

Role of Cobalamin in treating Pernicious Anemia

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Abstract:

Pernicious anemia (PA) which is also known as Biermer's disease is a type of disorder caused by deficiency of cobalamin (vitamin B12) and is also responsible for removal of myelin sheath at neurological sites. It's a very fatal disease if not diagnosed early may get other body systems malfunctioning. Its diagnosis must therefore be evoked and considered in the presence of neurological and hematological manifestations of undetermined origin. Biologically, it is characterized by the presence of anti-intrinsic factor antibodies. Its also seen that its most prominent in > 30 years of age and is also found in 4-28 months infants causing another type of megaloblastic pernicious anemia there. As along with treatment a daily intake of B12 rich food supplements can play a vital role in reducing a risk of PA to some extent. As vitamin B12 can help repairing the myelin sheath which reduces the neurological disorders related with pernicious anemia. In the present scenario we are updating with most of the facts and role of vitamin B12 in treating pernicious anemia.

Keywords: pernicious anemia, Biermer's disease, cobalamin, intrinsic factor, megaloblastic, macrocytic, myelopoiesis.

Introduction:

Pernicious anemia is a condition in which body is not able to make RBCs and also lacks vitamin B₁₂. Lacking of vitamin B₁₂ occurs due to the lack of gastric protein called intrinsic factor. As 'pernicious' means 'deadly' so it is a fatal disease which gradually grows inside body and affecting various other body systems. There exists a rare form of pernicious anemia in which babies are born without or in deficiency to produce intrinsic factor. But in most of the cases and studies its seen that pernicious anemia tends to occur after age of 30-35 years. This disease if remained undiagnosed or undetected may lead to neurological related aftereffects as nerve cells and blood cells both need vitamin B₁₂ to function. Pernicious anemia retaining in body for long time may cause damage to heart, nerves and brain. As moving towards the symptoms and signs of pernicious anemia in an affected body may include; 'Addison-bernier anemia', 'Addisonian pernicious anemia', 'Addison's anemia', 'primary anemia'. Other symptoms which are easily visible or recognizable are fatigue, shortness of breath, rapid heart rate etc. The following disease can be recognised through clinical evaluation and detailed report of patient's history which include intestine's ability to absorb vitamin B12. The risk of pernicious anemia can be slowed down or reduced by taking a proper diet of food containing vitamin B12. Vitamin B12 or cobalamin is the largest and most complex of all vitamins. The following vitamin must be taken through foods like eggs, meat, beef, chicken, yogurt, cheese, fortified breakfast etc. As many researches and studies found that people consuming more of cobalamin containing foods are away from the risk of pernicious anemia, especially women and elderly people above age of 60 years must take foods containing cobalamin on daily diet basis as these two categories lie in a high-risk zone of getting affected by pernicious anemia. [1]

Pernicious Anemia: An Overview

Pernicious anemia is a type of macrocytic disease (increase in the size of RBCs also known as megalocytosis or macrocythemia) which is caused due to deficiency of vitamin B12 whose deficiency is caused by lack of intrinsic factor. As per studies pernicious anemia is mainly a disease caused in elderly but as far as percentage of younger ones is concerned they contribute to 15% of the total affected population. Pernicious anemia usually infests more than 30 years of age (usually

adults >60 years of age) and has its influence on both the sexes equally. Also, pernicious anemia is associated with Atrophic Body Gastritis (ABG) and it is the end stage of ABG [2]. As pernicious anemia is last juncture of autoimmune process, it results in the severe damage to oxyntic gastric mucosa [3]. The long retainment of *Helicobacter pylori* (*Helicobacter pylori* is a gram-negative bacterium that causes chronic inflammation in the stomach and duodenum and is often termed as ulcer bacteria) infection in pathogenesis of pernicious anemia and ABG has been recorded in recent studies, but still it's in debate that pernicious anemia may be included in long term consequences of *Helicobacter Pylori Gastritis* [4]. Patients usually suffer from symptoms of anemia with pallor, fatigue, lightheadedness, with decreased mental concentration. Glossitis is a frequent sign of megaloblastic anemia (condition in which the bone marrow produces unusually large, structurally abnormal, immature red blood cells that is megaloblasts) in which patient tends to have red, smooth and painful tongue. The rising of bilirubin levels caused by ineffective erythropoiesis appears as jaundice. Patients may also develop neurological symptoms in which nerves other than brain and spinal cord (peripheral nervous system) is affected and sometimes the spinal cord may also take part in this. Some people become irritating and extremely depressed and some may suffer from Paranoia (megaloblastic madness). Autoimmune diseases like Autoimmune thyroid disease, Type 1 diabetes mellitus and vitiligo can also be noticed in same manner. [5]. In age group from 4 to 28 months another form of pernicious anemia that is Juvenile anemia is seen. Most affected infants are developing a form known as megaloblastic anemia in which large, immature RBCs are incapable of delivering oxygen to body tissues and other cells (white blood cells and platelets) are also affected in the same manner (pancytopenia). It is also seen that mental retardation is very frequent in infants along with juvenile pernicious anemia. The infants affected are facing the repeated episodes of extreme anemia and jaundice. As talking about the individuals suffering from congenital form have almost similar symptoms as juvenile anemia but the process of rupturing is comparatively slower. Symptoms may include weakness, shortage of breath and abnormal high heart rate. Affected ones may also have some gastrointestinal problems like lack in appetite, abdominal pain and many more. Some people suffering from pernicious anemia may have swollen liver or spleen and problems involving urinary functions may also develop. This disease is most common in northern Europe, Scandinavia, and

north America than other parts of world. This disorder becomes more frequent those who are suffering from diseases like multiple myeloma etc. [1].

What is vitamin B12?

Vitamin B12 or cobalamin is a water-soluble vitamin which is one of the most complex vitamins of all and can be derived from animal products like meat, eggs and other products. The normal requirement of cobalamin is 1-2 nmol/L in our stomach vitamin B12 is released from protein by peptic actions and bound to HC(Homocysteine) travels to duodenum where pancreatic proteases digest HC releasing B12 to bind intrinsic factor. [6]. The name vitamin B12 is generic for specific group of cobalt containing corrinoids with several essential biological activities in humans. [7].

Role of vitamin B12:

Cobalamin serves as a primary enzymatic cofactor in myelopoiesis (role in nucleotide synthesis) and also in the medullation of central nervous system and peripheral system. The enzymes through which cobalamin performs its functions are methionine synthase and methylmalonic COA-mutase. Thus, a deficiency of B12 leads to rupturing of myelin sheath which leads to malfunctioning of neurological system seen in vitamin B12 deficient patients. Asynchronism between maturation of cytoplasm and nuclei leads to macrocytosis, immature nuclei, hyper segmentation of granulocytes in peripheral blood. Deficiency of B12 leads to inhibition of DNA synthesis causing megaloblastic symptoms in bone marrow along with gastrointestinal tissue, causing gastrointestinal disorders in affected population by Pernicious anemia. [8]

How to diagnose:

There are certain methods through which the presence of pernicious anemia can be checked and the risk can be prevented:

- A complete blood cell count (CBC).
- Vitamin B12 level measures in blood.
- Folate levels (which are often reduced when vitamin B-12 levels are low)
- Presence of antibodies to intrinsic factor and stomach lining cells.

- Blood levels of methylmalonic acid or homocysteine, both of which may be sensitive indicators of vitamin B-12 deficiency
- A bone marrow biopsy maybe done if bone marrow disorders found in the tests and reports. [5]

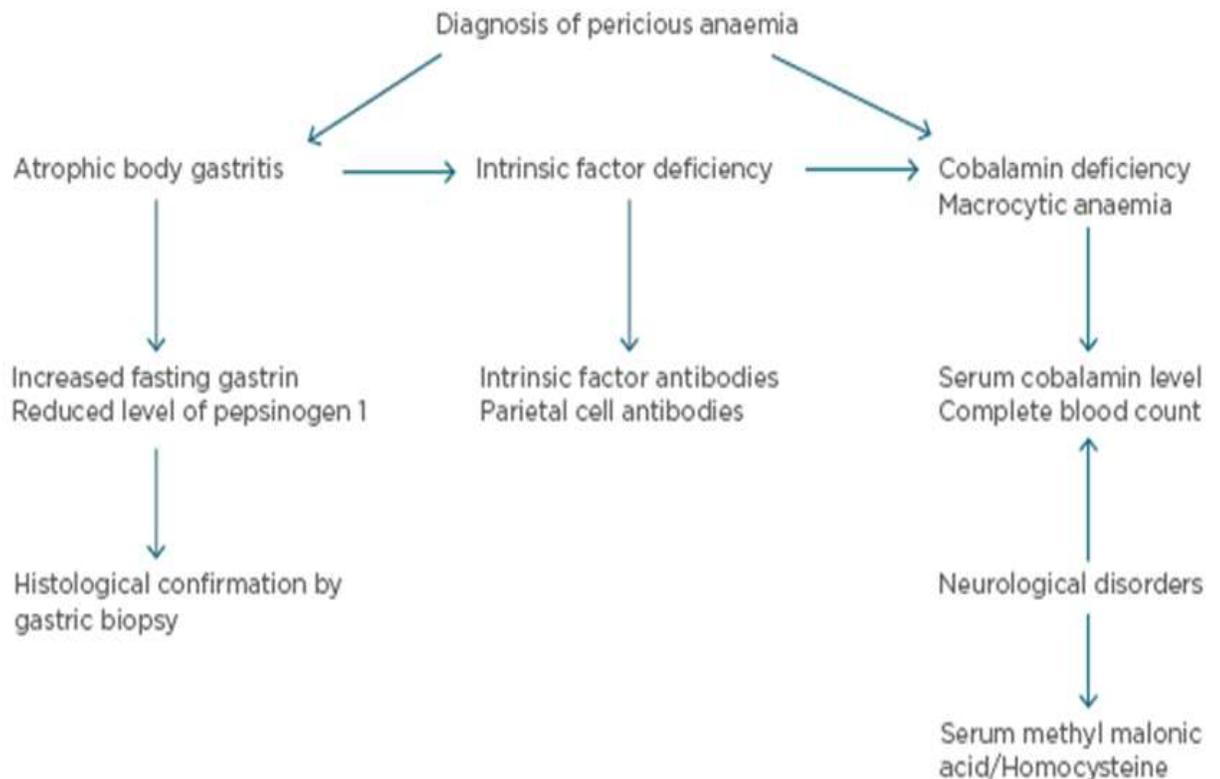


Fig: Diagnostic algorithm for pernicious anemia. [8]

Sources of vitamin B12:

Vitamin B12 is naturally found in food like meat, eggs, fish, yogurt, milk and other dairy products. In addition, fortified breakfast cereals and fortified nutritional yeasts are readily available sources of vitamin B12 that have high bioavailability. The estimated bioavailability of vitamin B12 from food varies by vitamin B12 dose because absorption decreases drastically when the capacity of intrinsic factor is exceeded (at 1–2 mcg of vitamin B12). For example, the bioavailability of vitamin B12 appears to be about three times higher in dairy products than in meat,

fish, and poultry, and the bioavailability of vitamin B12 from dietary supplements is about 50% higher than that from food sources. [9]

Table 1: Recommended intake of vitamin B12 [10]

Groups		Vitamin B12 (mcg/d)
Adults	Men	2.5
	Women	2.5
	Pregnant women	+0.25
	Lactating women	+1.0
Infants	6-12 months	1.2
Children	1-6 years	1.2
	7-9 years	2.5
Adolescents (girls)	10-12 years	2.5
	13-15 years	2.5
	16-18 years	2.5
Adolescents (boys)	10-12 years	2.5
	13-15 years	2.5
	16-18 years	2.5

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