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ORIGINAL ARTICLE

Plasma vitamins and essential trace elements in multi-drug resistant tuberculosis patients before and during chemotherapy

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Abstract Multi-drug-resistant tuberculosis (MDR-TB) is caused by *Mycobacterium tuberculosis* (Mtb) strain resistant to both rifampicin and isoniazid. Nigeria has an estimated MDR-TB rate of 2.9% and 14.3% among new and relapse cases respectively and is ranked among 4 high burden African countries for MDR-TB. Malnutrition has been implicated in the progression from dormant to active disease.

This study determined the plasma level of micronutrients (Fe, Zn, Cu, vitamins A, C, D and E) in MDR-TB patients before and throughout anti-TB chemotherapy. Plasma iron, zinc, copper, vitamins A, C, D and E were determined in twenty-four (24) MDR-TB patients before the commencement of anti-TB chemotherapy, 2 months, 4 months and 6 months post-commencement of anti-TB chemotherapy, as well as in twenty (20) healthy controls. Plasma vitamin A level was significantly decreased before chemotherapy compared with controls. At 2 months of anti-TB treatment there were significant decreases in plasma levels of iron, vitamins A, C and E compared to controls whereas plasma zinc level was significantly increased compared with levels before treatment. At 4 months of treatment, plasma levels of copper and vitamin D were significantly increased while plasma vitamin E level was reduced significantly compared with controls. There were significant increases in iron, zinc, copper, vitamin A and vitamin D levels with decreased plasma levels of vitamins C and E at 4 months of treatment compared with their levels before chemotherapy. At 6 months of treatment, plasma levels of iron, zinc, copper and vitamin D were significantly increased while vitamin E was significantly decreased compared with controls. Plasma levels of iron, zinc, copper, vitamins A and D were significantly increased whereas the levels of vitamins C and E were significantly reduced at 6 months of treatment compared with levels before chemotherapy.

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Plasma levels of iron, zinc, copper, vitamins A and D were raised while plasma levels of vitamins E and C were reduced in MDR-TB patients from 4 months post commencement of anti-TB chemotherapy. Thus, there is need to monitor micronutrient supplementation and plasma levels of these micronutrients to avoid complications associated with overload or deficiency.

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Background

Tuberculosis (TB) continues to be a major public health challenge globally and now ranks alongside HIV as a leading cause of death worldwide [1]. Recent statistics show a rise in the number of new TB cases from 9 million in 2013 to 9.6 million in 2014 with the number of TB associated deaths in 2013 and 2014 remaining constant at 1.5 million [1,2]. In recent years, progress in TB control and eradication has been threatened by the emergence of drug resistant strains of *Mycobacterium tuberculosis* (Mtb). Multi-drug-resistant tuberculosis (MDR-TB) is defined as a disease caused by Mtb strain resistant to both rifampicin and isoniazid, which are frontline anti-tuberculosis drugs presently used in chemotherapy. Nigeria is reported to have an estimated MDR-TB rate of 2.9% and 14.3% among new and relapse cases respectively and is ranked among 4 high burden African countries for MDR-TB [3]. Among other factors, malnutrition has been implicated in the progression from dormant to active disease [4].

The innate immune cells; macrophages, neutrophils and dendritic cells, play an important role in immunological response, as first responder, activator of adaptive immunity and effector cell in Mtb infection [5]. Mtb bacilli upon entry into the lungs are engulfed by resident innate immune cells (macrophages and dendritic cells). This leads to transformation of macrophages from a resting state to an activated state with characteristic feature of increased oxygen uptake, enlargement and increased protein synthesis [6]. Also there is increased influx of neutrophils to the lungs, and a report demonstrated that neutrophils are the most commonly infected phagocytes in human TB [7]. Macrophage and neutrophil apoptosis have also been reported to be a potent mechanism for control of inflammation and removal of infected cells in Mtb infection [8]. These lead to a high rate of cellular turnover during infection and increased demand for essential nutrients by the immune cells [9].

A close relationship was suggested between micronutrients and modulation of neutrophil and macrophage functions [10]. Micronutrient malnutrition has been described in pulmonary TB patients [11–14] and several studies have suggested that patients with TB are at high risk of deficiency of vitamins A, C, D and E as well as zinc [13,14]. Our previous study [15] reported micronutrient malnutrition in patients with drug-sensitive TB at diagnosis and throughout the period of anti-TB chemotherapy. Because micronutrient deficiency has been reported to impair resistance to infection, lead to active TB disease and poor outcome of anti-TB chemotherapy, this present study therefore determined the plasma level of micronutrients (Fe, Zn, Cu, vitamins A, C, D and E) in MDR-TB patients before and throughout anti-TB chemotherapy.

Materials and method

Study participants

Twenty-four (24) patients admitted into the MDR TB center, University College Hospital (UCH) Ibadan, Nigeria for anti-TB treatment were recruited for the study after obtaining written informed consent. Patients had been previously diagnosed as being infected with isoniazid and rifampicin resistant strains of Mtb using clinical history, chest X-ray and GENE Xpert test. Twenty (20) apparently healthy participants were recruited as controls. Five (5) milliliters of blood was drawn from the anti cubital fossa vien into lithium heparin tubes before the commencement of chemotherapy, and 2 months, 4 months and 6 months of anti-TB therapy. Blood samples were centrifuged and plasma obtained was analyzed.

MDR-TB treatment protocol

All bacteriologically confirmed MDR-TB patients received intensive phase for 6–8 months in the hospital followed by 12 months of continuation phase in the community based on WHO updated guidelines in 2011 [16]. Standardized treatment regimen was used including five drugs: kanamycin/Amikacin, Levofloxacin, Prothionamide, Cycloserine, Pyrazinamide (with Pyridoxine). This present study was conducted during the intensive phase of treatment.

While patients were admitted for MDR-TB treatment, they were supported by non-governmental organizations which provided nutritional support in the form of meals and micronutrient supplements. Vitamin C (Spartan C), folic acid (Vitabiotics), vitamin B complex (Vitabiotics), vitamin B6 (Pauco) and multivit (Pauco) supplements were administered daily with anti-TB drugs as part of the treatment regimen at the center where this study was conducted.

Micronutrient analysis

Plasma levels of micronutrient vitamins (A, C, D and E) were determined by high performance liquid chromatography method using WATERS 616/626 (USA) machine as previously carried out [17].

Plasma concentrations of trace metals (Fe, Zn and Cu) were determined using atomic absorption spectrophotometry (Buck Scientific, 210, Atomic Absorption Spectrophotometer, Connecticut, USA) as previously described [15].

Statistical analysis

Data obtained were analyzed using statistical package for social sciences (SPSS) version 17.0. Independent Student

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