

NEW INNOVATIVE METHODS OF TREATMENT OF ADVANCED ANEMIA IN PATIENTS WITH RHEUMATOID ARTHRITIS

Temirov Nuriddin Najmitdinovich

*Doctor ordinator of hematology center of
Samarkand regional multi-network medical center*

Azizova Shakhlo Majidovna

*Doctor of the Department of Rheumatology of
Samarkand regional multi-network medical center*

Dadajanov Uktam Utkurovich

*Teacher of the Department of Hematology
Samarkand State Medical University*

Madasheva Anajan Gazkhanovna

*PhD, Senior lecturer of the Department of Hematology
Samarkand State Medical University*

Annotation. In the context of treating advanced anemia in patients with rheumatoid arthritis, it's crucial to address both the underlying rheumatoid arthritis (RA) and the associated anemia. Anemia in RA can be multifactorial, with causes such as chronic inflammation, medication side effects, or nutritional deficiencies.

Keywords: anemia, treatment, systemic manifestations, individual manifestations, rheumatoid arthritis, chronic bleeding.

Rheumatoid arthritis (RA) is one of the most common inflammatory diseases of the joints, accounting for about 10% of rheumatological pathologies. It represents not only a medical but also an economic problem since the onset of the disease in most cases is observed in people of working age [9]. Research in recent years has shown the leading role of cytokines and other inflammatory mediators in the development of not only articular syndrome but also the entire range of systemic manifestations of this disease. Based on the data obtained, fundamentally new and more effective drugs, the action of which is based on the anti-cytokine principle, were developed and introduced into clinical practice [6]. However, despite these successes, several questions regarding the pathogenesis of individual manifestations of RA and especially their treatment remain open. These include the problem of anaemic syndrome – a frequent companion to rheumatoid inflammation.

In recent years, it has been established that the role of a universal humoral regulator of iron metabolism is played by hepcidin, a 25-amino acid peptide synthesized in the liver [7, 12]. The connection between



hepcidin and iron metabolism was first described by S. Pigeon et al. [4]. It has been noted that under the influence of pro-inflammatory cytokines, in particular IL-6, there is hyperproduction of hepcidin, which blocks the receptors of ferroportin, a transmembrane protein that transports iron adsorbed by enterocytes into the blood [5]. This assumption was confirmed in an in vitro experiment [3], in which the regulatory functions of ferroportin and hepcidin were studied. The authors used ^{59}Fe -labeled rat erythrocytes, which were phagocytosed by macrophages. The results showed that about 70% of ^{59}Fe was released into the blood, which is associated with the regulatory function of ferroportin. It was noted that the effect of hepcidin on macrophages led to a decrease in the level of ferroportin and a decrease in the amount of ^{59}Fe in the blood. A similar effect was found when synthetic hepcidin was administered to mice [2].

Changes in iron metabolism can also occur as a result of an increase in the phagocytic activity of macrophages. There is evidence that this is facilitated by IL-1, which, acting on neutrophils, leads to the release of lactoferrin from them [1]; the latter binds free iron and delivers it not to erythrocytes, but to macrophages.

Anemia is a common complication in patients with rheumatoid arthritis (RA). The development of anemia in RA can be attributed to various factors, and it is often multifactorial. Here are some key reasons why anemia may occur in individuals with rheumatoid arthritis:

1. Chronic Inflammation:

- RA is characterized by chronic inflammation, and the inflammatory response can affect the production and lifespan of red blood cells. Inflammation can interfere with the body's ability to use iron and other nutrients essential for red blood cell production.

2. Cytokine Release:

- Inflammatory cytokines, such as tumour necrosis factor-alpha (TNF-alpha) and interleukin-6 (IL-6), are elevated in RA. These cytokines can suppress the production of red blood cells in the bone marrow and contribute to anaemia.

3. Medication Side Effects:

- Some medications commonly used to treat RA, such as nonsteroidal anti-inflammatory drugs (NSAIDs) and disease-modifying antirheumatic drugs (DMARDs), may have side effects that can contribute to anemia.

4. Bone Marrow Suppression:

- Chronic inflammation and the autoimmune process in RA can affect the bone marrow's ability to produce red blood cells, leading to anemia.

5. Iron Deficiency:

- Inflammation in RA can lead to the sequestration of iron within cells, making it less available for the production of red blood cells. Additionally, chronic bleeding, often unnoticed, can contribute to iron deficiency anemia.

6. Folate and Vitamin B12 Deficiency:

- RA patients may be at an increased risk of developing deficiencies in folate and vitamin B12, both of which are essential for red blood cell production.

7. Renal Dysfunction:



- RA-related vasculitis or the use of certain medications may affect renal function, leading to decreased production of erythropoietin, a hormone crucial for red blood cell production.

To address anemia in patients with rheumatoid arthritis, a comprehensive approach is typically required. This may involve:

- **Treating the underlying RA:** Disease-modifying antirheumatic drugs (DMARDs) and biologics can help control inflammation and improve overall disease management.
- **Iron supplementation:** Oral or intravenous iron supplementation may be prescribed to address iron deficiency.
- **Vitamin and mineral supplementation:** Folate, vitamin B12, and other nutrient deficiencies should be corrected through diet or supplements.
- **Erythropoiesis-stimulating agents (ESAs):** In some cases, ESAs may be considered to stimulate red blood cell production.

Management should be tailored to each individual's specific circumstances, and healthcare professionals, including rheumatologists and haematologists, play a crucial role in determining the most appropriate course of action. Regular monitoring of hemoglobin levels and addressing the underlying causes are essential components of effective anemia management in patients with rheumatoid arthritis.

Here are some potential innovative methods for the treatment of advanced anemia in patients with rheumatoid arthritis:

- *Disease-Modifying Antirheumatic Drugs (DMARDs):*

The effective management of RA using advanced DMARDs can help control inflammation and subsequently improve anemia. Targeting the underlying disease process can contribute to the resolution of anemia.

- *Biologic Therapies:*

Biologic drugs that target specific pathways involved in RA, such as tumor necrosis factor (TNF) inhibitors, interleukin-6 (IL-6) inhibitors, or Janus kinase (JAK) inhibitors, may be beneficial. These drugs can help control inflammation and improve symptoms, including anemia.

- *Iron Supplementation:*

Innovative iron supplementation strategies, including intravenous iron infusions, may be considered. Intravenous iron can be more efficient in raising haemoglobin levels compared to oral iron supplements and may have a more rapid onset of action.

- *Erythropoiesis-Stimulating Agents (ESAs):*

In some cases, erythropoiesis-stimulating agents, such as erythropoietin, may be used to stimulate the production of red blood cells. However, the use of ESAs in RA-related anemia is somewhat controversial and should be carefully considered based on individual patient factors.

- *Nutritional Support:*

Addressing nutritional deficiencies, including iron, vitamin B12, and folic acid, is crucial. Innovative methods may include personalized nutrition plans or supplements to optimize nutrient levels.

- *Comprehensive Management Approach:*



Integrating a multidisciplinary approach that involves rheumatologists, haematologists, and nutritionists can help provide comprehensive care. Collaboration among specialists can lead to tailored treatment plans that address both RA and anemia.

- Patient Education and Empowerment:

Empowering patients with knowledge about the relationship between RA and anemia, as well as the importance of medication adherence, regular monitoring, and lifestyle factors, can contribute to better outcomes.

Always consult with healthcare professionals to determine the most suitable and up-to-date treatment options for individuals with rheumatoid arthritis and associated anemia. Advances in medical research and treatment options continue to evolve, so staying informed about the latest developments is essential.

References:

1. Adlerova L. Lactoferrin: a review / L. Adlerova, A. Bartoskova, M. Faldyna // *Veterinarni Medicina*. 2008. Vol. 9. P. 457–468.
2. Chaston T. Evidence for differential effects of hepcidin in macrophages and intestinal epithelial cells / T. Chaston, B. Chung, M. Mascarenhas, J. Marks // *Gut*. 2008. Vol. 57. P. 374–382.
3. Knutson M.D. Iron release from macrophages after erythrophagocytosis is up-regulated by ferroportin 1 overexpression and down-regulated by hepcidin / M.D. Knutson, M. Oukka, L.M. Koss, F. Aydemir, M. Wessling-Resnick // *Proc Natl Acad Sci USA*. 2005. Vol. 102. P. 1324–1328.
4. Pigeon C. A new mouse liver specific protein homologous to human antibacterial peptid hepcidin is overexpressed during iron overload / C. Pigeon, G. Ilyin, B. Courselaud // *J. Biol. Chem*. 2001. Vol. 276. P. 7811–7819.
5. Raj D.S. Role of Interleukin-6 in the Anemia of Chronic Disease / D.S Raj // *Semin Arthritis Rheum*. 2009. Vol. 5. P. 382–388.
6. Smolen J.S. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs / J. S. Smolen, R. Landewé, F. C. Breedveld // *Ann Rheum Dis*. 2011. Vol. 70. P. 1519.
7. Sun C. C. Targeting the hepcidin-ferroportin axis to develop new treatment strategies for anemia of chronic disease and anemia of inflammation / C. C. Sun, V. Vaja, J. L. Babitt, H. Y. Lin // *Am J Hematol*. 2012. Vol. 87. P. 392–400.
8. Theurl I. Pathways for the regulation of hepcidin expression in anemia of chronic disease and iron deficiency anemia in vivo / I. Theurl, A. Schroll, M. Nairz // *Haematologica*. 2011. Vol. 96. P. 1761–1769.
9. Коваленко В.М. Хвороби системи кровообігу: динаміка та аналіз / В.М. Коваленко, В.М. Корнацький // *Аналітично-статистичний посібник*. 2008. С. 66–79.
10. https://www.rmj.ru/articles/zabolevaniya_kostno_myshechnoy_sistemy/Anemiya_u_bolnyh_r_evmatoidnym_artritom_osobnosti_patogeneza_diagnostiki_i_lecheniya/#ixzz8Lc1JYT4J
11. Ruziboeva, O. N., Abdiev, K. M., Madasheva, A. G., & Mamatkulova, F. K. (2021). Modern Methods Of Treatment Of Hemostasis Disorders In Patients With Rheumatoid Arthritis. *Ученый XXI века*, 8.



12. Мадашева, А. Г., & Махмудова, А. Д. (2021). Биохимические показатели у больных гемофилией с мышечными патологиями до и после лечения. *Форум молодых ученых*, (4 (56)), 233-238.
13. Gazkhanovna, M. A., Makhmatovich, A. K., & Utkirovich, D. U. (2022). Clinical efficacy of extracorporeal and intravascular hemocorrection methods in psoriasis. *ACADEMICIA: An International Multidisciplinary Research Journal*, 12(2), 313-318.
14. Мадашева, А. Г. (2022). Коррекция диффузной алопеции при железодефицитной анемии. *Science and Education*, 3(12), 231-236.
15. Мадашева, А. Г. (2022). Клинико-неврологические изменения у больных гемофилией с мышечными патологиями. *Science and Education*, 3(12), 175-181.

