

Electromagnetic Affects and Hemoglobin Synthesis

Dinesh K. Garg, Pranav Pandya, Dhruv Garg*, Aanchal Garg**

Dev Sanskriti Vishwavidyalya, Shantikunj, Haridwar, INDIA

**Department of Electronics and Communication Engineering, Jaypee Institute of Information Technology, Noida, INDIA*

***Department of Biotechnology, Graphic Era University, Dehradun, INDIA*

Abstract: *The hemoglobin is a precious and has great significance in human life. Without hemoglobin human life is not possible because it is a great component of circulatory system to transfer of oxygen to all over body cells. The anemia may be develop due to the low content of hemoglobin and red cell count (RBC) and can create a severe problem in human beings. Anemia is generally caused by some infection, adverse effects of some toxicant, chemical/drugs, free radical (develop in metabolic reaction), some bi-product (pollutants) of motor – sprite as well as electromagnetic waves/ radiations and also genetic disorder. These bi-products inhibit the biosynthesis of hemoglobin at certain levels and create global problem mostly for blood banking and also some harmful hereditary diseases i.e., thalassemia, Banti's disease, Cooley's anemia etc. If the hemoglobin synthesis occurs properly, these genetic disorder/syndromic problems (porphyria) can be minimized and also the WHO problem.*

Key Words: - *Free radicals, carbon mono oxide, hemoglobin synthesis, and electromagnetic toxicant*

I. Introduction

The blood is most precious in human body. Indeed bloodletting represents one of the oldest human efforts of therapy to cure the different disease in eighteen century. It contains different type of cells, protein, liquid plasma, vitamins, carbohydrate, lipids, minerals and large number of micro -molecules including with different hormones in entire circulatory system. Primarily, in embryo at one stage all the blood elements are produced in spleen. After birth, this function is taken over by bone marrow, but if the bone marrow is put out of action, the spleen may resume its hematopoietic role. Undergoing as myeloid metaplasia. It is also believe that spleen also exert a subtle control over blood formation in the marrow possibly by means of a hormone which regulate the maturation of all the blood elements. The spleen remove the aged, damaged or deteriorated element from peripheral i.e. spleen is also known as graveyard or slaughter house of the red cells [1]. Spleen also plays an important role as a reservoir or blood bank when a sudden demand as in violent exercise, asphyxia or hemorrhage. After birth, the bone marrow three type of cells e.g. the erythrocyte (red blood cell, RBC), leukocyte (white blood cells) and the thrombocyte. It seems probable that three cells are derived from primitive mesenchyme, stem cells, the hemocytoblast, which is large and granular basophilic cytoplasm which contain large nucleus and several prominent nucleoli. The cytoplasm has a stroma and a membrane envelope which consists of proteins and lipids with very little amount of carbohydrate. The lipid lies mostly at the surface with an intensely negative charge. The proteins is present in the form of hemoglobin with biconcave disc like cells i.e. RBC in whole plasma. The formation of RBC is depend on the erythropoietin hormones, which is present in a small amount in normal blood and in increase amount in anoxia conditions.

The adult erythrocyte is a carrier of oxygen by the presence of hemoglobin. The erythropoiesis is controlled not only by the level of red cells but also by the level of circulating hemoglobin under the influence of a hormone i.e. erythropoietin (hemopoietin). In a condition of lack or shortage of erythrocyte stimulates specialized cells in the kidney to synthesize and secrete increased amount of erythropoietin into the blood stream. The erythropoietin in turn boosts the production of erythrocyte. The production of erythrocyte i.e. reticulocyte, which than leaves the bone marrow and possess into the blood stream and each reticulocyte will lose its mitochondria and ribosome within one or two days, become a mature RBC(2-3).

Anemia or loss of hemoglobin contents as well as RBC counts may be due to the presence of free radicals and other toxic biomolecule present in human body. The hemolysis or destruction of red cells within the body i.e. intra-corporcular hereditary hemolytic anemia or may be extra corporcular i.e. acquired hemolytic anemia. The impaired production of as in iron deficient and vitamin B and faulty construction of red cells which may be hereditary, as in sick cell and thalassemia or acquired as in any infections, renal failure or irradiation. Some RNA and proteins are abundant in the specialized cells in which they function. Hb (hemoglobin) is expressed specially in red cells, carries O₂ and tyrosine amino transferase enzyme in liver but not in other tissues (4). Hemoglobin consist of a Heme group which covalently attached to cytochrome 'C'. The porphyrin ring have six cytochrome in respiratory chain, each has a different affinity for an electron and a slightly different spectroscopic structure. The synthesis of Heme group play a central part in electron transfer between the

mitochondria and cytoplasm. Iron Sulphur clusters are essential for electron transfer in respiratory chain and also maintenance and stability of nuclear genome which produced in mitochondria. The instability of nuclear genome create the cancer and may sometime be linked to the decreased function of cellular protein that contain iron-Sulphur clusters (5). In new born baby, a dangerous stage of anemia develop hereditary problem of a sickle cell disease called homozygous beta thalassemia major i.e. Cooley Anemia. It is generally found in people in which the complete lack of beta protein in hemoglobin.

Presently, we have observed that hemoglobin synthesis in human beings is a great problem and it is necessary to resolve it and highlighted a focus to develop a healthy human community. There are different factors e.g. malnutrition, poverty, cell sickness, free radical toxicant develop in metabological reactions, drugs/chemical, electronic waves / radiations develop from electronic waste and also mis-metabolism are directly/indirectly affected to the heme synthesis in human beings. These factors create an anemia & severe syndromic as well as carcinogenic hereditary disease. In present paper, we are describing the data which represent the anemic conditions and influence and also generate new great problem in human beings.

II. Materials and Methods

The physiological and physio-chemical data of male and female persons of age group 15-40 years, who are suffering from low hemoglobin content. i.e. anemia were collected from different climatic regions. The female (pregnant as well as non-pregnant) and male persons who are treated under the kind supervision of physician and gynecological expert were considered in present study to observe the cause of anemia as well as some syndromic conditions/disease. The blood samples and data were collected and analyze for different hematological parameters e.g. hemoglobin, RBC, Ht%, platelets, and peripheral blood smear (PBS) were carried out by using auto cell counter, model Sysmex XP-100/A-1, 273, Transacia Company. The biochemical parameters, Blood urea, S. Creatinine, S. Bilirubin, SGPT and S. Calcium were carried out by using autoanalyzer, Erbacam, Em-360 of Transacia Company was used.

III. Result and Discussion

There are two hundred female and two hundred male anemic persons include in present study and divided into 5 different age groups i.e. 15-20, 21-25, 26-30, 31-35 and 36-40 years respectively. Few children (male/female) below 15 yr. of age were also considered as they are anemic in rural areas as well as in slum/semi slum area of urban locality. The female persons (200 total and 40 in each group) include pregnant and non-pregnant women. The observed values of different haematological parameters e.g., hemoglobin (Hb), red blood cell (RBC), hematocrit (Ht %), Platelet count are presented in Fig.1 . The observed value of different biochemical parameters such as blood urea, S. Creatinine (S. creat.), S. Bilirubin, SGPT, S. Calcium are summarized in table-1. The Hb content of all the anemic persons were found in the range of 4.5 to 8.0 gm% (in female) where as in male it was 5.5 to 8.5 gm%. Apart from that in few cases, the hemoglobin content was below 4.5 gm%. Other hematological parameters e.g. Ht %, RBC and platelets count details are also presented in Fig. 1 respectively. The peripheral blood smear details and MCV, MCH, MCHC values were also found low in comparison to normal standard value. The peripheral blood smear study was clearly indicate that most people were hypochromic, microcytic where as in few cases it was pernicious, hemolytic and also macrocytic anemia. In few male as well as female person those taking hematinic salts, the hemoglobin content did not increase significantly i.e. it is a sign of slow synthesis or non-synthesis of heme group. The toxicity, pollution, transportation (surrounding areas- male persons who are servicing in transport corporation) electronic tower/appliances present in their surrounding and using the electronic equipment e.g. mobile/laptop, using LED, sodium, light condition were also considered to determine the causes of anemia because of that these conditions are directly affects the human metabolism as well as physiological activities and produce different free radical and toxic substances/molecule produce in human body. These free radicals are more toxic and inhibit the synthesis pathway. The biochemical parameters observed mean values are summarized in Table-1 (male and female persons) and were found in normal range significantly except S. Calcium level. In few cases the SGPT (ALT, alanine transaminase enzyme) slightly increased whereas S. Bilirubin and bile pigment in urine did not found in increasing order. The S. Calcium ion level was found decrease in comparison to normal standard values.

The total leukocyte counts (WBC) were observed normal while in few cases of severe anemic condition, total leukocyte counts were found decreased in comparison to normal value. The differential count of these WBC were found abnormal, i.e., the Neutrophil polymorph percentage decrease and lymphocyte count slightly increased in few cases. Whereas, the monocyte percentage did not influenced. In few cases of severe anemic person (Hb % is 3.0 to 4.0), the blood urea and serum creatinine level were found increase in comparison to normal standard value and physical sign of edema develop on their body. The internal body temperature slightly increased i.e., up to 99 -100°F for a long period. But their serum bilirubin level did not

influenced. The alanine transaminase (ALT) level slightly increase whereas the serum calcium ion, Ht%, and RBC were also found decrease.

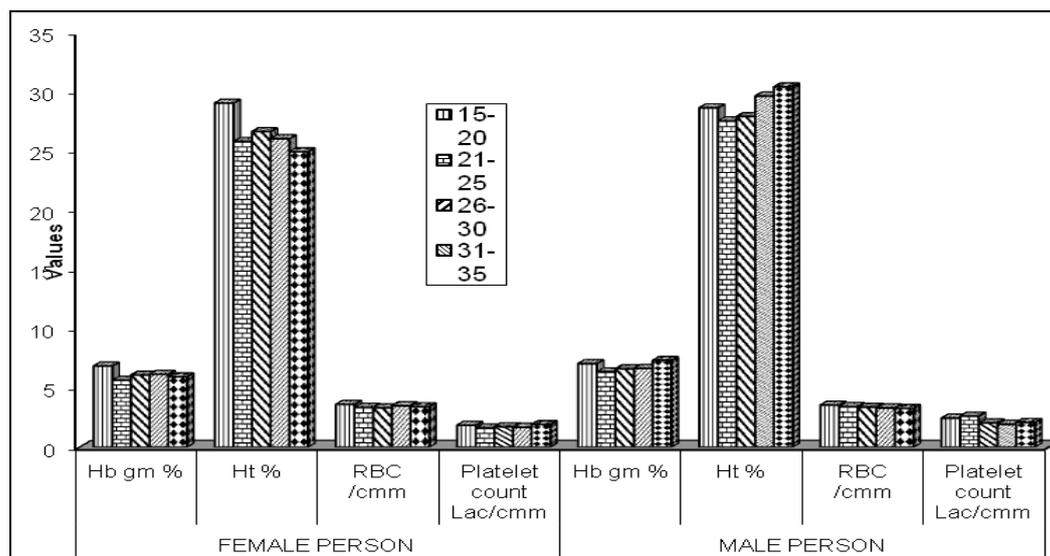


Fig.1: Hematological values of male and female anemic person

Table1: Observed values of Biochemical Parameters of Male and Female anemic Persons

AGE GROUP	MALE					FEMALE				
	Blood Urea mg/dl	S. Creat. mg/dl	S. Bilirubin (Total) mg/dl	SGPT mg/dl	S. Calcium mg/dl	Blood Urea mg/dl	S. Creat. mg/dl	S. Bilirubin (Total) mg/dl	SGPT mg/dl	S. Calcium mg/dl
15-20	20.15 ± 0.07	0.65 ± 0.02	0.25 ± 0.06	17.45 ± 0.65	9.45 ± 0.17	19.25 ± 0.06	0.56 ± 0.02	0.35 ± 0.07	24.15 ± 1.92	8.85 ± 0.27
21-25	19.55 ± 0.06	0.68 ± 0.03	0.42 ± 0.15	19.85 ± 0.43	8.85 ± 0.11	18.33 ± 0.07	0.58 ± 0.03	0.43 ± 0.11	28.85 ± 1.52	9.68 ± 0.35
26-30	23.12 ± 0.11	0.85 ± 0.07	0.65 ± 0.16	24.15 ± 0.31	8.93 ± 0.18	21.12 ± 0.09	0.76 ± 0.09	0.76 ± 0.09	31.18 ± 1.07	8.45 ± 0.24
31-35	21.45 ± 0.15	0.97 ± 0.15	1.08 ± 0.19	31.15 ± 0.65	8.69 ± 0.12	18.45 ± 0.05	0.83 ± 0.09	0.98 ± 0.17	32.07 ± 0.98	8.15 ± 0.21
36-40	24.65 ± 0.19	1.08 ± 0.17	0.95 ± 0.14	37.25 ± 0.95	8.15 ± 0.18	21.45 ± 0.18	0.95 ± 0.13	0.83 ± 0.14	31.55 ± 1.08	8.02 ± 0.35

± = mean value of 40 persons

Those person were residing near electronic tower in rural as well as in urban areas and also using more electronic appliances/devices etc. also should the lower value of Hb% for a long period. Their Hb content did not increase significantly during a long time treatment by some food & hematinic salts. Few persons those are diabetic or non-diabetic and follow some urological problems e.g. nephritis and other syndromic conditions, the hemoglobin content was found low in comparison to normal value. It may be due to the adverse effect of certain medicine/drugs/toxic elements.

In present study, we have observed that the hemoglobin content was found low up to 4.5 gm% (in most cases) and also up to 3.0 gm% (in few anemic persons). It may be due to the slow synthesis process of heme group. It occurred due to the climatic conditions affected by toxic elements, malnutrition, mis-metabolism and some unwanted rays/electronic radiations/waves. Which are always present surrounding us. During the physiological activities and metabolic reaction (oxidation and reduction) takes place in our body, free radical, toxic elements production bi-products and gases develop. These products creates the adverse effect and stimulate the entire physiological conditions. Carbon monoxide gas which is emitted from the combustion of diesel/oil/petrol (as motor spirit) and directly affected to the human beings and other mammals through breathing process. Carbon monoxide emitted in huge quantity and directly react with hemoglobin (Hb). It has great affinity (300 time faster) to absorb with blood i.e. in hemoglobin content and highly toxic to the human physiological conditions. It is a very fast coagulating agent for blood and block the circulatory system. Which causes the atherosclerosis and person get cardiac attack or severe respiratory problem. The supply of oxygen stop to the entire body system including to the brain and person may die. Carbon monoxide is great barrier of circulatory system and cause to stop or inhibit the heme group synthesis directly i.e. it may affect the

mitochondrial as well as ribosomal body where heme synthesis process takes place (6). And these slow process create a long term anemia in human beings, which latter on develop some dangerous and hereditary disease e.g. carcinoma of colon, cancer in any organ, Parkinson disease, respiratory problem (asthma) and also Alzheimer, disease (5, 6).

During this reaction the cardio-thoracic problem, some hormonal effects may develop which inhibit the heme synthesis process as cardiolipin structure and also catalase, peroxidase enzymes. Because of that adults Hb, structurally consist of 4- subunits (i.e. tetramer) which is held by non-covalent interactions; HbA, (2 alpha and 2 beta) is major term Subunit. Each subunit consist of heme (in-Ferro-protophyrin) and globin proteins. The heme is a combination of protophyrin IX and ferrous ion (Fe^{+2}) and globin protein fold as a protective hydrophobic pocket around heme group. The proto porphyrin IX contains 4 pyrrole rings and ferrous ion (Fe^{+2}) form six bonds in which four co-ordination bonds with proto porphyrin and fifth with Imidazole group of histidine on globin and sixth with distal histidine on globin that may be occupied by oxygen in oxy-hemoglobin. But during the effect of carbon monoxide, it effect on oxy-hemoglobin bond due to its great affinity (300 times more than oxygen) to bind with hemoglobin and hemoglobin get poisoned i.e. it affect the heme group synthesis directly. This reaction is just similar to the hydrogen cyanide (HCN) with hemoglobin (7,8). Those persons are living in polluted area where the poisonous gases are generated. The biosynthesis of heme is affected at two stages i.e. 1) at biosynthesis of porphobilinogen and 2) conversion of porphobilinogen to heme which takes places in mitochondria at TCA cycle. Where Delta- aminolevulinic acid (ALA) is formed by the interaction of glycine with succinyl -CoA under the reaction catalyzed by Aminolevulinic acid synthase (ALA Synthase) with pyridoxal phosphate (as B6- phosphate) as cofactor. ALA in mitochondria transported to cytosol which are converted to porphobilinogen by the biochemical reaction as catalyzed by ALA dehydratase. The conversion of porphobilinogen to heme takes place by the condensation of 4- porphobilinogen molecule to form an uroporphyrinogen-I to uroporphyrinogen-III under the catalyzed by synthase-I & co-synthase enzyme respectively in the cytosol and transported into mitochondria finally(9). It seems that the carbon-monoxide is a very toxic gas emitted in the environment by the transport vehicle and industries, which block the heme biosynthesize process in human beings. The heme synthesise regulate as heme biosynthesize occur in erythroid cells and hepatocytes and in RBC it control at ALA synthase, porphobilinogen deaminase Ferro chelatase stages. In the absence of globin, heme oxidize into hemin which contain Fe^{+3} (ferric ions) which also inhibits the transport of ALA synthase from cytosol to mitochondria (a site of action) as well as represses synthesis of enzyme. As Ferro chelatase and ALA synthase are highly sensitive to inhibition by heavy metals (lead etc.). The lead and other toxic molecules poisoning is another factor to decrease the hemoglobin content in anemic person (8).

Similarly, the depletion in RBC and hematocrit value both in male & female persons, observed in all age group clearly indicate that it occurred due to the hemolysis (destruction in RBC) as well as toxic effects of certain factors, which directly influence the formation of red cells in spleen and hemoglobin synthesis process. Later on these factors develop a chronic symptoms i.e. splenomegaly, blood cytopenia (neutropenia, thrombocytopenia, pancytopenia etc.) in human body. The chronic stages of anemia may also develop the Banti's disease i.e. liver cirrhosis with ascites (10-13). These adverse factors may affect the formation as well as development of erythrocyte (RBC) and hemoglobin synthesis process in human being at different stage of biochemical synthesis. Because of that the formation of RBC is that its nucleus to become an immature erythrocyte i.e. articuloocyte which than leaves the bone marrow and passes into the blood stream. The reticulocyte will lose its mitochondria and ribosomes with in a day or two to become a mature erythrocyte (14). During hemoglobin synthesis, some RNA and proteins are abundant in specialized cells in which they function and cannot be detected elsewhere. There are two α and β globin chains that associate to form hemoglobin molecule consisting of two α - chain and two β - chain. If the polluted gas i.e. carbon monoxide affect the human being directly, it absorbs by the blood due to its great affinity very fast and block the hemoglobin synthesis.

As in fetus condition, four oxygen-binding sites in $\alpha_2\beta_2$ molecule interact, allowing a co-operative, allosteric change in the molecule as it binds and release oxygen, which enables hemoglobin to take up and release oxygen more efficiently than single chain version. The β -chain gene apparently underwent duplication and mutation to give rise to a second β -like chain that is synthesized in fetus stages i.e. if oxygen binding breakup by toxic substances/gases (carbon-monoxide) this pathway lose and some hereditary problem may occur, because of the hemoglobin molecule has higher affinity for oxygen and help in the transfer of oxygen from mother to the fetus (15). The genes for new β -like chain subsequently duplicated and mutated again to produce two new genes ϵ and γ , the ϵ chain being produced earlier in development to form $\alpha_2\epsilon_2$ than the fetal γ chain which forms $\alpha_2\gamma_2$. Each of these duplicated gene has been modified by point mutation that affects the properties of the final hemoglobin molecule. These free radicals and other toxic biomolecules threatens the synthesis of heme protein in RBC and may develop the beta- thalassemia i.e. Cooley's Anemia mostly in new born baby, because of that it is a genetic disorder hereditary life threatening disease and needs regular blood

transfusion. The extensive life-long blood transfusion also leads to iron-overload which must be treated with chelating therapy to prevent early death from organ failure (16).

However, the hemolytic anemia may occur due to the malarial parasite as falciparum malaria profound hemolysis which create slightly higher serum bilirubin and creatinine levels. The long period malarial infections causes inhibition of suppressor T-cells which normally regulate IgM production. This leads to uninhibited β -cells production of IgM and the formation of myoglobin (17). In this view, peripheral blood smear show normocytic- normochromic anemia with increase reticulocyte count. It is a factor of splenomegaly syndromic condition and leukopenia and also thrombocytopenia due to the hypersplenism. The intravascular hemolysis can be due to the chronic malaria and create hemoglobinuria i.e. renal function gets affected, hepatic failure can occur in human beings (by great loss of hemoglobin i.e. up to 3.0 gm%)(17).

IV. Conclusion

Hemoglobin has great significance to control the human physiology as it is a carrier of oxygen molecule circulation throughout the human body, which is a basic need for metabolical reactions (oxidation/reduction). During this process some free radical develop and inhibit the biosynthesis of hemoglobin which takes place in mitochondria. At certain stages of biosynthesis process, several adverse reaction occurs due to the toxic substances, electromagnetic waves/ radiations, carbon monoxide gas and causes very harmful disease and hereditary syndromic problems in human beings. The gaseous reaction in blood occur due to the absorption of carbon monoxide content which also inhibit the biosynthesis of hemoglobin. If we prevent such pollutant or minimize the toxic reaction, the biosynthesis of hemoglobin may occur in human beings i.e. the synthesis of blood takes place in human body and can minimize the WHO problems.

Acknowledgement

The technical assistant provided by Dr. Neeraj Jain, Sr. Scientist, CBRI, Roorkee is gratefully acknowledged.

References

- [1]. Dameshek W and Welch C.S., Hypersplenism and surgery of spleen, New York, 1952.
- [2]. Wintrobe M.M., clinical Hematology, Philadelphia, 6th ed. 1967.
- [3]. Molecular Biology of the cell, The Problem Book, John Wilson, pub. By Garland Science Taylore Francis Group, LLC, New York, 6th ed., 1244-45.
- [4]. Molecular Biology of the cell, The Problem Book, John Wilson, pub. By Garland Science Taylore Francis Group, LLC, New York, 6th ed., 371.
- [5]. Molecular Biology of the cell, The Problem Book, John Wilson, pub. By Garland Science Taylore Francis Group, LLC, New York, 6th ed., 760-66.
- [6]. Boyd W "A Textbook of Pathology", Henry Kimpton, 8th Ed., 1970.
- [7]. Text book of biochemistry with clinical co-relation, Ed. By T M Devlin, 4th Ed.
- [8]. Hames B D., Hooper N M., J D Haughton. Instant notes in biochemistry, Blos. Scientific Pub., Springer UK.
- [9]. Musil J., Novakava O and Kunz K., Biochemistry in Schematic Perspective, Avicenum, med. Press Prague, 1977.
- [10]. Pick L: Am. J. med. Sci., 1933, 185, 453.
- [11]. Rich A R, Lewis M R and Wintrobe M M. Bull, Johns Hopkin Hosp., 1939, 65, 311.
- [12]. Wiseman B K and Doan C A: Am. Int. Med., 1942, 16, 1097.
- [13]. Harris J W, and Kellermeyer R W; the Red Cell production metabolism, destruction: Normal and Abnormal, rev. ed. Cambridge Harvard University, Press 1970.
- [14]. Molecular Biology of the cell, The Problem Book, John Wilson, pub. By Garland Science Taylore Francis Group, LLC, New York, 6th ed., 1245.
- [15]. Molecular Biology of the cell, The Problem Book, John Wilson, pub. By Garland Science Taylore Francis Group, LLC, New York, 6th ed., 229.
- [16]. <http://www.dshs.state.tx.US/newborn/Cooley.Sttm>.
- [17]. Bruneel F., Gachot B., Wolff M, Regnier B., Danis M., Resurgence of Black Water fever in Long-Term European Expatriates in Africa, Clinical Infection Disease, 2001; 32: 1133-1140.