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Review

The Impact of Spleen Disorders in the Pathogenesis of Anemia from the Viewpoint of Persian Medicine

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Abstract

Spleen is one of the main components of reticuloendothelial system and plays an important role in controlling of red blood cell quality with elimination of old and damaged cells. Physicians of Traditional Persian Medicine believed that spleen has a high incorporation with the liver, and liver has a main role in blood production. So its pathologic changes influence the production of hematologic elements in both aspects of amount and quality. In this study, chapters related to spleen disease in several Traditional Persian Medicine textbooks and available databases were reviewed. Further the relationship between anemia and spleen diseases were derived and evaluated. After interviewing two experts about the findings and reaching data saturation, the results were compiled and explained. Spleen dysfunction and diseases can lead to anemia, because of intercommunity with liver. This happens with different mechanisms such as: enlargement, cold distemperment, asthenia and crisis. Although there are many studies so far about anemia, but role of the spleen in the development of anemia is still not well known. Considering the role of the spleen in developing anemia, the drugs used in Persian medicine for spleen-originated anemia may provide an appropriate solution to treat the disease.

Keywords: Spleen; Anemia; Liver; Persian medicine

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Introduction

The spleen is a major organ in the reticuloendothelial system, which plays an important immune role and removing foreign material and damaged erythrocytes in the systemic blood circulation. It is a storage place where iron, erythrocytes, and platelets are stored in the human body. One of the most important roles of spleen is control of red blood cell (RBC) quality with elimination of old and damaged ones. Two morphologically and functioning compartments exist in the spleen; red pulp and white pulp. One common histological finding of the spleen is pigmented sediment in the red pulp which are mainly a result of the erythrocytes destruction and conversion of their iron to hemosiderin for reuse [1]. Naturally, about one third of whole platelets are stored in the spleen and released into the blood stream when necessary. An increase in these natural activities can lead to splenomegaly [2].

The spleen is a main organ contributing to anemia. Two frequently mechanisms have been discussed as the splenic mechanisms in the pathogenesis of anemia: the first being a site for iron retention in macrophages and the second, reduction of RBC half-life due to increased RBC removal in hypersplenism [3]. Furthermore, spleen has a key role in the pathogenesis of autoimmune hemolytic anemia [4]. Also, it is mentioned that anemia can lead to spleen disorder like splenomegaly. Therefore, there is a bidirectional relationship between the spleen and anemia.

Reviewing medical historical manuscripts demonstrates that, physicians of traditional Persian medicine (TPM) were aware of the impact of spleen disorders in the pathogenesis of anemia [5-7]. They carefully described the anatomy, functions and diseases of the spleen. They believed the spleen to be an important organ, which has different physiological functions and its disorders can affect other organs such as liver [8,9]. It is believed that spleen is the most important organ for storage of black bile. This organ takes black bile from blood circulation and holds it until it is needed in the body [8,10,11]. As regards one of the main functions of the spleen is trapping of malformed, damaged and old RBCs and then destroying them, maybe it can be matched with its function of removing the black bile from the bloodstream which has been mentioned in TPM [12].

Based on the viewpoint of TPM the liver is a main organ which produce blood and blood humors, also there is a relationship between spleen and liver, so some spleen disorders can influence the liver and cause secondary liver diseases that lead to development of anemia [9]. Therefore, both the spleen and liver are considered as the blood production unit and their pathologic changes influence the amount and quality of hematologic elements [13].

The relationship between the spleen disorders and anemia from the viewpoint of TPM is not considered properly, and thus, in this article, we aimed to review some TPM theories in the pathogenesis of anemia.

Methods

In this historical article, we reviewed the chapters related to the spleen diseases in several TPM textbooks including *Al-Hawi fi al-Tibb, Kamil al-Sinaa al-Tibbiya, Al-Qanun fi al-Tibb, Firdous al-Hikmah, Kholasatol-Hikmah, Daqaiq al-Ilaj fi al-Tibb, Exir-e Azam, Kholasat al-Tajarob, Kefayeh Mansoori and Connash fi al-Tibb* and collected the items related to the topic. Moreover, the search was accomplished in electronic databases including PubMed, Science Direct, Scopus, SID and other relevant databases up to March 2019 to review recent advances in this field. The keywords of the search were spleen, anemia, splenomegaly and other related terms. Furthermore, interviews were conducted with two experts in TPM about the

findings until data saturation was reached. Finally, the data was categorized and analyzed to notice the impact of spleen disorders in the pathogenesis of anemia.

Results

According to TPM, there are four humors in the human body including blood or sanguine (*Dam*), phlegm (*Balgham*), yellow bile (*Safra*) and black bile (*Sawda*) which are produced in the liver. Therefore, the liver has a main role in humor production, especially the blood. These humors contribute to the formation of body organs and feeding the whole body [9, 14]. Also, each of them has a pair of specific qualities called temperament and its related sign and symptoms. Equilibrium in the quantity and quality of these four humors has an important role in preserving human health; thus, any change in them can cause dystemperament and subsequently, a disease. In TPM textbooks, anemia has been discussed as blood humor deficiency named "*Qillat-ud-dam*" [5,6,11].

According to TPM, the spleen can cause anemia by various mechanisms including:

- *Spleen swelling*: this is an inflammation in the spleen as a result of a change in quality or quantity of the four humors. In this disease, absorption of the black bile from the bloodstream is increased. Black bile is considered as a dense humor, consequently, blood viscosity decreases and the blood becomes diluted [10].
- *Spleen enlargement:* It is believed that body slimming follows spleen enlargement. Hippocrates said:" *whenever the spleen is enlarged, the body and liver become lean and whenever the spleen is tiny, the body and liver become obese and corpulent*" [15]. In TPM, it is mentioned that, a large spleen can hold a large volume of blood resulting in anemia [due to decreased effective intravascular volume]. Also, a large spleen can induce liver weakness. As a result, proper blood production by the liver reduces [5,15].
- *Spleen cold dystemperament*: the liver needs adequate heat for appropriate functions. Coldness of some organs next to the liver, such as the spleen, makes its temperament cold and can lead to liver weakness. It is followed by dysfunction of this organ and a decrease in blood production as well [16].
- *Spleen asthenia*: in this disease, the spleen cannot take black bile from blood circulation and hold it properly; therefore, excessive black bile releases into the bloodstream and results in changes in circulating blood composition. In this case, liver dysfunction will pursue, followed by anemia due to inappropriate blood humor production [7,10,17]. Baha al-Dowleh *Razi said:* " *The spleen can receive a large amount of blood flow from the liver, which result in diminished liver function*"[18].
- *Spleen crisis "Bohran"* : Spleen crisis sometimes leads to releasing of stored black bile into the bloodstream then liver asthenia and anemia will happen [10].

Discussion

Current studies provide different reasons for the etiology of anemia, with nutritional deficiencies, chronic diseases, and bleedings considered as the main ones [4]. Moreover, many different factors contribute to the pathophysiology of anemia such as immune cells, erythron, nutritional factors, liver, spleen and kidney disorders [3]. The spleen is a site for iron retention in macrophages and can increased RBC removal through trapping and destroying old RBCs [3,4].

TPM comprises types of evidence based on humoral theories. Although its paradigms and terminology are different from the current medical ideas, it seems that considering these theories can be helpful as a source of new treatment strategies. According to TPM, the liver is a major hematopoietic organ, and to a lesser extent the spleen plays the same role, directly and in-

directly through the liver.

Spleen-related anemia is classified in three main categories: the first one is cold spleen dystemperament which leads to cold liver dystemperament and asthenia. The second category is spleen asthenia, which may increase the circulatory black bile and also produce or worsen liver asthenia.

The third category is spleen enlargement and stiffness. The inflammation and swelling of the spleen does not always lead to enlargement but almost always produces stiffness. This condition occurs in different diseases such as hemoglobinopathies and cirrhosis [19, 20]. Enlargement of the spleen can potentiate the sequestration and destruction of blood components, and demonstrate hypersplenic manifestations such as anemia, thrombocytopenia and leukopenia [21].

There is also evidence that spleen and anemia have a mutual relationship. Some hematologic diseases can lead to the spleen disorder like splenomegaly. In spherocytosis due to a loss of membrane surface area and defect in the shape of the RBCs, spherocytic red cells become trapped in the spleen and destroyed, so splenomegaly occurred [22].

In inflammatory diseases, abnormal and excessive accumulation of iron in macrophage cells occurs in the reticuloendothelial system including the spleen. So splenomegaly occurs due to increased RBC uptake by macrophages [3].

In addition, in some other diseases the spleen can cause anemia. In hemolytic anemia due to RBC injury, the remaining Heinz bodies are removed by the spleen and cause a large spleen [23]. The spleen is a major organ for antibody production and RBC destruction [4].

However, enlargement of the spleen by itself can lead to a decrease in the viscosity of the blood and anemia; in some cases, like infections, changes in the composition of blood may activate the spleen and produce splenomegaly to an extent that requires splenectomy [24,25]. Rhazes and Jorjani reported the following: *"Those patients who have congenital splenomegaly are also susceptible to liver asthenia and finally usually develop anemia"*. Therefore, whether congenital or a result of changes in the blood composition, splenomegaly can weaken the liver and be followed by anemia [13].

Based on TPM textbooks, splenomegaly leads to emaciation of the liver and weight loss. Some TPM physicians think that this symptom is mainly due to diffusion of black bile in the body. Dawud al-Antaki shared the following about splenomegaly: *"If the spleen is palpable in physical examination and the body is thin, the cause of the disease is definitely related to black bile"* [10].

Although many studies have been conducted on the pathogenesis of anemia, it seems that further evaluation about the role of the spleen and those drugs used in TPM for spleen related anemia may provide an appropriate source for new treatment strategies.

Conflict of Interest

None.

Acknowledgment

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