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Review Article

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Review on Iron Overload Disease in Human and Chelating Trap

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ABSTRACT

Iron is one of an element of periodic table with 26 atomic numbers. This element exists in second abandon of transition metal and it exists in earth's crust in fourth abundant. It found in the middle and in the first transition row of predict table. Mostly this metal presented in two forms of oxidation state II (d^6) and III (d^5). Overloading of iron and the infections of hemochromatosis are mostly common in humans and it is treatable circumstances. This excessiveness of iron overload has a genotypes said that HFE, most study recommended that it need a multiethnic primary care for affected population. The synthesis and characterizations of transition metal have important things. Most of transition metals have medicinal proprieties. Due to this metal have improvements in transfusion therapy in beta-thalassemia major patients; Trans fissional become the major cause of late morbidity and mortality. In the entire world spatially in developing country chelating therapy is best but it is expensive. For example in India and other developing countries, iron chelation therapy is still not strictly adhered to in these children, mostly due to financial constraints. An orally effective and cheap iron chelator is the need of the hour in the treatment of beta-thalassemia major. With the advent of Deferoxamine, Deferiprone and Deferasirox, there is new enthusiasm in this front. The main aim of this review gives the ways of chemotherapy, mechanism and the globally existence of those removed iron overload in our body.

Keywords: Chemotherapy; Iron overload; Chelation therapy; Deferoxamine; Deferasirox

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INTRODUCTION

Iron is one of an element of periodic table with 26 atomic numbers. This element exists in second abandon of transition metal and it exists in earth's crust in fourth abundant. It found in the middle and in the first transition row of predict table [1]. Its position in the middle of the predict table elements of the first transition row. This implies that due to the properties of transition metals iron has the possibility various oxidation states 2^- to 6^+, the principal in the electronic configuration ones being 2^+ in d^6 and 3^+ in d^5, Fe^{4+} or Fe^{5+} although dependent on the mono oxygenates generate high reactive intermediates during their catalytic cycle. While in the solubility in water, Fe^{2+} is highly water soluble, however $Fe^{3+}$is moderately water insoluble. When come to the acidic properties of iron, Fe^{3+} due to hard acidic it prefers hard oxygen legends even as Fe^{2+} due to in the borderline of hard and soft favor nitrogen and sulfur legends preferred. The interaction this both $Fe^{2+}$and $Fe^{3+}$and ligand supporter atoms will depend on the strength of the chemical bond formed between them. Both Fe^{2+} and Fe^{3+} most frequently found for coordination number of 6, this coordination number is giving octahedral stereochemistry although four- (tetrahedral) and, particularly, five-coordinate complexes [1,2].

Iron is present in the diet as either the form of reduced form of ferrous (Fe^{2+}) or in the oxidized form of ferric (Fe^{3+}). There are two cases iron in our body which means: If our body absorbs low iron concentration this condition known as iron deficiency; and if our body absorbs exes' concentration, this case known asiron overload. If the iron overload becomes severe; the condition is diagnosed as hemochromatosis [2]. Iron overload occurs when the body absorbs higher concentration of iron from diet or from hereditary. Contrarily the capacity of binding transferring for iron is surpassed, resulting in non-transferrin-bound iron (NTBI) circulating in the blood and the subsequent deposition and

lastly it storage of free iron in our tissues. The higher unnecessary accumulation and storage space of free iron in body tissues over time can occur with chronic transfusion therapy in patients with transfusion-dependent anemia's and following myeloablative allogeneic hematopoietic stem-cell transplantation [3]. The three habits of over accumulation iron:, first through absorption of dietary hemi (entreat route) and non-hemi iron (the parenteral route), second through transfusions or injections of iron containing compounds, and third placental route during fetal life of the human day today activities and life span [4,5]. Iron is very vital developing to healthiness of our body but unwarranted amounts of this iron in the body are highly toxic and difficult for controlling our body system [6]. Overload accumulation of iron can be coupled with a wide range of genetic and environmental factors and can lead to parenchyma damage of body organs [7]. Some iron-overload disorders *HFE*-associated hereditary hemochromatosis and β-thalassemia are quite common in body system, while others factors are exceedingly rare [8]. Hemochromatosis is one of the common diseases that happen as a result of significant duplications' of iron accumulation. Similarly Hereditary hemochromatosis is due to the body readily absorption iron that can lead to over total-body iron overload with secondary tissue damage in a wide range of organs [9]. The other on is Beta thalassemia. It was first described in 1925 by Thomas Cooley. In those days, thalassemia major patients rarely used to survive the first decade of life spam [10].

The blood disorder on the production of reducing hemoglobin can cause Beta-thalassemia. Hemoglobin is red blood cells which directly related with the concentration of iron that carries oxygen to cells throughout the body system. The decrements of this can cause pals skin, weakness, fatigue and more serious complications. A person which caused by Bata-thalassemia can pretend to increases risk of developing abnormal blood clots.There are two types of Bata thalassemia: thalassemia major and thalassemia intermedia. Thalassemia major symptoms: it appear within the first two years of life, loss of weight and height without proper growing per years, the skin of children is yellow and whites of eyes and it affect all the systems of the body thalassemia intermedia is mainly appears early childhood or later in life and it affected the growing systems of the body by slowing and bone abnormalities [11-13].

PHYSIOLOGY OF IRON TRANSPORT

The principle of biochemical cause of cell damage in iron overload is believed to be the generation of free radicals. These can damage membranes and DNA leading to cell damage, mutation and ultimately, cancer. A secondary effect seems to be the increased deposition of collagen, stimulated by both increased ROS and iron leading to tissue fibrosis. In the below Figure 1, there are presented the distribution of iron in tissue and accumulation [11,14].

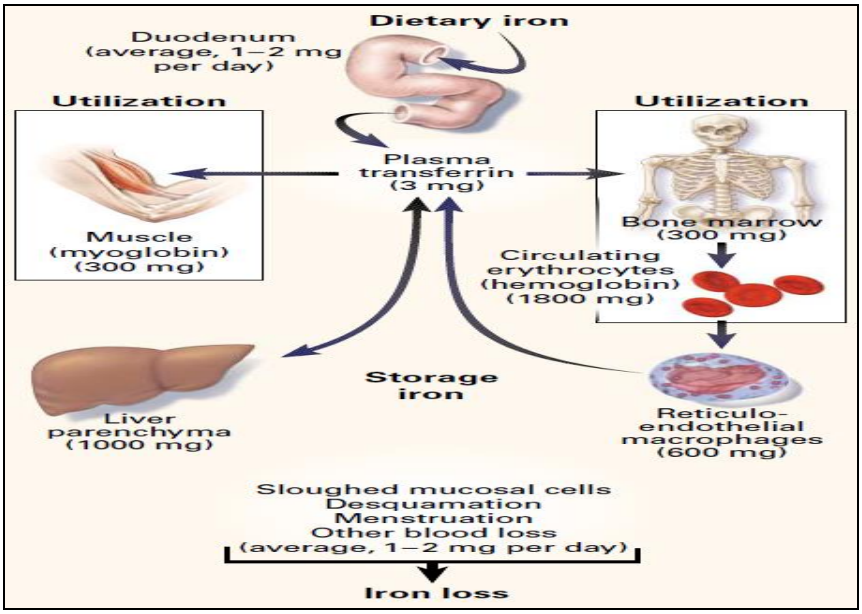

Figure 1: Accumulation and distribution of iron metabolism in the body organ

OXIDATION AND REDUCTION OF IRON

Oxidations and reductions of iron depends on the inter conversions of both Fe^{2+} (ferric) between Fe^{3+} (ferrous). It has the capacity to gain and los electrons readily. The interconvert ions of ferrous and ferric has capability makes it a useful component of cytochromes, oxygen-binding molecules (i.e., hemoglobin and myoglobin), and many enzymes. Yet, in our body if their exists free radicals of iron can also the possibility to damage tissues organs by catalyzing the conversion of hydrogen peroxideto free-radical ions that attack cellular membranes proteins and DNA [8,15].

$$Fe^{3+} + O_2^- \rightarrow Fe^{+2} + O_2 \quad 1$$
$$Fe^{2+} + H_2O_2 \rightarrow Fe^{3+} + {}^{\cdot}OH + OH^- \quad 2$$

CREATION OF FREE RADICALS IN OUR BODY

The free radicals formed by if the iron in our body undergoes oxidation with oxygen. This is oxidations of iron depends on the ages of the person, as the age increased the oxidation rapidly speedup and lastly they increments of rapid body's normal metabolism. The dangerousness of these free radicals, it also is created by the immune system to help destroy bacteria and viruses during an infection and they can form because of exposure to certain chemicals, environmental toxins like pollution and radiation and cigarette smoke [16,17]. But our body under normal conditions it easily duplicates frees radicals. But if the reproductions of this free radical increased day to day without any neutralization the body under dangerous conditions [17,18].

The Effects of Free Radicals Accumulations in our Body

The free radical is highly reactive. Contrarily it easily penetrates the cell membrane. "Infect at the molecular level, the chain reaction of electron "theft" can affect the cell membrane (the outer covering of the cell) by making it either too vulnerable or too resistant to outside influences". DNA cell's can affected easily by this free radical then this causes the cell to reproduce abnormally [16,17]. In addition to damaging cell membrane this free radicals can accumulates loadings of cholesterol in the blood. The increments of cholesterols results abnormality of body, increase accumulations of fat, stick to the walls of the blood vessels, cause of heart disease, abnormal cell reproductions, cause different forms of cancer and it damages some partes of our body [8,17].

HOW CAN REMOVAL OF EXCESS IRON IN HUMAN BODY

One of the most recent removals of iron overload in our body is using chelating therapy. The factors of this therapy, it talks longer treatment because if it caused once have rapid duplication of iron absorptions. Due to this it time to remove all too balanced conditions. There are two factors during chelators to remove excess iron: The first the rate at which the chelator depletes storage iron, and secondly the rate of continued iron accumulation [9,10]. "Most patients with trans fusional iron overload require transfusions indefinitely. Since each unit of blood deposits about 230 mg of iron, most patients who require, for instance, 2 units of blood per month will have at most a very slightly negative iron balance with chelating therapy". Deferoxamine mostly efficient for iron chelator therapy it removes between 35 and 70mg of iron per day in our body accumulated [10,15].

IRON CHELATOR THERAPY

Some Advantages and Properties of an Ideal Iron Chelator Therapy

The following pointes are the main advantages and its properties absorbing iron in chelation therapy: the ferric form of iron has high attraction but the ferrous form of iron low attractions to wards of the therapy [10,14]. This therapic system has attained negative balance on iron. It has in good tissues protection and cell penetration on the chelator organ. It is easily available, affordable and the doses rate once in daily intact are good on metabolic activities [18].

The Day to Day Developments of Chelators Therapy

In over the world nowadays iron overload dessis controlled by this chelation therapy. The over loaded iron is chelated, both from the reticulo-endothelial cells (RE cells) as well as various parenchymal organs and the chelated iron is cleared by the liver organ and excreted through the bile duct. The chelation therapy has ability to prevent myocardial cell iron uptake, remove iron directly from myocardial cells and exchange iron with DFO [6]. Iron chelation therapy is inevitable to prevent the consequences of trans fusional hemosiderosis in thalassemia major patients.

The absorptions of iron in the liver can be maintained at normal conditions or it can maintain at mildly elevated levels. On the facts of this therapy the hepatic fibrosis can be totally prevented and the induced cardiac infection decreased. It highly controlled the problems on the normal growing and sexual development achieved [10,11].

THE THERAPY USING DEFEROXAMINE, DEFERASIROX AND DEFERIPRONE

Deferoxamine

The Deferoxamine is derived from the amino functional groups of an organic compound. It is unsuccessfully immersed iron from gastrointestinal tract, in it must be attended the administered, the reason of, most of the available drug may be consists of in a single intramuscular injection without binding any iron after treatment. On the single treatments of iron chronic it absorb overload calls for 500–1,000 mg to be controlled intramuscularly each day plus an additional 2,000 mg to be infused intravenously with each unit of blood transfused [11,15]. On contrarily, the cell regimen for continuous intravenous infusion through an implantable venous catheter. From daily dose 1,000–2,000 mg an alternative regimen requires to be administered into the subcutaneous tissue of the abdomen over eight to 24 hours with a portable mini-infusion pump 40 or a balloon infuser. This drug is controls the normality of iron accumulation. In addition, the potential auditory, ocular, and neurological toxicity of Deferoxamine has meanly led to guidelines for monitoring of therapy including annual audiometric and eye examinations. Growth and skeletal abnormalities may also occur. 40 over 30 years of experience with Deferoxamine have shown iron chelation to be an effective therapeutic modality in the management of trans fusional iron overload [6,19] (Figure 2).

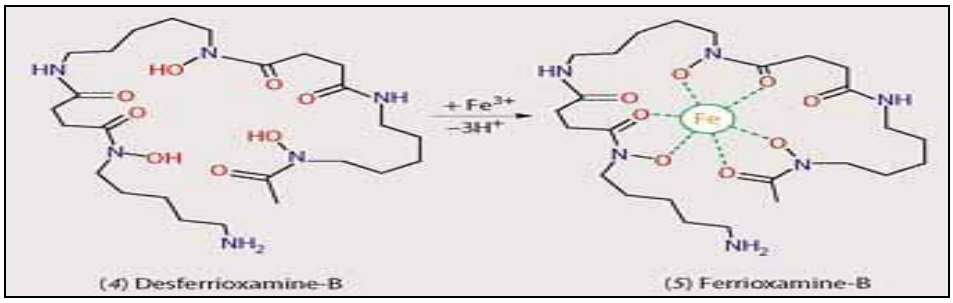

Figure 2: The chemical reaction and structure of Deferoxamine

Deferasirox

Deferasirox also an organic compounds which has amino group, have ability to reacts with iron. The daily intake of Deferasirox is once in a day for the person who's age greater than +18, it has eight to 16 hours long plasma half-life, which provides 24 hour chelation with a single dose. 20 mg/kg per day is the normal recommended dose in one day. It must take on an empty stomach at least 30 minutes before eating food [13,15]. There are no effect in the cell growing and other body system. The most advantages of Deferasirox are generally well-tolerated, with an acceptable safety profile in pediatric and adult patients; and common adverse effects are gastrointestinal disturbances and rash. Preclinical studies in animals suggested that the kidney is a potential organ of toxicity when Deferasirox is administered in high doses. Using Deferasirox can maintain good cellular reproduction but it is cost primarily due to the quality of life benefits derived from the simpler and more convenient mode of oral administration [19] (Figure 3).

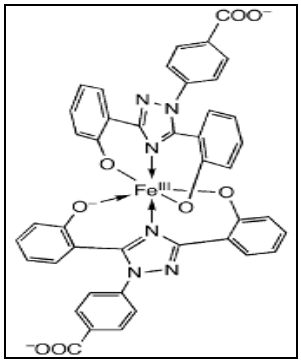

Figure 3: The chemical structure of Deferasirox

Deferiprone

Deferiprone is also one of organic functional group and it has a ketone functional. The drug Deferiprone can be orally administered and three times intake per day within the differences of eighteen hours. They have 43–136minutes of a relatively short plasma half-life and 75–100 mg/kg/day the range dose of adult person. And similarly it has to protect the cell systems and it is not to affect the normal growth of organs [6,16]. Deferiprone have the ability to penetrate the cell membrane and to chelator with iron in the affected cell membrane. But the Deferoxamine is poorly penetrating the cell membrane. Deferiprone have side effect on neutropenia and agranulocytosis, muscular skeletal and joint pain, gastric intolerance, hepatic dysfunction, and zinc deficiency [19] (Figure 4).

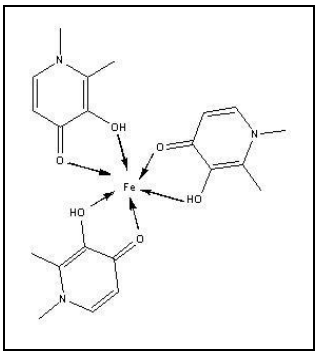

Figure 4: The chemical structure of Deferiprone

CONCLUSION

Deferoxamine is one to one reaction ratio, poor on the complainers and it is highly expensive in cost and it talks three monthly. Deferasirox has a two to one reaction ratio; good on compliance, expensive and it talk one monthly. Deferiprone is three to one ratio to react with iron, good result on the compliance, less cost and it talks three monthly. The synthesis and characterizations and application of this like treatment are a very difficult tax. But the output is incredible. Co-administration of antioxidant (natural or synthetic) or with another chelating agent has shown to improve removal of toxic metals from the system as well as better and faster clinical recoveries. However, we still lack in-depth clinical studies with pre-existing or newer chelating agents in order to understand the mechanism underlying the beneficial effects of antioxidants and to explore optimal dosage and duration of treatment in order to increase clinical recoveries in case of humans.

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