PB2250 GENETIC REGULATION IN IRON OMEOSTASIS IN SIDEROPENIC COVID19 DISEASE AFFECTED PATIENTS WITH NEW IRON ORAL FORMULATION: LESSONS FROM A DIFFERENT PERSPECTIVE

Topic: Iron metabolism, deficiency and overload

Background: Coronaviruses are able to upregulate gene chop/gadd153. This gene induces CD8 lymphocyte apoptosis and stimulates hepcidin production. Covid19 is also able to induce Asp-1 gene expression that degrades asparagine blocking NO production, impairing immune response and antithrombotic activity.

We know that iron deficiency is linked to an increase incidence of infection and impaired immune response, and anemia impact negatively on covid 19 survival.

Aims: To show how covid19 interferes in iron metabolism of sideropenic patients upregulating expression of genes as chop/gadd153 and arginase-1 and how sucrosomial oral iron support might change that.

Methods: We enrolled 60 patients with sideropenic anemia due to gastrointestinal bleeding, of whom 40 affected by documented COVID19 infection only with mild form with fever, diarrhea, bone or muscle pain or flu-like syndrome.

This study is a multicenter, retrospective study. The time of enrollment was 20 months. 20 Patients received 60 mg/die of elemental iron of Sucrosomial® iron (20 patients – group A). 20 patients received no iron support (group B). We enrolled also 20 patients without COVID19 infection, but with gastrointestinal bleeding, as control group (group C).

Characteristics of patients were superimposable in the three groups.

Whole blood was taken from the 60 COVID-19 patients and 20 healthy individuals as control group, and after RNA extraction and complementary DNA (cDNA) synthesis of Arg1, hepcidin and chop/gadd153 gene, expression of genes was measured by real-time PCR and was referred to gene expression of control group.

The circulating M1 proinflammatory macrophages (iNOS high/CD163 low/CD14+) and M2 antiinflammatory (iNOSlow/CD163high/CD14-) were analyzed by cytofluorimetry.

Data were collected at 0 and 3 months.

Results: At 0mo Chop gene expression was 2inA,4inB,1inC; Arg-1gene expression was 2inA,3inB,1inC, M1 expression was 0.4%inA,1%inB,0.4%inC,M2 expression was 0.6%inA,0.2%inB,0.5%inC.

At 3mo Chop gene expression was 1inA,1.5inB,1inC; Arg-1gene expression was 1inA,1inB,1inC, M1 expression was 0.4%inA,0.8%inB,0.4%inC,M2 expression was 0.5%inA,0.4%inB,0.5%inC.

Summary/Conclusion: Patients with gastrointestional bleeding with mild covid 19 disease show respect to patients with gastrointestinal bleeding and without covid19 disease an increased activation of chop gene and asp-1 gene, that leads to lymphopenia, immunodepression, functional iron deficiency, hencanced m1 macrophage polarization with an high inflammation, an higher transfusion need, an high number of hospitalized patients with a lenght of hospital stay higher. And these facts are evident mainly in the first phase of the mild disease.
When patients are supported with oral sucrosomial iron, the expression of chop and asp-1 gene and hepcidin gene are lower than we can see in sideropenic patients not supported. The level of inflammation, M1 macrophages proinflammatory polarization and functional iron deficiency is lower in patients supported, with no transfusion need, a slight level of anemia, no patients hospitalized. Also in this case differences are evident mainly in the early phase of disease.

Probably new oral iron formulation, as sucrosomial iron, are important to influence expression of genes as chop and asp-1, mainly in the early phase of covid19 disease, stopping functional iron deficiency and allowing a restart of a normal immune system functioning.