tool in diagnosis & monitoring of response to treatment. Supplementation of zinc in pulmonary T.B. may improve immunological response of patients, which helps in early recovery & effectiveness of therapy.

CONCLUSION

Our study shows significant low level of serum Zinc levels as compare to normal subjects. Zinc supplementation should be given along with other nutrients.

KEYWORDS

Cell Mediated Immunity, serum zinc, DOTS (Directly Observed Treatment Short Course) Pulmonary Tuberculosis (PTB), Tubercle bacillus.

BACKGROUND

Tuberculosis is a curable infectious disease causing significant morbidity and preventable deaths worldwide. India tops the first five countries ranked in terms of absolute number of cases. TB and HIV are lethal partners and thereby they have made the situation worse, which has been further complicated by the emergence of strains of multidrug resistance tuberculosis. These challenges can be better controlled by measures initiated by the Govt. which include effective surveillance system, accelerated identification of cases, expansion of DOTS program in hard to reach areas, laboratory facilities and monitoring of micronutrients status. Malnutrition is one among the many challenges in the effective control of Tuberculosis. The nutritional status, especially of micronutrients is still poorly documented.

Micronutrients study is related to addressing malnutrition which needs to be part of the efforts directed towards control of tuberculosis, as PTB can result in malnutrition. Moreover, malnutrition may account for a greater population attributable to risk of TB than HIV infection and certainly a much more correctable one. Malnutrition can predispose to PTB. Zinc is one of the micronutrients necessary for the normal functioning of the immune system.[1]

The World Health Organization (WHO) published the 18th global report on tuberculosis (TB) in a series that started in 1997. It provides a comprehensive and up-to-date assessment of the TB epidemic and of the progress made in TB prevention, care and control at global, regional and country level, using data reported by 197 countries and territories that account collectively for over 99% of the TB cases in the world.

TB remains a major global health problem although TB treatment has saved the lives of more than 22 million people, according to the report, which also reveals that the number of people who fell ill with TB in 2012 was 8.6 million, with 1.3 million TB deaths globally (including 320,000 deaths among HIV-positive people).[2]

TB is one of the top 10 causes of death worldwide. It is also the main cause of deaths related to antimicrobial resistance and the leading killer of people with HIV. During past 60 years, clinicians and researchers have devoted an immense amount of work to attempt to understand tuberculosis and factors which influence progression. To

arrest this, vast efforts have emerged with the present view and conclusions, which are used as guideline principles for those who have the responsibility of dealing with tuberculosis in individual patient in community and or in Laboratory.

In spite of the enormous amount of research that has been done since Robert Koch first reported the isolation of the etiological agent on 24th March 1882, we still have a very incomplete understanding of the nature of virulence of tubercle bacillus and the nature of host response to tubercle bacillus and the nature of host response to infection. Neither do we have a very clear understanding of the reason for the rise and fall in the number of cases of tuberculosis nor is there a general appreciation of inadequacies of public health control methods that have been used to combat the disease. However, in recent years there has been a great improvement in pure understanding of host parasite interaction in tuberculosis as we have started understanding the immunological basis of disease.[3]

Zinc is essential element in nutrition. It is a constituent of several enzyme systems including carbonic anhydrase, alcohol dehydrogenises, alkaline phosphatase, superoxide dismutase, RNA polymerase, carboxy peptidases' is also present in insulin of the B-cells of pancreas.

Zinc deficiency affects host defences by decreasing phagocytosis and reducing the number of circulating T-cells. Zinc in our body is involved in various activities such as metabolic function, immunity and wound healing. Because of limited data on the serum level of zinc in patients with pulmonary tuberculosis, it was decided to study serum zinc level in such patients and to compare them with the levels in healthy control.

It has been observed by so many researchers that the plasma Level was low in established cases of the pulmonary tuberculosis.[4]

Although malnutrition has been described in TB patients previously, contrary to what is commonly believed, little is known about nutritional status with respect to the micronutrients vitamin A, zinc and iron. Low concentrations of these nutrients may affect host defense.

The decrease in serum zinc level could explain the immune system dysfunction and the high level of oxidative stress in patients with MDR-TB. Therefore, the evaluation of the zinc and copper status could represent essential parameters in monitoring of TB second line treatment for better treatment management.[5,6]

Zinc deficiency affect host defense by detraining phagocytosis and reducing the number of T-cells. Several studies have demonstrated that the serum level of zinc decreases significantly during the active tuberculosis and increase following recovery after institution of antituberculous therapy and improvement of the nutritional status.[7]

Aims and Objectives
The present study was carried out with the objective to study the relation of plasma zinc levels in cases of pulmonary tuberculosis.

MATERIALS AND METHODS

It is an age and sex matched Case Control study, conducted in Pulmonary Medicine department in NKP Salve Institute of Medical Sciences, a tertiary care centre, Nagpur. From 1st May 2013 till 31st October 2013 (six months). The study participants included 40 (20 males and 20 females) sputum positive Pulmonary TB cases as per the DOTS guidelines and 40 control subjects (20 males & 20 females of same age groups). 10 ml blood sample was collected by venepuncture and it was diluted with equal volume of distilled water. Out of it, 1 ml of sample was aspirated into an atomic absorption spectrophotometer along with appropriate standard solution and zinc levels were determined at 213.9 nm.

All precaution of sterilization, preservation and processing was taken care as per the standard requirement.

RESULTS

Sr. No.	Subjects	No. of Cases	Range (microgm/dl)	Mean (microgm/dl)	Total Mean (Microgm/dl)
1	Male	20	52-163	106.05	100.8
2	Female	20	62-146	95.55	
Table 1. Plasma Zinc Levels in Male and Females					

Table 1. Shows, Serum Zinc levels in the control subjects (20 males and 20 females) Total mean plasma Zinc level was 100.8 microgram/lit. This shows the control subjects were having a normal concentration of plasma zinc.

| Sr. No.	Subjects	No. of Cases	Range(microgr/dl)	Mean(gm/dl)	Total Mean(Microgm/dl)
1	Male	20	26-126	59.06±7.7	
2	Female	20	24-124	55.04±6.6	57.05
Table 2. Plasma Zinc Levels in Active Pulmonary Tuberculosis					

Table 2. Shows, Serum Zinc levels in diagnosed subjects of study (20 males and 20 females), which was significantly low.

Subjects	Study	Control	P value
Male	59.06 (± 3.21)	106.05 (± 3.41)	< 0.01*
Female	55.04 (± 2.1)	95.55 (± 1.99)	< 0.01*
Table 3. Comparison of Plasma Zinc Levels in Active Pulmonary Tuberculosis and Control Group			

*Unpaired t test.

In the control subjects, the plasma zinc levels were, in males- 106.05 microgram/ lit & in females- 95.55 microgram/ lit. Mean plasma zinc was found 100.8 microgram / lit.
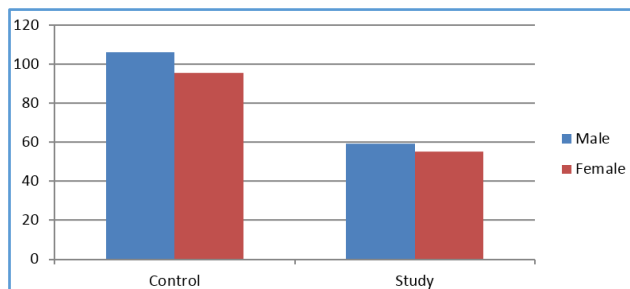
Zinc levels in Control and Study Groups

In the cases with pulmonary tuberculosis, the plasma zinc levels were 59.06 microgram/lit in males & 55.04 microgram/lit in females. Mean plasma zinc was found 57.05 microgram / lit. This shows the control subjects was having normal concentration of plasma zinc.

In study cases of active pulmonary tuberculosis, the serum zinc level was significantly low (p<0.01).

DISCUSSION

Since last few decades various researches have been done on same topic and found to have correlation between serum zinc levels and pulmonary tuberculosis. In 1968 J A Halsted also found low serum zinc levels in pulmonary tuberculosis and other diseases.[8] As also in our present study, the result in positive cases of pulmonary tuberculosis, shows the serum zinc level was significantly low. In the same way following studies have been carried which were also having the serum zinc level significantly low. As it was also observed by Kuppamuthu et al, in 2008, the level of serum zinc among TB patients was significantly lower than that of controls.[4] Karyadi et al, in 2000, in Indonesia, did the same study, they also found that in positive cases of tuberculosis, the serum zinc in levels was significantly low. In Karyadi's study the mean plasma zinc concentration in malnourished TB patients was 13% lower than in well-nourished healthy controls (P < 0.05) and was 7% lower than in well-nourished TB patients. Compared with malnourished healthy controls, malnourished TB patients had 10% lower mean plasma zinc concentration. In our study we also found the low plasma zinc levels, which matches with the present study.[5] Van Lettow et al in 2004 also observed malnutrition with specific reference to micronutrients zinc, which was also low in pulmonary tuberculosis with or without HIV co-infection.[6] H. Ghulam et al, carried out a study in United Kingdom to see the effect of Zinc in positive cases of pulmonary tuberculosis, they also observed significantly low serum zinc level along with other micronutrients. According to the study results he suggests estimation of serum zinc levels is an important tool in diagnosis and monitoring of response to treatment in pulmonary tuberculosis, and even a booster of the immunological mechanisms if instituted during the course of treatment.[9] A Koyanagi et al, carried out a study in 2004 to see the role of zinc in pulmonary tuberculosis along with silicosis and silico-tuberculosis, they also found significantly low serum zinc level in pulmonary tuberculosis.[10] K. Ramakrishnan et al, carried out the similar type of study, they also observed significantly low plasma zinc level in their positive cases.[11] The mean ± SD for zinc among the controls, HIV positive and HIV negative patients were; 117.13 ± 4.2, 53.9 ± 8 and 65.5 ± 9.8 m g/dL; respectively. The plasma zinc levels were significantly low in active PTB patients irrespective of HIV status, but more so in HIV-positive individuals. These results also match with our results. These changes may be attributable to nutritional factors, enteropathy and acute phase reactant proteins. C. Mythili and R Lalitha also carried out the study to see the role of Micronutrients zinc in pulmonary tuberculosis. Their study revealed significant decrease in mean level of Serum zinc level (39.76 ± 20.27) in pulmonary tuberculosis, as compared to (86.42 ± 16.51, p=0,001) microgram/dL in controls. In results of this study matches with our results.[1] M Muthuraj et al also studied the zinc levels in tuberculosis patients. The zinc and calcium levels of PTB patient co-infected with HIV is (Zn: 467.5bp, Ca: 20750bp) lower than the zinc and calcium levels (Zn: 1251bp, Ca: 41580bp) of normal (control) healthy individual. All three parameters were significantly low in active PTB patients with HIV. The results were concordant with present study.[12] The study done by J D Bogden et al also revealed. Mean (+/- SD) zinc concentrations 84.8 ± 15.5 micrograms/dL and 13.0 ± 2.4 micrograms/lit in pulmonary tuberculosis and controls respectively, for plasma. The results matches with present study.[13]

G. Mohan, S. Kulshreshtha. Also carried the similar type of study with following results as the average plasma concentration of serum zinc in healthy volunteers was 96±18 µg/dL. In tuberculosis patients, serum zinc levels 64.14 ± 3.97 µg/dL, before the start of treatment, which came down to 74.31 ± 3.60 µg/dL, after 4 weeks of anti-tubercular treatment. So, in the study, they observed significantly low level of plasma zinc level that matches with the present study.[14]

CONCLUSION

The present study reveals significantly low levels of serum zinc in active cases of pulmonary tuberculosis in comparison to normal control subjects. Normal level of Zinc is essential to combat the tubercular infection and to help in cell mediated immunological response. In the normal subjects,

zinc has to be supplemented in our diet and can be given as preventive nutrient to increase cell mediated immunity.

Overall the studies conclude that zinc supplementation improves the effect of TB medication as it serves as a booster of immunologic process and estimation of zinc levels could be used as a valuable laboratory tool to assess the effectiveness of ongoing antitubercular therapy. The study suggests that in view of the poor nutritional status in patients of pulmonary tuberculosis, zinc supplementation, be made a mandatory constituent of treatment protocol.

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