Evidencia ozonoterapia

Anotaciones acerca de la SSO3

Se conoce que..

- Un ensayo clínico es un estudio PROSPECTIVO donde se comparan efectos o valores de un grupo sujeto a una intervención Vs un grupo control, en población humana.
  - Los participantes se siguen en un periodo de tiempo X..
  - No necesariamente todos inician en la misma fecha calendario
  - Existe un T0 (inicio de l estudio).
  - Se emplea una o más técnicas de intervención, que se debe comparer contra la major terapia estándar
  - Los grupos al inicio deben ser comparables (aleatorización).
  - Idealmente doble ciego.

Fases de un ensayo

- Preclínico
  - Estudios in vitro
  - Modelos en animales.
- Clínicos
  - Fase I: Buscan
    - estimar la “tolerancia”
    - Caracterizar la farmacocinética y la farmacodinámica (emergen conceptos como biodisponibilidad y distribución compartimental en el organismo).
    - Establecer las dosis
      - Cual es el umbral de toxicidad. Por ejemplo 45 µg/mL para evitar daño al enterocito en IR. (la regla del 1/3)
    - Estimar la seguridad:
      - El caso de la deficiecnia de Gluocsa 6 fosfato deshidrogenasa.
    - Adelantados en “voluntarios sanos” (No necesariamente).
    - Pacientes que han fracasado con otras terapias.

Fase preclínica….Zotero….ISCO3..SSO3

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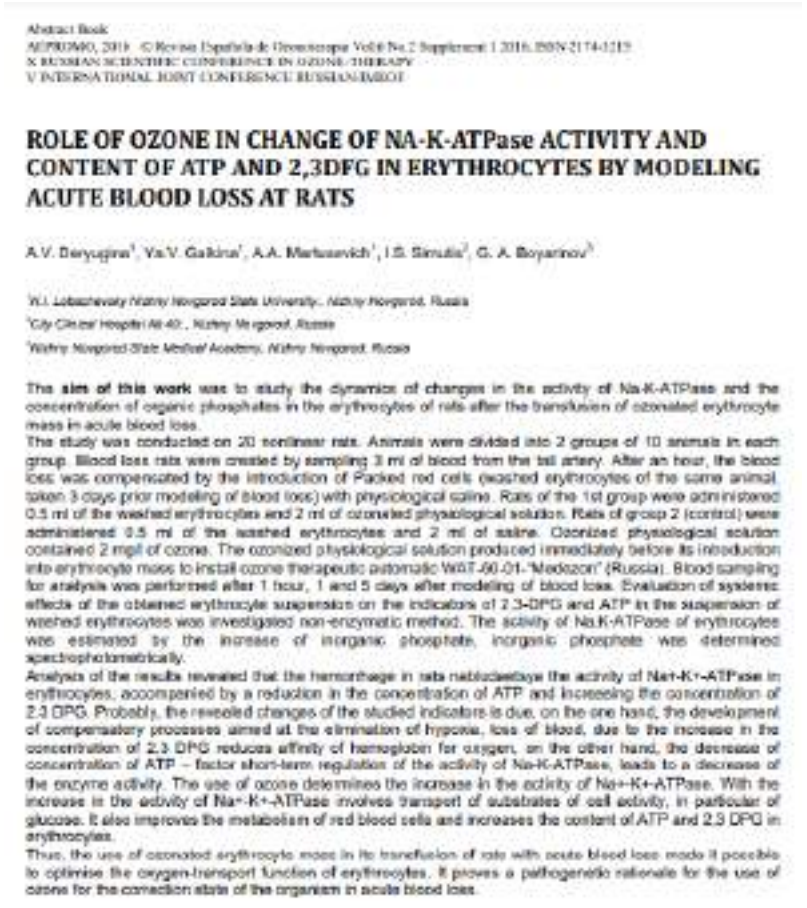


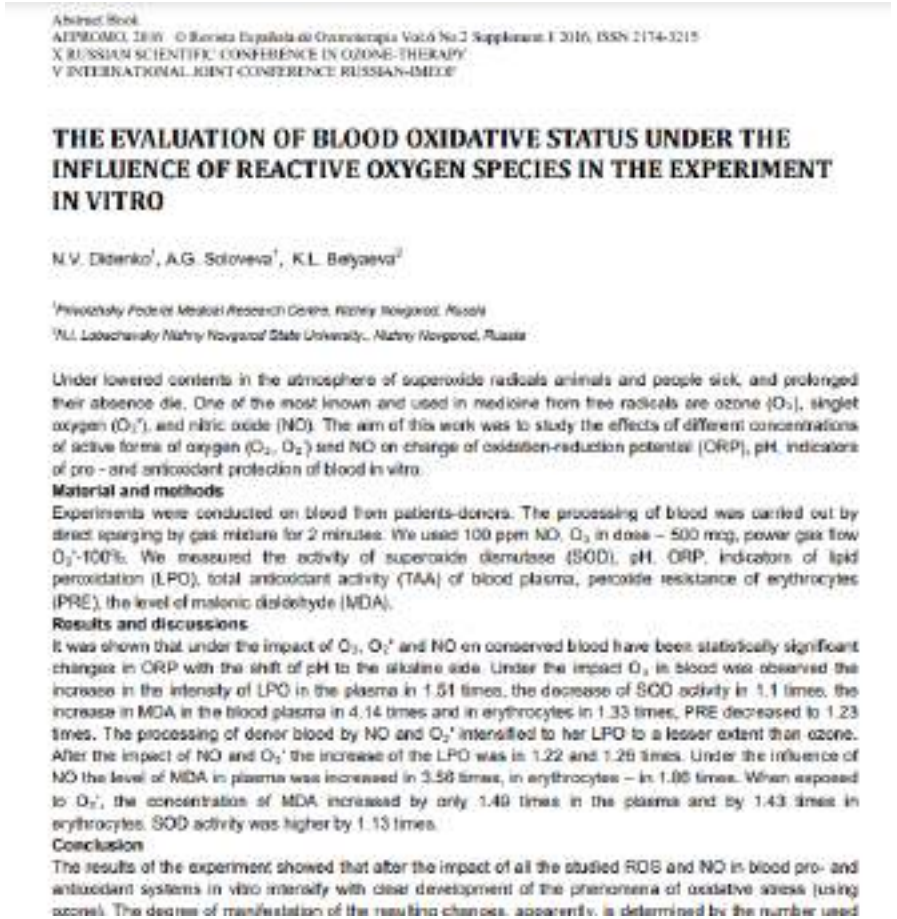
Abstract Book
AUPROMO, 2019 · © Revista Española de Ozonoterapia Vol.6 No.2 Supplement 1 2016, ISSN 2174-3215
X RUSSIAN SCIENTIFIC CONFERENCE IN OZONE-THERAPY
V INTERNATIONAL JOINT CONFERENCE RUSSIAN-IMEDF

ROLE OF OZONE IN CHANGE OF NA-K-ATPase ACTIVITY AND CONTENT OF ATP AND 2,3DFG IN ERYTHROCYTES BY MODELING ACUTE BLOOD LOSS AT RATS

A.V. Deryugina[1], Va.V. Galkina[2], A.A. Markusevich[1], I.S. Simulin[3], G. A. Boyarinov[3]

[1]N.I. Lobachevsky Nizhny Novgorod State University., Nizhny Novgorod, Russia
[2]City Clinical Hospital №40 , Nizhny Novgorod, Russia
[3]Nizhny Novgorod State Medical Academy, Nizhny Novgorod, Russia

The aim of this work was to study the dynamics of changes in the activity of Na-K-ATPase and the concentration of organic phosphates in the erythrocytes of rats after the transfusion of ozonated erythrocyte mass in acute blood loss.
The study was conducted on 20 nonlinear rats. Animals were divided into 2 groups of 10 animals in each group. Blood loss rats were created by sampling 3 ml of blood from the tail artery. After an hour, the blood loss was compensated by the introduction of Packed red cells (washed erythrocytes of the same animal, taken 3 days prior modeling of blood loss) with physiological saline. Rats of the 1st group were administered 0.5 ml of the washed erythrocytes and 2 ml of ozonated physiological solution. Rats of group 2 (control) were administered 0.5 ml of the washed erythrocytes and 2 ml of saline. Ozonized physiological solution contained 2 mg/l of ozone. The ozonized physiological solution produced immediately before its introduction into erythrocyte mass to install ozone therapeutic automatic WAT-90-01-"Medozon" (Russia). Blood sampling for analysis was performed after 1 hour, 1 and 5 days after modeling of blood loss. Evaluation of systemic effects of the obtained erythrocyte suspension on the indicators of 2,3-DPG and ATP in the suspension of washed erythrocytes was investigated non-enzymatic method. The activity of Na,K-ATPase of erythrocytes was estimated by the increase of inorganic phosphate, inorganic phosphate was determined spectrophotometrically.
Analysis of the results revealed that the hemorrhage in rats nebluclaetsya the activity of Na+-K+-ATPase in erythrocytes, accompanied by a reduction in the concentration of ATP and increasing the concentration of 2,3 DPG. Probably, the revealed changes of the studied indicators is due, on the one hand, the development of compensatory processes aimed at the elimination of hypoxia, loss of blood, due to the increase in the concentration of 2,3 DPG reduces affinity of hemoglobin for oxygen, on the other hand, the decrease of concentration of ATP – factor short-term regulation of the activity of Na-K-ATPase, leads to a decrease of the enzyme activity. The use of ozone determines the increase in the activity of Na+-K+-ATPase. With the increase in the activity of Na+-K+-ATPase involves transport of substrates of cell activity, in particular of glucose. It also improves the metabolism of red blood cells and increases the content of ATP and 2,3 DPG in erythrocytes.
Thus, the use of ozonated erythrocyte mass in its transfusion of rats with acute blood loss made it possible to optimise the oxygen-transport function of erythrocytes. It proves a pathogenetic rationale for the use of ozone for the correction state of the organism in acute blood loss.



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X RUSSIAN SCIENTIFIC CONFERENCE IN OZONE-THERAPY
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THE EVALUATION OF BLOOD OXIDATIVE STATUS UNDER THE INFLUENCE OF REACTIVE OXYGEN SPECIES IN THE EXPERIMENT IN VITRO

N.V. Dibenko[1], A.G. Soloveva[1], K.L. Belyaeva[2]

[1]Privolzhsky Federal Medical Research Centre, Nizhny Novgorod, Russia
[2]N.I. Lobachevsky Nizhny Novgorod State University., Nizhny Novgorod, Russia

Under lowered contents in the atmosphere of superoxide radicals animals and people sick, and prolonged their absence die. One of the most known and used in medicine from free radicals are ozone (O_3), singlet oxygen (O_2^*), and nitric oxide (NO). The aim of this work was to study the effects of different concentrations of active forms of oxygen (O_2, O_2^-) and NO on change of oxidation-reduction potential (ORP), pH, indicators of pro - and antioxidant protection of blood in vitro.

Material and methods

Experiments were conducted on blood from patients-donors. The processing of blood was carried out by direct sparging by gas mixture for 2 minutes. We used 100 ppm NO, O_3 in dose – 500 mcg, power gas flow O_2-100%. We measured the activity of superoxide dismutase (SOD), pH, ORP, indicators of lipid peroxidation (LPO), total antioxidant activity (TAA) of blood plasma, peroxide resistance of erythrocytes (PRE), the level of malonic dialdehyde (MDA).

Results and discussions

It was shown that under the impact of O_3, O_2^- and NO on conserved blood have been statistically significant changes in ORP with the shift of pH to the alkaline side. Under the impact O_3 in blood was observed the increase in the intensity of LPO in the plasma in 1.51 times, the decrease of SOD activity in 1.1 times, the increase in MDA in the blood plasma in 4.14 times and in erythrocytes in 1.33 times, PRE decreased to 1.23 times. The processing of donor blood by NO and O_2^- intensified to her LPO to a lesser extent than ozone. After the impact of NO and O_2^- the increase of the LPO was in 1.22 and 1.26 times. Under the influence of NO the level of MDA in plasma was increased in 3.56 times, in erythrocytes – in 1.86 times. When exposed to O_2^-, the concentration of MDA increased by only 1.49 times in the plasma and by 1.43 times in erythrocytes. SOD activity was higher by 1.13 times.

Conclusion

The results of the experiment showed that after the impact of all the studied ROS and NO in blood pro- and antioxidant systems in vitro intensify with clear development of the phenomena of oxidative stress (using ozone). The degree of manifestation of the resulting changes, apparently, is determined by the number used

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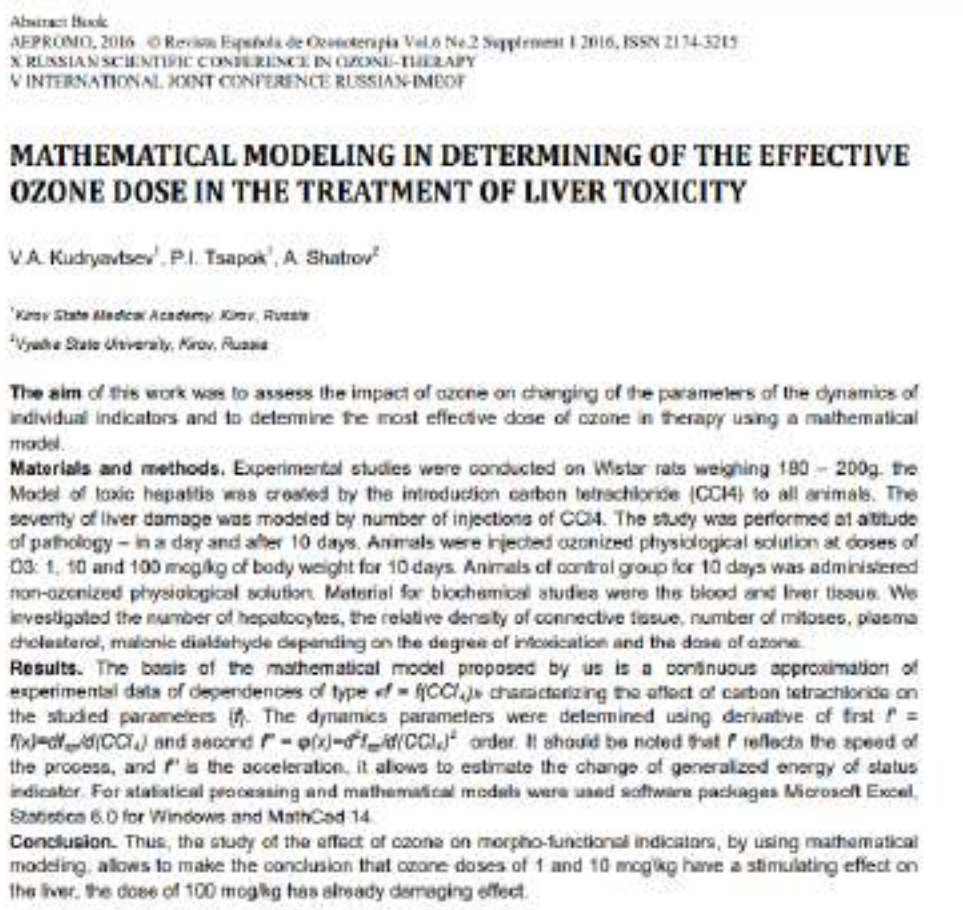
[Effect of ozonized saline on signaling passway of Keap1-Nrf2-ARE in rat hepatocytes]

Abstract



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X RUSSIAN SCIENTIFIC CONFERENCE IN OZONE-THERAPY
V INTERNATIONAL JOINT CONFERENCE RUSSIAN-IMEOF

MATHEMATICAL MODELING IN DETERMINING OF THE EFFECTIVE OZONE DOSE IN THE TREATMENT OF LIVER TOXICITY

V.A. Kudryavtsev[1], P.I. Tsapok[1], A. Shatrov[2]

[1]*Kirov State Medical Academy, Kirov, Russia*
[2]*Vyatka State University, Kirov, Russia*

The aim of this work was to assess the impact of ozone on changing of the parameters of the dynamics of individual indicators and to determine the most effective dose of ozone in therapy using a mathematical model.
Materials and methods. Experimental studies were conducted on Wistar rats weighing 180 – 200g. the Model of toxic hepatitis was created by the introduction carbon tetrachloride (CCl4) to all animals. The severity of liver damage was modeled by number of injections of CCl4. The study was performed at altitude of pathology – in a day and after 10 days. Animals were injected ozonized physiological solution at doses of O3: 1, 10 and 100 mcg/kg of body weight for 10 days. Animals of control group for 10 days was administered non-ozonized physiological solution. Material for biochemical studies were the blood and liver tissue. We investigated the number of hepatocytes, the relative density of connective tissue, number of mitoses, plasma cholesterol, malonic dialdehyde depending on the degree of intoxication and the dose of ozone.
Results. The basis of the mathematical model proposed by us is a continuous approximation of experimental data of dependences of type «$f = f(CCl_4)$» characterizing the effect of carbon tetrachloride on the studied parameters (f). The dynamics parameters were determined using derivative of first $f' = f(x)=df_{ex}/d(CCl_4)$ and second $f'' = \varphi(x)=d^2f_{ex}/d(CCl_4)^2$ order. It should be noted that f' reflects the speed of the process, and f'' is the acceleration, it allows to estimate the change of generalized energy of status indicator. For statistical processing and mathematical models were used software packages Microsoft Excel, Statistica 6.0 for Windows and MathCad 14.
Conclusion. Thus, the study of the effect of ozone on morpho-functional indicators, by using mathematical modeling, allows to make the conclusion that ozone doses of 1 and 10 mcg/kg have a stimulating effect on the liver, the dose of 100 mcg/kg has already damaging effect.

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X RUSSIAN SCIENTIFIC CONFERENCE IN OZONE-THERAPY
V INTERNATIONAL JOINT CONFERENCE RUSSIAN-IMSOF

Microcirculation state at prolonged use of ozonated saline in a chronic experiment

P.V. Peretyagin[1,2], A.K. Martusevich[1], V.N. Krylov[2]

[1]Privolzhsky Federal Research Medical Center, Nizhny Novgorod, Russia
[2]N.I. Lobachevsky State University of Nizhni Novgorod – National Research University, Nizhny Novgorod, Russia

The **aim of this study** was estimation of influence of ozonized saline infusions on rats' microcirculation state.

Material and methods

The experiment was performed on 40 Wistar rats, divided into 4 equal groups. Duration of experiment was 60 days, during the first 30 days the animals of the first experimental group daily intraperitoneally injected with 1 ml of 0.9% sodium chloride saturated with an ozone concentration of 3000 μg/ l ,(ozone dose of 0.6 μg). For animals of the second experimental group the saturated ozone concentration was 10,000 μg/l (the ozone dose - 2 mg), for the third experimental group – 40000 μg/l (the ozone dose of 8 mg). Animals in the control group received oxygenated physiological solution.

We evaluated the state of the microvasculature at the end of the experiment and 30 days after its completion with laser Doppler flowmetry using the LAKK-M ("LAZMA", Moscow), the intensity of microcirculation (microcirculation index - PM), the activity of its regulatory components and the degree of involvement of shunt paths were studied.

Results

It has been shown that long-term use of ozone for 30 days, has a dose-dependent effect on the microcirculation, while the effect of low concentration of the compound (0.6 mg) stimulating microcirculation surround keeps this effect even for 30 days after discontinuation of exposure. Large doses of ozone (2.0 and 8.0 mg), stimulating microcirculation system during long-term exposure, after its cancellation lose their modulatory effect on the microcirculation, compensating for it remains low shunt mechanisms.

Free Radical Research
Volume 50, 2016 - Issue 9

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Original Article

Ozone mediators effect on "*in vitro*" scratch wound closure

Giuseppe Valacchi, Claudia Sticozzi, Iacopo Zanardi, Giuseppe Belmonte, Franco Cervellati, Velio Bocci

Download citation | https://doi.org/10.1080/10715762.2016.1219751

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Abstract

The beneficial effect of low doses of ozone on wound healing has been well documented and attributed mainly to its bactericidal and pro-oxidant properties. Because ozone itself does not penetrate the cells but immediately reacts with polyunsaturated fatty acids, its effects are the results of oxidative mediators. Among the molecule produces by the interaction of ozone with biological systems, there are HNE and H_2O_2. As today, the cellular mechanisms accounting for the positive effects of mild ozonization on wound closure are still largely unexplored. The aim of the present study was to evaluate the effect of different non-toxic doses of ozonated saline ranging from 2 to 300 μM, in an *in vitro* wound scratch model by the use of human keratinocytes. The results showed that ozonated saline is able to improve *in vitro* wound healing by stimulating cell proliferation as measured by BrdU assay and PCNA protein levels. In order to better elucidate the molecules that play the main role in the beneficial effect of ozonated saline in wound healing, HNE and H_2O_2 were used alone or in combination to mimic ozonated saline effect. Surprisingly, keratinocytes treated with different doses of HNE and H_2O_2 did not significantly improve the wound closure, while the combination of the two compounds was able to improve wound closure. In addition, Nrf2 pathways were also activated as determined by its translocation to the nucleus and the increased HO1 gene expression. The present work suggests that ozonated saline effect on wound closure is the results of the combination of more molecules among which HNE and H_2O_2 play a key role.

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> Biomed Khim. Nov-Dec 2009;55(6):750-8.

[The effect of ozonated physiological solution on the postreperfused lipid composition and the level of carbohydrate metabolism substrates]

[Article in Russian]

N N Andreeva, T I Soloveva, M V Balandina, I V Mukhina

PMID: 20469723

Abstract

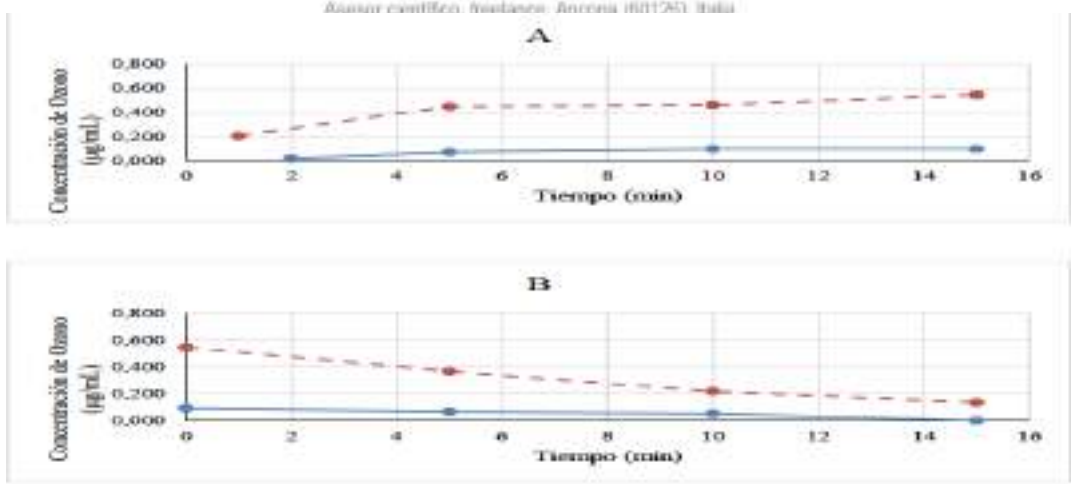
The effect of ozonated physiological solution on lipid composition, lipid peroxidation and level of carbohydrate metabolism substrates were investigated in the early reperfusion period. The total ischemia/reperfusion model was used. This study shows that injection of ozonated physiological solution in the early reperfusion period did not prevent cardiac myocyte membrane delipidization, activation of lipid peroxidation due to antioxidation exhaustion. Treatment with ozonated physiological solution promotes normalization in the lysophosphatidylholine and lysophosphatidylserine content, activation of hydrolytic degradation of neutral lipids, the decrease in membrane lipid microviscosity, activation of the aerobic glucose utilization and prevents lactic acidosis in the heart.

Ozone Therapy Global Journal vol. 10, nº 1 pp. 39-53, 2020
Official Journal of Aepromo (Spanish Association of Medical Professionals in Ozone Therapy). Madrid, Spain
Publicación Oficial de Aepromo (Asociación Española de Profesionales Médicos en Ozonoterapia). Madrid, España
ISSN: 2174-3215

Artículo original

Aspectos prácticos en ozonoterapia: Estudio de la concentración de ozono en la solución salina ozonizada

Gregorio Martínez-Sánchez



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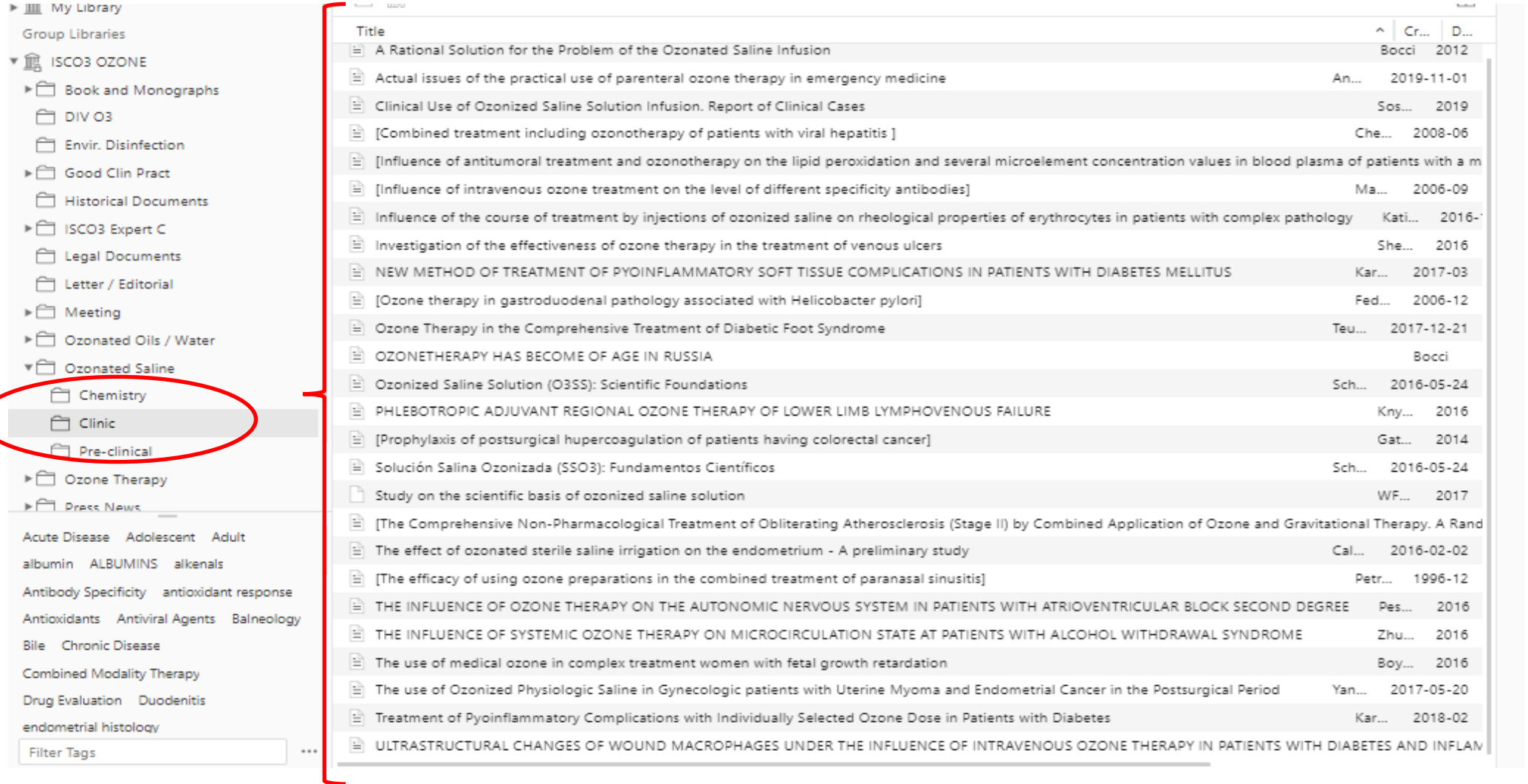

Ensayos clínicos. Múltiples congresos internacionales. Cuba, México, España, Rusia

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X RUSSIAN SCIENTIFIC CONFERENCE IN OZONE-THERAPY
V INTERNATIONAL JOINT CONFERENCE RUSSIAN-IMEDF

THE INFLUENCE OF OZONE THERAPY ON THE CONCENTRATION OF NITRIC OXIDE IN HYPERTENSION

I.E. Okrut, C.N. Kontorshikova, D.A. Dautova

[1]Nizhny Novgorod State Medical Academy, Nizhni Novgorod, Russia
[2]N.I. Lobachevsky Nizhni Novgorod State University, Nizhni Novgorod, Russia

The work is dedicated to the study a concentration of nitric oxide (nitrate and nitrite) during the arterial hypertension under the influence of ozone therapy. The object of the study was the blood samples of 80 persons with hypertension before and after treatment. The subject of the research was indicators of the exchange of nitric oxide - nitric oxide metabolites (nitrates/nitrites) in plasma in patients with arterial hypertension. The level of nitrates and nitrites was evaluated in a protein-free extract by spectrophotometry on a spectrophotometer Apel PD 303 (Japan). The course of treatment was 10 procedures for the introduction of ozonated physiological solution through the day. Ozone was generated using a ozone generator "Kvazar" when a current of the barrier discharge using medical oxygen. The ozonation of the solution was carried out by a 10-minute sparging with 200 ml of 0.9% NaCl solution, ozone-oxygen gas mixture with ozone concentration at the outlet of the ozonator from 1500 mcg/l of gas. The increase in the concentration of NO metabolites in blood of patients with arterial hypertension was marked compared to the control group at 40%, which indicated the presence and progression of pathological vascular mechanisms in the body. Conducted ozone therapy of patients with arterial hypertension led to a decrease in the concentration of nitrate and nitrite in 28% on average. Thus, the inclusion of ozone therapy in the treatment and prevention of hypertension allows to get a significant and lasting clinical effect.

Key words: ozone therapy, hypertension, nitrates, nitrites

Indice

Seguridad…eficacia

Ozone: Science & Engineering: The Journal of the International Ozone Association
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/bose20

Ozone Therapy in Patients with Viral Hepatitis C: Ten Years' Experience

M.N. Mawsouf [a], T.T. Tanbouli [b] & R. Viebahn-Hänsler [c]
[a] National Cancer Institute, Cairo University, Cairo, 11796, Egypt
[b] New Life Specialized Clinics, Mohandiseen, Giza (Greater Cairo), 12411, Egypt
[c] Medical Society for the Use of Ozone in Prevention and Therapy, Stuttgart, D-76473, Germany

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Ozone Therapy in Patients with Viral Hepatitis C: Ten Years' Experience

M.N. Mawsouf,[1] T.T. Tanbouli,[2] and R. Viebahn-Hänsler[3]
[1]National Cancer Institute, Cairo University, Cairo 11796, Egypt
[2]New Life Specialized Clinics, Mohandiseen, Giza (Greater Cairo) 12411, Egypt
[3]Medical Society for the Use of Ozone in Prevention and Therapy, Stuttgart D-76473, Germany

Hepatitis C is a medical problem in Egypt. The usual line of treatment is very expensive, with major side effects and low efficacy especially in genotype 4, which is common in Egypt. Several studies were performed between 1999 and 2008 to evaluate the role of ozone therapy in HCV (Hepatitis C). The first study included 60 genotype 4 Hepatitis C patients, who received combined ozone treatment with major autohemotherapy three times per week for 8 weeks, followed by twice per week for 16 weeks. It was found that, following 8 weeks of ozone therapy, the viral load decreased in 91.67% of the cases attaining negative PCR in 20%. Following 24 weeks of ozone therapy, there was a further decrease in viral load reaching 95% of the cases, with a negative PCR level in 36.67%. After 8 weeks of ozone therapy, the abnormal enzyme levels were back to normal in 21.67% of the cases for the SGPT enzyme, and were back to normal in 20% for the SGOT enzyme. A second study included 50 genotype 4 Hepatitis C patients. The number of visits was three times per week for 12 weeks followed by twice per week for 12 weeks. The general condition improved in 94% of the cases. There was a decrease in quantitative PCR in 71.8% of the cases that reached negative PCR in 24% after 8 weeks' treatment. The number of negative PCR cases for HCV virus increased to cover 36% of the cases after 24 weeks' treatment. There was a statistically significant improvement as regards the parameters of SGOT, SGPT, albumin, bilirubin and prothrombin after 8 weeks from the start of the study. A third study was carried out on 30 HCV patients, yielding results similar to the previous two.

Keywords Ozone Therapy, Hepatitis C (HCV)

AIM OF THE STUDIES

These studies were performed to evaluate the effectiveness and safety of ozone therapy in Hepatitis C genotype 4 infections, and to evaluate a proposed ozone therapy protocol in HCV genotype 4 treatment. Several studies and clinical observations were conducted between 1999 and 2008.

INTRODUCTION

Hepatitis C (HCV) is a worldwide medical problem. It is estimated that more than 300 million people are suffering from HCV (NIH 2009). Hepatitis C is a major medical problem in Egypt. It is postulated that more than 15%, i.e., over 10 million Egyptians are suffering from HCV (Sanara 1997). Progress of the disease is slow; it is mainly detected accidentally, and it is devitalizing and difficult to treat. The conventional line of treatment is very expensive and involves major adverse reactions in addition to having a low efficacy (Di Bisceglie and Bacon 1999).

Hepatitis C leads in most cases to complications, e.g., liver cirrhosis, ascitis, liver carcinoma and, ultimately, liver cell failure. It is estimated that liver cirrhosis develops in 20–25% of the patients with HCV within 20 years. Hepatocellular car-

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artículo original

The use of Ozonized Physiologic Saline in Gynecologic patients with Uterine Myoma and Endometrial Cancer in the Postsurgical Period

Dr. Olga S. Yanchenko
Dr. Elena U. Kontorschikova
Dr. Tatiana C. Kachalina
The Medical Academy of Nizhny Novgorod, Nizhny Novgorod, Russia
Dr. Victor V. Novikov
Nizhegorodsky State University Named after N.A. Lobachevsky, Nizhny Novgorod, Russia

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can be influenced by unforeseen influences from the environment. With the help of a process-based approach it is possible to model the deterministic, process based parts. By employing agent-based rules, it would then be possible to create a more realistic model of the complex system to be simulated.

The data for the simulation model built with this approach are to be selected by data mining.[6] In particular, not all data coming from ozone-based treatments can be useful for the model. Whereas in discrete event process simulation the emphasis is on the functional description of the modelled parts in detail, in agent-based simulation the most important facet is the interaction among those parts. As a matter of fact, it is interaction that produces a variety of behaviours that have could even not explicitly be described in the model of the individual parts. In agent-based simulation, there are therefore two main areas levels that use different data, with different goals. A micro level to describe a simple local behaviour and a macro level, whose effects partly result from the micro level and partly from the interaction of more elements. Such emerging behaviours could be revealed by non-explicit patterns in the simulation data and a subsequent phase may be needed for simulation to reveal the model that subdivides the data. Data mining techniques can therefore be the key to unveiling non-trivial knowledge through the initial assumption used to build the micro level, the model and structure of the agent aggregation that emerged from the simulation. Data mining and machine learning in general can be used in different ways in agent-based simulation;[6,7] it is possible to divide these contributions into two main tasks: i) *Ex ante*, where machine learning and data mining techniques can be used to achieve the one kind of intelligent behaviour that combines the data of past executions of simulation learning from experience and tuning some initial parameters of the simulation to a local maximum; ii) *Ex post*, where final results of a simulation are analysed using data mining techniques to uncover interesting patterns in data, helping to better model the behaviour of the overall systems. Note that the behaviour of the system is usually more than the sum of the parts and is not described in the first phase of the simulation task. Data mining could be used to create a model that is supported by statistical evidence that could be an initial hypothesis about the system.

Conclusions

This paper has a theoretical aim; its purpose is about introducing a hybrid simulation technique to be applied to the pharmacoeconomic analysis of ozone therapy. In particular, the approach of pharmacoeconomics is that of comparing the outcome of a traditional therapy with that of a different therapy. Ozone therapy is very interesting for medicine, since the effects and actions of O_3 are mainly positive and beneficial for many different diseases. This makes ozone therapy as a very good candidate to be studied with the approach of pharmacoeconomics. While costs (both direct, indirect and intangible) are very important for deciding which therapy should be favoured, also other factors have to be taken into account like, for instance, lives saved, life years after therapy, quality of life and so on. This is why traditional approaches to pharmacoeconomics could come short (*e.g.* statistics); that's where simulation could be an effective method for evaluating a broader range of outcomes. For this reason, two simulation paradigms are discussed in this work, namely discrete event process simulation - to simulate those parts of the process which are well known and easily mouldable as a flow of actions and if/then clauses – and agent based simulation – to represent those parts or interactions where only general rules are known and the emergent aggregate behaviour is not determined *a priori* but rather coming out from the whole system and its ever-changing essence. So the combination of these two approaches can be a powerful analytical method to be applied to pharmacoeconomics in general and to ozone therapy in particular, as a case study. Moreover, in order to select the data to be used in such simulations, but also to analyse results coming from them, a data mining approach is proposed.

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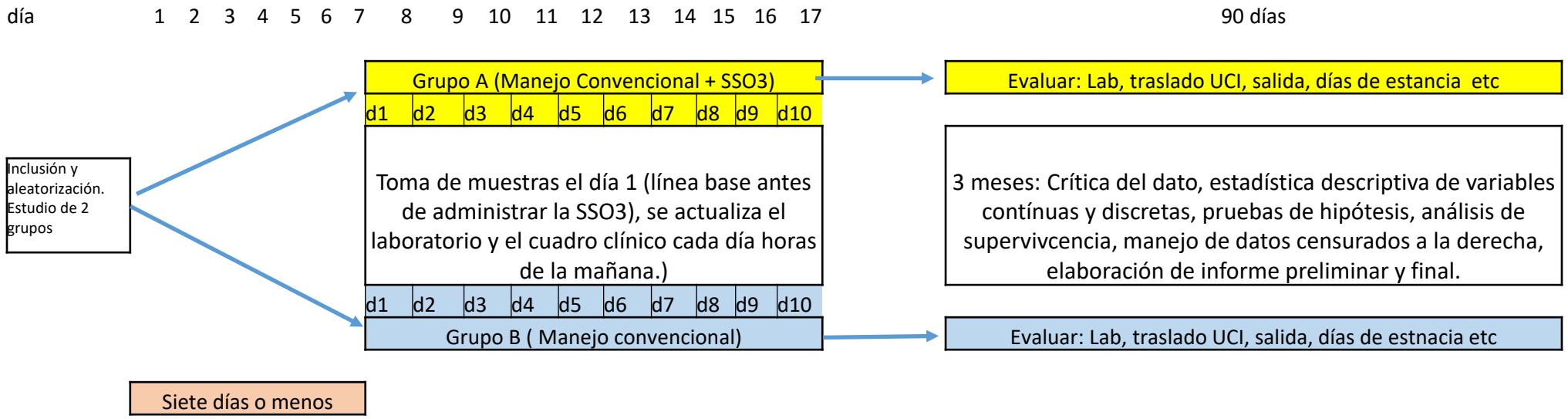
Pharmacoeconomic analysis of ozone therapy supported by agent based process simulation and data mining

Marco Remondino,[1-3] Luigi Valdenassi,[2,3] Marianno Franzini[2,3]

[1]Department of Economics, University of Genoa; [2]Department of Internal Medicine and Medical Therapy, University of Pavia; [3]Italian Scientific Society of Oxygen-Ozone Therapy (SIOOT), Gorle (BG), Italy

Esquema del ensayo clínico SSO3 (Diseño Add-on a grupo de control activo)



La regla del 3…fase 1.

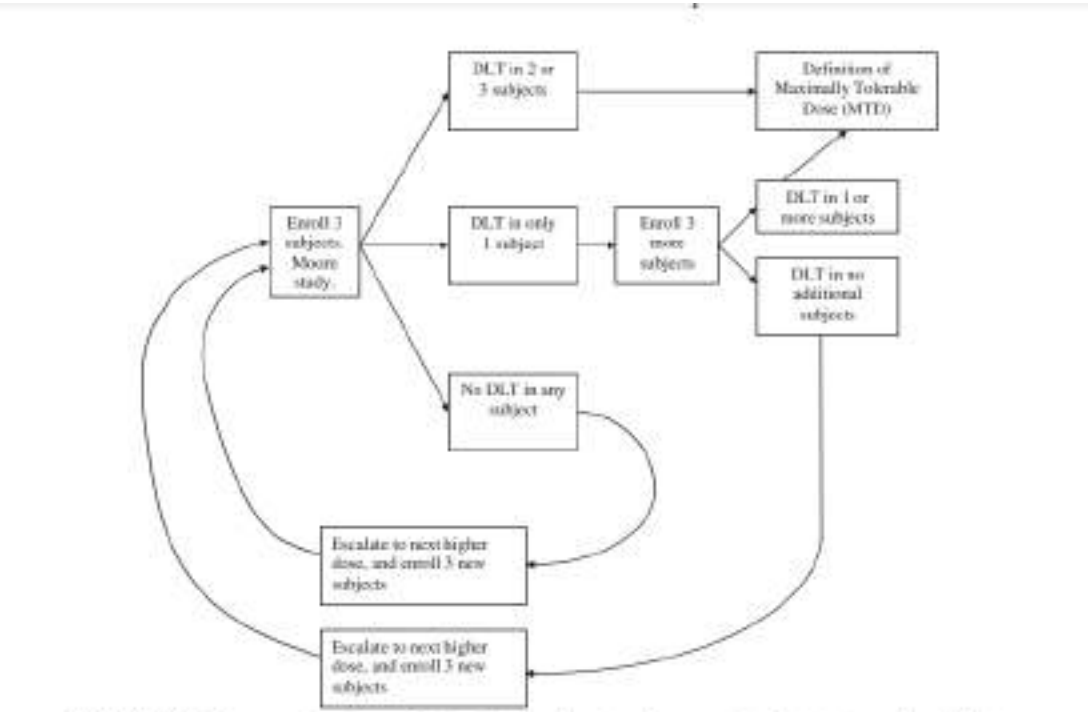


FIGURE 2-17 Schema used in dose-escalation study. The schema involves a number of decision trees where the decisions are in response to toxicities that are present in the study subjects, and where the decisions are to increase the dose for subsequently enrolled subjects.

- Con 100 µg/kg peso se observan efectos adversos por hepatotoxicidad en ratas.
- Dada la presunción de flebitis y ardor en zona de veno punción, en humanos no se aconseja burbujear SSN 0,9 % con una concentración mayor de 8 µg/ml -recordar que se diluye solo el 10 %, por tanto la concentración de O3 en la solución es de 0,8 µg/ml- (al aplicar 200 ml de SSN, la dosis total es de 160 µg de O3– equivale aprox a 2 µg de O3/kg de peso para una persona de 80 kg de peso corporal).
- Para mantenerse debajo del umbral de la flebitis y el dolor tipo ardor en zona de venopunción Se propone desarrollar el ensayo con un rango de dosis total de 60 µg a 100 µg de O3, equivale a dosis de 0,75 µg/kg a 1,25 µg/kg de peso corporal para una persona tipo de 80 kgr.

Ventajas del diseño Add-on a grupo de control activo.

- No se abandona manejo protocolizado establecido para reducir la mortalidad y morbilidad compleja en paciente hospitalizado. Se reduce el riesgo legal y de imagen corporativa.
- Si es superior el manejo convencional al obtenido con el grupo de SSO3, simplemente se descarta la SSO3 como opción terapéutica alternative para paciente COVID 19 en fase 2,
- Si el desempeño en la batería de laboratorios y los desenlaces resolutivos (traslado a UCI o salida del centro asistencial, es superior en el grupo de SSO3 respecto del manejo convencional, se propone avalar su uso como manejo COMPLEMENTARIO del paciente COVID 19 en fase 2. Se exploraría en otras fases (fase 1 y fase 3) modulando dosis. Desarrollar estudio de cohortes para explorar calidad de vida 3 y 6 meses después en pacientes con salida (en el contexto del síndrome post covid).
- Si NO HAY DIFERENCIAS –es decir son comparables en resultados o no es inferior el manejo con SSO3 respecto del manejo convencional, se debe explorar su uso en un contexto de manejo **seguro, flexible y complementario de manera discrecional**.