OZONE THERAPY IN MEDICINE

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Abstract: *Since its introduction in 1840, ozone therapy is providing to be a new therapeutic modality with great benefits for patients. The potent antimicrobial power of ozone, along with its capacity to stimulate the immune response, makes it a therapeutic agent in a lot of medical pathologies. The biological processes from the living organisms and pathogens agents can be stimulated or inhibited, according to requirements by using the electrostatic fields, of corona discharging or different concentrations of ozone. The nature, intensity and shape of the field, exposure times and ozone concentration represent as many influence modes on the biological processes. While in some medical domains ozon therapy proved its efficiency, in others the results are in validation process.*

Cuvinte cheie: *ozon, ozonoterapie, câmpuri electrice intense, antimicrobian*

Rezumat: *De la introducerea ei in anul 1840, ozonoterapia s-a dovedit a fi o terapie alternativă in medicină, cu beneficii importante pentru pacienti. Potentialul antimicrobian al ozonului, impreună cu capacitatea de stimulare a sistemului circulator si de modulare a raspunsului imun, au dus la utilizarea ozonului intr-o multime de afecţiuni. Anumite procese biologice ale organismelor vii şi ale agenţilor patogeni pot fi stimulate sau inhibate, in funcţie de necesităţi, utilizând câmpuri electrice, descărcări corona şi concentraţii diferite ale ozonului. Natura, intensitatea si forma câmpului, timpul de expunere şi concentraţia oxigenului pot influenţa in diverse moduri procesele biologice. In timp ce in unele domenii medicale ozonoterapia şi-a dovedit eficienţa, in altele aceasta urmează sa fie validată.*

SCIENTIFICAL ARTICLE OF BIBLIOGRAPHIC SYNTHESIS

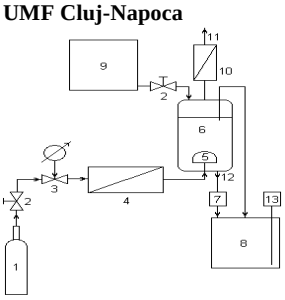
Although ozone was mentioned by Homer, only during the 19th and 20th century it was discovered the method of its generation and its chemical property. Ozone is a chemical compound made of three oxygen atoms (O3- tri-atomic oxygen), a form having a higher energy state compared to the normal atmospheric oxygen (1). There have been very few studies performed regarding the potential of ozone in medicine; the domain being controversial and is one of those that still pioneered in an international level. Therapy with ozone, i. e. the treatment of patients with a mixture of ozone and oxygen, was utilized from a long time ago as an auxiliary method to the conventional treatment, especially in those cases where the traditional treatment did not provide satisfactory results. Ozone is considered to be one of the strongest oxidizing agents, having antiseptic, especially antibacterial property which makes it very effective in combating microbial infections (2).

Obtaining ozone and its mode of action:

Principal modality of obtaining ozone for medical applications is the method of unloading the corona. Advantages of this method are its technical facility, production of ozone in an increased concentration and the possibility of adjusting concentration of ozone in different solutions (1).

In the last few years, strong oxidizing character of ozone was utilized complementarily along with other benefits offered by ultraviolet radiation, hydrogen peroxide, chlorines, strong electric fields etc., which had conferred enlargement of the area of applicability of ozone in preservation of some mediums as well as food products, in the process of obtaining medicine in stomatology, in the treatment of diseases refractory to medicinal treatments etc. Generally the strong antimicrobial property along with the phenomenon of local stimulation of leucocytes offered by ozone is utilized in medicine.

Figure no. 1. Plant for the ozonation of watery solution – UMF Cluj-Napoca



1 – tub (tank or rezervoir) of oxygen; 2 – valve ; 3 – regulator of pressure; 4 – controllable generator of ozone; 5 – porous diffusor of ozone; 6 – column for the diffusion of ozone in the watery solution (reactor with bubbles); 7 – measures rezidual of ozone in the watery solution; 8 – collecting vessel for the ozonated watery solution; 9 – vessel for watery solution to be ozonated; 10 – destroyer of rezidual ozone; 11 – evacuation route for gas; 12 – evacuation route for the ozonated solution,(samples); 13 – measuers the pH or other physio-chemical parametres of the watery solution.

Ozone represents a highly unstable form of oxygen, having a half life of less than an hour in the normal working conditions. Decomposition of ozone into oxygen can be controlled partially by association of liquid, "vector", whose composition, watery or viscous, can influence the speed of conversion of these two forms of oxygen.

As the process of solubilization of ozone in the watery solution more importantly in the process of its decomposition and recombination can result in a huge number of free radicals; so the behavior of ozone respectively the behavior of free radicals in the watery solution can be considered as approximately identical phenomenon (4).

Processing of the watery solution should be done with ozone resulting from oxygen or through application of strong

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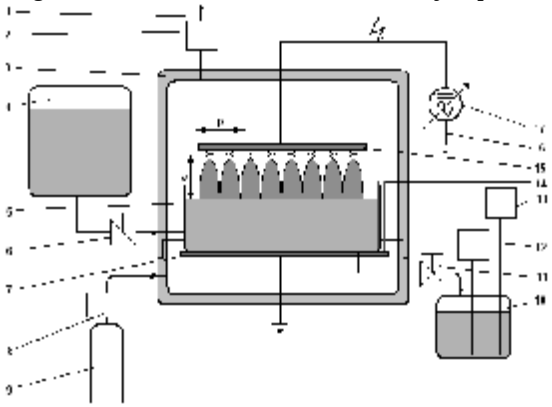
electric fields to the watery solution in the presence of oxygen and in complete absence of air, as it can result in ammonium dioxide which is harmful and can compromise totally the beneficiary effects of ozone (3,4).

Remnants of ozone or amount of free radicals found in the watery solution treated in the ozonizer or those found in the unit of processing electric field depends upon a lot of factors out of which the most important are: temperature of the watery solution (at a temperature above 50° C, the speed of decomposition and recombination of ozone increases highly), pH of the watery solution, type and the grade of the impurity in the watery solution, pressure of the solution, material of the stocking recipient and medium with which the watery solution comes into contact (4).

Figure no. 2. Plant for direct processing of watery solution in strong electric filed- Universitatea Tehnica Cluj-Napoca



1- evacuation route for gas; 2 – destroyer of rezidual ozone (optional); 3 – unit for direct processing; 4 – vessel for the watery solution to be processedt; 5 – petri dish for direct processing, with the liquid kept in a stationary state; 6 – valve for the alimentation Petri dish; 7 – electrode connected to earth, plate type; 8 – vavle to regulate the pressure; 9 - tub (tanc or reservoir) of oxygen; 10 – collecting vessel for the processed watery solution; 11 - valve (tap) for the collection of watery solution; 12 – measures the rezidual ozone in the watery solution; 13 - measuers the pH or other physio-chemical parametres of the processed watery solution; 14 – piece that connects the watery solution to earth; 15 – active electrode, corona, of high tension; 16 – bridge between the belt and socket of earthing; 17 – regulator of high tension.

The antimicrobial effect of ozone is due to both its direct action as well as its capacity to form very active peroxides with unsaturated fatty acids which has a destructive effect upon the microorganism. In small dozes ozone has a locally destructive action upon the cell membrane but in large doses it blocks some specific enzymatic systems and cellular receptors leading towards the death of the pathogenic microorganism. Bactericidal effect of ozone is twice that of chlorine and is equally effective in those cases resistant to antibiotherapy without inducing any resistance of its own. Equally good results were reported also against viruses, funguses and protozoa's (5).

The initial mechanism through which ozone acts upon microorganisms is by the oxidation of their cell membranes, the process where glycoprotein's, glycolipids and different amino acids of the cell membrane gets affected resulting in the intrusion of the ozone molecule inside the cell and in turn resulting in blocking the enzymatic system of the cell finally leading to death (6).

Other than its direct action upon microbial agents, ozone also has an immunomodulating action which is conferred by stimulating not only the cellular mechanism (T lymphocytes, Monocytes) but also the humoral mechanism (synthesis of cytokines, interferons and of tumoral necrosis factors) (7). Hence upon administration of an well judged concentration of ozone, it plays an important therapeutic role in different kind of infections through the generation of free radicals of oxygen (O2, OH, H2O, NO, HOCL), radicals that are produced also inside granulocytes and macrophages during the time of an infectious process (8).

The effect of ozone upon microorganisms is proportional to the concentration of ozone and the time of its exposure upon them. Studies performed had showed that ozone is equally effective upon gram positive as well as gram negative bacteria, only later needing a higher concentration of ozone for neutralization than the gram positive ones. Upon the anaerobes and micro-aerophils, ozone has a dramatic toxic effect mainly because of the energetic metabolism specific to these bacteria's which uses organic compounds as a final receptor of oxygen and also because of the fact that they does not possess protective enzymes against toxicity of oxygen (9).

The oxidation property of ozone was used in combating facial infections mainly those encountered in dental surgeries (10). In a study upon 83 patients undergoing surgical intervention for a complete prosthetic replacement of hips, Dr. Bioloszenski (11) did not find any septic complication in those patients who have received intraoperative prophylaxis of ozone therapy. In the same time there have not been reported adverse or negative effects of ozone upon the patients or on medical staffs. Chen H. in 2007 (12), had demonstrated the anti-apoptotic and anti-inflammatory potential of ozone in an experimental study performed on rats suffering from acute renal ischemia, and again Parkhishenko IuA in 2003 had obtained a more rapid amelioration of hepatic insufficiency and more rapid efficient detoxification of the organism in case of an icteric patient who had received par-eneteral ozone therapy (13). The antimicrobial effect of ozone was shown in the cases of necrotizing fascitis (14), maxillary osteonecrosis (15), prostatic surgeries (16), super infected wounds and ulcers refractory to treatment (17) where besides having an accelerated healing through continuous irrigation of ozone there was also obtained a reduction of pain, mental stress and hence a final reduction of overall cost of the treatment. Ozone therapy was also applied under the form of extracorporeal oxygenation and ozonation of blood. Di Paolo N in 2005 had performed a study upon 82 patients and demonstrated the stress controlling therapeutic property of ozone where the patients had suffered from different kinds of immune dysfunctions as well as some degenerative processes (18). Ozone therapy also had proved its efficacy in case of those patients suffering from degenerative muscular diseases, ischemic diseases, infections and refractory wounds where the conventional therapy had found to be failed (19). Oxidizing property and the antimicrobial property of ozone was proved also in the cases of peritonitis, by Ozmen V et al. who had used intraperitoneal irrigation of ozonated saline solution in the cases of mice and obtained a reduction in the rates of mortality and reduction in the rates of postperitonitic residual abscesses (20). Hence was obtained a reduction of mortality rate from 62.07% to 37.23% (21) in those mice suffering from acute severe peritonitis; an overall fall of 1.7 times in the rate of mortality and 1.8 times fall in the rate of infectious complications (22). In the patients who had developed sepsis or septic shock, use of ozone therapy as an adjuvant treatment had led to a reduction of mortality rate from 39.2% to 25.6% (23). Ozone can have an important therapeutic role in different types of infections as it generates free oxygen radicals (O2, OH, H2O2, NO, HOCL) similar to those produced by granulocytes and macrophages during the process of an infection (24). Ozone is extremely active and does not induce any resistance as they are highly efficient also against anaerobic bacteria's as well as bacteria's resistant to antibiotics.

In Romania, recent studies performed by University of Medicine and Pharmacy Cluj Napoca, had proposed the combined utilization of ozone and strong electric fields to treat different biologic mediums, as it led to the inhibition of noxious processes and at the same time bio-stimulation of useful processes of the respective treated medium (3,4).

As far as the mode of administration of ozone is concerned, according to the result desired ozone can be administered systemically, locally or in a combined way. Where there is an antimicrobial effect of ozone is desired, ozone is administered in a large concentration targeted directly at the foci of infection. In case of infections inside the abdominal cavity (infected pancreatitis, peritonitis of different causes) the optimal way of administration is intraperitoneally where one has to ensure a constant flux of ozonated solution in such a way that a constant concentration of ozone similar to that of minimal concentration having bactericidal effect is obtained in the respective zone of interest. The process can be obtained through a system of drainage tube that offers a continuous lavage.

Capacity of ozone (a strong oxidizing agent) to induce an increase in the level of cellular antioxidant enzymes thereby reducing oxidative stress forms the base of utilization of this form of oxygen in different diseases. The study on the effect of ozone upon acute pancreatitis with necrosis of the pancreas and peripancreatic tissues is still in an experimental level in University of Medicine and Pharmacy Cluj Napoca. Acute pancreatitis represents one of those pathological entities where the oxidative modifications caused by the access of free radicals remains the main mechanism of pathogenesis. In the same way, another point of interest is the enzymatic autodigestion of the gland itself. Some of the studies have showed that ozonated saline solution containing smaller doses of ozone produces a positive effect upon the proteolytic system and on the other hand larger doses induces a decrease in activity of plasmatic alpha 1 antitrypsin and of plasmatic alpha 2 macroglobulin levels (25).

CONCLUSIONS

In this was, in contrast to the dogma which says that "ozone is always toxic", recently it had been shown that at certain concentrations ozone can have properties like disinfectants, immuno-modulators, inducer of antioxidant enzymes, can contribute to stimulation of the metabolism, induction of the synthesis of endothelial nitric oxide and can also activate the stem cells with beneficial effects in neo-vascularization and tissue healing. Ozone therapy is a promising domain for the non-conventional medicine, proving its efficacy in certain pathologies and through studies and researches is on its way to prove its efficacy in the rest of the pathologies in the near future.

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