Original Article

The prevalence of anemia in rheumatoid arthritis

Smyrnova Ganna*

Department of Internal Medicine, Donetsk M. Gorky National Medical University, Ukraine

ARTICLE INFO

ABSTRACT

Objectives: The aim of this study was to evaluate the prevalence of anaemia in rheumatoid arthritis (RA).

Patients and methods: 89 patients who fulfilled American College of Rheumatology (ACR) criteria for RA were included in this study. The mean disease duration was 10.9 ± 8.8 years. All patients received methotrexate (10.5 ± 5.5 mg/week) in combination with folic acid. Steroid hormones were prescribed to 92% (19.3 ± 3.8 mg/day) of patients. Erythrocyte sedimentation rate (ESR) and levels of hemoglobin, C-reactive protein (CRP), tumour necrosis factor-alpha (TNFα) and interleukin-1 beta (IL-1β) were evaluated in all patients. The World Health Organization (WHO) criteria for anaemia uses a hemoglobin threshold of <120 g/L for women and <130 g/L for men.

Results: Anaemia was observed in 57 (64%) of the patients (1st group), the other patients (2nd group) had normal levels of hemoglobin (135.5 ± 10.7 g/L). Duration and activity of RA were significantly higher ($p < 0.05$) in the 1st group compared with the 2nd. ESR, CRP, TNFα, and IL-1β mean levels were significantly increased ($p < 0.05$) in the 1st group when compared with the 2nd group. Negative correlations between hemoglobin level and ESR, CRP, TNFα, and IL-1β concentrations were observed.

Conclusion: This study showed for the first time in Ukraine that in 46% of patients with RA, anaemia was diagnosed. A reduction of hemoglobin level was associated with a high activity of disease.

Prevalência de anemia na artrite reumatoide

RESUMO

Objetivos: O objetivo desse estudo foi avaliar a prevalência de anemia em pacientes com artrite reumatoide (AR).

Pacientes e métodos: 89 pacientes que satisfaziam os critérios do *American College of Rheumatology* (ACR) para AR foram incluídos nesse estudo. A duração média da doença foi $10,9 \pm 8,8$ anos. Todos os pacientes foram medicados com metotrexato ($10,5 \pm 5,5$ mg/semana) em combinação com ácido fólico. Hormônios esteroides foram receitados para 92% dos pacientes ($19,3 \pm 3,8$ mg/dia). Velocidade de hemossedimentação (VHS), níveis de hemoglobina,

* *Corresponding author.*
   E-mail: a.smyrnova@mail.ru (S. Ganna).

proteína C reativa (PCR), fator de necrose tumoral alfa (TNFα) e interleucina-1 beta (IL-1β) foram avaliados em todos os pacientes. Os critérios da Organização Mundial da Saúde (OMS) para anemia utilizam um limiar para hemoglobina de <120 g/L para mulheres e de <130 g/L para homens.

Resultados: Anemia foi observada em 57 (64%) dos pacientes (1º grupo); os demais pacientes (2º grupo) tinham níveis normais de hemoglobina (135,5±10,7 g/L). A duração e a atividade de AR foram significativamente maiores (p<0,05) no 1º *versus* 2º grupo. Os níveis médios de VHS, PCR, TNFα e IL-1β estavam significativamente aumentados (p<0,05) no 1º *versus* 2º grupo. Foram observadas correlações negativas entre o nível de hemoglobina e as concentrações de VHS, PCR, TNFα e IL-1β.

Conclusão: Esse estudo demonstrou pela primeira vez que, na Ucrânia, 46% dos pacientes com AR apresentavam anemia. Um nível reduzido de hemoglobina foi associado à atividade intensa da doença.

Introduction

Rheumatoid arthritis (RA) is a polyarticular autoimmune disease, affecting about 1% of the adult population.[1] The disease is characterized by hyperplasia of synoviocytes, mainly the synovial fibroblasts, resulting in bone and joint destruction.[2] Recent studies have revealed a key role of cytokines and other mediators of inflammation in the development not only of the articular syndrome, but also a whole range of systemic manifestations of the disease.[3] In particular, anemic syndrome is a very common manifestation of rheumatoid inflammation. However, the prevalence of anemia in Ukrainian patients has never been investigated as it relates to RA.

The aim of this study was to determine the prevalence of anemia in RA patients.

Methods

Eighty-nine patients who fulfilled the American College of Rheumatology (ARA) criteria for RA were included in this study. The mean disease duration was 10.9±8.8 years. All patients received methotrexate (average dose 10.5±5.5 mg/week) in combination with folic acid. Steroid hormones were prescribed to 92% (average dose 19.3±3.8 mg/day). All of the subjects were submitted to the following battery of tests: erythrocyte sedimentation rate (ESR), levels of hemoglobin, C-reactive protein (CRP), tumor necrosis factor-alpha (TNF-α) and interleukin-1 beta (IL-1β). The World Health Organization (WHO) criteria for anemia uses a hemoglobin threshold of <120 g/L for women and <130 g/L for men.[4] Pregnant or breast-feeding patients, patients with a history of other inflammatory or non-inflammatory arthritis, megaloblastic anemia, malignancies, renal disease with severe renal insufficiency, chronic infectious and inflammatory diseases, and other diseases in the stage of decompensation were excluded from the study. In addition, the study was approved by the local ethics committee, and all participants gave their written consent for inclusion.

Statistical analysis

The Kolmogrov-Smirnov and Shapiro-Wilk tests were used to test normality while non-parametric tests were preferred for testing the results and scales. The differences in proportions between the groups were compared using a chi-square or Fisher's exact test where appropriate. Continuous variables, including disease duration, and morning stiffness (MS) duration were compared using the Mann-Whitney-U test among categories of grouped variables, and the degree of correlation between the variables was calculated using Spearman's rho correlation coefficients. General descriptive statistics were summarized using numbers and percentages for categorical variables and median (min-max) while mean ± standard deviation (SD) was utilized for continuous variables. Statistical analyses were performed with the "MedStat" version 4.0 for Windows software program, and a p-value of less than 0.05 was considered to be statistically significant.

Results

Anemia was observed in 57 (64%) of the patients (1st group); the other (2nd group) had normal levels of hemoglobin (135.5±10.7 g/L). The patients from the 1st and 2nd groups were statistically similar with regard to age (p=0.21) and gender (p=0.33).

Duration and activity of RA were significantly (p<0.05) higher in 1st group compared with the 2nd (Table 1). The mean ESR, CRP, TNF-a, IL-1b levels were significantly increased in the 1st group when compared with the 2nd (Table 1).

The results of a correlation analysis between the hemoglobin level and the laboratory parameters of RA activity are shown in Table 2. There were negative correlations between the hemoglobin level and ESR, CRP, TNF-a, IL-1b concentrations (Table 2).

Discussion

According to the literature,[5] anemia develops in 30%-70% of patients with RA. There are different types of anemia,

Table 1 – Comparison of the RA activity of the two groups

Parameters	P-values	1st group	2nd group
Duration of RA	0.004	11,67±3,62	7,63±3,48
ESR, mm/h	0.03	51,26±24,67	29,65±19,84
CRP, mg/dL	0.001	48,27±12,18	4,38±1,28
TNFα, pcg/mL	0.001	32,54±9,71	7,69±3,45
IL-1β, pg/mL	0.04	166,32±18,54	102,28±16,34
DAS28 index	0.004	5(5;6,5)	3(2,5;3)

Table 2 – The results of a correlation analysis between the hemoglobin level and the laboratory parameters of RA activity

Laboratory test	Correlation coefficient (r)	p values
ESR, mm/h	-0,62	p<0,001
CRP, mg/dL	-0,61	p<0,001
TNF-α, pcg/mL	-0,59	p<0,001
IL-1β, pg/mL	-0,57	p<0,001

including iron deficiency anemia (IDA), anemia of chronic disease (ACD), megaloblastic anemia, hemolytic anemia and COMBI anemia that could occur in patients with RA. Some causes of anemia include changes in iron metabolism due to lesions of the mucous membrane of the gastrointestinal tract by steroid drugs, methotrexate; shortening of red blood cells' life or its inadequate production by bone marrow.[6] Our results are consistent with the data of literature. A characteristic of this disorder is a blunted erythropoietin response by red blood cell precursors, decreased survival of the red blood cells, and defective iron absorption. Defective macrophage iron retention may also contribute to the disorder by interrupting iron delivery to erythroid precursor cells. It may be precipitated by impaired iron utilization, where functional iron is low but tissue iron is normal or high. It is the second most common form of anemia worldwide after IDA. It is also clear now that inflammatory cytokines released during ACD can alter systemic iron metabolism by inducing excess synthesis of hepcidin, the iron regulatory hormone. Since hepcidin inhibits iron export from cells by blocking ferroportin activity, excess hepcidin is the root cause of the hypoferremia and iron-restricted erythropoiesis seen in ACD.

Conclusions

In conclusion, we believe that this is the first study to evaluate the prevalence of anemia in Ukrainian patients with RA. We suggest that RA patients undergo a routine analysis of their hemoglobin levels, and when decreased hemoglobin level is suspected, adequate investigation should be performed. Moreover, patients should be advised about estimation of clinical and laboratory RA activity parameters.

Conflicts of interest

The author declares no conflicts of interest.

REFERENCES

1. Lawrence RC, Helmick CG, Arnett FC, Deyo RA, Felson DT, Giannini EH et al. Estimates of the prevalence of arthritis and selected musculoskeletal disorders in the United States. Arthritis Rheum. 1998;41:778-799.
2. Neumann E, Lefèvre S, Zimmermann B, Gay S, Müller-Ladner U. Rheumatoid arthritis progression mediated by activated synovial fibroblasts. Trends in Molecular Medicine. 2010;16:458-468.
3. Choy EH, Panayi GS. Cytokine pathways and joint inflammation in rheumatoid arthritis. N Engl J Med. 2001;12:907-916.
4. World Health Organization. WHO/NHD/01.3: Iron deficiency anaemia. Assessment, prevention and control. A guide for programme managers. Geneva, 2001. 114p.
5. Bloxham E, Vagadia V, Scott K, Francis G, Saravanan V, Heycock C et al. Anaemia in rheumatoid arthritis: can we afford to ignore it? Postgrad Med J. 2011;1031:569-600.
6. Kullich W, Niksic F, Burmucic K. Effects of the chemokine MIP-1alpha on anemia and inflammation in rheumatoid arthritis. Z. Rheumatol. 2002;61:568-576.