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Iron Deficiency Anemia Caused by Chronic Kidney Disease Complicated by Chronic Heart Failure, Treatment, Improvement of Prognosis

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Abstract: ***In the presented review, the prevalence of anemia and iron deficiency (railway) with CXN, their influence on the course of the course and forecast of this state are affected. The definition of anemia and a railway is formulated based on the assessment of various laboratory data. In particular, the diagnostic significance of the determination of serum iron, serum ferritin, transferin saturation coefficient, a common iron-binding ability of blood serum and transferlic soluble receptor levels are discussed. It is emphasized by the importance of determining the level of iron in the bone marrow, although being the "gold standard" diagnosis of railway, but rarely used in wide clinical practice. Pathogenetic mechanisms for the development of the CHD for CHD, including the lack of iron intake, the role of inflammation, erythropoietin, RAAS, and the influence of some pharmacological preparations. The physiological consequences of the railway and anemia are described, the activation of hemodynamic and non-aggative compensatory mechanisms developing in response to anemia and often exacerbating CXN. Particular attention is paid to modern approaches in the treatment of anemia and railway with HSN, including discussion of the effectiveness and safety of oral, intravenously administered iron and hematopoiesis stimulants.***

Keywords: ***anemia, iron deficiency, chronic heart failure, Diagnostics, Erythropoietin, Ferritin, Transfirin, Hepsidine, Pathogenesis, Forecast, Treatment***

I. INTRODUCTION

Chronic CN is a widely distributed disease - today it is about 26 million people's population and it is assumed that in the near future the number of such patients will increase significantly. Thus, the share of patients with HSN in the United States, compared with 2012, most likely will increase by more than 46% by 2030 [3], which is associated with an increase in the life expectancy of the population, improving the prevention and treatment of CVD, and First of all, IBS.

II. MAIN PART

Nevertheless, despite significant progress in the methods of treating CHF, a huge number of patients remain symptoms, with limiting the possibilities of performing physical exertion and high risk. of death. It is also important that such patients often have other concomitant states that make it difficult to treat HSN [6]. Patients with HT most often suffer from coronary artery disease, hypertension, chronic kidney disease, chronic obstructive pulmonary disease, obstructive sleep apnea syndrome and SD. In addition, there are more and more data on the presence of iron deficiency (railway) and anemia, which are independent FR adverse predictions at CXN [7-9]. HSN anemia is more often found in women, elderly and having a deterioration in the kidney function and is associated with severe myocardial remodeling, inflammation and overload. The presence of anemia is associated with more pronounced symptoms of HSN, the worst functional status of CH, high risk of hospitalization and decrease in survival. According to the latest information, therapy aimed at the correction of hemoglobin levels (HB) is not associated with a significant improvement in the course of CHF, while the treatment of the railway leads to a significant favorable clinical effect, even in patients without anemia. In this regard, there are a number of informed issues: is there a low HB indicator of the main therapeutic goal? Should I consider the reduction of HB as a marker of gravity of the underlying disease or comorbide pathology? How justified the events for the Correction of the railway, and which of them are the most efficient and safe today? An accurate understanding of the mechanisms through which anemia and the CHRD worsen the flow of CXN will allow for a more pathogenetically reasonable treatment, which with greater probability will improve the quality of life of such patients and reduce the risk of deaths. The submitted review is devoted to the issues of the definition, epidemiology, pathogenetic aspects, diagnosis and treatment of anemia and the railway in patients with HSN.

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Definition of anemia and iron deficiency with As noted, anemia and railway are among the most common concomitant states in patients with HSN [7, 12], which are associated with poor clinical status and adverse outcomes of the disease. At the same time, it is important to note that the presence of anemia is not always due to the existing railway, and the latter can exist without anemia. In order to differentiate these states in clinical practice, it is necessary to clearly understand the difference between them. According to the definition of WHO experts, anemia is characterized as a reduced level of HB (<130 g / l in men and <120 g / l in women). Despite the fact that these values are most often used in modern studies, some authors use other criteria according to which anemia for CXN is diagnosed with a decrease in Hb ≤120 g / l in men and HB ≤110 g / l in women. Accordingly, the prevalence of anemia among patients with XSN varies significantly depending on the HB reference intervals used. In patients with anemia, along with measuring the HB level, the level of iron in the body is determined to confirm or clarify the causes of anemia. According to the definition of WHO, the railway is a state in which the decrease in the iron serum content is noted due to the lack of mobilization of it from the depot, and there are signs of violation of iron intake in tissue, including erythron [20]. The international expert group Iron Core in 2017 proposed the following wording: "The railway is a state associated with health, in which the lack of iron does not comply with the needs of the body and which may be present with both anemia and without it.".

Prevalence of anemia and iron deficiency The prevalence of anemia among patients with HSN varies from 9 to 69.6%. According to the results of a meta-analysis, which included more than 150 thousand patients with CH, anemia was observed in 37.2% of cases, while its frequency reached 49% among patients with acute decompensation of HSN. As already noted, the prevalence of anemia with CXN depends on which HB levels were used to diagnose it. Thus, with the value of Hb <130 g / l in men and <120 g / l in women, the frequency of anemia is 16-49%. Whereas with the values of Hb ≤120 g / l in men and ≤110 g / l, the prevalence of this state decreases to 11-17%. According to a study conducted in Poland, Spain and Holland and covered more than 1,500 patients with low FV (SNNFV) LV, the prevalence of anemia (HB <130 and <120 g / l for men and women, respectively) amounted to 28.3%. For the first time, the anemia occurred at CHN met with a frequency of 9.6%, according to Solvd research, 14.2% - COMET [3] and 16.9% - VAL-HEFT. According to Research results, still failed to establish which criteria it is advisable to use to determine anemia [7]. It was also revealed that hemodilution caused by an excess fluid in 46% of cases can cause anemia, even in patients with HSN without clinical signs of fluid overload. Therefore, it should be noted that the prevalence of anemia, in addition to the diagnostic criteria, additional factors may influence, for example, the severity of the decompression of the CHF. There are data indicating the high prevalence of anemia among patients with a railway compared with patients having a normal iron level. At the same time, the frequency of the railway in patients with XSN is very variable. This is evidenced by its detection in 30-50% of patients with HSN and in 70-80% with acute CH. According to other authors, these indicators vary within 37-61%. Most likely, the prevalence of the railway with HSN patients is higher, compared to anemia, and it is found both in combination with it and without. It is necessary to emphasize that the railway and iron deficiency anemia (waiting) are often mistakenly considered as identical states. According to the expression A. J. Stewart Coats "Not every CSD is associated with anemia, as well as not any anemia is associated with the railway, therefore the doctor must be aware of the probability of the LA even in patients without anemia".

Diagnosis of anemia and iron deficiency in patients For diagnosis of anemia in patients, the concentration of HB in the blood serum is determined primarily (Fig. 1, step 2) [5]. According to WHO recommendations, with a mild anemia, the HB level is 110-129 g / l in men and 110-119 g / l in women; with moderate - 80-109 g / l; With severe - less than 80 g / l, regardless of gender. To determine the railway, there are many tests, but, unfortunately, there are no uniform diagnostic standards, which complicates the distinction of the railway from the WD and perception of it, as an independent state with separate clinical consequences. In addition, not all tests are closely correlated with each other, since each of them characterizes the different stones of iron metabolism [16]. A more accurate assessment of the CHD associated with anemia, in patients with CH can be carried out in the study of additional indicators presented in Table 1 [13, 36-38]. To form an accurate diagnosis, it is necessary to determine the content of serum iron (SZh), serum ferritin, transferrin saturation coefficient (CST), overall iron binding ability of blood serum (EHSKSK), transferparin receptor level (RRT) and evaluate additional edges of erythrocytes and reticulocytes (hypochromic content Erythrocytes (GE/C) and HB in reticulocytes (HBR / C)) [1]. The concentration of SZh reflects the balance between the amount of iron coming and released from the plasma. In the absence of inflammation or chronic diseases, the content of SZH has a strong relationship with a margin of iron in the body: 1 mg / l SB corresponds to 10 mg of fabric. Normal import values in men - 8.9-26.8, in women - 6.3-25.9 μmol / l [13]. When measuring the SE, it is necessary to take into account the exposure to its daily oscillations (in the morning clock iron level above) and other influences (diet, blood transfusion, taking iron-containing drugs, etc.) [39, 41]. The serum level of ferritin is directly proportional to the accumulation of iron in macrophages and hepatocytes. Normal values of serum ferritin 24-336 μg / l in men and 11-307 μg / l in women.

However, with CHF, as with systemic chronic inflammatory syndrome, the level of serum ferritin rises, acting as a non-specific inflammation marker, which makes the determination of the absolute and functional railway and inaccurate [6]. In this case, the functional railway can be observed at a normal or slightly elevated level of ferritin. The HSN train is diagnosed as absolute with a decrease in serum ferritin <100 μg / l and CNT (SZH / OHSSKKH100%) <20% or relative (functional) - at the level of serum ferritin 100-299 μg / l and KST <20%.

Параметр	Референтный интервал	Абсолют- ный ЖД без анемии	Абсолют- ный ЖД с анемией	Функциональ-ный ЖД с и без анемии	Чувстви-тельность, %	Специ-фичность, %
Депо железа вп КМ		Отсутствие ЭКП ретикулоэндо-телиальных клеток	Отсутствие ЭКП иретикуло-эндотелиальных клеток	Низкое исодержание ЭКП нормальное количество ретику-лоэндотелиальных клеток	«Золотой истандарт»	«Золотой стандарт»
Hb, г/л	М: 135–175; Ж: 120–155	N	□□□□	N/□	Слабая	Слабая
MCV, f L	М: 81–95; Ж: 82–98	N/□	□□□□	N/□	Слабая	88,3
Ферритин, мкг/л	М: 24–336; Ж: 11–307	≈20	<15–30	N/□	35–48	75–100
СЖ, мкмоль/л	М: 8,95–26,86; Ж: 6,27–25,96	□	□	□	Слабая	Слабая
ОЖССК, мкг/л или трансферрин, мкмоль/л	44,77–71,63; 25,12–45,23	N	□	N/□	Слабая	Слабая
КНТ, %	≈15–50	≈30	<15	N/□	59–88	63–78
РРТ, мг/л	1,8–4,6	□	□□	□	70–81	59–71
РРТ/ферритин	≤1,03	□	□□	□	81	83
Гепсидин, нг/мл	М: 29–254; Ж: 17–286	N	□	□	50–92,5	85–90
ГЭ/ц, %	<2,5	N/□	□	N/□	64–78	77–78
HbP/ц	≈28–35	N/□	□	N/□	53–78	53–100

Table 1. Laboratory tests for the diagnosis of iron deficiency

With a serum railway, the level of RRT also rises, which, unlike ferrithin, does not change under inflammation. Among the available blood parameters of the RRT and CST are the strongest correlation with the level of iron depletion in the bone Mozens (km). A significant scientific achievement in the field of study of iron metabolism was the discovery of heptisdin - hormone gum, regulating the metabolism of iron. It modulates the ferluorine-dependent iron yield into the bloodstream in response to the system level and the need for SZh. Normally, in response to an increase in the SE, an increase in heptisidine expression occurs, and on the contrary, the level of hepsidine decreases with the railway. Unfortunately, in clinical practice, the definition of indicators such as RRT, the ratio of RRT to ferritine or hepsidine level is difficult.

These parameters in a comprehensive examination of CHN patients could serve as more accurate diagnostic indicators of the detection of absolute or relative railway [49, 50]. Definition of GE / C and HBR / C is a sensitive and accurate method of screening on the railway. The HBR / C assessment is the advantage over the counting of GE / C, since due to the larger life expectancy of the erythrocytes, their indices acquire their diagnostic significance only in the manifest form of anemia with explicit clinical symptoms. In turn, the reticulocyte that turns into red blood cell after 1-2 days, more accurately reflects the content of iron in it, which makes this parameter an important additional marker of the railway. The "gold standard" diagnostics of the railway is to determine the level of iron in km by studying its aspirate painted by the peers dye, since the values of bone marrow gland are not subject to change in inflammation. Nevertheless, the study of the CM in ordinary clinical practice is very limited due to the invasiveness of the method, its high costs, the subjectivity of the interpretation of the results and the complexity of re-execution. According to a small study, which included 37 hospitalized patients with decompensated CHN and anemia, it was revealed that even at normal levels of SZH, ferritin and erythropoietin (EPO) in 73% of cases, iron depletion is observed in km. The variability of Ferritin and CST indicators can be partially explained by the inconsistency between the content of iron in the blood and km.

In a recent study N. GROTE BEVERBORG and Whise of the group conducted in 42 patients with SNNFV, which revealed the aorto-coronary shunting, during the study of the CM in 40% (n = 17) of patients was diagnosed by the RA. A. V. Hoffbrand and P. A. H. Moss believes that it is necessary to investigate km only in severe, complicated cases, with high suspicion of complete depletion of iron depot in macrophages and developing erythroblasts. Widely used method for determining the railway (ferritin <100 μg / l and 100-299 μg / l with KST <20%) It has a sensitivity of 82% and specificity of 72%. It should be noted that among patients with low levels of ferritin (<100 ng / ml), but normal CNT (> 20%) is not observed reduction in the level of SZh. It was revealed that the ferritin level is a more accurate indicator of the determination of an excess of iron than its deficiency [13].

III. CONCLUSION

In recent years, the role of comorbide pathology has been given more and more attention to the medical community. It is not by chance that in the recent recommendations of the European Society of Cardiologists [10] and the Russian Cardiology Society for Patients with Acute Decompensated and HSN [43] Sections devoted to comorbide pathology are very significant in size. Along with inflammation and neurohumoral activation, anemia and railway are one of the most common states in CXN, the frequency of which reaches 70% of cases. If the definition of anemia, the degree of its severity is based on the estimation of the HB level values, the diagnostics of the railway requires accounting not only the level of SZh, but also the definition of additional parameters, including the evaluation of the concentration of ferritin and CST. At the same time, taking into account the negative effect of the LEG in patients with SN for a forecast and quality of life, it is considered to be appropriate to conduct all patients with HSN examination on identifying iron deficiency for reasonable and adequate replenishment of its lack.

Among the methods of correction of anemia and a railway, seemingly a wide range of therapeutic capabilities, encouraging treatment results are currently obtained only by GDP. Oral gland preparations, PSE have a number of restrictions and adverse side effects that limit their widespread use in clinical practice. Obviously, it is necessary to conduct further research on the study of the efficiency and tolerability of both various forms of iron and PSE preparations, given the pathogenetic features of the railway, the presence of concomitant diseases and the state of the LV function.

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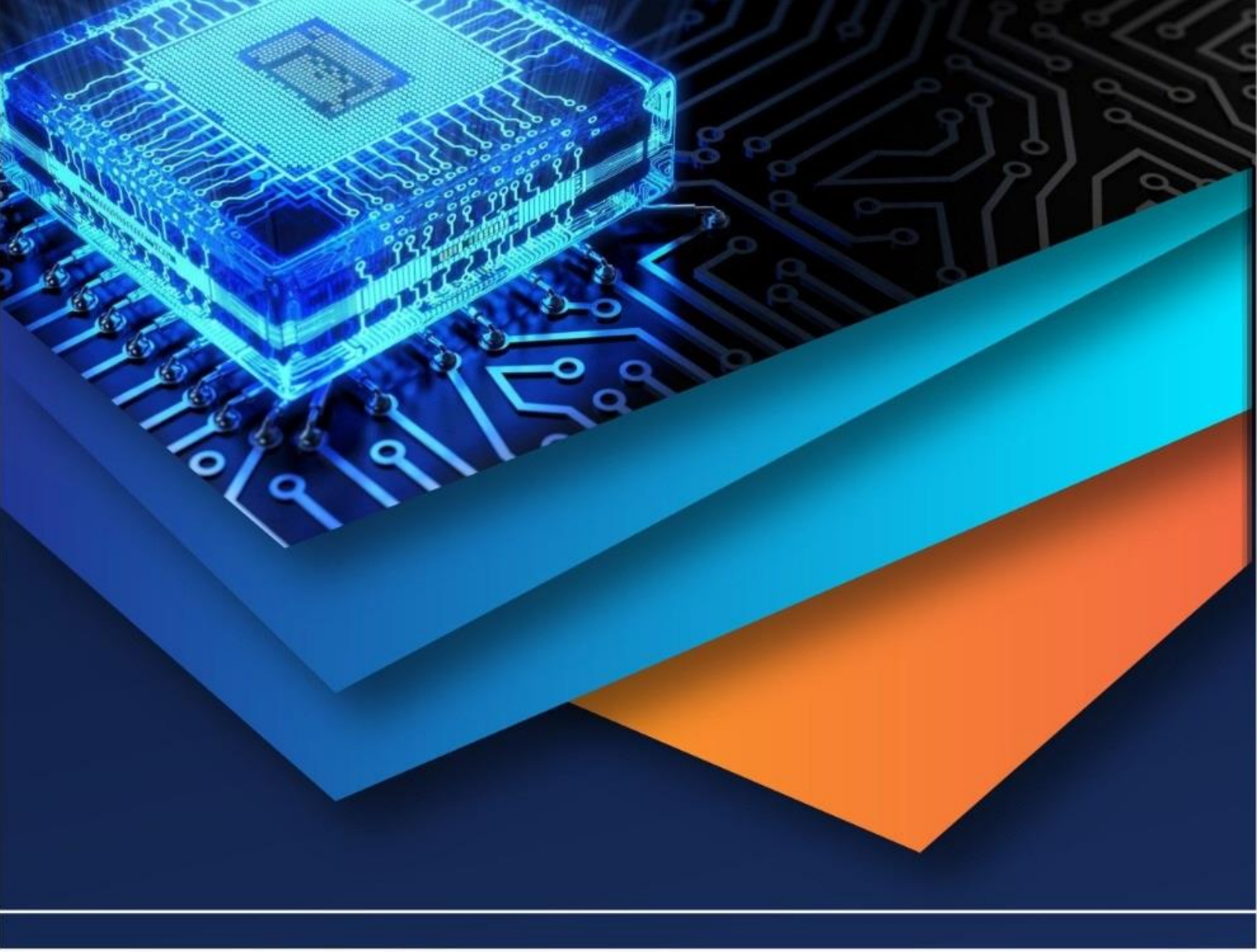
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