JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue

JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)

An International Scholarly Open Access, Peer-reviewed, Refereed Journal

USAGE OF OZONE THERAPY AND ITS IMPACT ON GENERAL HEALTH.

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Abstract : Ozone treatment is a type of alternative medicine that uses ozone gas. It is divisive because of worries about its efficacy and safety. Researchers are now investigating the effects of ozone treatment on the human body in order to determine whether it has any therapeutic promise. Humans are poisonous to ozone gas, and little study has been done on the safety of ozone treatment. As a result, official organizations are now opposed to its use. Anyone with questions regarding ozone therapy or whether treatment is best for them should consult their physician. In this overview, I have put in efforts in gathering information about ozone treatment and its effects on human health. It would assist anyone who are considering this therapy or would like to learn more about it in making their decision.

***IndexTerms* – ozone therapy,autohemotransfusion,Phleboclysis,Ozonated Saline,Bimosiamose's influence.**

I. INTRODUCTION

Ozone is a colorless gas made up of three atoms of oxygen (O3). Ozone (O3) is a triatomic molecule, consisting of three oxygen atoms. Its molecular weight is 47.98 g/mol. Ozone is thermodynamically highly instable compound that is dependent on system conditions like temperature and pressure, decomposes to pure oxygen with a short half-life. Ozone in the upper atmosphere filters potentially damaging ultraviolet light from reaching the Earth's surface. It has many different applications in various fields; one of them is usage of ozone in medicine. Ozone therapy is one of the modern non-medication methods of treatments. It has been in use for over 100 years. Medical reports on successful application of ozone in therapy of different diseases and studies of its effects caused a rapid growing interest in it. The other factors that are responsible for its wide spread are simplicity of performance, good tolerance by patients, absence of side-effects or adverse reactions and high medical-social and economic efficiency. Although ozone therapy is still being ignored by most of medical establishment because of facts that gaseous ozone is quite toxic and has strong oxidative properties.

The word ozone was first used by Schonbein in 1840. He subjected oxygen to electrical discharges and noted "the odour of electrical matter". Schonbein concluded that odour was due to a gas which he named ozone, from the Greek ozein (odorant), and described several of its properties. Numerous researchers since that time have worked to interpret the nature and actions of ozone. Mariniak and Delarive showed that it is an allotropic form of oxygen, and Mulliken and Dewar shed light on its molecular architecture.

Ozone has the ability to destroy toxic or noxious industrial impurities (phenols, cyanides, tetraethyl lead among others) and to inactivate bacterial contaminants has made it an attractive alternative. Due to its ability to inactivate bacterial contaminants in sewage, it has been used as an alternative to chlorination. In 1901 Wiesbaden, Germany became the first city to use ozonation for purification of its drinking water, followed by Zurich, Florence, Brussels, Marseille, Singapore and Moscow (the largest installation in the world), among others. By the end of the 19th century the use of ozone to disinfect drinking water of bacteria and viruses was well established in mainland Europe. Ozone is 25 times more powerful than hypochlorite acid and 500 times faster. Ozone has greater disinfection effectiveness against microbes like bacteria, virus and cyst compared to chlorination. In addition, the oxidizing properties of ozone can also reduce the concentration of Iron, Manganese and reduce or eliminate the taste and odour problems in water.

II. HISTORY OF OZONE THERAPY

Ozone therapy refers to the process of administering ozone gas into your body to treat a disease or wound. Ozone is a colorless gas, O3 is highly water-soluble inorganic molecule composed of three oxygen molecules.

The history of ozone's medical applications has nebulous and anecdotal beginnings. A. Wolff, Payr and Aubourg are those researcher who will always be linked with pioneering research, especially in the field of locally applied medical ozone. Hansler, another researcher developed one of the first reliable models of medical ozone generators During WWI, A. Wolff successfully treated putrescent wounds, suppurating bone fractures, fulminating inflammations (phlegmons), and abscesses, reporting his findings in 1915. The work of surgeon and ozone therapist Erwin Payr, who presented his epoch-making paper "Ozone Treatment

in Surgery" (Über Ozonbehandlung in der Chirurgie) at the 59th Meeting of the German Surgical Society (Deutsche Gesellschaft für Chirurgie) in 1935, gave this discipline a substantial boost. This can be considered the true start of ozone treatment.

Medicinal ozone, on the other hand, was not used until the 1950s, considerably later in the twentieth century. Because there were no ozone-resistant materials, such as plastics, it was difficult for the practitioner to deliver ozone locally in wound therapy or by rectal insufflation because any measurable quantity of ozone in the ambient air made it practically impossible. In 1958, Hänsler showed off his first medical ozone generator, which could produce a therapeutically variable ozone/oxygen mixture (concentrations). Together with H. Wolff, they introduced ozone therapy as we know it today.

Following a large number of publications by Payr and Aubourg in his research, H. Wolff was the first to introduce extracorporeal blood treatment into medical practice; Werkmeister developed local treatment methods in the form of "sub-atmospheric ozone gas application," and Rokitansky – as a surgeon – presented the first comprehensive studies on the topical and systemic treatment of diabetic gangrene. Ozone has several known effects on the human body, including immune-stimulating and analgesic, antihypoxic and detoxicating, antimicrobial (bactericidal, viricidal, and fungicidal), bio-energetic and biosynthetic (activation of carbohydrate, protein, and lipid metabolism), and antimicrobial (bactericidal, viricidal, and fungicidal). The antimicrobial action of ozone has received the greatest attention. The cytoplasmic membrane damage produced by ozonolysis of dual bonds, as well as ozone-induced alterations in intracellular contents (protein oxidation, loss of organel functions) owing to secondary oxidants' effects, are the principal causes of cell death. Due to their significant anti-oxidative capabilities, this activity is non-specific and selective to microbial cells; it has no effect on human body cells.

Ozone is very efficient in antibiotics resistant strains. Its antimicrobial activity increases in liquid environment of the acidic pH. In antibiotic-resistant bacteria, ozone is quite effective. Its antibacterial activity rises in an acidic pH liquid environment. The mechanism of ozone action in viral infections is based on infected cells' resistance to peroxides and a shift in reverse transcriptase activity, which is involved in viral protein production.

III. DYNAMICS OF ACTION

Bacteria, viruses, fungus, yeast, and protozoa inactivation:

Ozone therapy compromises the integrity of the bacterial cell membrane by oxidizing phospholipids and lipoproteins. At some phases of fungal formation, ozone decreases cell proliferation. Ozone damages the viral capsid and inhibits the viral reproduction cycle by breaking virus-to-cell interface via peroxidation. Cells with weakened enzyme coatings, which make them vulnerable to viral infection, are vulnerable to oxidation and removal by the body, which then replaces them with healthy cells.

- The cell wall comes into touch with ozone (green). The bacteria's cell wall is essential because it allows the organism to keep its form.
- When ozone comes into contact with a cell, it causes an oxidative burst, which forms a microscopic hole in the cell wall.
- A view of the cell wall from a close distance.
- An image of the cell after it has been bombarded by ozone for a long time.
- The bacterial wall can no longer keep its form after a few seconds and millions of ozone hits, and the cell dies.

Stimulation of oxygen metabolism:

As a result of ozone therapy, the rate of glycolysis in red blood cells rises. This stimulates 2,3-diphosphoglycerate, which leads to an increase in the amount of oxygen given to the tissues. Ozone boosts oxidative carboxylation of pyruvate, which starts the Krebs cycle, and so boosts ATP production. It also lowers NADH levels and assists in cytochrome C oxidation. Glutathione peroxidase, catalase, and superoxide dismutase, which act as free radical scavengers and cell-wall defenders, have their production enhanced. The production of prostacyline, a vasodilator, is likewise stimulated by O3.

Activation of the immune system: At 30 to 55 g/cc, ozone causes the greatest increase in interferon production, as well as the highest levels of tumor necrosis factor and interleukin-2. The production of interleukin-2 triggers a cascade of immunological reactions.

3.1Dynamics of action of O3 on the human lung:

On average, ozone causes a considerable reduction in critical ability. It causes a considerable increase in mean and specific airway resistance while having no effect on dynamic or static pulmonary compliance, viscous or elastic work. It also significantly decreases maximal transpulmonary pressure. There is also a significant increase in respiratory rate and a decrease in tidal volume.

IV. CLINICAL TRIAL

Bimosiamose's influence on O3-induced sputum neutrophilia was investigated in the following study: Biomosiamose is a glycomimetic that acts as a selective inhibitor and anti-inflammatory. It has been reported to be beneficial in diseases involving inflammatory cells, such as asthma. As of the most recent update, this medication was in phase 2 studies, being assessed for effectiveness and safety in the treatment of chronic pulmonary obstructive disease (COPD). The study was sponsored by Revotar Biopharmaceuticals AG and conducted by NCT00962481 (ClinicalTrials.gov Identifier).

Evaluation of the effects of the drug (SB-656933-AAA) on the body after a single dose in subjects who have inhaled O3: GlaxoSmithKline created the drug SB-656933-AAA, which was proven to be effective in treating COPD and cystic fibrosis. The administration of a single dosage of O3 prior to the administration of the aforementioned medicine was shown to improve this activity. NCT00551811 conducted a phase 1 investigation on this medication until the most recent updated data was available.

Intra-articular O3 treatment for knee osteoarthritis pain relief: Patients with osteoarthritis of the knee are presently being studied to see if ozone will help them feel better. The study is now in phase 2 and is being done by NCT00832312. It is supported by Ben-Gurion University of the Negev.

The Effect of Ozone Therapy on Lumbar-Herniated Discs: Ozone is being studied for its efficacy in infiltration and effectiveness in comparison to microdiscectomy in the treatment of lumbar-herniated discs that meet surgical requirements. The experiment is presently in phase 2 and is supported by the Kovacs Foundation, with trials being conducted by NCT00566007. The study compares the efficacy of infiltration in the presence of corticoids and anesthetics to that of replacing O3 with oxygen.

V. POSITIVE OUTCOME OF OZONE THERAPY

It was revealed that O3 stimulates the antioxidant system, which has an impact on blood glucose levels. By activating superoxide dismutase, which regulates organic peroxide levels, ozone lowered oxidative stress.

- Ozone was shown to completely inactivate HIV in vitro; this action of O3 was dose-dependent. It was established that the inactivation concentration was not cytotoxic. A reduction in the HIV p24 core protein resulted in inactivation.
- Ozone has also been found to improve host immunity by increasing the production of cytokines.
- In an in vitro study, O3 was found to be particularly effective in reducing the amounts of Acinetobacter baumannii, Clostridium difficile, and methicillin-resistant Staphylococcus aureus in both dry and wet samples, indicating that it might be used as a disinfectant.
- An oxygen/O3 combination was discovered to prolong the onset of arrhythmia produced by potassium chloride, aconitine, and other drugs in experimental animals such as rats.
- It boosts the immune system's activity.
- Purifies the blood and lymphatic system
- Lowers the risk of shock and stroke
- Prevents/reverses degenerative illnesses
- Removes auto-immune disorders.
- Increases metabolic rate, leading in a 200-450 calorie reduction in a 30-minute session.
- Increases blood circulation, which aids in the faster recovery of damaged muscles. Stimulates blood vessels, which relieves pain and accelerates the healing process.
- Kills all types of bacterial and viral illnesses
- Mineral absorption is improved.
- Reduces lactic acid build-up and increases muscular flexibility, which relaxes and loosens muscles.
- Oxidizes toxins, allowing them to be excreted through the skin, lungs, kidneys, and colon.
- Far infrared radiation enters the joint and surrounding tissues, improving blood flow, lowering inflammation, and alleviating pain.
- There is some indication that ozone therapy for COVID-19 patients has favourable results, although there have been no large-scale research on the subject.
- Oxygen-ozone treatment has been shown in certain studies to lessen the size of herniated discs, which may play a role in musculoskeletal problems.
- Patients with serious cardiopulmonary illnesses who received ozone treatment saw various degrees of improvement in their oxygen levels.

VI. DRAWBACKS OF OZONE THERAPY

Ozone aggravates respiratory illnesses like asthma and impairs the body's capacity to fight infections. Air embolism, myocardial infarction, temporary blindness, blood flow interference, irritation and damage to the vaginal mucous barrier, and an increased risk of infection are all dangers connected with ozone treatments.

- The Herxheimer response occurs in certain people who get ozone treatment. This can create flu-like symptoms in the individual and make them feel worse in the short term.

Due to O3's reactivity, such as oxidation, peroxidation, or the formation of free radicals, a cascade of events such as lipid peroxidation leading to changes in membrane permeability is seen, and lipid ozonation products (LOP) operate as signal transducer molecules.

The presence of unsaturated fatty acids in both lung lining fluid and pulmonary cell bilayers is the fundamental cause for this. O3 combines with unsaturated fatty acids to produce particular products, such as LOP, which activates lipases, causing the release of endogenous inflammatory mediators.

Inactivation of enzymes is caused by the removal of functional groups. These responses cause cell harm or death as a result of the reactions.

Photochemical smog contains mixtures of O3 and NO2, which are toxic to lung alveoli and operate additively or synergistically. Antioxidants or free radical scavengers in the diet, such as vitamin E, C, and others, can counteract the effects of O3.

Arachidonic acid was shown to be oxidised in the presence of O3 to produce peroxides, namely arachidonic acid peroxides (AAP), with activity equivalent to prostaglandin endoperoxides, in an in vitro research. In the presence of indomethacin and Vane's combination of vasoactive hormones, these peroxides were reported to demonstrate contraction of rabbit aortic strips and rat fundus strips in dosages equivalent to spontaneously produced prostaglandin peroxides. AAP induced human platelets to clump together in platelet-rich plasma, but these effects were not seen in the presence of indomethacin or vitamin E, suggesting that these drugs may be utilized to treat O3 toxicity.

VI. RECENT DEVELOPMENT:

Chronic pain, such as low back pain, coronary artery disease, osteoarthritis, and peripheral artery disease, is now a major social and economic burden, making Gaskin et al study's all the more important. The national cost of chronic pain management in the United States is estimated to be between $560 and $635 billion dollars. India too, is on its path for effecting pain management. Many centers focus mainly on chronic pain management .To effectively prevent and manage chronic pain, further research is required.

Anti-inflammatory medicines, such as corticosteroids, immunosuppressive drugs, and antibiotics, are commonly used to alleviate pain caused by a herniated disc or osteoarthritis of the joints. These medications are only partially and only temporarily effective. There are also possible adverse effects, which in some circumstances do not even ease the pain.

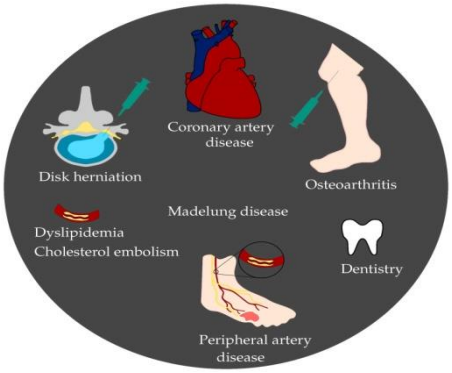

Fig:1

Ozone gas, on the other hand, is already widely used for a variety of therapies and health conditions. Figure 1 depicts several examples of circumstances. Ozone is an extremely unstable gas that decomposes into oxygen very fast. As a result, it must be produced prior to treatment. Ultra-pure medical oxygen is used as the input for the ozone generator during the production of ozone for medical purposes. As a result, an oxygen–ozone combination is produced for future use. Because the ozone generator uses ultra-pure medical oxygen instead of air as an input, humidity interference is not taken into account when measuring ozone gas for medical purposes.

VII. METHODS OF OZONE THERAPY

7.1 Autohemotransfusion treatment

The most successful type of ozone therapy is autohemotransfusion (LAH – Large AutoHemotherapy), which is administered intravenously. It entails drawing the patient's blood into a vacuum container, which is subsequently filled with an oxygen-ozone combination. Following that, ozone-saturated blood is delivered intravenously back to the patient's body in a closed circuit. One intravenous injection is required for the operation, which takes around 15 minutes.

Materials and Methods used:

1.Major autohaemotherapy treatments are carried out in accordance with established procedures. To avoid blood coagulation and increase flow properties, a plastic container is filled with 50mL saline and 0.25 mL heparin, followed by 100mL venous blood. The blood is then soaked with an ozone/oxygen combination and returned to the venous circulation.

Major Autohemotherapy : A roll-type peristaltic pump with a microprocessor monitoring system is utilised to pump the blood and return it to the venous circulation, making the operation of Major Autohemotherapy easier. The pump is meant to manage blood flow rate and is integrated with a safety device that prevents air from entering the vein during the reinfusion of ozonized blood.

Procedure of Major Autohaemotherapy

Drip Phleboclysis of Ozonated Saline

- In Russia, however, an alternative to Major Autohemotherapy has grown more generally accepted and popular. It's called ozonated saline drip phleboclysis. The procedure is easy to follow. Sterile saline will be administered intravenously after being barbotaged with an ozone/oxygen combination in a flask. (The detailed description is presented in the manual “Ozone Therapy in Practice” - www.ozonmed.ru).

Result: The approach has proven to be highly effective, even when using very low ozone concentrations (1-3 mg/l) and dosages (50- 600mcg)

- Any claims that sodium hypochloride is generated when saline is ozonized were proved to be false. Three unique testing were conducted, all of which proved that the amount of hypochloride used was far too little to have any effect on the human body.

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7.2 Ozonated saline, administered intravenously

Ozone saline - a method that allows for the use of relatively low dosages of ozone. Individuals with the following conditions may benefit from this type of ozone therapy: -CVD, autoimmune disease, Lyme disease, chronic fatigue syndrome, diabetes

Advantages:

Ozonated Saline IV Therapy can bring amazing comfort and healing to people suffering from the illnesses described above. This therapy works in a variety of ways, including:

- Stimulates the immune system of the patient
-Improves blood and oxygen circulation throughout the body
-Reduces inflammation caused by sickness, injury, or illness
-Eliminates the harmful burden in the body
-Kills germs, viruses, mould, and fungi
-Improves general health and wellness.

7.3 Enteral treatment

Because ozone supplied this manner has a systemic impact, enteral therapy (rectal delivery of the oxygen-ozone combination in gaseous form, RI – Rectal Insufflation) can be employed as an alternative to intravenous administration. Ozone is delivered rectally as a gas using a particular rectal delivery device. Ozone reaches the big intestine's wall, where it then enters the bloodstream. It is a straightforward and painless process. Because the patient controls the pace and strength of gas supply, the set promotes patient comfort during the process.

Three enteral operations are judged to be equivalent to two autohemotransfusion treatments in terms of efficacy.

The approach is highly advised for patients with big intestinal problems, because the local action of ozone will add up to the systemic effect in this scenario. Children can also benefit from this form of therapy.

7.4 External application of an oxygen-ozone mixture on wounds

External use of an oxygen-ozone mixture for wounds (also known as a "ozone shoe") – necessitates a closed gas cycle, which is given by a tight, adequately approved siliconized bag that we place on the injured leg and then fill with an oxygen-ozone gas combination. The medication is used to treat difficult-to-heal wounds, leg ulcers, pressure sores, dermatitis, and "diabetic foot," among other things.

7.5 Subcutaneous injection

Subcutaneous injection — an adequate amount of the oxygen-ozone combination is injected beneath the skin near the afflicted area. It possesses anti-inflammatory and hence analgesic properties (e.g. facial nerve), as well as antimicrobial properties (which is important in local treatment of severe acne).

7.6 Vessel injection

After Vessel (spider) injection — a trace quantity of oxygen-ozone combination is injected directly into dilated vessels (spider veins) using a precision needle, causing the vessel walls to "glue together" and the vessel to be excluded from the bloodstream, with a highly positive cosmetic result.

The next step of the study is to compare these competing models to evaluate that which one of these models is more supported by data.This study follows the methods used by Chen (1983), the Davidson and Mackinnon equation (1981) and the posterior odds ratio (Zellner, 1979) for comparison of these Models.

VIII. SUMMARY

Ozone treatment is a type of alternative medicine that uses ozone gas. It is divisive because of worries about its efficacy and safety. Researchers are now investigating the effects of ozone treatment on the human body in order to determine whether it has any therapeutic promise. Humans are poisonous to ozone gas, and little study has been done on the safety of ozone treatment. As a result, official organizations are now opposed to its use. Anyone with questions regarding ozone therapy or whether treatment is best for them should consult their physician. In this overview, I have put in efforts in gathering information about ozone treatment and its effects on human health. It would assist anyone who are considering this therapy or would like to learn more about it in making their decision.

IX. CONCLUSION

I conclude, by adding that the review done shows the different methods that are being used in ozone therapy. Although few researcher are contraindicating the use of ozone in medical field, research on the ill effects are still under progress. The medical field has been on a drastic change every single day. We would be seeing a lot of research and positive outcome in the future..

X. ACKNOWLEDGMENT

I'm overwhelmed in all humbleness and gratefulness to acknowledge my depth to all those who have helped me to put these ideas, well above the level of simplicity and into something concrete. I would like to express my special words of gratitude to my colleague Mrs. Jannet Reena Purani, Mrs. Sudarshini George, Mrs. Jennifer Roshni Paka & Mr. Jeevan who has helped me do this work and gave me great ideas in making this project unique.

REFERENCES

[1] Noel L. Smith., Anthony L. Wilson, et al,. 2017. Ozone therapy: an overview of pharmacodynamics, current research, and clinical utility. National Center for Biotechnology Information, 7(3): 212–219.

[2] Sri Sri College of Ayurvedic Science & Research Hospital**.** 2022. Ozone Therapy. Available from: https://srisriayurvedahospital.org/ozone-therapy/#:~:text=Ozone%20shows%20general%20revitalizing%20capacity,and%20clinical%20dizziness%20or%20vertigo..

[3] Omar Seyam, Noel L. Smith, et al,. 2018. Clinical utility of ozone therapy for musculoskeletal disorders, National Center for Biotechnology Information 8(3): 103–11

[4] Seidler V., Linetskiy I., Hubálková H., et al,. 2008. Ozone and Its Usage in General Medicine and Dentistry A Review Article. Prague Medical Report 109 (2008)1, 5–13

[5] Wikipedia. Available from: https://en.wikipedia.org/wiki/Ozone_therapy

[6] Elvis A. M., Ekta J. S. March 2011. Ozone therapy: A clinical review. The Journal of Natural Science, Biology and Medicine 2(1):66-70

[7] Catia Scassellati, Antonio Carlo Galoforo, et al,. 2020. Ozone: a natural bioactive molecule with antioxidant property as potential new strategy in aging and in neurodegenerative disorders. National Center for Biotechnology Information, 63: 101138

[8] Roycroft JH, Gunter WB, Menzel DB. Ozone toxicity: Hormone-like oxidation products from arachidonic acid by ozone-catalyzed autoxidation. Toxicol Lett. 1977;1:75–82.

[9] Mustafa MG. Biochemical basis of ozone toxicity. Free Radical Biol Med. 1990;9:245–65. [PubMed] [Google Scholar]

[10] Donovan DH, Williams SJ, Charles JM, Menzel DB. Ozone toxicity: Effect of dietary vitamin E and polyunsaturated fatty acids. Toxicol Lett. 1977;1:135–9. [Google Scholar]

[11]Bimosiamose: An Antiinflammatory Glycomimetic.[cited in 2010]; available from: http://www.revotar.de/pdf/BioTOPics24_Bock.pdf . [Google Scholar]

[12] Mustafa MG. Biochemical basis of ozone toxicity. Free Radical Biol Med. 1990;9:245–65. [PubMed] [Google Scholar]

[13] Donovan DH, Williams SJ, Charles JM, Menzel DB. Ozone toxicity: Effect of dietary vitamin E and polyunsaturated fatty acids. Toxicol Lett. 1977;1:135–9. [Google Scholar]

[14] Hazucha MJ, Bates DV, Bromberg PA. Mechanism of action of ozone on the human lung. J Appl Physiol. 1989;67:1535–41. [PubMed] [Google Scholar]
[15] Martínez-Sánchez G, Al-Dalain SM, Menéndez S, Re L, Giuliani A, Candelario-Jalil E, et al. Therapeutic efficacy of ozone in patients with diabetic foot. Eur J Pharmacol. 2005;523:151–61. [PubMed] [Google Scholar]
[16] Study to evaluate the effect of bimosiamose on ozone induced sputum neutrophilia. [cited in 2010]. Available from: http://clinicaltrials.gov/ct2/show/NCT00962481.
[17] Beeh KM, Beier J, Meyer M, Buhl R, Zahlten R, Wolff G. Bimosiamose, an inhaled small-molecule pan-selectin antagonist, attenuates late asthmatic reactions following allergen challenge in mild asthmatics: a randomized, double-blind, placebo-controlled clinical cross-over-trial. *Pulm Pharmacol Ther.* 2006;19:233–41. [PubMed] [Google Scholar]
[18] The Effect of Ozone Therapy for Lumbar Herniated Disc. [cited in 2010]. Available from: http://clinicaltrials.gov/ct2/show/NCT00566007?term=ozone+therapyandrank=1 .
[19] D'Erme M, Scarchilli A, Artale AM. Ozone therapy in lumbar sciatic pain. *Radiol Med.* 1998;95:21–4. [PubMed] [Google Scholar]
[20] Evaluate the effects of the drug (SB-656933-AAA) on the body after a single dose in subjects who have inhaled ozone. [cited in 2010]. Available from: http://clinicaltrials.gov/ct2/show/study/NCT00551811 .
[21] Groenewald C.B., Essner B.S., Wright D., Fesinmeyer M.D., Palermo T.M. The Economic Costs of Chronic Pain Among a Cohort of Treatment-Seeking Adolescents in the United States. J. Pain. 2014;15:925–933. doi: 10.1016/j.jpain.2014.06.002. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
[22] Margolis J., Barron J.J., Grochulski W.D. Health Care Resources and Costs for Treating Peripheral Artery Disease in a Managed Care Population: Results From Analysis of Administrative Claims Data. J. Manag. Care Pharm. 2005;11:727–734. doi: 10.18553/jmcp.2005.11.9.727. [PubMed] [CrossRef] [Google Scholar]
[23] Gaskin D.J., Richard P. The Economic Costs of Pain in the United States. J. Pain. 2012;13:715–724. doi: 10.1016/j.jpain.2012.03.009. [PubMed] [CrossRef] [Google Scholar]
[24] Salus Ozone Institute, 2021. OZONE TREATMENT METHODS Methods of medical administration of the oxygen-ozone mixture. Available from: https://instytutozonoterapii.pl/ozone-treatment-methods/
[25] Longevity effect integrative health & wellness. 2022. Tulsa Ozonated Saline IV Therapy. Available from: https://longevityeffect.com/tulsa-wellness-services/ozonated-saline-iv/
[26] Oleg V. Maslennikov, Irina A. Gribkova,. 2008. Ozone Therapy Method. Absolute Ozone. Available from: http://www.absoluteozone.com/ozone-therapy-method.html