ISSN 2475-5451

Review Article

International Journal of Diabetes & Metabolic Disorders

Potential of Electronic Water as a Therapeutic Treatment for Oxidative Stress-Related Diseases

Masahiro Onuma[1]*, Teijiro Wakatuki[2] and Ryusuke Fujiki[3]

[1]*Trisguide Co., Ltd*

[2]*Crystal Lab Co., Ltd*

[3]*Medical Corporation Foundation Keijinkai Hospital*

***Corresponding author:**
Dr. Masahiro Onuma, President, Trisguide Co., Ltd, Shinagawa East One Tower 4F 2-16-1 Konan Minato-ku Tokyo Japan Email: onuma@trisguide.com

Submitted: 11 July 2018; **Accepted**: 20 July 2018; **Published**: 23 July 2018

Introduction

The significance of "oxidative stress" as an underlying factor in metabolic syndrome-related diseases and lifestyle diseases was discussed in our 2008 review [1]. Nine years later, we feel this subject has gained considerable importance with regard to medical cost control measures of a national budget of 96 trillion yen in the 2015 fiscal year (FY 2015); 41 trillion yen was allocated for national health-related expenditures. More than a third of this was for metabolic syndrome-related diseases. In this regard, many issues such as improvement of dietary habits as a measure to prevent accumulation of visceral fat, making exercise therapy habitual, and acceptance of designated health checks remain unresolved. Currently, local governments are making an effort to solve issues related to these areas. However, progress has been slow, and a more suitable approach may be required at the 'preliminary reserve' stage prior to drug treatment. Thus, we examined whether "electron rich water" is a viable counter-measure to oxidative stress.

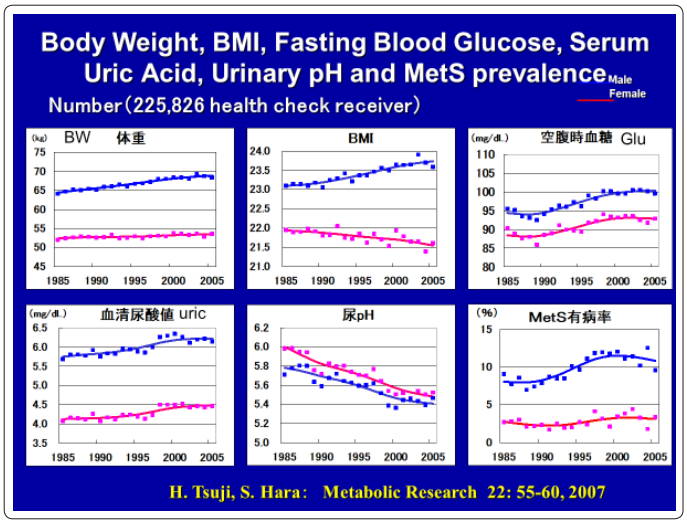
Status of Designated Health Checks

In FY 2014, 53,847,427 citizens were eligible for designated health checks. Of these, the number of people who actually received consultations was 26,163,456 (48.6%). Additionally, of those who received consultations, 4,403,850 (16.8%) qualified for designated health guidance. Of these, 783,118 patients completed the guidance, which is a completion rate of 17.8%.

Compared to FY 2008 (38.9%), the rate for receiving consultations for designated health checks had increased by 9.7 percent in FY 2014 (48.6%). On the other hand, compared to FY 2008 (19.9%), the rate of qualifying for designated health guidance had fallen by 3.1 percent in FY 2014 (16.8%). The current situation in Japan, where the consultation rate has fallen below 50% and the completion rate for designated health guidance has dipped below 20%. This indicates that the proportion reaching the final goal of designated health guidance is less than 10%. Therefore, future measures to counteract this downward trend are urgently needed.

Metabolic Syndrome and Oxidative Stress

Data (Figure 1) from studies conducted at Toranomon Hospital Health Management Center from 1985 to 2005 revealed that fasting blood glucose levels, serum uric acid values, and urinary pH values were proportionally correlated to an increase in both body weight and the body mass index (BMI) [2]. This indicates that an increase in serum uric acid values and the acidification tendency of urine may be an indicator of increasing "oxidative stress" in the body. Therefore, the presence of the metabolic syndrome may be considered as an indirect expression of "oxidative stress disease."



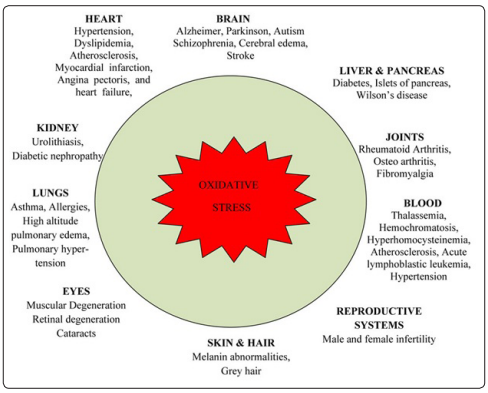
Various Diseases that are Causally Linked to "Oxidative Stress"

Oxidative stress is described as a state in which an imbalance exists between oxidizing and reducing actions due to reactive oxygen species (ROS) in the body causing the oxidizing action to become dominant. ROS consists of oxygen radicals (O_2), hydrogen peroxide (H_2O_2) and hydroxyl radicals (-OH), produced by NADPH oxidase, xanthine oxidase, and mitochondrial respiratory chain enzymes. ROS removal mechanisms in living organisms utilize antioxidant substances and antioxidant enzymes to suppress the oxidizing action. Oxidative stress arises when the balance between production and removal is disrupted through excessive production of ROS and the impairment of the antioxidant system. Oxidative stress is reported to be involved in the onset and progression of various diseases, including diabetes, chronic kidney disease (CKD), arteriosclerosis, and non-alcoholic steatohepatitis among others. Type 2 diabetes is characterized by insulin secretion failure and insulin resistance.

However, reports indicate that oxidative stress may play a major role in insulin secretion failure. Resistance to oxidative stress weakens when the concentration of superoxide dismutase (SOD), a component of the ROS elimination system in insulin secreting β cells of Langerhans islets in the pancreas, decreases. As the oxidative stress of β cells progresses and insulin resistance increases, the hyperglycemic state continues. Furthermore, superoxide production from mitochondria of vascular endothelial cells increases and this increase is further enhanced due to the activation of vascular cell NADPH oxidase, leading to the onset and progression of further complications.

The effects of oxidative stress on the skin may include "skin rust." Skin rust is a skin condition in which skin cells oxidized by ROS cause deterioration of nutrient intake and waste disposal, excessive melanin production, poor generation of collagen (which imparts tightness to skin), and disorders in skin turnover [3].

More recent studies also indicate that oxidative stress may be related to Alzheimer's disease, as glucose metabolism and oxidation of energy metabolism-related enzymes are accelerated from the early stages of Alzheimer's disease [4].Furthermore, a new study reports that "fatigue" may be caused by oxidation of neurons by ROS, thereby increasing the fatigue factor (FF) protein, which causes fatigue [5]. A list of representative oxidative stress-related diseases is shown in (Figure 2). Therefore, when considered in combination these studies indicate that oxidative stress may affect the human body in many ways, and that it may directly or indirectly cause many other diseases that are yet unknown [6].



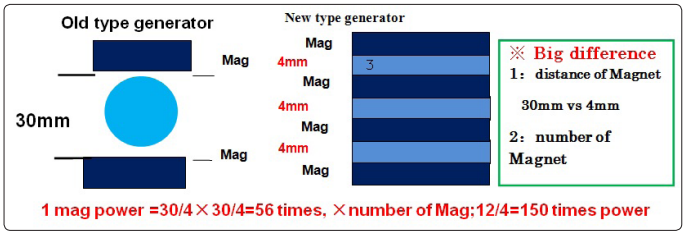
"Oxidative Stress" Mitigation Measures As A Solution

As shown in (Figure 3), there are many types of oxidative stress related diseases [7]. These include diabetic retinopathy, diabetic neuropathy, diabetic nephropathy, metabolic syndrome, chronic kidney disease, ischemic heart disease, myocardial infarction, cerebral stroke, peripheral atherosclerosis, cerebrovascular atherosclerosis, left ventricular hypertrophy, congestive heart failure, arterial hypertension, hepatic fibrosis, Parkinson disease, Alzheimer's, dementia, pulmonary hypertension, erectile dysfunction, emphysema, asthma, allergosis, osteoporosis, osteoarthritis, gastric ulcer, septic shock, pulmonary fibrosis, pains, rheumatic arthritis, psoriatic arthritis, ulcerative colitis, scleroderma, pathogenic vascularization, graft rejection, chronic pain, hypersensitivity, and cataract among others.

The most promising solution may be able to provide electrons externally. As a case in point, allopurinol (a xanthine oxidase inhibitor) is widely used clinically as a uric acid-lowering drug. Converting allopurinol into oxypurinol creates a powerful "oxidation stress suppressing capability," and several applications have been reported even in actual clinical practice [8]. However, allopurinol is a medical drug, which cannot be used in practice as a countermeasure in non-symptomatic cases. Currently, this poses a critical issue. Therefore, we focused on "electronic water." Research to prevent rusting and scaling by applying magnetism to water pipes has already been carried out in the former Soviet Union. A publication called "Magnetic Treatment of Water" was issued by Vuyi Klassen in Russia in 1977. Subsequently additional research has been conducted, but the results have not met or exceeded initial expectations [9, 10].

The New "Electronic Water Generator"

We studied the "electronic water generator" of Crystal Lab Co., Ltd. The differences between the "electronic water generator" and the "magnetic processor or water activator" mentioned previously are as follows: (1) By reducing the distance between the magnetic forces from 30 mm to 4 mm, that is one-seventh of the previous gap, generation of electrons increased in inverse proportion to the square of the distance as per "Faraday's law." (2) Compared to 4 pairs of magnets in a normal water activator, the electric water generator has 12 pairs. In summation, electron generation was increased threefold. Therefore, this generator optimizes the synergistic effect of (1) and (2) (resulting in 150 times more electron production) to increase "oxidative stress inhibition capability" to previously unseen levels (Figure 3) (Patent No. 5939215).



Clinical Test Results

The relationship between oxidative stress, ageing and diseases resulting from ROS and free radicals has been previously characterized, and it is widely believed that all pathologies may involve these two factors. Reduction of oxidative stress is thought to be important not only from the viewpoint of preventive medicine but also from that of disease treatment. In living cells homeostasis is established by maintaining a neutral pH both inside and outside the cell, proper osmotic pressure, a normal ion balance, and electrical neutrality in the cell. Oxidative stress is a major disruptor of homeostasis.

Therefore, we attempted to verify whether oxidative stress that is excessive in certain disease states (advanced cancer patients and diabetic patients) can be alleviated using water generated from the new electronic water generator of Crystal Lab Co., Ltd. Oxidative stress and antioxidant levels were measured using a FRAS4 free radical analyzer (Wismer Co., Ltd., Tokyo Japan), in order verify efficacy of the new electronic water generator. The results are described below.

Test Subjects

A treatment sample of 10 people (8 cancer patients and 2 Type 2 diabetes patients) who were fully informed in regard to the consent form concerning the use of personal information and provided written consent, and a control sample of 2 healthy people (1 male, 1 female), were selected as test subjects (Table 1).

Table 1
List of Test Subjects

1	58 years	Male	Postoperative recurrent scirrhous stomach cancer stage IV
2	81 years	Female	Unresectable gastric cancer stage IV
3	78 years	Female	Unresectable gastric cancer stage IV
4	77 years	Female	Unresectable pancreatic cancer stage IV
5	68 years	Female	Unresectable pancreatic cancer stage IV
6	76 years	Female	Unresectable pancreatic cancer stage IV
7	72 years	Female	Recurrent breast cancer stage II
8	79 years	Male	Postoperative recurrent liver cancer stage IV
9	62 years	Male	Type 2 diabetes (HbAlc: 8.7)
10	80 years	Female	Type 2 diabetes (HbAlc: 11.7)
• 1. Healthy person: male 64 years			
• 2. Healthy person: female 58 years			

Control Subjects - healthy individuals without a history of lifestyle-related diseases were chosen.

Test Method

Oxidative stress and antioxidant tests for serum were measured using a FRAS4 free radical analyzer FRAS4.
Oxidative capacity was determined according to the Diacron-Reactive Oxygen Metabolites (d-ROMs) method, either by Fenton's reaction or by Haber-Weiss reaction, using a hydroperoxyl radical (ROO•), lipid peroxide radical, and alkoxy radical (R•) as substrates. CARR units (dynamic range: 200-300 units) were used as the measurement units.

Antioxidant capacity was determined using the biological oxidant potential method (BAP) by allowing the total amount of bio-reductive substances centered on ascorbic acid to act on iron trichloride ($FeCl_3$). Additionally, the thiocyanate-hue binding method was used as the indicator reaction to derive the total amount of reduction. The amount of reduced iron (Fe) ions was calculated in μmol (reference value: 2,201 μmol/L or more).

Electronic water was consumed for three weeks as follows: after meals, between meals and before sleeping 6 times a day, and during time periods convenient to the test subjects. The volume of drinking water consumed was 750-1000 mL. BAP and d-ROMs checks for all cases were carried out at 4:30 pm. As for the degree of oxidative stress, it is said that the fluctuation within a day is small as long as there is no cause that may bring about a change in particular.

Result

The electronic water generated from the new electronic water generator supplied electrons to the antioxidants in the living body (Figure 4 & 5). The d-ROMs value in the degree of oxidative stress test by the FRAS4 free radical analyzer exhibited a decreased, and the BAP value, which is an indicator of plasma antioxidant capacity, improved significantly. In addition, it is thought that friction between the vascular wall and blood corpuscle accompanying high oxidative stress in blood vessels in cancer and diabetes was reduced through improvement of ion balance, resulting in electrical neutralization and reduction of oxidative stress.

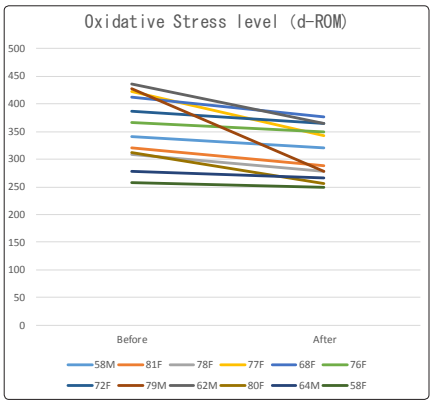


Figure 4

200-300 Normal
300-320 Borderlines
321-340 Low degree of oxidative stress
341-400 Medium degree of oxidative stress
401-500 High degree of oxidative stress

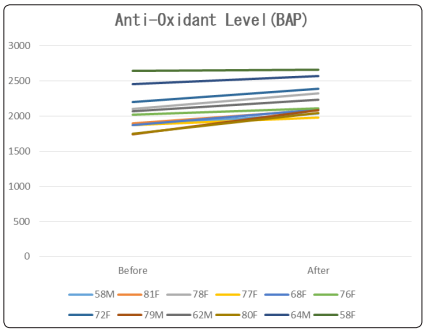


Figure 5

2,000-2,200: Borderline
1,800-2,000: Slight deficiency
1,600-1,800: Insufficient antioxidant power
1,400-1,600: High deficiency in antioxidant power
Under 1,400: Very high deficiency in antioxidant power

Discussion

In regard to diabetes, a study conducted by Masayuki Yamamoto et al. using mice, indicated that the mechanism involving the onset of diabetes and obesity in the brain is related to an increase in oxidative stress of the brain (11). It was clarified that, as oxidative stress increases, the hypothalamus, which regulates systemic metabolism, decrease in nerve cells and the actions of hormones (such as insulin and leptin), atrophies leading to diabetes and obesity. Although it is known that oxidative stress is elevated in diabetes, sufficient knowledge regarding the significance of oxidative stress elevation in the hypothalamus region, and its role in regulating metabolism in particular is lacking, due to various limitations affecting current research on the subject. In the above study, it was found that mice with decreased tRNA $^{[Ser]\ Sec}$ (Trsp) gene expression in the hypothalamus and pancreatic Langerhans islets developed obesity and diabetes. In the brains of mice with increased oxidative stress, nerve cell death was accelerated in the hypothalamus. As nerve cells (which play an important role in metabolic regulation) decreased, resistance to insulin and leptin (an obesity inhibition hormone) increased. The above study regards reducing "oxidative stress" as an important strategy for the prevention of diabetes, and attention is directed towards its future development.

We believe that our study indicates that the effect of suppressing oxidative stress via "electronic water" may be an option for the prevention and treatment of diabetes. This is because the data suggests that "oxidative stress relief" may be related to the functional recovery of pancreatic β cells, and the resultant recovery of insulin secretion ability. When insulin binds to the insulin receptor, phosphorylation of the amino acid tyrosine normally occurs in the insulin receptor substrate. Under "oxidative stress conditions," instead of the tyrosine, the amino acid serine is phosphorylated and glucose is not metabolized. Cellular proliferation and apoptosis occur in response to the stress conditions, resulting in impaired glucose metabolism of insulin, causing insulin resistance and simultaneously causing various ageing-related diseases such as arteriosclerosis and cancer.

It is known that chronic inflammatory conditions increase the risk of carcinogenesis. Cells such as neutrophils and macrophages are activated in the inflamed area leading to an increase in the production of ROS and nitric oxide. These free radicals cause DNA mutations and cell proliferation thereby promoting cancer development. When chronic inflammation is present, cancer develops more easily. It also promotes the rapid growth of cancer that is already present, as when there is inflammation, a large volume of ROS is generated in that area, thereby increasing the opportunities for DNA mutations to occur. Furthermore, when cell proliferation occurs in order to compensate for cells that have died due to inflammation, the very factors that promote cell proliferation also become promoters of carcinogenesis.

Because cancer cells depend on anaerobic glycolysis for energy production, they need much more glucose than normal cells. In addition, within cancer cells, a large amount of lactic acid is produced by anaerobic glycolysis leading to oxidation of surrounding tissues. In oxidized tissue, blood vessels contract and a hypoxic area is formed. Repeating ischemia-reperfusion results in excessive generation of ROS, thereby producing a cycle of cancer progression. Research indicates that inhibition of mitochondrial function in cancer cells is not irreversible, and that mitochondrial function can be reversed back to a normal state, which then activates oxidative phosphorylation in the mitochondria of cancer cells. In other words, addition of external electrons may normalize the action of apoptosis (cell death) inducing substances such as ROS and cytochrome C generated in the mitochondria. Since this tends to cause apoptosis of cancer cells, it may improve the cellular microenvironment, and thereby contribute to cancer treatments, including immunotherapy which is currently attracting much interest.

The results of the current study indicate that electronic water may be useful for the prevention of many diseases originating from oxidative stress, as also for the improvement of many other disease conditions.

References

1. Suzuki I, Yamauchi H, Onuma Masahiro (2009) New development of uric acid synthetic inhibitor – Toward a new target for xanthine oxidation-reduction enzyme inhibitor allopurinol. Drugs Today (Barc) 45: 363-378.
2. Tsuji H, Miyagawa M, Arimoto S (2007) Relationship between serum uric acid level as well as urinary pH and metabolic syndrome- related factors from health screening data gathered over 21 years. Health screening 22: 383-388.
3. Miyaji Y Eds (2006) Oxidative stress and skin diseases - Skin also rusts. History of Medicine - Oxidative Stress Ver.2. Tokyo: Medical Dentistry Publication.
4. Sonoda N, Inoguchi T (2015) "Mechanism and pathology of onset of dementia due Oxidative stress"
5. Kajimoto O (2016) all fatigue is caused by the brain. Tokyo: Shueisha.
6. Advances in Bioscience and Biotechnology (2012) 3: 7A.
7. Terawaki H1, Nakayama M, Miyazawa E, Murata Y, Nakayama K, et al. (2013) Effect of allopurinol on cardiovascular incidence among hypertensive nephropathy patients: the Gonryo study. Clin Exp Nephrol 17: 549-553.
8. Sofie Haglund, Svante Vikingsson, Sven Almer, Jan Söderman (2017) Combination treatment with 6-mercaptopurine and allopurinol in HepG2 and HEK293 cells – Effects on gene expression levels and thiopurine metabolism PLoS One 12: e0173825.
9. Ying Huang, Chunya Zhang, Jinghua Shen, Xiaogang Zhang, Huanhua Du, et al. (2017) Clinical Study on efficacy of allopurinol in patients with acute coronary syndrome and its functional mechanism. Hellenic J Cardiol DOI: 10.1016/j.hjc.2017.01.004
10. Ritsumi Saito, Daisuke Saigusa, Jingbo Pi, Akiyoshi Fukamizu, Fumihiro Sugiyama, et al. (2017) Nrf2 Improves Leptin and Insulin Resistance Provoked by Hypothalamic Oxidative Stress. Cell reports 18: 2030-2044.