RESEARCH ARTICLE

The Role of Vitamin B12 on Adenosine Monophosphate-activated Protein Kinase in Anemic Patients

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Received: 05th October, 2022; Revised: 26th November, 2022; Accepted: 04th December, 2022; Available Online: 25th December, 2022

ABSTRACT

Background: Anemia affects people at all stage of their lives, but it is most common in pregnant women and young children. Iron deficiencies are metabolic stress since it affects both the abilities to provide oxygen to tissue and the abilities to use oxygen (mitochondrial capability impairment). Vit.B12 plays role in the metabolism of AMP-activated protein kinase which considers as protection against inflammation *in-vitro* and *in-vivo*.

Methodology: This study includes 30 samples of the patient and 30 samples as control groups, by centrifugation, blood samples were separated and stored at minus twenty centigrade. Different questions were asked of all patients and control groups. like duration of anemia, malabsorption, malnutrition, history, drugs, weight, height, and smoking

Results: The results showed that the mean value of height levels in patients (162.2 ± 4.495) no significant difference (*p-value* = 0.6) as compared to control groups (165.6 ± 5.359) also in weight levels showed no significant difference (p-*value* = 0.9) between control (69.3 ± 3.418) and patients groups (63.8 ± 4.654). In vit.B12 levels, the mean value of patients (295.923 ± 162.241) showed a significant difference (*p-value* = 0.012*) as compared with mean of control groups (482.2 ± 158.12). In transferrin levels, there was a significant difference (*p-value*=0.04**) in vit.B12 levels between mean of patients (29.307 ± 11.604) and mean of control groups (42.4 ± 8.711). In addition to that, the mean value of Hb levels in patients (9.7 ± 2.200) showed significant difference (*p-value* = 0.03*) as compared to control groups (14.1 ± 0.94), finally, PCV levels showed a significant difference (*P-value* = 0.02*) in Polycythemia Vera (PCV) levels between mean of patients (43.3 ± 3.82) and mean of control groups (30.1 ± 6.601).

Conclusion: In this study, further demonstrate that vit.B12 plays role to decrease inflammations by macrophage inhibition; we identify the mechanism of AMP pathway mediate vit.B12 action of anti-inflammations, and reported the relation between vit. B12 and AMP-activated protein kinase (AMPK) phosphorylation, therefore vit.B12 is considered as a novel action of anti-inflammatory reagent responses.

Keywords: AMP-activated protein kinase, Transferrin, Vit.B12.

International Journal of Drug Delivery Technology (2022); DOI: 10.25258/ijddt.12.4.38

How to cite this article: Raoof IB, Abdalah ME, Mohsin RA. The Role of Vitamin B12 on Adenosine Monophosphate-activated Protein Kinase in Anemic Patients. International Journal of Drug Delivery Technology. 2022;12(4):1722-1724.

Source of support: Nil.

Conflict of interest: None

INTRODUCTION

According to various studies, anemia is one of the most commons disorder worldwide due to iron deficiencies is the prevalent form according to multiple analyse.[1] Thus, iron deficiencies lead to an inability to supply the large amounts of iron required by the bone marrow to supply a sufficient number of red blood cell to maintain tissue oxygenation.[2] Moreover, when anemia is severe, the coexist hypoxia stimulates the kidney to increase the synthesis of erythropoietin.[3]

Iron supplying occurs by dietary absorption in the duodenum, and through the recycling of age erythrocytes by macrophage, ferroportin is responsible for iron entry into the bloodstream from these sources, as well as released from hepatocyte store.[4] Thus the ferroportin axis strongly influence erythropoiesis by regulation plasma iron and systemic iron homeostasis, potential lead to anemia.[5] Furthermore, anemia is a common complication in patients with autoimmune disorder and other inflammatory disorder; these conditions is known as anemia of chronic diseases.[6] A similar condition is seen in the elderly, often seen in the absence of a specific underly diseases.[7]

According to the Adenosine monophosphate (AMP) activate protein kinase (AMPK) is a heterotrimeric protein that consist of three subunit: and. α, β and γ subunit.[8] The

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α subunit provides catalytic activities, and it also includes a glycogen binding domains that control activities.[9] The subunit is required for AMP binding and form the broad bases of the proteins. By suppressing oxidative stress, AMPK activation has multiple protective effects.[9]

In addition, previous studies demonstrate that the AMP-activated protein kinase (AMPK) enzyme is essential for maintaining cellular energy homeostasis. It develops as a mechanism to control the whole body's energy balances and feeding behaviors that is responsive to cellular energy status, as well as hormone and cytokine. AMPK may have none metabolic role such as maintaining cell polarities and normal cell divisions, or controlling cell growth and survival, in addition to regulating energy homeostasis.[10]

AMPK has been identify as a critical cellular energy sensors. As results, AMPK plays a crucial role in how cell respond to changes in their energy status, and iron homeostasis is essential for energy transduction within the cells.

Exercise cause cellular metabolic stress, which has been shown to increase AMPK activation.[11] AMPK activation is disrupted when oxygen supplies or consumption is reduced.[12] It is a heterotrimer made up of two regulatory subunit and one alpha catalytic subunit.[13] Pyridoxal, pyridoxine, and pyridoxamine, which are important cofactor for enzyme involved in different metabolic activities, make up vitamin B6 (vit. B6).[14.] B12 deficiencies, a nutritional deficiencies disease primarily caused by vitamin malabsorption, is now recognized as a global issue, frequently cause by dietary inadequacy, especially among children and women of reproductive age, clinical B12 deficiencies as opposed to state of vitamin metabolic inadequacy.[15]

Other research showed that transferrin has an ellipsoidal form and two iron binding site; transferrin saturation (TS) determine it is functional status; in a healthy subject, about 30% of transferrin is saturated with iron; when both iron binding site are occupy, it is named diferric transferrin; while in the one site is link to iron, it's named monoferric transferrin; and when no site contains iron, it's named apotransferrin.[16] Transferrin saturation determine the amounts of iron bound in the bodies under physiological condition.[17]

MATERIALS AND METHODS

This study includes 30 samples of patients and 30 samples of control groups, blood samples were separated by centrifugation and stored at minus 20°C. Different questions were asked to all patients and control groups like duration of anemia, malabsorption, malnutrition, history, drugs, weight, height, and smoking.

Table 1: Distribution of different parameters in patients and control groups

Parameters	*Mean ± St (Control)*	*Mean ± St (Patient)*	*p-value*
Height cm	165.6 ± 5.359	162.2 ± 4.495	0.6
Weight Kg	69.3 ± 3.418	63.8 ± 4.654	0.9
Vit.B12 Pg/mL	482.2 ± 158.12	295.923 ± 162.241	0.012*
Transferrin µmol/L	42.4 ± 8.711	29.307 ± 11.604	0.04*
Hb	14.1 ± 0.94	9.7 ± 2.200	0.03*
PCV (%)	30.1 ± 6.601	43.3 ± 3.82	0.02*

Statistical Analysis

Sensitive and specifics data was analyzed by used Microsoft word office 2010, database were performed by used Statistical packages for the social science software programs, Ver.18.0. Categories were showed as mean and st. The central trends measure for quantitative varieties and quality iteration. Significant differences *p-value* was performed as equal to or less than 0.05.

RESULTS AND DISCUSSIONS

The result demonstrate different parameters in patients and control groups, there was decreased significant value in anemic patients compared to control groups in each of vit. B12, transferrin, haemoglobin (Hb) and packed cell volume (PCV) as showed in Table 1.

The results showed that the mean value of height levels in patients (162.2 ± 4.495) no significant difference (p-*value* = 0.6) as compared to control groups (165.6 ± 5.359) also in weight levels showed no significant difference (*p-value* = 0.9) between control (69.3 ± 3.418) and patients groups (63.8 ± 4.654).

In vit.B12 levels, the mean value of patients (295.923 ± 162.241) showed a significant difference (*p-value* = 0.012*) as compared with mean of control groups (482.2 ± 158.12). In transferrin levels, there was a significant difference (*p-value* = 0.04**) in vit.B12 levels between the mean of patients (29.307 ± 11.604) and mean of control groups (42.4 ± 8.711). In addition to that, the mean value of Hb levels in patients (9.7 ± 2.200) showed significant difference (*p-value* = 0.03*) as compared to control groups (14.1 ± 0.94). Finally, PCV levels showed a significant difference (*p-value* = 0.02*) in PCV levels between mean of patients (43.3 ± 3.82) and mean of control groups (30.1 ± 6.601)

Our results are identical to the previous studies, there was decreased level of vitamin B.12 in anemic patients can led to decrease level of AMP-activated protein kinase because of vit. B12 playing role in the metabolism of AMP-activated protein kinase which consider as protection against inflammations *in-vitro* and *in-vivo*. AMP-activated protein kinase play an important role to inhibit inflammations in macrophages. vit.B12 activate AMPK in macrophage by increase AMPK phosphorylation and reversible mechanisms in macrophage, then activated AMPK produce an inhibitory effect on inflammations in multiple cell, therefore pre-treatment of cell with vit.B12 dose-dependent to prevent the elevation of inflammation by Lipopolysaccharides (LPS) which induced inflammation in macrophage. The major discovery of the present studies is that vit.B12 produce several beneficial effect to prevent inflammations.[18] In addition, AMPK stimulates catabolic process which increased adenosine triphosphate (ATP) production, and subsequently inhibit anabolic process which consumed ATP.[19] Iron deficiencies with low transferrin

saturations in patients is characteristic a disorder of patients.[20] Iron is an essential element to brain cell because it was used to maintains metabolism, in addition to myelin production and neurotransmitter synthesis.[21] Also, Transferrin used to transport iron into tissue, it was necessary for oxidization to ferric iron via oxidizing actions of the enzyme ceruloplasmin.[22]

CONCLUSION

In this study, further demonstrate that vit.B12 plays role to decrease inflammations by macrophage inhibition; we identify the mechanism of AMP pathway mediating vit.B12 action of anti-inflammations, and reported the relation between vit. B12 and AMPK phosphorylation, therefore vit.B12 consider as a novel action of anti-inflammatory reagent responses.

ACKNOWLEDGMENT

We would like to thanks Mustansiriyah University to provide incorporeal support to complete the review.

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