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A CRITICAL REVIEW OF PITTADHARA KALA AS MAJJADHARA KALA W.S.R. TO ANAEMIA

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ABSTRACT

Kala is '*dhatwashayanter maryada'* which is not well explained in literature. *Kala* are seven in number which lies in between *dhatu* and *ashaya,* correlated with fibrous, serous and mucous membranes. *Pittadhara kala* is sixth in number, present in between *amashaya* and *pakwashaya* that is *grahani* correlated as Small intestine. This *kala* holds *Pachaka pitta* and *Agni* which promotes complete digestion, assimilation and absorption of the *chaturvidha anna*. *Pittadhara kala* is correlated with the lining membrane of small intestine which plays vital role in digestion and absorption of all nutritive substances like vitamin $B_{12,}$ folate and iron which is the main source of development and maturation of RBCs. *Majja dhatu* is present in the cavity of long bones which is correlated with bone marrow, a major site of RBC production and blood formation. Impaired *pitta dhara kala* causes malabsorption of vitaminB_{12} and iron leading to anaemia. Impaired majjadhara kala will affect the production of RBCs and will also lead to anaemia. Hence this can be one of the reasons that *Acharya Dalhan* had stated *Pittadhara kala as Majjadhara Kala* in chapter '*Sarpadashta visha vigyanam'*.

Keywords: *Pittadhara kala, Majjadhara kala, Grahani*, Vitamin $B_{12,}$ Anaemia, Small intestine.

INTRODUCTION

Ayurveda is the science which is based on various concepts, one of them is *kala* which is considered as an anatomical part only and remained neglected, whereas *kala* is having physiological and clinical relevance. *Kala* is '*dhatwashayanter maryada'* which separates *dhatu* and *ashaya*. There are seven *kalas* explained in *samhita* whereas *pittadhara kala* is on sixth, which is present in between *pakwashaya* and *amashaya* i.e. *grahani*, and which is correlated as small intestine. *Grahani* not only store the *chaturviddhaanna* but also promotes complete digestion, assimilation and absorption with the help of *pachaka pitta* which is produced by *pittadharakala* with the help of *samanvayu*.

Small intestine is present in between stomach and large intestine, which is the major site of digestion and absorption of all nutritive substances like Vitamin $B_{12,}$ iron, folic acid, cobalt, manganese, calcium and proteins into the peripheral blood circulation. *Majjadhatu* is present in the cavity of long bones and which is cor-

related with bone marrow. The function of bone marrow is production and maturation of the RBCs i.e. erythropoiesis.

For production and maturation of RBCs body needs Vitamin B_{12}, iron and folate which are absorbed from *grahani* which is nothing but *pittadhara kala*. Through blood circulation these factors reaches to the bone marrow which is correlated with *majja dhatu* where they get utilized in the formation of RBC and lack of these factors leads to anaemia. During the stages of development and maturation of RBC megaloblast is converted into primary erythroblast in presence of VitaminB_{12} and folate and primary erythroblast is converted into normoblast in presence of iron, copper, cobalt and other metals. Vitiation of bone marrow will lead to impairment of RBCs production and vitiation of small intestine lead to alter the maturation of RBCs ultimately resulting anaemia.

Acharya Dulhan stated that *pittadhara kala* as *majjadhara kala* in *sarpadashtavisha adhyaya* in *kalpasthana* of *sushrut samhita* because both the *kala* plays vital role in RBC production. So this attempt is made to correlate *pittadhara kala* as *majjadhara kala* w.s.r. to anaemia.

AIM

To study *pittadhara kala* as *majjadhara kala* w.s.r. to anaemia.

OBJECTIVE

1. To study *kala* and *pittadhara kala*.
2. To study absorption of influencing factors responsible for erythropoiesis from small intestine i.e. pittadhara kala
3. To study utilization of these factor during erythropoiesis in bone marrow.
4. To correlate *pittadhara kala* as *majjadhara kala* w.s.r.to anaemia.

REVIEW OF LITERATURE

KALA

Kala is '*dhatwashayanter maryada'* which separates *dhatu* and *ashaya*[1]. The *ashaya* is cavity which gives *ashraya* to the *Dosha*, *Dhatu* and *Mala* [2]. *Snayu*, *jarayu* and *shleshma* are the three basic principles in the formation of *kala,* these three structures can be compared with fiber, serous and mucous layers respectively [3]. *Kala* are the pith of the stem in the tissues. While describing *kala*, it is said as the duramen of cores of a piece of wood or stem becomes exposed to view by cutting into it, so the *dhatus* of the body may be seen by removing the successive layers. These *kalas* are extensively supplied with *snayus* bathed in *jarayu* and encased in *shleshma*[4]. Acharaya Vagbhata says the *kleda* which is lies in the internal part of the *ashaya* that becomes *pakwa* by *dhatwagni* and forms as *kala*[5]. It covers the internal and external layers of the organ, and it may separate the muscle. It helps for holding, movement, supporting, absorption and lubrication in the different parts of the body [6].There are seven *kalas* explained in *samhita*.

PITTADHARA KALA

Pittadhara kala is on sixth number which is said to be lies in between *Amashaya* and *Pakwashaya* i.e. *Grahani*, which is correlated as small intestine [7]. *Grahani* not only store the *chaturviddha anna* propelled from the *amashaya* and on its way to the *pakvashaya*[8], but also promotes complete digestion, assimilation and absorption with the help of *Pachaka pitta* which is secreted by *pitta dhara kala*[9]. *Amashaya* is the part before the small intestine i.e. stomach of modern anatomy. *Grahani* is a *sthan* of *pachakagni* which helps in digestion of food [10]. After digestion of food *Ahar* is converted into *Aharras* which is then absorbed by the *pittadhara kala* for the further nourishment of the seven *dhatus*[11].

MAJJA DHATU

It is the sixth tissue in *ayurveda* which corresponds to bone marrow. It is present in cavity of the long bones [12]. The *Vayu mahabhut* creates spaces in the bone and these spaces are filled up with the *snigdhaamsa* of *medas* as a *Majja*[13]. The function of *majja dhatu* is to provide unctuousness, strength and nourishment to *shukradhatu* and fills *asthi dhatu*[14].

PITTADHARA KALA* AS *MAJJADHARA KALA

Dalhan had stated that *Pittadhara kala as Majja dhara Kala [15]*. When *vishvega* enter sixth *kala* i.e. *majja dhara kala* it vitiates *Grahani* and show the symptoms like heaviness in the body, dysentery, pain in heart and syncope [16].

SMALL INTESTINE

It is the part which is present in between stomach and large intestine having three parts i.e. duodenum, ileum and jejunum. The intestinal wall has serous, muscular, sub mucous and mucous layers. The submucous is a loose connective tissue carrying blood vessels, lymphocytes and nerves. The mucosa of the small intestine is lined by a simple columnar epithelium which consists primarily of absorptive cells i.e. enterocytes with scattered goblet cells and occasional enteroendocrine cells. The enterocytes secrets enzymes, goblet cells secrets mucus,enteroendocrine cells secretes intrinsic factor of castle, paneth cells secrete cytokines and Brunner glands secrets mucus and enzymes[17]. The columnar epithelial cells forms circular folds and the whole surface is covered by filiform or linguiform intestinal villi. The circular folds are large, crescentic folds of mucosa which project into the intestinal lumen. These folds slow down the passage of contents and increase the absorptive surface. Intestinal villi are highly vascular processes just visible by the naked eye and project from the entire intestinal mucosa. Small intestine is the major site of digestion and absorption from where all nutritive substances are absorbed like vitamin B12, folic acid, iron, cobalt, copper, manganese, calcium and proteins [18].

Absorption of vitamin B $_{12}$[19]

Vitamin B_{12} is called extrinsic factor since it is obtained from dietary supplement. Its absorption from intestine requires the presence of intrinsic factor of castle which is secreted by parietal cells of gastric gland and makes it available for absorption by the small intestine. Vitamin B_{12} is important for the formation and maturation of red blood cells. Within the stomach, the Vitamin B_{12} is released from the food by proteolytic enzymes (proteases). The freed Vitamin B_{12} now combines with R binders obtained from saliva. In the small intestine, pancreatic enzymes remove 'R binders' and the freed Vitamin B_{12} now combine with IF. IF is secreted by parietal cells of the stomach which secretes HCL. The Vitamin B_{12}-IF complex is resistant to digestion and travels down to reach lower part of ileum. In the membrane of the epithelial cells of the terminal part of ileum receptors for Vitamin B_{12}-IF complex exist the complex is taken up by cubilin part of these receptors, and the complex is absorbed by the enterocytes. After absorption from the intestine, Vitamin B_{12} being bound with transcobalamin II (β globulin) goes to the liver where it is stored. From the liver, the Vitamin B_{12} goes to red bone marrow when the need of Vitamin B_{12} is very high.

Absorption of Iron [20]

Iron is important for the formation of hemoglobin. Dietary iron is available in two forms called heme and non heme. Iron is absorbed mainly from the duodenum of the small intestine through the intestinal cells called as enterocytes by pinocytosis and transported into the blood. Bile is essential for the absorption of the iron. Hydrochloric acid from gastric juice makes the ferrous iron soluble so that it could be converted into ferric iron by the enzyme ferric reductase from enterocytes. From enterocytes, ferric iron is transported into the blood by a protein called ferroportin. In the blood ferric iron is converted into ferrous iron and transported into the blood.

Absorption of Folic Acid [21]

The form of folic acid occurring naturally in food is called folate. It is essential for the formation of DNA, RNA and metabolic amino acids. Folic acid is essential for final maturation of the red blood cells folate is mainly absorbed in the duodenum and jejunum.

BONE MARROW

Bone marrow is a semisolid tissue which may be found within the spongy or cancellous portions of bones which is the site of new blood cell production [22]. In the bone marrow are cells called pluripotential hemopoietic stem cells, these cells are the primitive cells in the bone marrow, which give rise to the blood cells. In early stages, the PHSC are not designed to form a particular type of blood cell hence the name uncommitted PHSC. When the cells are designed to form a particular type of blood cell, the uncommitted PHSCs are called committed PHSCs. The different committed stem cells, when grown in culture, will produce colonies of specific types of blood cells. Committed stem cell that produces erythrocytes is called a colony-forming unit-erythrocyte (CFU-E).

Changes during erythropoiesis [23]

Cells of CFU-E pass through different stages and finally become the matured RBCs. During these stages four important changes are noticed.

1. Reduction in size of the cell (from the diameter of 25 to 7.2 μ)
2. Disappearance of nucleoli and nucleus.
3. Appearance of hemoglobin.
4. Change in the staining properties of the cytoplasm.

Factors necessary for erythropoiesis are:

1. General factors: Erythropoietin, Thyroxin, Hemopoietic growth factors and Vitamins
2. Maturation factors: Vitamin B_{12}, intrinsic factor and folic acid are necessary for the maturation of RBCs.
3. Factors necessary for hemoglobin formation:

Stages of erythropoiesis

Various stages between CFU-E cells and matured RBCs are –

1. Primary erythroblast
2. Early normoblast
3. Intermediate normoblast
4. Late normoblast
5. Reticulocyte
6. Matured erythrocyte

Folic acid works closely with vitamin B_{12} in making red blood cells and helps iron function properly in the body. The normal proliferation of cells depends on adequate folate and vitamin B_{12} . Folate is necessary for efficient thymidylate synthesis and production of DNA. Vitamin B_{12} is needed to successfully incorporate circulating folic acid into developing RBCs, retaining the folate in the RBCs [24].

Primary erythroblast (megaloblast)

It is the first cell derived from CFU-E having large size with diameter of about 20μ, having large nucleus occupies the cell almost completely. Proerythroblast multiplies several times and finally forms the early normoblast. Synthesis of hemoglobin starts in this stage. Erythroblast requires folate and vitamin B_{12} for proliferation during their differentiation. Vitamin B_{12} and folate helps to make DNA, the genetic material in all cell[24]. Deficiency of vitamin B_{12} and folate inhibits purine and thymidylate synthesis, impared DNA synthesis would be expected to result in chromosomal breakage and possibly nuclear damage causes erythroblast apoptosis resulting in anaemia from ineffective erythropoesis. Erythroblasts requires large amount of iron for hemoglobin synthesis which starts in this stage [25].

Early normoblast[26]

It is smaller than Proerythroblast with a diameter of about 15μ. In the nucleus, the nucleoli disappear, condensation of chromatin network occurs which is essential for cell differentiation and liberate more spaces for hemoglobin enrichment.

Intermediate normoblast[26]

It is smaller than the early normoblast with a diameter of 10 to 12μ. The nucleus is still present; the chromatin network shows further condensation. Hemoglobin starts appearing.

Late normoblast[26]

It is smaller than intermediate normoblast with a diameter of about 8 to 10μ. Nucleus becomes very small with very much condensed, dark and clumped chromatin network, ready to be extruded. Once it is extruded, the cell is known as a reticulocyte. Quantity of hemoglobin increases. In the final stage of late normoblast just before it passes to next stage, the nucleus disintegrates and disappears.

Reticulocyte[26]

In this stage RBCs are immature and slightly larger than matured RBCs. The cytoplasm contains the reticular network which is formed by remnants of disintegrated organelles so the cell is called reticulocyte. During this stage the cell enter the blood capillaries through capillary membrane from the site of production.

Matured erythrocyte [26]

Reticular network disappears and the cell becomes the mature RBC and attains the biconcave shape with size 7.2μ diameter. The matured RBC is with hemoglobin but without nucleus.

ANAEMIA [27]

The impaired RBCs production and destruction of defective RBCs in the bone marrow before release

into the peripheral blood (ineffective erythropoesis) results in an anaemia.

- Due to deficiency of nutritive substances necessary for erythropoesis like iron, protein, vitamin B_{12} and folic acids leads to nutritional deficiency anaemia.
- Due to inadequate availability of iron for hemoglobin synthesis results into iron deficiency anaemia.
- Due to deficiency of proteins, the synthesis of hemoglobin is reduced leads to protein deficiency anaemia.
- Due to deficiency of vitamin B_{12} occurring as a result of failure of secretion of intrinsic factor leads to pernicious anaemia.
- Due to deficiency of vitamin B_{12} and folic acid which is the maturation factor leads to megaloblastic anaemia.
- Due to disorder of redbone marrow aplastic anaemia is produced.

DISCUSSION

1. **Role of *Pittadhara kala* in anaemia:**

- *Pittadhara kala* is present between *amashaya* and *pakwashaya* i.e. *grahani* which is correlated as small intestine.
- Small intestine is the major site of digestion and absorption from where all nutritive substances are absorbed like vitamin B_{12}, folic acid, iron, cobalt, copper, manganese, calcium and proteins.
- Intrinsic factor of castle is secreted by the parietal cells of the stomach and enteroendocrine cells of small intestine which helps in absorption of vitamin B_{12}. Due to failure of secretion of intrinsic factor megaloblastic anaemia occur.
- Structural abnormality in small intestine and gastric mucosa develops mal-absorption syndrome which includes crohn's disease, tropical sprue, due to all these conditions there is lack of absorption of erythropoietic factors which are responsible for development and maturation of RBCs leads to pernicious anaemia.

2. **Role of Majja dhatu in anaemia:**

- Majja dhatu is correlated with bone marrow which is present in cavity of long bones where erythropoiesis occurs.
- Any kind of disorder in bone marrow cannot produce RBCs resulting in aplastic anaemia.
- vitamin B_{12} and folic acid are absorbed in small intestine which is utilized in the bone marrow during first stage of erythropoiesis i.e. megaloblast and these helps to make DNA a genetic material. Lack of these vitamins causes diminished DNA and consequently failure of nuclear maturation and division of RBC.

3. **Pitta dhara kala as Majja Dhara kala:**

Small intestine is the major site of absorption of all nutrients where as bone marrow is the site of production of blood cells.

Efficient absorption of vitamin B_{12}, folic acid and iron, which are the influencing factors of blood formation results in healthy and matured RBCs in bone marrow by the process erythropoiesis.

4. **Vishvega Avastha:**

Acharya Sushruta has mentioned *Kala* which lies in between *dhatu* and *ashaya.* After snake bite the visha (poison) enters from one dhatu to another through kala and manifest into vega. It vitiates *Dhatu* and its respective *Kala*. When visha penetrates majja dhatu (bone marrow) through majjadhara kala it deranges the grahani giving rise to a sense of heaviness of the limbs, dysentery, and pain in heart and syncope.

CONCLUSION

As both the sites plays vital role in formation and maturation of RBCs and vitiation of any one of these may lead to anaemia so this may be one of the reason that *Acharya Dalhana* had stated *Pitta dhara kala* as *majja dhara kala.*

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