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Short Communication

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Transcutaneous ozone therapy: an underestimated medical practice

Abstract

In this work it has been investigated the effects on fifteen healthy volunteers of a transcutaneous ozone exposition in a sauna cabin. A large numbers of parameters were determined before the exposition, at the end and 0.5, 1 and 24 hours after the ozone treatment. A control group (6 volunteers) has been exposed to oxygen alone with the same experimental conditions of the ozone treated group. The subjects exposed to ozone showed no significant intragroup and intergroup differences respect to control group in body mass modification, blood pressure, and hematological parameters except to a significant increase in plasma levels interleukin 8, total antioxidant status (TAS) and thiobarbituric reactive substances (TBARS) at the end of the treatment. However, all values returned to normal 24hours after the ozone treatment. These results suggest a possible induction, with a transdermal ozone application, of an acute and calculated oxidative stress similar to that observed after the major ozonated autohemotherapy. Moreover, no side effects after the ozonated sauna were observed.

Keywords: thiobarbituric reactive substances, ozone treatment, total antioxidant status, stratum corneum

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Abbreviations: SC, stratum corneum; TAS, total antioxidant status; TBARS, thiobarbituric reactive substances

Introduction

Ozone (O3) is a gas naturally present in the troposphere and it becomes one of the major oxidizing and pollutant agents in the atmosphere. The human skin represents, together with the respiratory system, the organ most exposed to environmental ozone, and it can be said that O3 is the most reactive chemical component to which the human epidermis is in contact. It has been undertaken numerous studies to evaluate the effect of ozone on antioxidants and lipids in the skin. In particular, the stratum corneum (SC), the thin border between the air and the organism, would seem to be the most susceptible to the oxidative action of ozone. The statum corneum consists of a single bicompartmental system of cells without a nucleus (corneocytes) wrapped in an intercellular matrix rich in lipids (such as ceramides, cholesterol and free fatty acids) and vitamin E. From experimental studies it has been showed that the damaging action of ozone, at high and prolonged doses, appears to be expressed in an increase in lipid peroxidation and a simultaneous decrease in vitamin E present in the stratum corneum.

Starting from these premises, it is inevitable to ask what is the "rationale" for the use of ozone transcutaneously. A first doubt to be clarified is whether ozone, administered for therapeutic purposes through the skin (and therefore in doses and methods different from some of the in vitro experiments described above), can cause harmful effects on the epidermis. It is useful to remember that oxygen-ozone for topical cutaneous use, by applying bags to the lower limbs in case of atrophic ulcers and in localized infections, is used by many decades in Europe, and that during these treatments no skin damage has ever been reported due to the contact of ozone with the skin. It should also be remembered that even the use of ozonated baths presupposes the interaction of the entire epidermis with the action of ozone, and, even in these cases, no side effects are known. Therefore, the phenomena of lipoperoxidation described by Thiele et al. on animal models would not seem to have harmful effects in humans during a brief and controlled exposure as in the case of transcutaneous oxygen-ozone therapy. On the other hand, lipoperoxidation, could prove to be "therapeutic" rather than harmful if, for example, these lipid peroxides, interacting with other molecules and coming into contact with the blood circulation, were able to reproduce those phenomena of stimulation of the antioxidant and immune system described for the major ozonated autohemotherapy. Even in the case of transcutaneous oxygen-ozone therapy, it would therefore seem that there is a fine line between the toxicity and the therapeutic effect of ozone. Obviously, in order to trigger a "therapeutic" oxidative stress, it is necessary that the ozone comes into contact with an extensive skin surface, and for this reason we have turned our attention to transcutaneous ozonation in the sauna. In Canada the ozonated sauna has been widely used. It consists in the almost total exposure of the body (with the exception of the head and neck) to oxygen-ozone dispersed in a hot-humid environment. With this therapeutic modality a wide spectrum of pathologies are treated, from chronic infectious diseases, to joint trauma, to neoplastic pathologies, with "positive" results, as usual not reported in any scientific journal. The ozonated sauna also combines the benefits of ozone, temperature and a hot-humid environment. However, due to the presence of three important factors (temperature, oxygen, ozone), it is not known what is the role of ozone. Since the ozonated sauna could represent a valid alternative to GAET in cases where venous access is difficult to find, we conducted a study on healthy volunteers exposing them to oxygen-ozone or oxygen alone.

Methods

The study described was authorized by the Ethical-Deontological Committee of the University of Siena and was performed on 15 healthy volunteers who gave their informed consent for execution of the study. The selected volunteers had homogeneous anthropomorphic characteristics (male subjects, aged between 32 and 48years, non-smokers, with similar lifestyles) and did not suffer from any pathology in progress. In a control group of healthy volunteers (n=6) it has been performed the same protocol of the ozone treated group but it has been used oxygen alone as gas flow in the sauna. A venous blood sample was taken from all subjects at set times: before the treatment in

the sauna, immediately at the end, after 30minutes, after an hour and after 24hours from the end of the treatment. Various parameters were analyzed on these samples: venous oxygen pressure (PvO2), total plasma antioxidant status (TAS) according to Rice-Evans and Miller, thiol protein groups (PTG) according to Hu, malonyldialdehyde plasma expressed as reactive substances to thiobarbituric acid (TBARS) according to Buege and Aust. As clinical monitoring in the subjects were measured body temperature, weight, systolic-diastolic blood pressure; an electrocardiogram was also performed before and after the sauna to ascertain any thermal stress arrhythmias. The plasma levels of Interleukin 8 (IL-8), of myeloperoxidase (MPO) and of transforming growth factor beta (TGF beta) were also determined with ELISA methods.

Technical conditions of use of the ozonized sauna

The sauna cabin was kindly offered by Plasma fire International (Langley, BC, Canada) and consisted of a plastic laminate structure with an internal volume of approximately 440 liters. The gas flow through the cabin (both in the case of treatment with O2-O3 and with O2 only) was 1 liter / min, and was produced by an ozone generator from the company Ozonosan (Hansler, Germany) with photometric concentration control of O3.

The maximum ozone concentration reached at the end of each session did not exceed about 0.90micrograms /ml, a value 12 times lower than the minimum ozone concentration during the treatment of ulcers of the lower limbs.

The hot steam was generated in the cabin by means of a thermos stated resistance that was adjusted to 90 °C, in order to obtain an internal temperature of 46-50°C. The cabin doors were closed during the treatment, but to avoid the loss of ozone polyethylene sheets were placed on the door opening and around the neck.

Each treatment lasted 20 minutes and at the end of each session, before opening the cabin doors, the gas flow was interrupted and the internal gas rapidly aspirated to prevent any accidental inhalation of O3 by the subject or the experimenters. At the end of the treatment the subject was placed lying down for a few minutes on a bed during the classic reaction to the temperature of the sauna.

Results

As previously reported, each volunteer underwent to a sauna treatment with oxygen-ozone or oxygen (control group). The body temperature increases achieving the maximum at the end of the treatment (37.5-39.3 °C), and then decreases rapidly in the following minutes. The body weight decreases by about 200-600 grams at the end of the sauna, probably due to intense sweating. Blood pressure also showed a slight decrease and return to baseline values in 30 minutes. Of particular interest are the data relating to venous pressure of O2 and CO2. The venous pO2 increases significantly and the pCO2 decreases consequently at the end of the sauna treatment, and this situation persists for about an hour after the end of the sauna. The increase in venous pO2 is greater after an oxygen-ozone sauna respect to an oxygenated sauna (Table 1).

Table 1 A summary of parameters measured before (PRE), at the end (END) and 0.5h, 1 hour and 24 hours after a period in the sauna cabin in the presence of either oxygen ozone gas mixture (ozone) or oxygen only (control). Value is given as the mean (SD). Intergroup and intergroup comparison revealed no significant differences

Parameters	PRE		END		0.5h		1.0h		24h	
	ozone	control	ozone	control	ozone	control	ozone	control	ozone	control
RBC(x10^{6}mm^3)	4.94(0.22)	4.66(0.16)	5.06(0.22)	4.73(0.1)	4.71(0.14)	4.54(0.1)	4.62(0.21)	4.39(0.1)	4.87(0.26)	4.56(0.2)
HT(%)	45.37(1.91)	42.54(2.02)	46.5(1.92)	43.3(1.8)	43.27(1.19)	41.68(1.8)	42.5(1.82)	40.5(1.82)	44.13(2.91)	42.36(1.58)
PLT(x10^{3}mm^3)	183.5(17)	187.3(16)	207(20)	199.5(20)	182.5(19)	162.8(3.9)	173.2(23)	169(11.7)	191.5(26)	178.3(12.3)
pH	7.33(0.03)	7.3(0.02)	7.43(0.04)	7.4(0.02)	7.38(0.04)	7.38(0.01)	7.39(0.03)	7.37(0.01)	7.38(0.03)	7.36(0.04)
[HC03] mmol/l	28.8(0.98)	27.68(1.40)	25.3(1.24)	24.03(1.20)	26.9(2.32)	25.30(1.31)	26.07(1.34)	26.70(1.18)	27.32(1.02)	27.20(1.60)
Sv02sat(%)	54.2(21.8)	50.1(19.3)	88.3(8.7)	93.2(2.8)	76.3(20.3)	91.1(4.3)	86.5(6.4)	81.7(12.6)	62.4(32.2)	60.1(18.25)
TGFbeta(pg/ml)	54.5(10.9)	n.d.	32.8(9.7)	n.d.	32.7(9.2)	n.d.	30.5(7.3)	n.d.	45.7(8.7)	n.d.
AST(U/l)	23.2(3)	21(4)	24(2.5)	22(2)	23.7(6.3)	22(4)	23.2(4.7)	23(6)	24(2.9)	24(4.8)
ALT(U/l)	19.8(3.5)	20(2)	21.3(4.6)	22(3)	21.7(3.9)	21(3)	20.3(3.8)	20(4)	22.6(4)	20.8(4.5)
Creatine(mg/dl)	1.03(0.2)	1.01(0.1)	1.17(0.2)	1.08(0.3)	0.97(0.1)	1(0.2)	0.92(0.1)	0.98(0.1)	1.02(0.45)	0.99(0.38)

nd, not determined; RBC, red blood cells; HT, hematocrit; PLT, platelets; HCO3, bicarbonate concentration; SvO2, venous oxygen saturation; TGF, beta, transforming growth factor beta; AST, aspartate aminotransferase; ALAT, alanine aminotransferase

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Regarding the blood count, the data show an increase in hematocrit at the end of the treatment, with a subsequent decrease. The same trend was recorded in the number of leukocytes, which increase and renormalize after ozonated sauna. Plasma TAS and thiol levels and the PTG statistically decreased after the treatment. TBARS increase significantly after exposure to O2-O3 in sauna.

It is important to note that there was no increase in hemolysis. We also evaluated the changes in three fundamental parameters after treatments with O2-O3: IL-8 significantly increases 30 minutes after treatment, but no modifications of the MPO and TGF were observed (Tables 2&3).

As for the liver and kidney function parameters, they remained unchanged, as was the electrocardiogram performed before and after treatment.

Table 2 Modification of Thiobarbituric Acid Reactive Substances (TBARS) in the plasma of the 15 healty volunteeers before (PRE) , at the end of the ozonated sauna (END), 30 minutes after the end of the sauna(0.5 HR), 1 hour after the end of the sauna (1 HR) and (24 HRS) twenty four hours after the end of the sauna

TBARS (MICROMOLS/ml)	
PRE	0.9±0.2
END	1.2±0.3*
0.5 HR	1.4±0.2*
1 HR	1.7±0.3*
24 HRS	0.8±0.2

Values are expressed as mean±standard deviation.* = P< 0.05 compared to baseline value

Table 3 Modification of Interleukin 8 plasma value in the 15 healty volunteeers before (PRE), at the end of the ozonated sauna (END), 30minutes after the end of the sauna (0.5 HR), 1 hour after the end of the sauna (1 HR) and (24 HRS) twenty four hours after the end of the sauna

Interleukin 8 (PICOGRAMS/ml)	
PRE	2±0.1
END	6±0.2*
0.5 HR	14±0.1*
1 HR	3±0.1
24 HRS	2±0.2

Values are expressed as mean±standard deviation

* = P< 0.05 compared to baseline value

Discussion

The potential toxicity of ozone always requires particular caution with regard to possible innovative routes of administration; this is in fact the first study that scientifically evaluates the effect of oxygen-ozone by transdermal route on healthy volunteers, monitoring any changes in the main plasma lipoperoxidation parameters. During the ozonated sauna it is necessary to assure, given the continuous flow of O3, the absence of dangerous gas leaks outside of the cabin. During the 20 minutes of exposure to ozone, the body temperature increases, as usually reported in the sauna, but the values quickly return to normal. Body weight and systolic pressure also decrease slightly due to the intense sweating and vasodilation that occurs in the sauna. Of particular interest is the data relating to the considerable increase in venous pO2, indicating a marked transcutaneous passage of oxygen. In addition, both the total antioxidant state and the thiol group's decrease in the plasma while TBARS increase, and this effect are specific to ozone exposure. In our opinion this effect is not attributable to a direct passage of O3 through cell membranes (ozone decomposes rapidly at the epidermal level), but rather to the formation of LOP on the skin surface which, together with ROS including hydrogen peroxide, can pass the transcutaneous barriers and, favored by the intense vasodilation, penetrate the bloodstream. The increase in TBARS is transitory, as the peroxidative levels in the plasma return to normal after 24 hours, and the hypothesis that this oxidative stress is short-lived is supported by the total lack of side effects.

All these changes occurring after treatment with an ozonated sauna emphasize the possible role of this method in the panorama of oxygen-ozone therapy. The advantages of this procedure consist in the total lack of invasiveness, in the simplicity of use, in its low cost. Since the ozonated sauna seems to exert the same biochemical modifications as the major ozonated autohemotherapy, its use appears promising in the course of:

a. diseases of the musculoskeletal system
b. as an immune adjuvant in neoplasms
c. peripheral arteriopathies
d. ulcers
e. dermatitis, psoriasis, high severity lipodystrophy
f. chronic degenerative diseases (COPD, neurodegenerative diseases)

Conclusion

Studies are needed to establish the exact benefit of the ozonated sauna in the chronic diseases, and especially the absence of side effects following repeated treatments.

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Conflicts of interest

Author declares that there are no conflicts of interest.

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