FERROKINETIC STUDIES IN PATIENTS WITH GEOPHAGIA, GROWITH RETARDATION HYPOGONADISM, HEPATOSPLENOMEGALY IRON DEFICIENCY ANEMIA AND ZINC DEFICIENCY

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SUMMARY: Ferrokinetic investigations were performed in ten patients with prolonged Geophagia. Plasma Iron Clearance (T ½) was increased. Plasma Iron Transport Rate (PIT) was decreased in five. Red Cell Iron Utilization (RCU %) was decreased in six, while it was normal in three cases. Erythrocyte Iron Turnover Rate (EIT) was found to be decreased in five, normal in one and increased in three cases. Erythrocyte Survival Time (EST) was found to be shortened in all cases except one. The radioiron distribution obtained by surface counting over sacrum (marrow), spleen and liver was performed in three cases. The surface countings over spleen showed that red cell sequestration increased in two cases. Ferrokinetic data indicated that erythropoiesis was disturbed in children with geophagia.

Key Words: Ferrokinetics, Geophagia, Zinc Deficiency.

INTRODUCTION

Geophagia, the habit of eating clay or soil, has been a well known and studied health problem in Turkiye for many years (1-8). The geophagia syndrome characterized by iron deficiency anemia, hepatosplenomegaly, hypogonadism and zinc deficiency was first described by Prasad (9-10).

In some cases, iron absorption was decreased contrary to the expected (5). So the iron deficiency recurred in some patients despite adequate iron therapy (7). Recently, we showed that pathologic alterations in small intestinal mucosa healed after zinc therapy and iron absorption increased in these patients (8).

Zinc deficiency is responsible for some of the symptoms present in Prasad Syndrome. Because of the important effects of zinc deficiency on cell division, the rapidly proliferating tissues like intestinal mucosa, immune and haematopoietic systems are most affected (11).

Zinc deficiency might affect aminolevulinate dehydratase (ALAD) enzyme which contains zinc and is also essential for heme synthesis (12,13).

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Erythropoiesis in Geophagia syndrome was not studied previously. So we determine the erythropoiessis by using ferrokinetic studies.

MATERIALS AND METHODS

Ten patients admitted to the Pediatric Hematology and Oncology Research Center of Ankara University with prolonged geophagia were included in this study. They were investigated clinical, hematological and ferrokinetic points of view. Their age ranged from 7 to 27 years and 8 of them were girls. Five healthy children were included also as controls.

Routine hematological tests were performed through the standard techniques. The plasma, erythrocyte (RBC) and hair zinc levels were measured by atomic spectrophotometer Perkin-Elmer Model 103 [14] 3. Ferrokinetic studies were performed with 59 Fe. Iron 59 is obtained commercially as sterile ferrous citrate. Fe 59 solution (Amersham) with specific activity at least 10 ug per mg. 40 uCi 59 Fe citrate is injected to the patient. Another 40 uCi 59 Fe citrate is prepared to be used as the standard.

Following the injection, blood samples are drawn in Heparin at 15, 30, 60, 90, 120, 180, 240 min intervals. These samples for 59 Fe utilization curve are collected on days 1, 3, 5, 7, 10 and 14 after injection. These samples are collected in Heparin and counted as whole blood. Blood samples are counted (CPM) using a Gamma counter

(LKB Wallac 1280 Ultrogamma). Plasma Iron Clearance (T 1/2); Plasma Iron Transport (PIT); Red Cell Iron Utilization (RIU); Erythrocyte Iron Turnover (EIT) and Erythrocyte Survival Rate (RCS) were investigated in our Patients (15,16).

RESULTS

Clinical and hematological data of the Patients are shown in Table 1. Age range of the patients were 7 and 27. The duration of geophagia of the patients varied from 5 to 7 years. Eight cases had splenomegaly. We noted leukopenia in four patients with huge splenomegaly (8 to leukopenia in four patients with huge splenomegaly (8 to 22 cm). Six had delayed puberty and six had growth retardation (Below 3rd percentile in height according to the Turkish standards) (16). Reticulocyte counts were within normal limits, bone marrow examination were normocellular, erythroid/myeloid rate was normal.

Plasma, erythrocyte and hair zinc levels were found to be significantly lower when compared to the healthy controls. Data obtained from ferrokinetic studies with 59 Fe are shown in Table 2. Plasma Iron Clearance (T1/2) was increased in all cases. Plasma Iron Transport Rate (PIT)

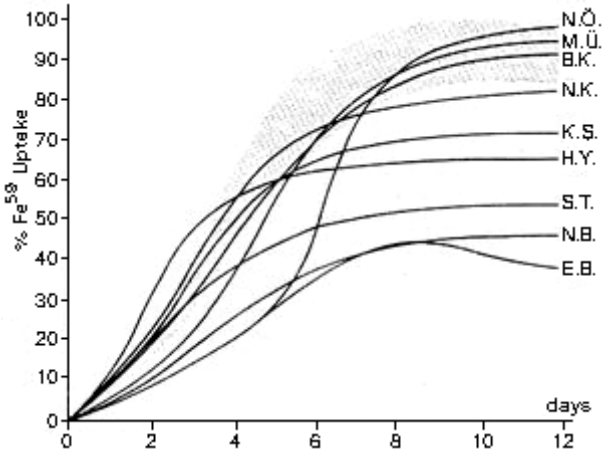

Figure1: Red Cell Utilization of Fe 59 in patients with Geophagia. Utilization of Fe 59 in these six patients was reduced, normal in four. This indicates that a proportion of the iron leaving plasma dose not appear in circulating red cell.

was increased in five cases (Cases 1, 3, 6, 8, 9), Red Cell Iron Utilization (RCU%) was decreased in six cases (cases 1, 5, 7, 8, 9, 10); normal in 3 (Cases 3, 4, 6) Figure 1). Erythrocyte Iron Turnover (EIT) was found to be decreased in five, (cases 1, 3, 6, 8, 9); normal in one (case 7) and increased in three (Cases 4, 5, 10). Erythrocyte Survival Time (EST) was found to be shortened in all cases except one (case 6).

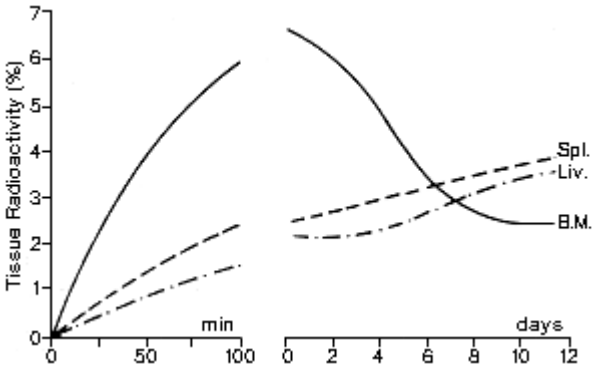

Figure 2: The radioactive iron content of bone marrow (sacrum) liver and spleen, after intravenous injection of radioactive iron labelled transferrin. The bone marrow shows an initial uptake, with a subsequent decrease because of bone marrow release of red cells with radioactive hemoglobin. In our patient, the splenic and to a lesser degree the hepatic uptake of radioactivity reflects red cell sequestration and destruction in these organs (BM: Bone Marrow, Liv: Liver, Spl: Spleen).

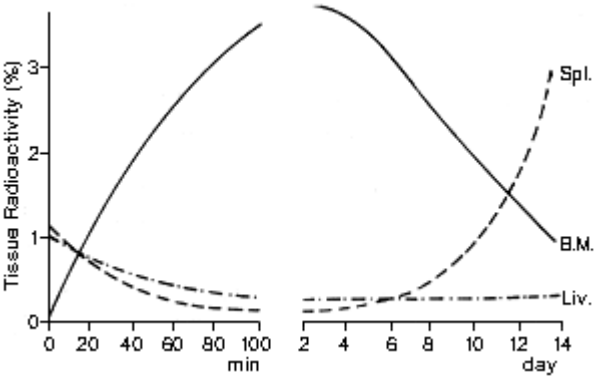

Figure 3: The radioactive content of bone marrow (sacrum), liver and spleen, after intravenous injection of radioactive iron labelled transferrin. In the patient, a late rise in the spleen radioactive content at increased level indicates splenic sequestration of circulating red blood cells (BM: Bone Marrow, Liv: Liver, Spl: Spleen).

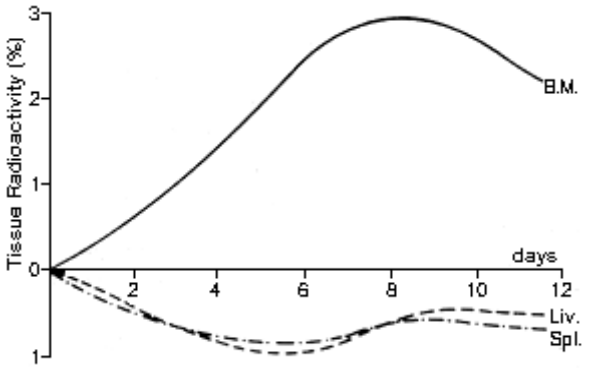

Figure 4: The radioactive content of bone marrow (sacrum), liver and spleen, after intravenous injection of radioactive iron labelled transferrin. The patient showed a normal variation (BM: Bone Marrow, Liv: Liver, Spl: Spleen).

Normally Bone Marrow activity rapidly increases in two or three days. Then erythrocytes begin to leave marrow. Activity over spleen and liver is minimal. The proportion or both activities to marrow activity shows the extramedullary activity. In cases 1 and 4, there was accumulation more than expected. In case 4, accumulation over spleen started after 14 the day and showed an increasing pattern thereafter. In case 2, there was no organomegaly and Fe 59 counts over spleen and liver was in normal limits (Figures 2, 3 and 4).

DISCUSSION

In the usual ferrokinetic study, transferrin is labelled with 59 Fe. The tracer is then monitored as it moves from the plasma to the bone marrow and into the circulating red cells.

Plasma Iron Clearance (T 1/2) was increased in all cases as expected in simple iron deficiency.

Plasma Iron Transport (PIT) was decreased in five patients, contrary to the expected values of iron deficiency.

Red Cell Iron Utilization (RCU %) was found to be reduced in our six patients.

The normal red cell iron utilization of radioactive iron may be as high as 90 percent, a further increase has little significance. A decreased utilization, however, is an important finding and suggests that mature red cells are destroyed shortly after their release from the marrow (Hemolysis), that immature red cells are destroyed in the bone marrow before their release to the circulation (ineffective erythropoiesis) or that serum iron, because of slow bone marrow uptake, is diverted to nonerythropoietic tissues.

Zinc deficiency might be responsible for the decrease of RCU % uptake in our patients because zinc is necessary for the ALAD enzyme, which has an important role in heme synthesis (12,13). As it is very well known that in iron deficiency, iron utilization is increased. In our cases bone marrow was normal, plasma clearance was rapid. These two findings indicate that bone marrow is ineffective.

The Erythrocyte Iron Turnover (EIT) which is an index of effective erythropoiesis was also found decreased in five cases contrary to the expected values of simple iron deficiency.

Erythrocyte survival time (EST) was found to be shortend in the majority of the patients, as expected in iron deficiency anemia.

Normally bone marrow activity rapidly increases in two or three days. Then erythrocytes begin to leave marrow. Activity over spleen and liver is minimal.

With radioactive iron, it is possible to determine whether the spleen is the site of red cell formation or destruction. Production of red cells in the spleen is demonstrated by an increased uptake of radioactive iron in the spleen, followed by rapid discharge and release of the iron into peripheral blood in red cells.

In two cases, case 1 and 4, there was radioactive iron accumulation more than expected. A progressive increase in radioactivity over splenic area suggests splenic destruction of red cells. An initial high level of radioactivity with little subsequent increase is more compatible with splenomegaly without red cell sequestration and destruction (17,18). In case 1, a progressive increase in radioactivity was observed over splenic and liver area. In case 4, accumulation of radioactive iron over spleen started after 14 th day and showed an increasing pattern thereafter, suggesting splenic destruction of red cells.

In summary, ferrokinetic data in this study indicated that erythropoiesis is disturbed in children with Geophagia. Ineffective erythropoiesis and increased splenic sequestration were shown in some cases with this syndrome.

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