

## IMPORTANCE OF INVESTIGATIONS IN AYURVEDA W.S.R TO VITAMIN B12 DEFICIENCY IN PATIENTS OF GRAHANI

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### ABSTRACT

*Ayurvedic* science is based on very strong basic principles of its own and has unique way of ascertaining a disease. Use of investigations in *Ayurveda* have been controversial. But there are various conditions in which the use of investigations have turned out to be beneficial and supportive to the *Ayurvedic* parameters. A comprehensive literature search was thus conducted and an observational, analytical study based on Authentic *Ayurvedic* texts, modern texts and Internet sources was done. Data was collected and analysed for further discussion and for conclusion to be drawn. In this attempt the role of investigations as an aid has been put forth with reference to *grahani*. In *grahani*, as absorption is hampered there is a possibility of Vitamin B12 (Cobalamin) deficiency which can be confirmed only through an investigation. When Investigations are not to be fully relied upon they should also not be fully neglected as well. Considering the opinion put forth by *Sushrutaacharya* that a *chikitasaka* may decide on a condition based also on preachings of other *shastras* and not on one's own shastra alone (*sushruta samhita.sutra sthana.4<sup>th</sup> chapter/7<sup>th</sup> shloka*) there is no harm in making use of investigations. It is with the help of these investigations that Vitamin B12 deficiency gets detected and further complications can be avoided in patients of *grahani*. Hence, investigations could be taken into consideration without deviating from the principles laid down by the science, *Ayurveda*.

**Keywords:** Investigations, Malabsorption, *Grahani*, Vitamin B12

### INTRODUCTION

Use of investigations in *Ayurveda* has always been a subject of debate. But there are various conditions in which the use of investigations has turned out to be beneficial and supportive to the diagnosis made purely on the basis of *Ayurvedic* parameters. Vitamin B12 deficiency is a commonly found feature, these days, in the people with vegan diet. It is because these people lack animal products in their diets including milk, major source of this vitamin being food of animal origin, e.g., meat, fish, and dairy products. Vegetables, fruits, and other foods of non animal origin are free from Cobalamin unless they are contaminated by bacteria. But Cobalamin deficiency is usual-

ly due to malabsorption. The only other cause is inadequate dietary intake. *Grahani roga* as explained in classics exhibits dysfunctioning of digestive system followed by elimination of either formed or incompletely formed faeces. Therefore, patients of *Grahani* are likely to be prone to Vitamin B12 deficiency.

**Materials and Methods** - A comprehensive literature search was conducted. It is an observational and analytical study based on Authentic *Ayurvedic* texts, Modern texts and Internet sources. Data was collected and analysed for further discussion and conclusion to be drawn.

**Role of Investigations in *Ayurveda***

Ayurvedic science is based on very strong basic principles of its own and has unique way of ascertaining a disease and its diagnosis. Yet there are certain areas where the diagnosis could be entirely correct but treatment may not be yielding any results. For instance, *Pandu* could be as a result of Iron deficiency Anaemia, megaloblastic Anaemia, hemolytic anaemia or due to anaemia of Chronic disorders etc. Similarly Investigations may also be useful for following the prognosis in a patient. For example, keeping a check on Blood sugar levels in patients of Diabetes Mellitus. On the other hand, matter of factly, when Investigations are not to be fully relied upon they should also not be fully neglected as well. Investigations also help in preventing the further consequences or *Upadrava* that might occur because of a prevailing disease as in case of *Grahani* wherein deficiency of Vitamin B12 might occur leading to further complications.

#### **Disorders of Absorption and Grahani**

Disorders of absorption constitute a broad spectrum of conditions with multiple etiologies and varied clinical manifestations. Almost all of these clinical problems are associated with diminished intestinal absorption of one or more dietary nutrients and are often referred to as the malabsorption syndrome.

Malabsorption is faulty absorption of nutrient materials from the alimentary canal (malassimilation). Malabsorption occurs when the small intestine is unable to transport broken down products of digestive materials from the lumen of the intestine into the lymphatics or mesenteric veins, where they are distributed to the rest of the body.

In *grahani roga* due to *durbala agni* there is elimination of *pakavaama mala* as there occurs *vidaha* of the *anna*. Therefore, there is *atisrushta* or *vibadha* or *drava mala pravrutti*.

(*charaka samhita, chikitsa sthana, 15<sup>th</sup> chapter/ 52<sup>nd</sup> -53<sup>rd</sup> shloka*)

Thus, the disorders of absorption exhibiting the cardinal feature of *grahani* (“*muhurbadham muhurdravam*”) can be incorporated under *grahani* – as a disease or *grahani* can be considered as one of the features found in some of the disorders of absorption, such as Irritable Bowel Syndrome, tropical sprue etc. In simple words, in either case, the pathophysiology occurring is that of Malabsorption and this defect in absorption could be of any nutrient be it macro or micro.

#### **Absorption of Vitamin B12**

Two mechanisms exist for cobalamin absorption. One is passive, occurring equally through buccal, duodenal, and ileal mucosa; it is rapid but extremely inefficient, with <1% of an oral dose being absorbed by this process. The normal physiologic mechanism is active; it occurs through the ileum and is efficient for small (a few micrograms) oral doses of cobalamin, and it is mediated by gastric intrinsic factor (IF). Dietary cobalamin is released from protein complexes by enzymes in the stomach, duodenum, and jejunum; it combines rapidly with a salivary glycoprotein that belongs to the family of cobalamin-binding proteins known as haptocorrins (HCs). In the intestine, the haptocorrin is digested by pancreatic trypsin and the cobalamin is transferred to Intrinsic factor (IF).

IF (gene at chromosome 11q13 coding for 9 exons) is produced in the gastric parietal cells of the fundus and body of the stomach, and its secretion parallels that of hydrochloric acid. Normally, there is a vast excess of IF. The IF-cobalamin complex passes to the ileum, where IF attaches to a specific receptor (cubilin) on the microvillus membrane of the enterocytes. Cubilin appears to traffic by means of amniolless (AMN), an endocytic receptor protein that directs sublocalization and endocytosis of cubilin with its ligand

IF- cobalamin complex. The cobalamin-IF complex enters the ileal cell, where IF is destroyed. After a delay of about 6 h, the cobalamin appears in portal blood attached to transcobalamin (TC) II. Between 0.5 and 5 g of cobalamin enter the bile each day. This binds to IF, and a major portion of biliary cobalamin normally is reabsorbed together with cobalamin derived from sloughed intestinal cells. Because of the appreciable amount of cobalamin undergoing enterohepatic circulation, cobalamin deficiency develops more rapidly in individuals who malabsorb cobalamin than it does in vegans, in whom reabsorption of biliary cobalamin is intact.

Owing to the mechanism of absorption of Vitamin B12 it can be said that small intestines play a major role in its absorption, especially Ileum, along with stomach, liver and gall bladder. Thus, basically the entire digestive mechanism if does not function properly it leads to improper digestion and malabsorption leading to its deficiency. The pathophysiology in the occurrence of *grahani* as stated above if is taken into consideration it can be said that as the defect lies in the absorption, the absorption of Vitamin B12 is also most likely to be hampered in the patients of *grahani*. Hence, in the patients of *Grahani* the deficiency of Vitamin B12 should be looked for because its deficiency may further lead to various other complications as follows. Also, *grahani*-like signs and symptoms are found in various diseases as stated above, which are also the causes responsible for Vitamin B12 deficiency.

#### **Clinical presentation of cobalamin deficiency**

Vitamin B12 deficiency causes a wide range of hematological, gastrointestinal, psychiatric and neurological disorders. Megaloblastic anemia is a common early symptom leading to the diagnosis, although neurological symptoms may occur in the absence of he-

matological abnormalities.

**Epithelial Surfaces**-After the marrow, the next most frequently affected tissues are the epithelial cell surfaces of the mouth, stomach, and small intestine and the respiratory, urinary, and female genital tracts. The cells show macrocytosis, with increased numbers of multinucleate and dying cells. The deficiencies may cause cervical smear abnormalities.

**Complications of Pregnancy**-The gonads are also affected, and infertility is common in both men and women with either (cobalamin or folate) deficiency. Maternal folate deficiency has been implicated as a cause of prematurity, and both folate deficiency and cobalamin deficiency have been implicated in recurrent fetal loss and neural tube defects.

**Cardiovascular Disease**- Coronary heart disease is produced due to atherosclerosis of coronary arteries and it is suspected that one of the risk factors of atherosclerosis is high level of homocysteine. However, Methionine is harmless substance. (Vitamin B12 converts homocysteine into harmless substance methionine). Children with severe homocystinuria (blood levels  $\geq 100 \mu\text{mol/L}$ ) due to deficiency of one of three enzymes, methionine synthase, MTHFR, or cystathionine synthase, have vascular disease, e.g., ischemic heart disease, cerebrovascular disease, or pulmonary embolus as teenagers or in young adulthood.

**Neurologic Manifestations** - Cobalamin deficiency may cause a bilateral peripheral neuropathy or degeneration (demyelination) of the posterior and pyramidal tracts of the spinal cord and, less frequently, optic atrophy or cerebral symptoms.

The patient, more frequently male, presents with paresthesias, muscle weakness, or difficulty in walking and sometimes dementia, psychotic disturbances, or visual impairment. Long-term nutritional cobalamin deficiency

in infancy leads to poor brain development and impaired intellectual development.

An important clinical problem is the non anemic patient with neurologic or psychiatric abnormalities and a low or borderline serum cobalamin level. Associations between lower serum folate or cobalamin levels and higher homocysteine levels and the development of decreased cognitive function and dementia in Alzheimer's disease have been reported.

Hematologic findings in peripheral blood - Oval macrocytes, usually with considerable anisocytosis and poikilocytosis, are the main feature. The MCV is usually  $>100$  fL unless a cause of microcytosis (e.g., iron deficiency or thalassemia trait) is present. Some of the neutrophils are hypersegmented (more than five nuclear lobes). There may be leukopenia due to a reduction in granulocytes and lymphocytes, but this is usually  $>1.5 \times 10^9/L$ ; the platelet count may be moderately reduced, rarely to  $<40 \times 10^9/L$ . The severity of all these changes parallels the degree of anemia. In a non anemic patient, the presence of a few macrocytes and hypersegmented neutrophils in the peripheral blood may be the only indication of the underlying disorder.

Bone marrow - In a severely anemic patient, the marrow is hypercellular with an accumulation of primitive cells due to selective death by apoptosis of more mature forms. The erythroblast nucleus maintains a primitive appearance despite maturation and hemoglobinization of the cytoplasm. The cells are larger than normoblasts, and an increased number of cells with eccentric lobulated nuclei or nuclear fragments may be present. Giant and abnormally shaped metamyelocytes and enlarged hyperpolyploid megakaryocytes are characteristic. In less anemic patients, the changes in the marrow may be difficult to recognize.

Chromosomes – Deficiency of Vitamin B12 (in association with folic acid) causes defective DNA synthesis (that is, defective chromosomal synthesis) in the precursors of RBC leading to diminution of cell division and maturation but normal formation of cytoplasm resulting in megaloblast and ultimately macrocyte.

Ineffective hematopoiesis - There is an accumulation of unconjugated bilirubin in plasma due to the death of nucleated red cells in the marrow (ineffective erythropoiesis). Other evidence for this includes raised urine urobilinogen, reduced haptoglobins and positive urine hemosiderin, and a raised serum lactate dehydrogenase.

Other effects of cobalamin deficiency - Cobalamin deficiency may sometimes result in defective bactericidal activity, and increased susceptibility to *Mycobacterium tuberculosis* may occur for poorly understood reasons.

As the effects of Vitamin B12 deficiency on the human body are enormous, there is a need for investigations to be carried out to rule out the deficiency of Vitamin B12 in the patients of *Grahani*. Thus, the investigations play a major role in diagnosis, prognosis of any disease as well as in avoiding the complications.

#### **Diagnosis of cobalamin deficiencies**

The diagnosis of cobalamin or folate deficiency has traditionally been depended on the recognition of the relevant abnormalities in the peripheral blood and analysis of the blood levels of the vitamins.

Serum cobalamin -This is measured by an automated enzyme-linked immunosorbent assay (ELISA). Normal serum levels range from 118–148 pmol/L (160–200 ng/L) to 738 pmol/L (1000 ng/L). In patients with megaloblastic anemia due to cobalamin deficiency, the level is usually  $<74$  pmol/L (100 ng/L). In general, the more severe the deficiency, the lower the serum cobalamin level. In patients with spinal cord

damage due to the deficiency, levels are very low even in the absence of anemia. Values between 74 and 148 pmol/L (100 and 200 ng/L) are regarded as borderline. They may occur, for instance, in pregnancy, in patients with megaloblastic anemia due to folate deficiency. The serum cobalamin level is sufficiently robust, cost-effective, and most convenient to rule out cobalamin deficiency in the vast majority of patients suspected of having this problem.

Schilling test (Radioisotope absorption test) – it is done to detect Vitamin B12 deficiency as well as to detect lack of IF and malabsorption.

Serum enzyme levels - methylmalonate and homocysteine - In patients with cobalamin deficiency sufficient to cause anemia or neuropathy, the serum MMA level is raised. Sensitive methods for measuring MMA and homocysteine in serum have been introduced and recommended for the early diagnosis of cobalamin deficiency, even in the absence of hematologic abnormalities or subnormal levels of serum cobalamin. Serum homocysteine is raised in both early cobalamin and folate deficiency but may be raised in other conditions. Thus, homocysteine levels are not used for diagnosis of cobalamin or folate deficiency.

#### OTHER TESTS

Studies of cobalamin absorption once were widely used, but difficulty in obtaining radioactive cobalamin and ensuring that IF preparations are free of viruses has made these tests obsolete. Tests to diagnose Pernicious Anaemia (PA) include serum gastrin, which is raised, and serum pepsinogen I, which is low in PA (90–92%) but also in other conditions. Tests for IF and parietal cell antibodies are also used as well as tests for individual intestinal diseases.

#### CONCLUSION

Based on the above discussion that has been put forth it can be said that Investigations thus carried out in patients of *grahani* may help in preventing the complications caused by the deficiency of Vitamin B12. Investigations in Ayurveda can therefore prove to be beneficial and thus when Investigations are not to be fully relied upon they should also not be fully neglected as well. As rightly said by *Sushrutacharya* that a *chikitasaka* may decide on a condition based also on preachings of other *shastras* and not on one's own *shastra* alone, investigations could be taken into consideration without deviating from the principles laid down by the science, Ayurveda

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