Intralipid in the Target Treatment of Lipid Peroxidation Disorder Caused by Oxidative and Nitro-Galogenic Stress in Patients with SARS-Cov2 / COVID / 19

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Authors’ contributions
This work was carried out in collaboration among all authors. Authors Ilie Vasiliev, MV and Irina Vasilieva designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Authors SG, GG, MB, VD, NB, ED, Olga Tagadiuc, Pavel and Tania Globa, NR, GP, LV, JB, GC, Lilian and Elena Globa, SI, LS, AC, MD’A, Oleg Tarabrin and Ilie Vasiliev managed the analyses of the study. Author Ilie Vasiliev managed the literature searches. All authors read and approved the final manuscript.

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1. INTRODUCTION

Scientists Eldor J., Javid M.J., Zebardast J. has been published [1-8] the successful use of intralipid in postoperative cognitive impairments, the antitoxic effect of local anesthetics during neuraxial anesthesia, and also as an antidote to the toxic manifestations of calcium blockers, and since 2020, the anticoVID / 19 effect. Coronavirus enters intracellularly thanks to both the molecule the protein Cluster of Differentiation (CD147) [also called extracellular matrix metalloproteinase inducers (EMMPRIN), or basigin (BSG), and belong to the immunoglobulin superfamily] and the Angiotensin-Converting Enzyme 2 (ACE2) receptors due to immunocompromising (IC) mechanisms. The predominance of the hyperinflammatory response (SIRS), due to the immune-paralysis of the anti-inflammatory response (CARS), manifests itself as IC CHAOS dissonance [9-10]. Vascular-pulmonary tissue is rich in ACE2 receptors, which contributes to rapid damage membranes to endothelium cells and alveocytes and the development of SARS-Cov2 / COVID19 respiratory failure, due to the accumulation of cytokine storm mediators. In other cases, protective cytokines aimed at destroying pathogenic bacteria, viruses, in cases of IC CHAOS dissonance, generates an imbalance between: Reactive oxygen species (ROS) / the antioxidant system (AS); reactive nitrogen species (RNS) / anti nitro oxidant system (ANOS) manifest themselves as Oxidative and Nitro-halogenic stress [11-13]. Accumulated metabolites ROS: oxygen free radicals (O2•− - superoxide radical anion, HO• - hydroxyl radical), H2O2 molecules - hydrogen peroxide, singlet oxygen 1O2, ozone O3, hypochlorite HOCl; and RNS (main forms of NO (dinitrogen trioxide - N2O3; peroxynitrite – ONOO− ; nitric oxide radical – NO•; nitrosonium cation – NO2+; nitrosoperoxy carbonate anion – ONOOOCOO− ; nitrogen dioxide NO2) behave aggressively against their own biological membranes. Reduction of ROS is carried out by activation of the ratio of prooxidant / antioxidants (GSH, Ascorbate, Retinols, Tocopherols, Urates, Carotenes, Bilirubin) and the ΔpH + mechanism [14] and optimal use of O2 in the respiratory chain, thereby reducing ROS and O2. The predominance of RNS> ANOS activates the intracellular synthesis of the p53 protein, which induces the expression of apoptogenic proteins Bcl-2, Bax, Fas, p53AIP (Apoptosis inducing protein). Simultaneously with the destruction of membrane proteins, DNA and RNA, lipid peroxidation (LPO) of cell membranes occurs with the formation of: lipid radicals L•; peroxyls LOO•; hydroperoxyls LOOH; alkoxyls LO•. In such cases, necrosis> apoptosis is clearly exceeded, since the predominant ROS> AS system also reduces the transmembrane potential on the inner mitochondrial membrane, provoking the Maria & Irina Vasilieva (electro-ion membrane distress syndrome) [15-17], disrupting the opening / closing of the Mitochondrial permeability transition pore-dependent Ca uniporter, mPT pore [18], conjugate process reflecting homeostasis of lysosomal mitochondrial autophagy clearance (mitophagy). Microcirculatory-mitochondrial distress syndrome, MMD is formed, with an increase in pCO2 (AV gap)> 6 mm Hg, as a reliable marker of tissue hypoxia. Extreme / Abnormal myelopoiesis exacerbates IR CHAOS dissonance, mediates MOD, and creates extreme genomic, transcriptomic, proteomic, metabolic, and phenomenal functional-structural disorders [17,19,20].

1.1 Purpose of the Study

Finding that Intralipid in the SARS-Cov2 / COVID / 19 treatment guidelines is recommended only in...
2. MATERIALS AND METHODS

In the COVID / 19 Intensive Care Unit, critical patients are hospitalized only with the positive confirmed diagnostic test RT-PCR (Coronavirus) (RNA, qualitative) in the nasopharyngeal exudate, were also examined for RPR, HIV etc. Intralipid was intravenously into a central vein used in 40 MODS SARS-Cov 2 / COVID-19 patients in the COVID19 Intensive Care Unit. Which developed Multiple Organ Dysfunction Syndrome (MODS) [21-30] against a background of various concomitant diseases: cancer, leukemia, diabetes mellitus, obesity, arterial - pulmonary hypertension, gastrointestinal bleeding, after surgery, with a pacemaker, liver cirrhosis, hormonal disorders and so on. The determination of the severity of SARS-Cov2 / COVID / 19 was determined according to the scales: HScore (P. Mehta et al.), high CRP, ESR, ferritin, fibrinogen, D-dimer, lymphopenia, thrombocytopenia; Thromboembolic risk (PADUA); Disseminated intravascular coagulation, DIC (ISTH); level of Consciousness (FOUR) in intubated patients; Organ failure (SOFA); Liver failure (Child - Turcotte - Pugh). Also determined: LDH ferments, Troponins, Creatinine phosphokinase, INR, ionogram, Oxygenation Index SpO2/FiO2 ratio, pCO2 (AV gap) and so on. Treatment of patients with SARS-Cov2 / COVID-19 was carried out in accordance with National Protocols, WHO with the manifestation of MODS was guided by the “Surviving Sepsis COVID-19” using (ECMO) MOST-ELSO [31]. Mechanical ventilation with alveolar recruitment [32]. Antiviral treatment: RNA-dependent RNA polymerase inhibition (Remdesivir); Inhibition of coronavirus fusion with the cell membrane by altering the pH of the cell membrane surface (Hydroxychloroquine); Protease inhibitors (Lopinavir / Ritonavir); Systemic Corticosteroids as Anti-Inflammatory (Dexamethasone); Immunomodulators (Tocilizumab - Selective IL-6 Receptor Antagonist; Anakira - Selective IL-1 Receptor Antagonist). Other authors have also used immunomodulators: Siltuximab, Baricitinib, Sarilumab. We also applied Convalescent plasma as a anti-COVID19 antibody carrier and active in IL-6 neutralization, with donor testing, including the absence of anti-HLA to prevent the risk of TRALI (Transfusion Related Acute Lung Injury); HNF (Unfractionated Heparin) Injectable Anticoagulant / HGMM (low molecular weight Heparin: Enoxaparin, Dalteparin, Nadroparin) in the treatment of Coagulopathies and for the prophylaxis of Venous Thromboembolism, Deep Venous Thrombosis, Pulmonary Embolism, DIC. We did not apply oral anticoagulants Intensive Care Patients, being recommended only to outpatients: Apixaban; Rivaroxaban. Antibiotics according to the de-escalation antibiotic therapy method for mono or multi inflammatory syndrome. Enteral and parenteral nutrition by applying Glucose; Amino Acids and Intralipid.

3. RESULTS

Severely ill patients with MODS SARS-Cov 2 / COVID-19 who were prescribed Intralipid for the purpose of parenteral nutrition, we noticed that they recover faster. The oxygenation index (OI) increased faster, SpO2 / FiO2 up to 400; The SpO2 saturation rose above 92 at FiO2 0.21; improved INR; enzyme activity decreased LDH, troponins, creatinine phosphokinase, including pCO2 (AV gap) <6 mm Hg, since the affected lung tissue was recovering, which was confirmed by X-ray.

4. DISCUSSIONS

We consider the observed improvement in the general condition in patients with SARS-Cov2 / COVID-19 after the use of Intralipid simultaneously with the energy carrier of parenteral nutrition and as its role in countering the development of lipid peroxidation disorder caused by Oxidative and Nitro-Galogenic stress. The observed encouraging therapeutic results after the use of Intralipid in patients with SARS-Cov2 / COVID-19 coincided with an improvement in the corresponding scales: HScore, PADUA, ISTH, FOUR, SOFA, Child - Turcotte - Pugh. The improvement of these rates was demonstrated by the universal membrane-cytotoxic mechanism of Intralipid in suspending and decreasing the aggressiveness of LPO in two possible ways: a) a direct decrease in the excess of ROS and RNS metabolites; b) increased activity of AS and ANOS. This also confirms the increase in OI to and above 400, which is possible with the restoration of destroyed endothelial and epithelial cells of the alveolar acini, capable of maintaining adequate
pulmonary gas metabolism. The actions of Intralipid to stop the ongoing destruction of cell membranes of LPO and a laboratory-proven decrease in cellular enzymes: LDH, Troponins, Creatinine phosphokinase are confirmed. Thus, Intralipid, acting on LPO, reduces the disorderly membrane-cell destructive actions: membrane destruction, swelling of plasma, lysosomes, mitochondria, karyorrhexis, DNA destruction, karyolysis. Also, these statements are confirmed by the regression of Maria&Irina Vasilieva syndrome [33] and Microcirculatory Mitochondrial Distress syndrome (MMDS) with a decrease in the tissue hypoxia marker pCO2 (AVgap) <6 mm Hg [34-40]. In this case, Intralipid also plays the role of microcirculatory-mitochondrial recruitment, reducing tissue hypoxia. As a result, MODS regressed, including the rapid recovery of consciousness and appetite [41-49]. We present X-ray images of two seriously ill MODS SARS-Cov 2 / COVID-19, of which one (A) received an Intralipid infusion, and the other (B) was not given, due to the absence of Intralipid in the hospital for financial and technical reasons. Apart from Intralipid, the treatment was the same for both patients. And the results are different. Patient A with repeated A2 X-ray of the lungs after 4 days showed a clear improvement in comparison with the X-ray of A1 lungs upon admission to the Intensive Care Unit, which made it possible to transfer the patient from the Intensive Care Unit, reducing the number of bed days, which is very important in a Pandemic. And in-patient B, who did not receive intralipid (was absent from the hospital), a repeated X-ray of the lungs after 6 days B2, was without improvement in relation to X-ray image B1, upon admission to the Department of COVID Intensive Care. Patient B continues intensive treatment [50-57].

**Fig. 1. X-ray.** A X-ray of the lungs of the patient "IJ" MODS SARS-Cov 2 / COVID-19 before the Intralipid infusion, during transfer to the Department of Intensive Care COVID-19. 16 November 2020. (A1)
Fig. 2. X-ray. A X-ray of the lungs of the patient "IJ" MODS SARS-Cov 2 / COVID-19 after the Intralipid infusion, when transferring from to the Department of Intensive Care COVID-19. 20 November 2020. (A2)

Fig. 3. X-ray. X-ray of the lungs of the patient "ChN" MODS SARS-Cov 2 / COVID-19 during transfer to the Department of Intensive Care COVID19. 24 November 2020. (B1)
5. CONCLUSIONS

1. Intralipid at Oxidative and Nitro-Galogenic stress in patients with SARS-Cov2 / COVID / 19, favors the predominance of the membrane-cytoprotective action of ROS / RNS over the membrane-cyto destructive action, restoring the balance between [ROS / AS] / [RNS / ANOS].

2. Membrane-cytoprotective mechanism Intralipid is due to a decrease in ROS and RNS and an increase in the activity of AS and ANOS, stopping LPO, reduces Maria&Irina Vasilieva syndrome, accelerates the regeneration of endothelial and epithelial cells of alveolar acinus, restoring gas-respiratory metabolism and the predominance of physiological cell apoptosis over necrosis.

3. Intralipid at SARS-Cov 2 / COVID / 19 opposes MMDS by microcirculatory - mitochondrial recruitment, as a result of which pCO2 (AVgap) <6 mm Hg, since LPO decreases and at the level of mitochondrial membranes, improving the function of Mitochondrial permeability transition pore-dependent Ca uniporter, mPT pore, support energy metabolism, eliminating energy deficits, restoring Extreme / Abnormal myelopoiesis and impaired autophagy (mitophagy).

Thus, Intralipid has shown in the strategy of targeted treatment of LPO in Oxidative and Nitro-Galogenic stress in patients with SARS-Cov2 / COVID / 19.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

As per international standard or university standard, patients’ written consent has been collected and preserved by the author(s).
ETHICAL APPROVAL
It is not applicable.

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COMPETING INTERESTS
Authors have declared that no competing interests exist.

REFERENCES


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