SCI-CONF.COM.UA

INNOVATIVE DEVELOPMENT OF SCIENCE, TECHNOLOGY AND EDUCATION

PROCEEDINGS OF XI INTERNATIONAL SCIENTIFIC AND PRACTICAL CONFERENCE AUGUST 1-3, 2024

VANCOUVER 2024

TABLE OF CONTENTS

AGRICULTURAL SCIENCES

BIOLOGICAL SCIENCES

MEDICAL SCIENCES

MEDICAL SCIENCES

DYNAMICS OF INTERLEUKIN-6 IN PATIENTS WITH COMMUNITY-ACQUIRED PNEUMONIA ASSOCIATED WITH CORONAVIRUS INFECTION UNDER THE INFLUENCE OF TREATMENT

Avgaitis S. S.
Zaporizhzhia State University Of Medicine And Pharmacy
Department of General Practice - Family Medicine and Psychiatry

Introduction.

In December 2019, a series of cases of pneumonia with an unknown cause presented in Wuhan, China, with clinical manifestations very similar to viral pneumonia. In-depth analysis identified a new coronavirus, which was named the novel coronavirus 2019. Severe Acute Respiratory Syndrome-Coronavirus 2 (SARS-CoV-2) is characterised by a long incubation period, high contagion and multiple transmission routes. However, there is currently no effective treatment, so patients are treated symptomatically. A better understanding of the mechanisms of pathological changes will help to identify potential drugs from the currently available ones (Wang C., 2020; Huang C., 2020).

Several clinical trials have shown that the ‘cytokine storm’ is an important mechanism underlying the exacerbation of the disease and death of patients with COVID-19. In particular, interleukin-6 (IL-6) levels in severely ill patients were significantly higher than in mild cases. Reducing IL-6 levels and decreasing its activity can prevent or even reverse the cytokine storm syndrome, thereby improving the condition of patients with COVID-19 (Wan S., 2020; Ye, Q., 2020).

Studies have shown that low-molecular-weight heparin has various non-anticoagulant properties that play an anti-inflammatory role by reducing the release of IL-6. However, the anti-inflammatory effects of heparin in COVID-19 are

currently not well understood. It is assumed that anticoagulation will have a beneficial effect in controlling the ‘cytokine storm’ and slow the progression of community-acquired pneumonia associated with coronavirus infection (Chen S., 2020; Gozzo L., 2020).

Objective.

To evaluate the dynamics of cytokines in patients with community-acquired pneumonia associated with coronavirus infection under the influence of treatment.

Material and methods: An open, prospective, observational study was conducted to achieve the aim and solve the problems. In the period from January 2021 to February 2022, patients with community-acquired pneumonia associated with SARS-CoV-2 aged 40 to 65 years were examined at the outpatient clinic of the Kherson City Clinical Hospital named after Afanasii and Olga Tropin of the Kherson City Council, 143 patients were admitted to the hospital. To participate in the study, patients signed the Voluntary Informed Consent to Participate in the Study form.

Study inclusion criteria: male and female patients aged 40 to 65 years; community-acquired pneumonia; informed consent of the patient to participate in the study.

Exclusion criteria for the study: pregnant women; uncontrolled hypertension; stage III hypertension; decompensated diabetes mellitus; congenital and acquired haemodynamically significant heart defects; stage II B - III chronic heart failure; oncological diseases; lung damage of more than 75% according to CT scan; contraindications to the administration of drugs and their components; alcohol dependence, drug addiction, mental disorders; patient refusal to participate in the study.

All patients were carefully examined for compliance with the inclusion/exclusion criteria. The diagnosis of community-acquired pneumonia was verified on the basis of the adapted evidence-based clinical practice guideline Community-Acquired Pneumonia in Adults, 2019. COVID-19 was diagnosed in accordance with Order No. 722 of the Ministry of Health of Ukraine dated 28.03.2020 as amended by Order No. 2122 of the Ministry of Health of Ukraine

dated 17.09.2020.

Allocation of the study subjects to subgroups. After randomisation, 143 hospitalised patients with severe APE associated with COVID-19 were divided into subgroups depending on the anticoagulant included in the treatment regimen:

- the first subgroup consisted of 71 patients who were prescribed standard heparin infusions;

- the second subgroup included 72 patients who received enoxaparin.

Interleukin-6 was measured in blood plasma by enzyme-linked immunosorbent assay using standard kits: 'IL-6-ELISA-Best', according to the attached instructions, in the certified laboratory of the Kherson City Clinical Hospital named after Afanasiy and Olga Tropin of the Kherson City Council. The amount of extension was determined using a HTI Immunochem-2100 plate analyzer (High Technology Inc., USA).

Drug treatment of patients.

At the stage of inpatient treatment, all patients (n = 143) received oxygen support. Systemic corticosteroids were prescribed: dexamethasone (KRKA, Slovenia) at a dose of 6 mg once daily. Ibuprofen, a non-steroidal anti-inflammatory drug, was prescribed at a dose of 400 mg twice daily (Ibuprofen-Zdorovye, manufactured by Pharmaceutical Company Zdorovye, Ukraine). In the hospital, remdesivir (Corovir, Bruck Pharma PVT, LTD) was also prescribed on the first day in a single dose of 200 mg, and 100 mg per day intravenously on the following days. The course of treatment lasted 5 days.

After randomisation, 71 patients were additionally prescribed infusions of standard heparin (Heparin-Pharmex, Farmex Group LLC, Ukraine) at the rate of 1000 IU/h for 10 days, and 72 patients received enoxaparin (Flenox, Farmak JSC, Ukraine) at the rate of 100 IU anti-Xa/kg (1 mg/kg) twice daily for 10 days. The study parameters were assessed on day 3 and 14 after randomisation.

Statistical processing of the data obtained during the study began with descriptive statistics, including the calculation of the median and interquartile range (Me [Q25; Q75]). When testing statistical hypotheses, the null hypothesis was

rejected at a level of $p < 0.05$.

Results.

Both treatment subgroups had comparable values of IL-6 at screening: 9.12 [8.12; 10.12] pg/ml in the first subgroup and 9.05 [8.00; 10.17] pg/ml in the second subgroup ($p > 0.05$). After 72 hours of treatment, the level of IL-6 significantly decreased in the first subgroup from 9.12 [8.12; 10.12] pg/ml to 8.01 [7.07; 9.00] pg/ml ($p < 0.05$) by $\Delta 1\% = -12.93\%$. Whereas in the second subgroup, this indicator significantly decreased by $\Delta 2\% = -4.75\%$ to 8.72 [7.36; 9.55] pg/ml, ($p < 0.05$). The values of IL-6 after 72 hours significantly differed between the first and second subgroups - 8.01 [7.07; 9.00] pg/ml vs. 8.72 [7.36; 9.55] pg/ml, respectively ($p < 0.05$). After 14 days, the decrease in IL-6 levels in both subgroups was significant and amounted to $\Delta 1\% = -49.76\%$ in the first subgroup and $\Delta 2\% = -40.70\%$ in the second subgroup ($p < 0.05$). There were no statistically significant differences in this indicator between the subgroups after 14 days of treatment ($p > 0.05$).

Our results coincide with those of C. Shi et al., statistical analysis of inflammatory cytokine levels in the two groups of patients showed that IL-6 was significantly reduced in the heparin group compared to the control group. Reducing IL-6 levels can prevent the ‘cytokine storm’ syndrome caused by the virus, thereby improving the condition of patients with COVID-19, which is consistent with the above (Shi C., 2020).

Thus, the results of our study showed that heparin significantly reduces IL-6 levels. Although the study has limitations, as it includes a small number of patients and no patients with comorbidity, it is reasonable to recommend the use of heparin for patients with a low risk of bleeding, while others use enoxaparin to prevent thrombotic complications.

Conclusions.

1. Combination therapy is effective in reducing IL-6 levels.

2. Heparin at a dose of 1000 IU/h is more effective in reducing IL-6 after 72 hours, whereas after 14 days both treatment regimens were comparable.

REFERENCES:

1. Wang, C., Horby, P. W., Hayden, F. G., & Gao, G. F. (2020). A novel coronavirus outbreak of global health concern. *The lancet*, *395*(10223), 470-473. DOI: 10.1016/S0140-6736(20)30185-9.

2. Huang, C., Wang, Y., Li, X., Ren, L., Zhao, J., Hu, Y., ... & Cao, B. (2020). Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The lancet*, *395*(10223), 497-506. DOI: 10.1016/S0140-6736(20)30183-5.

3. Wan, S., Yi, Q., Fan, S., Lv, J., Zhang, X., Guo, L., ... & Chen, Y. (2020). Characteristics of lymphocyte subsets and cytokines in peripheral blood of 123 hospitalized patients with 2019 novel coronavirus pneumonia (NCP). *MedRxiv*. DOI: 10.1101/2020.02.10.20021832.

4. Ye, Q., Wang, B., & Mao, J. (2020). The pathogenesis and treatment of the Cytokine Storm'in COVID-19. *Journal of infection*, *80*(6), 607-613. DOI: 10.1016/j.jinf.2020.03.037.

5. Chen, S., Wang, C., Wang, H., Yang, C., Cai, F., Zeng, F., ... & Zhang, Y. (2020). The Potential of Low Molecular Weight Heparin to Mitigate Cytokine Storm in Severe COVID-19 Patients: A Retrospective Cohort Study. *Clinical and Translational Science*, *13*(6), 1087-1095. DOI: 10.1111/cts.12880.

6. Gozzo, L., Viale, P., Longo, L., Vitale, D. C., & Drago, F. (2020). The potential role of heparin in patients with COVID-19: beyond the anticoagulant effect. A review. *Frontiers in pharmacology*, *11*, 1307. DOI: 10.3389/fphar.2020.01307.

7. Shi, C., Wang, C., Wang, H., Yang, C., Cai, F., Zeng, F., ... & Zhang, Y. (2020). The potential of low molecular weight heparin to mitigate cytokine storm in severe COVID-19 patients: a retrospective cohort study. *Clinical and translational science*, *13*(6), 1087-1095. DOI: 10.1111/cts.12880.