The Primary Physico-Chemical Mechanism for the Beneficial Biological/Medical Effects of Negative Air Ions

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Abstract—The primary chemical mechanism of the beneficial medical/biological action of negative air ions necessary for life was studied. Air ion deficiency is the cause of many illnesses and treatment with air ion inhalation is effective in many cases. However, its application is limited by the absence of knowledge of the primary mechanism of its action.

The superoxide anion $O_2^-$ was detected in the flow of negative air ions generated by an electroeffluvial air ionizer. Earlier, the appearance of hydrogen peroxide in solutions treated with air ions was shown. The presence of these reactive oxygen species in ultralow and low concentrations ($10^{-12}$–$10^{-6}$ M) suggested that the primary mechanism for the beneficial medical/biological action of negative air ions is moderate activation of free radical peroxidative oxidation within a physiological range that is lower than in tissues under pathology.

It was shown in patients that treatment with inhalation of negative air ions did not induce pathological changes in superoxide dismutase activity and, under simultaneous administration of a food antioxidant, led to its mild increase. The latter, along with some previous results, supports the proposed mechanism. In addition, taking the proposed mechanism into consideration, air ion doses for treatment can be selected on an individual basis and should depend on the redox state of the patient. This should achieve better results for medical treatment with ionized air.

Index Terms—Air ions, antioxidants, hydrogen peroxide, ionized air, reactive oxygen species, superoxide, superoxide dismutase, therapy with ionized air.

I. INTRODUCTION

A NEW theory for the primary physico-chemical mechanism of the beneficial biological/medical action of negative air ions is presented in this paper. Therapy using artificially generated negative air ions is a valuable application of ionized gasses, but unfortunately development of this application is currently very limited and has even declined compared to previous years. Cold ionization of air is used mostly as a tool for bacterial and chemical decontamination, as can be seen from the program of the ElectroMed99 Symposium. [see Guest Editorial in this special issue.] In our opinion, the main cause for the decreasing use of ionized air for medical purposes is the absence of knowledge of the primary mechanisms of its action. Without this knowledge, therapies with ionized air have explained variations in results for different groups of patients. Our theory explains the possible origin of these variations and allows us to propose new ways to improve the therapeutic effect. This provides a basis to correctly extend the use of artificial air ionization for the improvement of air quality at work and at home, which is become an increasingly important issue.

A. Brief History of the Medical Application of Artificially Ionized Air

Numerous investigations in the course of this century have provided evidence that the presence of a certain amount of negatively charged ionized gasses in inhaled air is necessary for normal vital activity [1]. Their presence is detected by measurement of the amount of negative charge, and they are called “negative air ions.” The number of negative air ions is high in clean natural air. This number increases under the influence of such factors as electrical discharges, movement of water and water drops, and radioactive decay. In some health resorts negative air ions are particularly numerous, reaching several thousands and tens of thousands per cm$^3$. On the other hand, the amount of negative air ions falls dramatically to several tens per cm$^3$ or even to a complete absence of ions in polluted city air, in closed and conditioned rooms, in moving cars and aircraft, and near television sets and computers.

Tchijevsky discovered the biological and physiological action of unipolar air ions in 1919. As has been stated in a special international memorandum, Tchijevsky’s pioneering investigations stimulated the biological and medical study of air ionization in different countries [2]. In the 1930’s, Tchijevsky advanced the concept of artificial ionization of air for medical treatment and for the prevention of disease. He designed a high-voltage air ionizer called “Lustre.” Beneficial medical/biological effects of negative air ion inhalation were demonstrated by Tchijevsky in animals and later in patients [3]. In particular, hypertension and bronchial asthma were cured in one to three weeks by daily half-hour sessions of negative air ion inhalation. In some cases, bronchial asthma attacks stopped immediately when inhalation was started.
Many cases of successful treatment with negative air ions were observed in different countries. In particular, Kornbluch effectively used negative air ions for burn treatment [4]. Krueger investigated the biochemical mechanisms of the beneficial biochemical effects of negative air ion inhalation [5]. He found that inhalation of negative air ions decreases excessive levels of the neurotransmitter serotonin. Serotonin levels become elevated under unfavorable conditions and cause various pathological symptoms. A dramatic example of illness caused by an excess of serotonin is the mental depression and feeling of exhaustion that develop with a rise of the positive ion content in the respired air. This physiological state can be induced by dry, hot winds that have various names in different countries. In Israel and in Arab countries, they are known as sharaf or hansim. Sulman obtained pronounced relief in the state of patients affected by sharaf conditions through the inhalation of negative air ions. He showed that such inhalation also decreased their excessive levels of serotonin [6].

We found in rats that negative air ion inhalation abolishes the stress-induced impairment of the “power stations” of the cell and the mitochondria in the brain and liver, and improves mitochondrial energy processes under adrenaline administration [7]–[9]. Many other examples of the beneficial medical/biological effects of negative air ions are described in the reviews cited here and elsewhere [10]–[13].

In spite of the above clear-cut evidence of the beneficial medical/biological effects of negative air ion inhalation, its medical application in recent years has diminished. This has been caused by the accumulation of unexplained cases of the absence of therapeutic effects or of unfavorable reactions. Such cases could not be explained by existing theories of negative air ion action, which were based mostly on consideration of the amount of inhaled charge.

This study presents new data, which implies novel mechanisms of the beneficial effect of negative air ions based on the chemical nature of the negative charge carriers and their interaction with the biochemical processes in the organism. Using this new model, the effect of negative air ion inhalation can be controlled in the organism and can be improved by antioxidants.

II. MATERIALS AND METHODS

For the studies we report on here, air ions were generated by an electroeffluvial ionizer, ELION-131M (a product of the DIOD Company in Moscow) through silent or dark (not corona) discharge. Electrons are generated at the tips of needle-shaped electrodes placed along wires positioned like the spines of an inverted open umbrella (see Fig. 1). This ionizer is a modern variation of the original design by that pioneer of medical treatment with air ions, Tchijevsky, and is called in his honor the “Tchijevsky Lustre.” The electrodes are fed by a high-voltage generator with square impulses of 50 kV, 1 Hz, and 30 ms. Impulse ion current is 25 μA, and its mean value is ~2 μA. A special feedback device prevents ozone formation. The Lustre is a powerful source of ions. A volume of air about 20 m² in cross-section containing light negative ions is formed with intensities from $2.5 \times 10^6$ charges per cm$^3$ to $0.5 \times 10^6$ charges per cm$^3$ at distances from 0.5 to 3 m, respectively. Near the Lustre, the “electrical wind” can be felt with the palm of the hand. Maximal saturation with air ions is reached within no more than 60 s. Ionization disappears two minutes after the generator is switched off. The concentration of air ions was measured by the aspiration condenser method with an ion counter SAI-TGU-66m (Tartu, Estonia). The counter differentiates negative, positive, light, and heavy air ions. The beneficial biological effects are typically related to the light negative air ions, and therefore for the rest of this paper we will present data only for those ions.

The concentration of negative air ions at the point of treatment of solutions was $6 \times 10^5$ charges per cm$^3$ and at the place of inhalation by a patient was $2 \times 10^5$ charges per cm$^3$. These concentrations lie within the ultralow molar range of $10^{-12}$–$10^{-25}$ M.

$O_2^-$ was measured using a free radical trap, Tiron (a product of Sigma, USA), by electron paramagnetic resonance (EPR) spectra measurement with a Brucker 400-MHz spectrometer.

Superoxide dismutase (SOD) activity was measured in erythrocyte hemolysates. The preparation of hemolysate is described by Kosenko et al. [14]. SOD activity was measured using an original modification [15] of the McCord and Fridovich method [16] based on adrenaline autooxidation.

The inhalation sessions for patients were carried out at the Clinical Center of Pushchino (Russia) by physicians Kosyakova and Lange according to clinical protocols and recommendations. Time of inhalation was 15–30 min once a day. The amount of air ions administered corresponds to a prophylactic dose which is 1/5 of the therapeutic dose, with air ion concentrations of $2 \times 10^5$ cm$^{-3}$ and $1 \times 10^6$ cm$^{-3}$, respectively.

III. RESULTS

A. Superoxide and Hydrogen Peroxide as Negative Charge Carriers in Ionized Air

Knowledge of the chemical nature of negative charge carriers in air is necessary to elucidate the primary mechanisms of the biological effects of negative air ions. Ionized, negatively charged oxygen $O_2^-$, superoxide, is the most expected candidate for this function. Superoxide can be formed by an electron generated by the ionizer combining with an oxygen molecule. It is difficult to detect as it exists for only a short time and does not accumulate in considerable amounts. Two molecules of superoxide spontaneously form hydrogen peroxide and oxygen according to the reaction

$$O_2^- + O_2^- + 2H^+ = H_2O_2 + O_2.$$

Hydrogen peroxide is a more stable substance than superoxide and is therefore more easily detected.

Even though superoxide had not yet been discovered, Tchijevsky suggested that the biological effect of negative air ions could be due to the presence of a special activated oxygen [17]. Krueger and Reed suggested that biological activity of negative air ions is mediated by an oxygen free radical [18]. The presence of superoxide in negative air ions was detected biochemically through the sensitivity of their effect to the specific enzyme [19]. The presence of superoxide and hydrogen peroxide among negative air ions was shown by Goldstein who suggested that...
the biological activity of negative air ions is attributable to superoxide [20]–[24]. The content of ionization products depends on the parameters of the generator. Some studies using different models of air ionizers also reported the presence of superoxide in the treated air.

In this work, we attempted to detect superoxide in solutions treated by the Tchijevsky Lustre. Earlier, we found the presence of micromolar concentrations of hydrogen peroxide in solutions treated by a flow of negative air ions [14]. The appearance of hydrogen peroxide suggested that its precursor, superoxide, is probably the primary product of air ionization. We used the free radical trap, Tiron, to detect superoxide by EPR spectra measurement. Initial experiments show that the EPR signal is easily observed in sea water and in solutions similar to intracellular media: 120-mM KCl, 10 mM of the buffer solution HEPES, pH 7.2. The signal increases greatly with an increase of pH to 10.0. The signal is diminished or extinguished by EDTA, sucrose, and Tris, which block free-radical processes. As shown in Fig. 2, the increase of EPR signal was in direct proportion to the duration of treatment, i.e., to the dose of air ions. The rate of $O_2^-$ accumulation was 0.5–1.0 $\mu$M/min.

Thus our previous study and data presented in this report show the presence of both superoxide and hydrogen peroxide in negative air ions. This is probably evidence that these substances are responsible for the beneficial biological/medical action of negative air ions. However, it is not easy to defend such a statement. The problem is that these two forms of oxygen were widely known to be harmful and damaging to living tissues. This classic view will be briefly considered below.

B. What is Oxidative Stress and Antioxidant Defense by Superoxide Dismutase?

In the 1960’s, Fridovich opened “The Superoxide Era” in biochemistry [25]. He found that under unfavorable conditions,
ionized oxygen, superoxide, is formed in the organism. This form of oxygen is highly reactive and is used in the organism for killing microorganisms. This can also damage the macroorganism’s own tissues. Oxidative damage in the organism is called “oxidative stress.” A special biological system exists to defend against oxidative stress. The first step of defense is the enzyme SOD. It greatly (10 000-fold) accelerates superoxide transformation into hydrogen peroxide as described above. Hydrogen peroxide is less toxic than superoxide; however, it is also very active. Therefore, both of them are called “reactive oxygen species.” Moderate SOD activity is typical for the normal quiescent state of an organism. SOD activity rises in response to the presence of superoxide. Mild increase in SOD activity is evidence of good antioxidant defense. Very high activity (50% and more above the basic level) is evidence of the development of oxidative stress. High activation is unstable and can turn into deep inhibition to lower than the normal level. This points to the exhaustion of the internal antioxidant system. To prevent this, external antioxidants are administered, which support the antioxidant defense mechanism of the organism.

C. What is the Effect of Ionized Air Inhalation on SOD Activity?

The molar concentrations of superoxide and hydrogen peroxide detected in our experiment are rather low: \(10^{-15}\) and \(10^{-6}\) M, respectively. Both of these are considerably lower than the level in pathological tissues in the organism. Therefore, we theorized that inhalation of ionized air will not damage the organism but will stimulate its antioxidant defense. This theory was tested in patients with arterial hypertension. In the 1940’s, hypertension was effectively cured by air ion inhalation. We measured activity of SOD in the blood as a conventional test of the state of the antioxidant system of the organism under pathology [26]–[29].

Twenty-three patients with arterial hypertension were under observation. All patients received their usual antihypertensive medicine. They were divided in three groups. One group received ionized air inhalations for ten days for 15–30 min once a day. The second group was administered the food antioxidant, amber acid (also known as succinic acid) [30], [31], with a dose of 100 mg once a day for ten days. The third group received both treatments.

The first result, which was noticed before the end of the inhalation course, was the improvement of the psychoemotional state of the patients. Anxiety, which is characteristic for these patients, was diminished: they were relaxed, their sleep improved, and they felt refreshed, more active, and a greater sense of well-being. Additional hypotensive effects beyond that already reached with antihypertensive drugs were not observed. The distinct improvement of how the patients felt suggested that inhalation had a positive effect on their metabolism. We investigated this by SOD activity measurements.

Typical data for three patients from each group are given in Fig. 3. Individual variations of the initial level of SOD activity are due to genetics and pathogenetic heterogeneity of the patients but not due to measurement error. The latter is within 1%–2% for two to three repeated measurements. The effect of treatment should be considered individually for each patient in order to avoid the contribution of the initial individual variations to the mean data. Indeed, as shown in Fig. 3, inhalation of ionized air did not induce a pathogenic rise in SOD activity. A mild decrease of SOD activity was observed only in the patient with the highest initial level. Administration of the food antioxidant, amber acid, resulted in a mild decrease in SOD activity in all cases. Joint treatment with ionized air and antioxidant produced a mild rise of SOD activity in all cases.

D. The Interpretation of the Observed Changes in SOD Activity

A careful consideration of these results leads us to the following five conclusions.

1) The results obtained show clearly the absence of oxidative stress from inhalation of ionized air at the doses administered.

2) The test used in this experiment can serve as a sensitive indicator of the individual effect of ionized air inhalation on patients. In particular, the single case of decrease in SOD activity was observed in the patient with the highest of all initial activity. This probably was due to his individual treatment with medicine containing iron, which can induce peroxidative oxidation [29], [32]. In this case, the interaction of ionized air and the enhanced internal peroxidative oxidation led to an overload of the antioxidant defense system and to an initial decrease of SOD activity. The decrease of SOD activity by ionized air, which is a potential activator of internal peroxidative processes, should be considered as an indication to diminish its dose.

3) The mild decrease of SOD activity by the food antioxidant, which does not increase but decreases internal peroxidative oxidation, can indicate the existence of some
Fig. 3. Activity of erythrocyte SOD in nine patients (left bar) before and (right bar) after treatment. For patients 1–3, the treatment was with negative air ions; for 4–6, treatment with amber acid (also known as succinic acid); and for 7–9, treatment with air ions supported by amber acid. SOD activity is given on the ordinate in arbitrary units.

4) The appearance of mild stimulation of SOD by inhalation of ionized air supported with an antioxidant shows that such a combination provide a more stable activation of antioxidant defense.

5) The proposed theory of the primary physico-chemical mechanism of the beneficial medical/biological action of negatively charged air ions as a mild activation of peroxidative processes in the organism allows control of the effect of inhalation, selection of individual doses of inhalation, and support of their effect by antioxidants. The measurement of SOD activity in the blood in our modification is sensitive and is a test available for clinic investigations.

IV. DISCUSSION

The key conclusion that can be drawn from our studies is that mild activation of free-radical peroxidative oxidation is the primary physico-chemical event contributing to the beneficial biological/medical effects of negative air ions.

The data presented show that in spite of the presence of such harmful oxygen species as superoxide and hydrogen peroxide among the air ions generated by the ionizer we used, they exhibit beneficial and not damaging effects. This agrees with our previous observations, which show that inhalation of negative air ions in therapeutic doses improves the function of mitochondria under stress and adrenaline administration [7]–[9]. Their direct influence does not damage isolated mitochondria but improves their energy processes and structure organization [33]–[36] and also improves the function of the heart muscle [37]. Inhalation was also accompanied by a small activation of peroxidative processes within the range of at least one order of magnitude lower than activation levels related to pathology [9]. In addition, we have unpublished observations that treatment of an incubation medium with negative air ions increases such typical peroxidative processes as the respiratory burst of neutrophils (Pocelueva) and that inhalation of ionized air stimulates endogenous hydrogen peroxide generation in rat heart mitochondria isolated after such treatment (Stavrovskaya). The key evidence of the free-radical nature and the beneficial biological action of negative air ions is provided by the increase in SOD activity caused by micromolar hydrogen peroxide that formed in solutions illuminated by the Lustre [14]. It was stated earlier that hydrogen peroxide inhibits SOD. This was at concentrations 700–6000-fold higher than in our experiments. The dual action of hydrogen peroxide on SOD activity serves as a good example of the opposite effects that low and high concentrations of active oxygen species have on biological systems. Their dose-dependent effect on biological systems is biphasic: initial activation by low concentrations is turned into inhibition by higher concentrations. Such kinetics are typical of free-radical peroxidative processes.

A. Recommendation for Individual Selection of Air Ion Doses

The important conclusion from the theory that activation of peroxidative processes is a primary mechanism of negative air ion action is guidance for the selection of individual doses for medical treatment. Determination of dose is usually based on some abstract average amount of negative ion consumption by a person per day and its relation to concentrations in the surrounding air [13]. For clean air, consumption is approximately \( 8 \times 10^6 \) ions, which is accepted as one biological unit. The prophylactic dose for healthy people is 23 biological units, while the therapeutic dose used to be considerably higher—up to 20 biological units for a session. Doses are corrected depending on air ion concentration in the surrounding air and the air’s humidity.
However, these prescriptions do not consider such important matters as the state of the patient: more specifically, the redox state of the patient. Taking into consideration that superoxide and hydrogen peroxide initiate free-radical peroxidative processes in the organism, it is necessary to determine the level of these processes in the individual patient. The level of peroxidative processes in healthy organisms is low and rises progressively under pathology. Therefore, in order to provide a stimulatory effect and to avoid inhibition, higher doses should be used for healthy people and progressively lower doses used for patients depending on their initial state. Indeed, too high a dose can be harmful for more at-risk patients. The initial dose in such cases should be low and then can be increased over the course of a successful treatment. Such an approach has been effectively used for treatment of broncho-lung diseases [38].

Support with antioxidants is also necessary for individuals with excessive peroxidative oxidation. The oxidative state of patients can be monitored by SOD activity as shown above or by other tests.

Last but not least, now that ionizers are available in the home, office, or car, another method of treatment can be recommended. We believe this to be safer with respect to possible excessive activation of free radical processes. The dose should be given not for a short time, e.g., the 1530 min for a clinic visit, but for several hours during the day. Such mild and prolonged exposure to air ions is closer to the desired natural condition and improves the air in the places where people spend much of their time.

B. Vital Necessity of Ultralow Concentrations of Ionized Oxygen

As previously noted, many observations show that ultralow concentrations (micromolar and lower) of superoxide and hydrogen peroxide play a regulatory role in the organism and do not damage tissues. Many important processes are initiated by these reactive oxygen species (e.g., see [39–[43]). The theory of the necessity of physiological concentrations (low in molar respect) for normal vital activity is not paradoxical.

It is worth mentioning that in low concentrations, superoxide and hydrogen peroxide are natural components of an ecologically clean environment. Low concentrations of \( \text{H}_2\text{O}_2 \) are inherent to natural water and air [44]. Its appearance is also due to the ionization of natural air and water in different ways: electrification, mechanical movement, radiation, and generation by plants and bacteria. In a thunderstorm, the concentration of \( \text{H}_2\text{O}_2 \) in the rain can reach \( 10^{-4} \text{ M} \). Exhaustion of \( \text{H}_2\text{O}_2 \) in artificial stagnant ponds leads to impairment of development of young fish and to their death. This damage can be restored by the addition of \( \text{H}_2\text{O}_2 \) or oxidants, e.g., iron, into the water. Similar disturbances can develop in the tissues of an organism whose ionized oxygen and hydrogen peroxide has been exhausted. External reactive forms of oxygen activate the internal. Exhaustion of reactive oxygen in the environment impairs the internal medium of the organism and leads to pathology.

Artificial ionization of air can compensate for this deficiency and cure the primary cause of many illnesses. One more reason for the decrease of air ion applications in medicine is the appearance of numerous drugs that did not exist in the 1930’s–1950’s. Many hypotensive, anti-asthmatic, anti-inflammatory means are now used for the treatment of hypertension, bronchial asthma, and burns. Their prompt effects are attractive to both physicians and patients. However, it should not be forgotten that many of them have unfavorable side effects on the organism. Their chronic administration brings pollution into the internal medium. In contrast, negative air ions clean the organism. That is why this natural method of sanitation should be widely used for medical treatment and not only for air cleaning. The goal of this paper is to remind scientists dealing with ionized gases of the great medical/biological importance of ultralow concentrations of ionized oxygen and to outline a new approach that can help extend its application to the sanitation of people.

REFERENCES


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