Improvement of neurological conditions and recovery of the left ventricular ejection fraction subsequent to oxygen-ozone therapy through auto-hemoinfusion of ozonated blood

Sergio Pandolfi,1,2 Claudio di Giovanni,3 Eleonora Marinari,3 Marianno Franzini1
1Oxygen-Ozone Therapy Scientific Society, Gorle (BG); 2Villa Mafalda Nursing Home, Rome; 3Department of Anesthesia and Intensive Care, La Sapienza University, Rome, Italy

Abstract

Here we present the case of a 76-year-old patient who suffered from ischemic cardiopathy and myocardial infarction in January 2014, arterial hypertension, kidney failure, Parkinsonism, vascular multifactorial ischemic cerebro pathology, cerebral ictus, neurogenic bladder, and inguinal hernia. The left ventricular ejection fraction evaluated through repeated echocardiographic examinations remained reduced to 33% from January 2014 to March 2015. The left ventricular ejection fraction, after 14 months from acute myocardial infarction and despite the coronary angioplasty and medical therapy, remained constantly reduced to 33%.

On 3rd July 2015 he started the oxygen-ozone therapy with 2 auto-hemoinfusions of ozonated blood per week. Over the first two months of therapy we noticed a marked improvement of his heart conditions with a net reduction in asthenia and neurological status, the improvement of heart conditions was corroborated by the echocardiogram of 5th November 2015 which showed an increase in the left ventricular ejection fraction from 33% to 50%. In this case the heart function improvement of left ventricular ejection fraction was noticed only after having started the systemic oxygen-ozone therapy through large auto-hemoinfusion. In April 2015, before starting the oxygen-ozone therapy we assessed the patient’s inguinal hernia to be inoperable due to the lapsed heart conditions, while the subsequent reassessment in December 2015, after the patient underwent oxygen-ozone therapy for 5 months, we assessed him to be operable considering the heart function improvement.

Introduction

Ozone is a gas characterized by instability, therefore it cannot be preserved but produced when needed to be used; it is naturally present in the organism of living beings, and performs several essential functions to life, it is produced by white blood cells and nowadays it is used to treat ischemic vascular pathologies since it reactivates the micro-circle and increases the oxygen transfer to different organs and systems, it increases the production of energy in cells, it does not show any side effects, and does not cause any pharmacological interactions. It acts on cell metabolism and favours the elimination of toxic substances produced into cells. Oxygen-ozone therapy is a macro-therapy having a multi-organ protective action because it reactivates the micro-circle with a better oxygenation into the different body districts, it induces an increase in erythrocyte deformability and filterability with a further increase in the oxygen transfer to cells due to the increase in the production of glycerophosphate and a rightward displacement of the hemoglobin dissociation curve, it increases the mitochondrial oxidative phosphorylation, the nitric oxide release at precapillary sphincter level and the neoangiogenesis. We have constantly observed a marked improvement in his central and peripheral circulatory conditions, showing clinical outcomes which are hardly achievable with other therapies in patients suffering from ischemic cardiopathy, kidney failure, respiratory failure, ischemic vascular cerebropathy, lower limb peripheral arterial disease. Other improvements we noticed were related to the heart function in those patients suffering from ischemic cardiopathy or from myocardial infarction, with a reduction in asthenia, arrhythmia, and in vascular claudication in those patients suffering from lower limb peripheral arterial disease. In cerebrovascular pathologies and in senile dementia we notice that those patients treated with oxygen-ozone therapy show an improvement of their cognitive and mnestic faculties, of their attention, memory, motor coordination, and a reduction in micturition disorders in neurogenic bladders.

The anti-inflammatory action of ozone, leads to a reduction in the production of prostaglandins by acting on the arachidonic acid and has an antioxidant action activating the endogenous protective enzymatic functions of cells against free radicals, because it increases the transcription at DNA level of protective enzymes against free radicals.

Thanks to these characteristics it represents an essential therapy in the prevention and treatment of ischemic cardiopathy, in post-infarction rehabilitation, kidney failure, in lower limb arterial failure, in...
cerebral vascular pathologies, in ischemic ictus, and in other patholo-
gies of the micro-circle on an ischemic and inflammatory basis.

**Case Report**

We present the case of a 76-year-old patient who suffered from acute myocardial infarction in January 2014, ha also suffered from Parkinsonism, arterial hypertension, chronic kidney failure, and dys-
lipidemia. On 15th January 2014 he arrived at the Reception of a 2nd
level Emergency Department after a drowsiness state associated with
negative dysarthria due to angina pectoris and dyspnea, the arterial
pressure was 80/50, the electrocardiogram (ECG) showed sinus tachy-
cardia at 104 bpm, isolated ventricular ectopic beats, ST depression
both in the front and in the back part. The ECG showed the left ventricle
within the size limits, a 40% left ventricular ejection fraction (EF), with
widespread hypokinesia without marked sectionality. The enzymes of
myocardial necrosis were serum taking positive. The thorax computed
tomography (CT) without contrast agent showed a pulmonary edema
with multiple emery glass areas above all in lower lobes associated with
pleural effusion. The brain CT was positive due to chronic ischemic
vascular cerebropathy. During his stay in cardiac intensive care unit we
noticed the progressive improvement of his general case history. On 21st
January 2014, an echocardiographic examination showed EF 35%,
widespread hypokinesia with akinesis of the basal segment of the
lower wall and of the medium segments of side wall, plus a 2° degree
diastolic dysfunction. On 28th January 2014 the patient underwent
coronary angioplasty with a direct implantation of a drug-eluting stent
on the descending coronary artery and of three metal stents on the
coronary artery. On 31st January he was discharged with the pre-
scription of medical therapy. On 16th April 2014 the patient underwent
an ECG that showed an increase in the mass index of left ventricle,
while segmentary asynergy documented a severe EF global and longitudi-
dinal systolic impairment of 33%, an increased diastolic filling pressure
and a mild mitral valve insufficiency. The subsequent echocardiograph-
ic examinations performed on 31st October 2014, 29th January 2014,
and 20th April 2014 respectively, the ECG showed an EF of 33%.
In July 2015 the patient started the oxygen-ozone therapy through large auto-
hemoinfusion of ozonated blood, during the sessions 240 mg of blood
were taken through venous access with needle-cannula, the blood was
collected in a closed-circuit SANOS bag specifically certified, and then
mixed with 200 cc of O2/O3 gaseous mixture at 35 mg through a MED95
Computerized Photometric System medical device [Multissigen srl.,
Gorle (BG), Italy] and subsequently re-infused into the vein.

In the first two months from the beginning of the therapy the patient
already showed a marked improvement of his heart conditions with
a reduction in asthenia and a marked improvement of neurological
conditions.

The improvement of heart conditions was corroborated by the ECG
performed on 5th November 2015, which showed an increase in the left
ventricular ejection fraction from 33% to 50%. In April 2015, before
starting the oxygen-ozone therapy we assessed the patient’s inguinal
hernia to be inoperable due to the lapsed heart conditions, while the
subsequent reassessment in December 2015, after the patient under-
gen oxygen-ozone therapy for 5 months, we assessed him to be oper-
able considering the heart and kidney function improvement.

**Discussion**

Ozone is a gas characterized by instability, it is naturally present in
the organism and in the atmosphere. Its therapeutic applications have
been unacknowledged for a long time. Its administration in the organ-
ism, even if at the very beginning shows an oxidizing action, leads to an
initial and transitory oxidative stress, the blood and plasma redox poten-
tial is made up of several high performing systems cooperating with
each other and effective in opposing the initial oxidizing action of ozone
that performs a real preconditioning from oxidative damage, its ther-
apeutic concentrations do not exceed the blood antioxidant potential.1,3

The ozone put in contact with plasma reacts instantly with the
antioxidant systems [above all uric acid, ascobic acid, glutathione
(GSH), cysteine, albumin] therefore only a small part of the initial dose
reacts with polyunsaturated fats, which are mainly present at the three
albumin hydrophobic cavities level (Eq. 1):

\[-\text{CH} = \text{CH} + \text{O}_2 + \text{O}_3 = 2\text{RCHO} + \text{H}_2\text{O}_2\]

Therefore the potential ozone energy is transferred to two main mes-
geners, such as H2O2, and the aldehyde 4-hydroxynonenal molecules
(4HNE) molecules and trans-4-hydroxyhexanal (HHE). Given the high
reactivity of ozone such reactions take place in a few seconds, and usu-
ally a few minutes of contact between blood and oxygen-ozone mixture
are enough for the ozone to exhaust completely and for the oxygen to
saturate the hemoglobin system and dissolve into plasma. The antioxi-
dant systems are mainly reintegrated in the 20 min following the expo-
sure to the gaseous mixture.

The deionized H2O2, enters mainly all hematic cells quickly and makes
some changes: i) erythrocytes: glycolysis activation, increase in intracel-
lular concentrations of ATP and 2,3-diphosphoglycereate. This turns
into a rightward displacement of the hemoglobin dissociation curve, which, therefore, releases oxygen to peripheral tissues more easily;3 ii) leucocytes: the phagocytic activity of neutrophils increases. In lymphocytes and macrophages the IkB intracellular patterns are acti-
vated, IkB is one of the IkB nuclear transcription factor components.
Trimer, which is degraded in the proteasome into heterodimer p50-p65,
can activate the transcription of more than 100 genes. Interleukins and
some acute-phase proteins are produced. Furthermore interferon and
tumor necrosis factor are produced;4 iii) platelets: platelet-derived
growth factor polypeptide, transforming growth factor β 1 and growth
factors are produced.

Aldehydes, reacting with GSH, carnosine and, above all, albumin, are
carried into the different body tissues. The toxicity of 4HNE and HHE is
opposed by compensatory mechanisms such as detoxification, dilution
and excretion; since they are recognized as oxidizing agents, the body
responds by producing superoxide dismutase, heme oxygenase, glucose-
6-phosphate dehydrogenase and other powerful antioxidants. Moreover,
aldehydes stimulate the production of endothelial nitric oxide synthase
(eNOS),3 improving the peripheral perfusion and the tissue oxygena-
tion. The auto-hemoinfusion of ozonated blood proved to be safe and well
tolerated by patients. Furthermore, it has been pointed out in a random-
ized clinical study on 140 patients, 70 of which underwent oxygen-ozone
therapy and the other 70 representing the control group, that the hema-
tochemical parameters showed a reduction in reactive oxygen metabolytes [300±10.1 Carratelli units (U.CARR.)] after 12 months com-
pared to an initial value of 380±10.4 U.CARR., P<0.05] and an increase
in the values of the plasma biological antioxidant potential (2100±34.8
µmol/vitamin C after 12 months compared to the initial value of
1610±56.2, P<0.05) in treated patients compared to the control group.5

These data demonstrate that the auto-hemoinfusion of ozonated
blood plays a crucial role in reducing the oxidative stress by endoge-
nously stimulating the production of antioxidant enzymes.

The oxygen-ozone therapy is a safe method, having no side effects,
which does not cause any allergic reactions and is currently used to
treat several pathologies (lower limb obliterative arteriopathy, cuta-
neous ulcers, atrophic maculopathy of retina, vascular pathologies on
ischemic and degenerative basis, brain pathologies on vascular and
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CD34 and CD117/c-kit. Moreover we have monitored the heart eNOS. These data indicate that the damage associated with ischemia cells we have evaluated in the infarcted tissue the immunoreactivity to and in the inflammation (CD68) and immune response (CD8 and CD4) and the myocardial immunohistochemistry with EPCs search. For these carried out the measurements of the size of the myocardial infarction (IS) and myocardial reperfusion can be opposed by a pre-treatment through the systemic administration of the oxygen-ozone gaseous mixture.

Recent studies showed that after a myocardial infarction the levels of endothelial progenitor cells (EPCs) reduced into the myocardium. These cells derive from the bone marrow and aim at mobilizing, migrating, and differentiating into endothelial cells in situ and creating a cell reserve able to make up for endothelial damage. Strategies aimed at increasing the EPCs into an ischemic heart seem to improve the neovascularization in the ischemic tissue, and could improve the myocardial blood flow and reduce the ischemic damage. An experimental study on animals pointed out that the oxygen/ozone protects the heart from acute myocardial infarction thanks to the local increase in the eNOS activity and to the recruitment of endothelial progenitor cells.

The purpose of this study has been to establish whether a mixture of oxygen/ozone (O3) protects the heart from acute myocardial infarction through the local increase of eNOS activity and endothelial progenitor cells recruitment. A critical evaluation of the various methods clarifies positive and negative aspects. Med Gas Res 2011;1:6.

Conclusions

The oxygen-ozone therapy through large auto-hemoinfusion protects the heart of patients suffering from ischemic cardiopathy and it is essential in the rehabilitation of those patients who had an acute myocardial infarction as clinical outcomes and experimental evidence pointed out.

References


[Ozone Therapy 2016; 1:5840]