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revisión

Ozonized Saline Solution (O3SS): Scientific Foundations

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Ozonized saline solution, O3SS, ozone, hypochlorites, hydrogen peroxide, Henry's Law, major autohemotherapy, AHTmajor, toxicity, Nrf2, dose, Madrid Declaration on Ozone Therapy.

Abstract

Ozone therapy is a technology that is currently being used to treat a variety of diseases, with a growing spread in the medical field.
Given the decision passed by the Spanish regional health authorities of Catalonia and Madrid to assimilate the major autohemotherapy to a blood drawn and to apply it the Royal Decree (Real Decreto)1088/2005, this paper presents a bibliographic review on the ozonized saline solution as a valid alternative method of use in daily practice by the ozone therapist.
At the same time taking into account the controversies that this method has raised, the scientific foundations of O3SS are analyzed, leading to the conclusion that is safe, effective, low cost and ease of application, and having a broad scientific support

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Objective

To synthesize and analyze scientific information on the effectiveness and safety of ozonized saline solution (O3SS) for therapeutic purposes.

Method

A literature review (2005-2016) and translation from Russian into Spanish of some researches published in Russian databases was conducted. Other sources of information were: The Cochrane Library; the reports of three autonomous communities (states) evaluation agencies published by the Spanish Ministry of Health; web pages related to the subject; bibliographical references hand searching from relevant papers and specialized journals.

Conclusions:

The ozonized saline solution is a safe, effective method, inexpensive and easy to apply, also has an extensive scientific support in terms of clinical studies.

Interest Conflict

The author states that she does not have interests that may compete with the primary interest and the aims of this report and influence her professional judgment in this regard.

Legal Issue

Two Spanish Regional Health Ministries (Catalonia in 2012, Madrid in 2016) out of the 17 that has the kingdom, decided that the major autohemotherapy (AHTmajor) is a medical technique that must be applied as per the stipulations spelled out in the Spanish Royal Decree 1088/2005, which “states down the technical requirements and minimum conditions of the hemodonation, and the centers and transfusion services”. These two Spanish Regional Health authorities have assimilated the major autohemotherapy (AHTmajor) to a blood transfusion and therefore have decided that the current legislation for blood transfusion must be strictly applied to the major autohemotherapy (AHTmajor).

AEPROMO (Spanish Association of Medical Professionals in Ozone Therapy) has officially came out against this legal interpretation. In dense and well structured documents it refuted with solid medical and legal arguments the decisions of both communities (Catalonia[1], Madrid[2]), asking them not to apply the Spanish Royal Decree 1088/2005 to the major autohemotherapy.

The Regional Catalan Ministry did not answer the request of AEPROMO dated July 23, 2012.

On the contrary the Regional Madrid Ministry did answered the petition of Aepromo stating that it was not “possible to accede” to its request and stressing "the required and necessary compliance" of the Royal Decree 1088/2005 to practice AHTmajor. [3]

What does mean for the medical centers in the Communities of Catalonia and Madrid? It means that the authorities allow to apply the AHTmajor but under the condition to stick to the requirements spelled out in article 30 of the Royal Decree 1088/2005. I.E., the medical centers must:

- To hire a physician specialist in hematology and hemotherapy with at least two years of experience in one or more centers or transfusion services.
- To appoint this specialist as director of the center.
- In addition the legislation allows the specialist to delegate its functions. So the appointed specialist could be remunerated financially by the center only for signing.

To our knowledge no other similar decision has been adopted by any of the other 15 Spanish autonomous communities (what it might happen given the great reference importance that have Madrid and Catalonia in the rest of the country) nor by other countries so far.

Based on what is currently happening in these two Spanish communities, I have decided to issue this bibliographical review to remember physicians that there is an alternate route of application for the major autohemotherapy (AHTmajor): The ozonized saline solution (O3SS).

It is worth remembering that both AHTmajor and O3SS are systemic routes of applications that have received full support by the Madrid Declaration on Ozone Therapy (ISCO3, 2nd. ed., 2015, items 3.11 and 3.1.22). [4] Both methods are safe and effective and with no side effects if done properly. It is clear that as any other ozone therapy technique, the health professional that performs either one or both procedures must have the appropriated training. For ISCO3 (International Scientific Committee of Ozone Therapy) both techniques are equivalent and their results are similar.

Pioneers of the Ozonized Saline Solution (O3SS)

It is a widespread practice in Russia and developed by the Russian school of ozone therapy in the city of Nizhny Novgorod (Volga Federal District).

The method consists in the prior saturation of the saline solution with a mixture of oxygen-ozone and its intravenous infusion to the patient. This route of application was approved by the Ministry of Health of the Russian Federation in the early 80s of the last century, specifically for the branches of orthopedics, dermatology, gynecology/obstetrics and neonatology. Since then it has been officially implemented in public health hospitals. [5,6, 7]

Ukraine officialized its application in 2001.[8]

Russians have an important number of published papers and clinical experiments, along with a strong clinical experience about the benefits of this therapy.[9] At the same time it has been recorded more than 500 Russian doctoral theses in ozone therapy using saline solution, as the primary route of ozone administration, with excellent results.
In April 1979, for the first time in the world a cardioplegic ozonized saline solution was administered in the coronary system of a patient with congenital heart injury. [10]
Russia has a large and proven scientific foundation at all scientific levels and I believe that we are far from what this country has managed to advance concerning ozone therapy.

Exclusion of Researches by Language in Scientific Journals

It is true that most of the Russian research papers are only written in Russian. Due to the lack of translations into English (the most conventional languages for scientific publications) no many health professionals are aware of the advances made by the Russians and Ukrainians in the field of ozone therapy and particularly on ozonized saline solution. However that does not mean that those researches and publications do not exist.

Occasionally it has been heard statements like this: *"In western scientific journals, or at least in those published in English, it has never been found a paper supporting the use of ozonized saline solution"*.

Ironically this argument has received support in three Spanish official reports from the autonomous communities of Galicia (2006) [11], Andalusia (2008) [12] and the most recent one of Catalonia (2014). [13] In all of them Russian investigations were conspicuous by their absence.

The Andalusian Report[12] states that "ozone therapy is being used for years in different countries, mainly Italy, Russia, Germany and Cuba." (P. 16). Nevertheless it recognizes that only it took into account for the report documents published in English, French, Italian and Spanish. (P. 22). Thus the important German and Russian investigations were discarded, in spite of having acknowledged that Germany and Russia were, along with Italy and Cuba, the main countries where ozone therapy was practiced.

For the sake of completeness the Andalusian report states: "As far as the limitations of this report it concerns, it is assumed that the MEDLINE and EMBASE referential mass databases suffer a language bias on the subject of publications indexed by them." (P.47).

The report from the Galicia Community[11] pins down that only took into account "the studies published in the following languages: Spanish, English, French, Portuguese and Italian" (P.16). Therefore research written in German and Russian were excluded.

The Catalonian report[13] confirms the above by stating that "it is very important to keep in mind the language limitation. The second most important reason for exclusion [from the report] given the number of discarded papers is precisely the language. From the title and abstract, usually published in English, it was selected a series of papers in which it was outlined the analysis of experimental groups with comparison groups but due to the language, had to be excluded. This may have influenced at the very moment of deciding the efficacy / effectiveness of ozone therapy." (P. 40).

The Catalonian report recognizes that 38 researchers were excluded only for reasons of language. (P. 48). In reviewing the literature consulted by the report it is confirmed the total absence of Russian investigations.

Controversy and Criticism

The OSS3 debate should be done exclusively on the scientific basis of this route of application and not through the prism of marketing. This point is very convenient to have it very present because while for the major auto-hemotherapy the use of specific bottles is indispensable is not the case in the saline solution. Objectively this translates into a reduction of bottles selling for AHTmajor and likely in the therapy price decrease. Hence the need that any debate motivated by the interests of those who sells the bottles for AHTmajor not be disguised with supposedly scientific arguments.

The ozonized saline solution (O3SS) procedure is not only effective and secure, but is much cheaper and easy to implement.

In addition it solves the big problem we are facing with different health administrations that assimilate the AHTmajor to a blood extraction. Nobody would question a procedure done with physiological saline solution keeping offering a good therapy to our patients along with others types of ozone systemic administration.

In places where auto-hemotherapy is viewed with skepticism, saline solution goes unnoticed. On the other hand patients that due to religious grounds do not accept blood manipulation, OSS3 is the first-order option.

Scientific Elements of the Ozonized Saline Solution (O3SS)

There is an ongoing discussion about the claim that the mixture of ozone with saline solution would generate H_2O_2 and NaCl, substrates that might cause complications in the body. However this question has been solved long time ago.

According to research conducted by Professor Claudia N. Kontorshchikova in saline solution at 0.9% ozonized (0.55mg/L O3) on average were found 0.004 mM/L of chloride ions. Analysis of hydrogen peroxide in samples of 0.9% NaCl done by analytical chemistry methods did not reveal any accumulation of hydrogen peroxide in concentrations exceeding 0.002% in any of the ozonation schemes, although it was found even much lower concentrations, in the order of 0.0004%.[14]

At the same time a research team led by Professor S. Razumovski verifies through a research that the ozone decomposition processes in NaCl aqueous solutions is not accompanied by formation of products other than oxygen. In particular, no noticeable amounts of hypochlorites and chlorates are observed. This is particularly significant for medicinal application of ozonized isotonic solutions". [15]

Professor Sergey Peritiagyn demonstrated that the concentration of sodium hypochlorite in the OSS3 was less than 0.001 g/mL. [16]

It is clear that the concentration of hydrogen peroxide and sodium chloride is not visible or even noticeable.

Regarding to mutagenicity and toxicity of ozone, studies in any of its administration ways show that the body can deal with it perfectly and trigger Nrf2 response, as long as repetitive stimuli of low doses of ozone are used. [17,18, 19]

It has been provided strong evidence that the induced damage to DNA by the O3 (chain breakage) in human leukocytes of the peripheral blood has a reversible effect; this indicates that the cells quickly recover the genotoxic effect induced by treatment with the gas.[20]

The genomic mechanism of action of ozone was described much earlier in ozonized saline solution than in major autohemotherapy. I am referring to Korean and Russian studies published in 2004-2011-2013. These studies have demonstrated that the response is dependent on the activation of the transduction mechanisms of nuclear signals Nrf2 (nuclear factor erythroid 2), which is a powerful protein located within each cell in the body and which is driven by the activator Nrf2 inducing protein synthesis, such as SOD (superoxide dismutase), CAT (catalase), and HO1 (heme oxygenase 1) among others. [21, 22, 23]

Ozone therapeutic indications are based on the knowledge that the use of low physiological doses of ozone plays an important role within the cell.

In 2013 and 2014 the same experiment as performed with saline solution was done *in vitro* and *in vivo* with the major auto-hemotherapy (AHTmajor). These studies demonstrated that the results were exactly the same as those that were found in the OSS3. [24,25]

These data point for the first time the activation of Nrf2 pathway by low doses of ozone with the consequent promotion of feedback mechanisms which induce protein synthesis thus favoring collectively cell survival.

Thus Nrf2 system contributes to the protection against various pathologies, including carcinogenesis, liver toxicity, respiratory and chronic inflammatory diseases, neuronal ischemia and renal problems. [25]

Doses Used in the Ozonized Saline Solution (OSS3)

The recommended doses of ozone to be used in O3SS are very low and are calculated by weight of the patient. These have been detailed and endorsed in the item 3.1.22 of the Madrid Declaration on Ozone Therapy (ISCO3, 2nd. ed., 2015). [4]

Ozonized Saline Solution (OSS3) as Alternative to Major Autohemotherapy (AHTmajor)

As indicated above both routes are safe and effective and with no side effects if done properly. It will depend of each health professional to decide which apply. For ISCO3 both techniques are equivalent and their results are similar.

What Are the Differences Between AHTMajor and OSS3?

The first is the amount of treated blood: since saline solution is a plasma expander, the O3SS represents a greater quantity of treated blood in relation to the AHTmajor, and therefore the number of sessions may need to be reduced. Perhaps this is the crucial point of the effectiveness of the Russian method.

The second difference is the physical law that applies to the O3SS, this is the Henry's Law (gas diffusion law) which says that a gas dissolves in a liquid (at constant temperature) in a directly proportional way to its pressure (either partially or not). If it is spoken of partial pressures then it is assumed that the gas is a mixture of two or more gases.

If we introduce in a bottle pure water and oxygen to 1 bar, this gas dissolves in the water until saturation. If we increase the pressure, oxygen begins to dissolve again until the new level of saturation. Thus, the amount of gas dissolves directly proportional to the pressure.

If there was a mixture of gases, for example, air containing 21% oxygen and 79% nitrogen then it would dissolve in relation to their partial pressures.

Diffusion and dissolution are different concepts in physics. Henry's statement refers to inorganic liquids and blood is an organic and living fluid. In the case of blood the ozone does not diffuse nor dissolve, but reacts with the blood. The reaction is much more complex since it reacts immediately with biomolecules such as fatty uric acid, unsaturated fatty acids, etc. resulting in the formation of mediators, of ozone metabolites: hydrogen peroxide, lipid peroxides, ozonides, etc. Therefore, the reaction of ozone in blood does not follow the Henry's Law.

Conclusions

- The OSS3 method has proven to be effective, safe and easy to perform.
- It is much cheaper than other methods.
- It can be applied to people with religious values opposing to blood transfusions.
- It does not represent a threat or risk to the eyes of the health authorities, since they could not question the administration of a physiological solution.
- It has a broad scientific support.

Last but not least the ozonized saline solution helps in solving the bureaucratic and economic vexed problem that the ozone therapist may face with different health administrations which assimilate AHTmajor to extraction and blood donation; forcing the health center, for example in the Spanish communities of Catalonia and Madrid, to hire a hematology and hemotherapy specialist to perform a major autohemotherapy.

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