Água rica em hidrogênio. Hidrogênio possui efeito antioxidante

11/06/11

O Hidrogênio possui 1 elétron na camada de valência e assim possui efeito redutor (antioxidante), principalmente contra o grande vilão da história oxidativa , o radical hidroxila, e contra o radical peroxi-nitrito,fato esquecido por muito médicos incluindo eu.

Jose de Felippe Junior

Hydrogen acts as a therapeutic antioxidant by selectively reducing cytotoxic oxygen radicals.
Ohsawa I, Ishikawa M, Takahashi K, Watanabe M, Nishimaki K, Yamagata K, Katsura K, Katayama Y, Asoh S, Ohta S.
Nat Med. 2007 Jun;13(6):688-94.

Source

Department of Biochemistry and Cell Biology, Institute of Development and Aging Sciences, Graduate School of Medicine, Nippon Medical School, 1-396 Kosugi-cho, Nakahara-ku, Kawasaki City 211-8533, Japan.

Abstract

Acute oxidative stress induced by ischemia-reperfusion or inflammation causes serious damage to tissues, and persistent oxidative stress is accepted as one of the causes of many common diseases including cancer. We show here that hydrogen (H(2)) has potential as an antioxidant in preventive and therapeutic applications. We induced acute oxidative stress in cultured cells by three independent methods. **H(2) selectively reduced the hydroxyl radical, the most cytotoxic of reactive oxygen species (ROS), and effectively protected cells; however, H(2) did not react with other ROS, which possess physiological roles.** We used an acute rat model in which oxidative stress damage was induced in the brain by focal ischemia and reperfusion. The inhalation of H(2) gas markedly suppressed brain injury by buffering the effects of oxidative stress. Thus H(2) can be used as an effective antioxidant therapy; owing to its ability to rapidly diffuse across membranes, it can reach and react with cytotoxic ROS and thus protect against oxidative damage.

Comment in

Nat Med. 2007 Jun;13(6):673-4.

PMID:17486089

Água rica em hidrogênio. Inalação do gás H2 protege sepse polimicrobiana reduzindo estresse oxidativo e liberação de HMGB1(High-mobility group protein B1)

11/06/11

Protective effects of hydrogen gas on murine polymicrobial sepsis via reducing oxidative stress and HMGB1 release.
Xie K, Yu Y, Pei Y, Hou L, Chen S, Xiong L, Wang G.
Shock. 2010 Jul;34(1):90-7.
Source
Department of Anesthesiology, General Hospital of Tianjin Medical University, Tianjin, P. R. China.
Abstract
Despite recent advances in antibiotic therapy and intensive care, sepsis is still considered to be the most common cause of death in intensive care units. Excessive production of reactive oxygen species plays an important role in the pathogenesis of sepsis. Recently, it has been suggested that molecular hydrogen (H2) exerts a therapeutic antioxidant activity by selectively reducing hydroxyl radicals (*OH, the most cytotoxic reactive oxygen species) and effectively protects against organ damage induced by I/R. Therefore, we hypothesized that H2 treatment had a beneficial effect on sepsis. In the present study, we found that H2 inhalation starting at 1 and 6 h after cecal ligation and puncture (CLP) or sham operation significantly improved the survival rate of septic mice with moderate or severe CLP in a concentration- and time-dependent manner. Furthermore, moderate or severe CLP mice showed significant multiple organ damage characterized by the increases of lung myeloperoxidase activity, wet-to-dry weight ratio, protein concentration in bronchoalveolar lavage, serum biochemical parameters, and organ histopathologic scores at 24 h after CLP operation, which was significantly attenuated by 2% H2 treatment. In addition, we found that the beneficial effects of H2 treatment on sepsis and sepsis-associated organ damage were associated with the decreased levels of oxidative product, increased activities of antioxidant enzymes, and reduced levels of high-mobility group box 1 in serum and tissue. Thus, H2 inhalation may be an effective therapeutic strategy for patients with sepsis.
PMID:19997046

Água rica em hidrogênio. Inalação de hidrogênio molecular suprime colite induzida por sulfato de sódio: aumenta o peso e diminui IL-1beta, TNF-alfa, IL-12 e infiltração de macrófagos na lesão do colon

12/06/11

Hydrogen mediates suppression of colon inflammation induced by dextran sodium sulfate.

Kajiya M, Silva MJ, Sato K, Ouhara K, Kawai T.

Biochem Biophys Res Commun. 2009 Aug 14;386(1):11-5.

Source

Department of Immunology, The Forsyth Institute, Boston, MA 02115, USA.

Abstract

By its antioxidant effect, molecular hydrogen gas (H2) was reported to protect organs from tissue damage induced by ischemia reperfusion. To evaluate its anti-inflammatory effects, we established a mouse model of human inflammatory bowel disease (IBD) by supplying mice with water containing (1) dextran sodium sulfate (DSS) (5%), (2) DSS (5%) and H2, or (3) H2 only ad libitum up to 7 days. At day-7, DSS-induced pathogenic outcomes including, loss of body weight, increase of colitis score, pathogenic shortening of colon length, elevated level of IL-12, TNF-alpha and IL-1beta in colon lesion, were significantly suppressed by the addition of H2 to DSS solution. Histological analysis also revealed that the DSS-mediated colonic tissue destruction accompanied by macrophage infiltration was remarkably suppressed by H2. Therefore, the present study indicated that H2 can prevent the development of DSS-induced colitis in mice.

PMID:19486890

Água rica em hidrogênio mais N-acetilcisteína (NAC) suprime estresse oxidativo e a conseqüente angiogênese após queimadura da córnea por alcalinos

12/06/11

Hydrogen and N-acetyl-L-cysteine rescue oxidative stress-induced angiogenesis in a mouse corneal alkali-burn model.
Kubota M, Shimmura S, Kubota S, Miyashita H, Kato N, Noda K, Ozawa Y, Usui T, Ishida S, Umezawa K, Kurihara T, Tsubota K.
Invest Ophthalmol Vis Sci. 2011 Jan 21;52(1):427-33.
Source
Department of Ophthalmology, Keio University School of Medicine, Shinjuku-ku, Tokyo, Japan.
Abstract
PURPOSE:
To investigate the role of reactive oxygen species (ROS) as the prime initiators of the angiogenic response after alkali injury of the cornea and observe the effects of antioxidants in preventing angiogenesis.
METHODS:
The corneal epithelia of SOD-1-deficient mice or wild-type (WT) mice were removed after application of 0.15 N NaOH to establish the animal model of alkali burn. ROS production was semiquantitatively measured by dihydroethidium (DHE) fluorescence. Angiogenesis was visualized by CD31 immunohistochemistry. The effects of the specific NF-κB inhibitor DHMEQ, the antioxidant N-acetyl-L-cysteine (NAC), and hydrogen (H2) solution were observed.
RESULTS:
ROS production in the cornea was enhanced immediately after alkali injury, as shown by increased DHE fluorescence (P<0.01). NF-κB activation and the upregulation of vascular endothelial growth factor (VEGF) and monocyte chemoattractant protein-1 (MCP-1) were significantly enhanced (P<0.01), leading to a significantly larger area of angiogenesis. Angiogenesis in SOD-1-/- mice corneas were significantly higher in WT mice (P<0.01), confirming the role of ROS. Pretreatment with the specific NF-κB inhibitor DHMEQ or the antioxidant NAC significantly reduced corneal angiogenesis by downregulating the NF-κB pathway (P<0.01) in both WT and SOD-1-/- mice. Furthermore, we showed that irrigation of the cornea with hydrogen (H2) solution significantly reduced angiogenesis after alkali-burn injury (P<0.01).
CONCLUSIONS:
Immediate antioxidant therapy with H2-enriched irrigation solution is a new potent treatment of angiogenesis in cornea to prevent blindness caused by alkali burn.
PMID:
20847117

Água rica em hidrogênio melhora a memória em modelo beta-amiloide de doença de Alzheimer por redução do estresse oxidativo

11/06/11

O Hidrogênio possui 1 elétron na camada de valência e assim possui ação redutora (antioxidante), principalmente contra o grande vilão da história oxidativa , o radical hidroxila e também contra o radical peroxinitrito, fato esquecido por muito médicos incluindo eu. Acresce que o hidrogênio por ser molécula muito pequena chega facilmente nas mitocôndrias e no núcleo. Jose de Felippe Junior

Hydrogen-rich saline improves memory function in a rat model of amyloid-beta-induced Alzheimer's disease by reduction of oxidative stress.

Li J, Wang C, Zhang JH, Cai JM, Cao YP, Sun XJ.

Brain Res. 2010 Apr 30;1328:152-61. .

Source

Department of Neurology, the First Affiliated Hospital of China Medical University, Shengyang, PR China.

Abstract

This study is to examine if hydrogen-rich saline reduced amyloid beta (Abeta) induced neural inflammation, and learning and memory deficits in a rat model. S-D male rats (n=84, 280-330g) were divided into three groups, sham-operated, Abeta1-42 injected and Abeta1-42 plus hydrogen-rich saline-treated animals. Hydrogen-rich saline (5ml/kg, i.p., daily) was injected for 14days after intracerebroventricular injection of Abeta1-42. The levels of MDA, IL-6 and TNF-alpha were assessed by biochemical and ELISA analysis. Morris Water Maze and open field task were used to assess the memory dysfunction and motor dysfunction, respectively. LTP were used to detect the electrophysiology changes, HNE and GFAP immunohistochemistry were used to assess the oxidative stress and glial cell activation. After Abeta1-42 injection, the levels of MDA, IL-6, and TNF-alpha were increased in brain tissues and hydrogen-rich saline treatment suppressed MDA, IL-6, and TNF-alpha concentration. Hydrogen-rich saline treatment improved Morris Water Maze and enhanced LTP (Long Term Potentiation) in hippocampus blocked by Abeta1-42. Furthermore, hydrogen-rich saline treatment also decreased the immunoreactivitiy of HNE and GFAP in hippocampus induced by Abeta1-42. In conclusion, hydrogen-rich saline prevented Abeta-induced neuroinflammation and oxidative stress, which may contribute to the improvement of memory dysfunction in this rat model.

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PMID: 20171955

Água rica em hidrogênio melhora o perfil lipídico e o metabolismo da glicose no Diabetes mellitus tipo-2.

12/06/11

Randomizado, duplo-cego e controlado com placebo:
n= 30 pts diabéticos-2 controlados/dieta e exercício
n= 6 pts intolerância à glicose no teste de tolerância à glicose
Grupo tratamento: 900 ml /dia de água rica em hidrogênio / 8 semanas
placebo : 900 ml/dia de água filtrada / 8 semanas
No grupo Diabético que ingeriu a água rica em hidrogênio:

1. Diminuição significante do LDL-colesterol modificada(<carga negativa e <pequena densidade)
2. Diminuição da LDL-oxidada
3. Diminuição dos ácidos graxos livres
4. Aumento de adiponectina plasmática

- Aumento da superoxido-dismutase extracelular

No grupo intolerância à glicose: 4 de 6 pts normalizaram o teste de tolerância à glicose

José de Felippe Junior

Supplementation of hydrogen-rich water improves lipid and glucose metabolism in patients with type 2 diabetes or impaired glucose tolerance.

Kajiyama S, Hasegawa G, Asano M, Hosoda H, Fukui M, Nakamura N, Kitawaki J, Imai S, Nakano K, Ohta M, Adachi T, Obayashi H, Yoshikawa T.

Nutr Res. 2008 Mar;28(3):137-43.

Source

Kajiyama Clinic, Kyoto 615-0035, Japan.

Abstract

Oxidative stress is recognized widely as being associated with various disorders including diabetes, hypertension, and atherosclerosis. It is well established that hydrogen has a reducing action. We therefore investigated the effects of hydrogen-rich water intake on lipid and glucose metabolism in patients with either type 2 diabetes mellitus (T2DM) or impaired glucose tolerance (IGT). We performed a randomized, double-blind, placebo-controlled, crossover study in 30 patients with T2DM controlled by diet and exercise therapy and 6 patients with IGT. The patients consumed either 900 mL/d of hydrogen-rich pure water or 900 mL of placebo pure water for 8 weeks, with a 12-week washout period. Several biomarkers of oxidative stress, insulin resistance, and glucose metabolism, assessed by an oral glucose tolerance test, were evaluated at baseline and at 8 weeks. Intake of hydrogen-rich water was associated with significant decreases in the levels of modified low-density lipoprotein (LDL) cholesterol (ie, modifications that increase the net negative charge of LDL), small dense LDL, and urinary 8-isoprostanes by 15.5% ($P < .01$), 5.7% ($P < .05$), and 6.6% ($P < .05$), respectively. Hydrogen-rich water intake was also associated with a trend of decreased serum concentrations of oxidized LDL and free fatty acids, and increased plasma levels of adiponectin and extracellular-superoxide dismutase. In 4 of 6 patients with IGT, intake of hydrogen-rich water normalized the oral glucose tolerance test. In conclusion, these results suggest that supplementation with hydrogen-rich water may have a beneficial role in prevention of T2DM and insulin resistance.

PMID: 19083400

Água rica em hidrogênio pode ser usada no tratamento da intoxicação por Monóxido de carbono (CO)

12/06/11

O Hidrogênio possui 1 elétron na camada de valência e assim possui ação redutora (antioxidante), principalmente contra o grande vilão da história oxidativa , o radical hidroxila e também contra o radical peroxinitrito, fato esquecido por muito médicos incluindo eu. Acresce que o hidrogênio por ser molécula muito pequena chega facilmente nas mitocôndrias e no núcleo. Jose de Felippe Junior

Hydrogen as a novel and effective treatment of acute carbon monoxide poisoning.
Shen M, He J, Cai J, Sun Q, Sun X, Huo Z.
Med Hypotheses. 2010 Aug;75(2):235-7.
Source
Department of Emergency, Changhai Hospital,168 Changhai Road, Shanghai 200433, PR China.
Abstract
Hydrogen is a major component of interstellar space and the fuel that sustains the stars. However, it is seldom regarded as a therapeutic gas. A recent study provided evidence that hydrogen inhalation exerted antioxidant and anti-apoptotic effects and protected the brain against ischemia-reperfusion injury by selectively reducing hydroxyl radical and peroxynitrite. It has been known that the mechanisms underlying the brain injury after acute carbon monoxide poisoning are interwoven with multiple factors including oxidative stress, free radicals, and neuronal nitric oxide synthase as well as abnormal inflammatory responses. Studies have shown that free radical scavengers can improve the neural damage. Based on the findings abovementioned, we hypothesize that hydrogen therapy may be an effective, simple, economic and novel strategy in the treatment of acute carbon monoxide poisoning.
PMID: 20347528

Água rica em hidrogênio. O Hidrogênio molecular reduz o estresse oxidativo e melhora a função mitocondrial

12/06/11

Desde 1997, descreveu- se na literatura médica o papel benéfico da água rica em hidrogênio em 38 doenças, estados fisiológicos e testes clínicos . O Hidrogênio possui 1 elétron na camada de valência e assim possui ação redutora (antioxidante), principalmente contra o grande vilão da história oxidativa , o radical hidroxila e também contra o radical peroxinitrito, fato esquecido por muito médicos incluindo eu. Acresce que o hidrogênio por ser molécula muito pequena chega facilmente nas mitocôndrias e no núcleo. Jose de Felippe Junior

Molecular hydrogen is a novel antioxidant to efficiently reduce oxidative stress with potential for the improvement of mitochondrial diseases.

Ohta S.

Biochim Biophys Acta. 2011 May 20.

Abstract

BACKGROUND:

Mitochondria are the major source of oxidative stress. Acute oxidative stress causes serious damage to tissues, and persistent oxidative stress is one of the causes of many common diseases, cancer and the aging process; however, there has been little success in developing an effective antioxidant with no side effect. We have reported that molecular hydrogen has potential as an effective antioxidant for medical applications [Ohsawa et al., Nat. Med. 13 (2007) 688-694].

REVIEW:

We review the recent progress toward therapeutic and preventive applications of hydrogen. Since we published the first paper in Nature Medicine, effects of hydrogen have been reported in more than 38 diseases, physiological states and clinical tests in leading biological/medical journals. Based on this cumulative knowledge, the beneficial biological effects of hydrogen have been confirmed. There are several ways to intake or consume hydrogen, including inhaling hydrogen gas, drinking hydrogen-dissolved water, taking a hydrogen bath, injecting hydrogen-dissolved saline, dropping hydrogen-dissolved saline into the eyes, and increasing the production of intestinal hydrogen by bacteria. Hydrogen has many advantages for therapeutic and preventive applications, and shows not only anti-oxidative stress effects, but also has various anti-inflammatory and anti-allergic effects. Preliminary clinical trials show that drinking hydrogen-dissolved water seems to improve the pathology of mitochondrial disorders.

MAJOR CONCLUSIONS:

Hydrogen has biological benefits toward preventive and therapeutic applications; however, the molecular mechanisms underlying the marked effects of small amounts of hydrogen remain elusive.

GENERAL SIGNIFICANCE:

Hydrogen is a novel antioxidant with great potential for actual medical applications. This article is part of a Special Issue entitled Biochemistry of Mitochondria.

PMID: 21621588

Água rica em hidrogênio possui efeito anti-diabético no diabetes murino induzido por estreptozotocina e no camundongo diabético geneticamente

12/06/11

A água eletrolizada reduz a glicemia e melhora a tolerância à glicose no diabetes murino induzido por estreptozotocina e no camundongo diabético geneticamente e aumenta a insulinemia e a sensibilidade à insulina no diabetes genético. José de Felippe Junior

Anti-diabetic effects of electrolyzed reduced water in streptozotocin-induced and genetic diabetic mice.

Kim MJ, Kim HK.

Life Sci. 2006 Nov 10;79(24):2288-92.

Source

Department of Obesity management, Graduate School of Obesity Science, Dongduk Women's University, 23-1 Wolkgukdong, Seoul, 136-714, South Korea. mijakim@dongduk.ac.kr

Abstract

Oxidative stress is produced under diabetic conditions and is likely involved in progression of pancreatic beta-cell dysfunction found in diabetes. Both an increase in reactive oxygen free radical species (ROS) and a decrease in the antioxidant defense mechanism lead to the increase in oxidative stress in diabetes. **Electrolyzed reduced water (ERW)** with ROS scavenging ability may have a potential effect on diabetic animals, a model for high oxidative stress. Therefore, the present study examined the possible anti-diabetic effect of ERW in two different diabetic animal models. The genetically diabetic mouse strain C57BL/6J-db/db (db/db) and streptozotocin (STZ)-induced diabetic mouse were used as insulin deficient type 1 and insulin resistant type 2 animal model, respectively. ERW, provided as a drinking water, significantly **reduced the blood glucose concentration and improved glucose tolerance in both animal models.** However, ERW fail to affect blood insulin levels in STZ-diabetic mice whereas **blood insulin level was markedly increased in genetically diabetic db/db mice.** This improved blood glucose control could result from **enhanced insulin sensitivity, as well as increased insulin release**. The present data suggest that ERW may function as an orally effective anti-diabetic agent and merit further studies on its precise mechanism.

PMID:
16945392

Água rica em hidrogênio previne a formação de radical superóxido no cérebro deficiente em vitamina C

12/06/11

Hydrogen-rich pure water prevents superoxide formation in brain slices of vitamin C-depleted SMP30/GNL knockout mice.
Sato Y, Kajiyama S, Amano A, Kondo Y, Sasaki T, Handa S, Takahashi R, Fukui M, Hasegawa G, Nakamura N, Fujinawa H, Mori T, Ohta M, Obayashi H, Maruyama N, Ishigami A.
Biochem Biophys Res Commun. 2008 Oct 24;375(3):346-50. .
Source
Department of Biochemistry, Faculty of Pharmaceutical Sciences, Toho University, Chiba 274-8510, Japan.
Abstract
Hydrogen is an established anti-oxidant that prevents acute oxidative stress. To clarify the mechanism of hydrogen's effect in the brain, we administered hydrogen-rich pure water (H(2)) to senescence marker protein-30 (SMP30)/gluconolactonase (GNL) knockout (KO) mice, which cannot synthesize vitamin C (VC), also a well-known anti-oxidant. These KO mice were divided into three groups; recipients of H(2), VC, or pure water (H(2)O), administered for 33 days. VC levels in H(2) and H(2)O groups were <6% of those in the VC group. Subsequently, superoxide formation during hypoxia-reoxygenation treatment of brain slices from these groups was estimated by a real-time biography imaging system, which models living brain tissues, with Lucigenin used as chemiluminescence probe for superoxide. A significant 27.2% less superoxide formed in the H(2) group subjected to ischemia-reperfusion than in the H(2)O group. Thus hydrogen-rich pure water acts as an anti-oxidant in the brain slices and prevents superoxide formation.
PMID:18706888

Água rica em hidrogênio previne aterosclerose em modelo murino de aterosclerose espontânea (camundongo sem apolipoproteina E) : diminui o estresse oxidativo na parede da aorta, o acúmulo de macrófagos nas lesões ateroscleróticas e o número de lesões ateromatosas

12/06/11

O estresse oxidativo está implicado na aterogênese, entretanto a maioria dos trabalhos clínicos com antioxidantes da dieta falharam e prevenir as placas ateroscleróticas. Com a ingestão da água rica em hidrogênio houve diminuição do estresse oxidativo na parede da aorta, diminuiu o acúmulo de macrófagos nas lesões ateroscleróticas, diminui o número de lesões ateromatosas. O Hidrogênio possui 1 elétron na camada de valência e assim possui ação redutora (antioxidante), principalmente contra o grande vilão da história oxidativa , o radical hidroxila e também contra o radical peroxinitrito, fato esquecido por muito médicos incluindo eu. Acresce que o hidrogênio por ser molécula muito pequena chega facilmente nas mitocôndrias e no núcleo. Jose de Felippe Junior.

Consumption of hydrogen water prevents atherosclerosis in apolipoprotein E knockout mice.

Ohsawa I, Nishimaki K, Yamagata K, Ishikawa M, Ohta S.

Biochem Biophys Res Commun. 2008 Dec 26;377(4):1195-8.

Source

Department of Biochemistry and Cell Biology, Institute of Development and Aging Sciences, Nippon Medical School, 1-396 Kosugi-cho, Nakahara-ku, Kawasaki, Kanagawa 211-8533, Japan.

Abstract

Oxidative stress is implicated in atherogenesis; however most clinical trials with dietary antioxidants failed to show marked success in preventing atherosclerotic diseases. We have found that hydrogen (dihydrogen; H(2)) acts as an effective antioxidant to reduce oxidative stress [I. Ohsawa, M. Ishikawa, K. Takahashi, M. Watanabe, K. Nishimaki, K. Yamagata, K. Katsura, Y. Katayama, S, Asoh, S. Ohta, Hydrogen acts as a therapeutic antioxidant by selectively reducing cytotoxic oxygen radicals, Nat. Med. 13 (2007) 688-694]. Here, we investigated whether drinking H(2)-dissolved water at a saturated level (H(2)-water) ad libitum prevents arteriosclerosis using an apolipoprotein E knockout mouse (apoE(-/-)), a model of the spontaneous development of atherosclerosis. ApoE(-/-) mice drank H(2)-water ad libitum from 2 to 6 month old throughout the whole period. Atherosclerotic lesions were significantly reduced by ad libitum drinking of H(2)-water (p=0.0069) as judged by Oil-Red-O staining series of sections of aorta. The oxidative stress level of aorta was decreased. Accumulation of macrophages in atherosclerotic lesions was confirmed. Thus, consumption of H(2)-dissolved water has the potential to prevent arteriosclerosis.

PMID:18996093

Água rica em hidrogênio produzida por eletrolise neutraliza radicais livres de oxigênio e protege o DNA da lesão oxidativa

12/06/11

Electrolyzed-reduced water scavenges active oxygen species and protects DNA from oxidative damage.

Shirahata S, Kabayama S, Nakano M, Miura T, Kusumoto K, Gotoh M, Hayashi H, Otsubo K, Morisawa S, Katakura Y.
Biochem Biophys Res Commun. 1997 May 8;234(1):269-74.

Source

Institute of Cellular Regulation Technology, Graduate School of Genetic Resources Technology, Kyushu University, Fukuoka, Japan. sirahata@grt.kyushu-u.ac.jp

Abstract

Active oxygen species or free radicals are considered to cause extensive oxidative damage to biological macromolecules, which brings about a variety of diseases as well as aging. The ideal scavenger for active oxygen should be 'active hydrogen'. 'Active hydrogen' can be produced in reduced water near the cathode during electrolysis of water. **Reduced water exhibits high pH, low dissolved oxygen (DO), extremely high dissolved molecular hydrogen (DH), and extremely negative redox potential (RP) values.** Strongly electrolyzed-reduced water, as well as ascorbic acid, (+)-catechin and tannic acid, completely scavenged O.-2 produced by the hypoxanthine-xanthine oxidase (HX-XOD) system in sodium phosphate buffer (pH 7.0). **The superoxide dismutase (SOD)-like activity of reduced water is stable at 4 degrees C for over a month and was not lost even after neutralization, repeated freezing and melting, deflation with sonication, vigorous mixing, boiling, repeated filtration, or closed autoclaving, but was lost by opened autoclaving** or by closed autoclaving in the presence of tungsten trioxide which efficiently adsorbs active atomic hydrogen.

Water bubbled with hydrogen gas exhibited low DO, extremely high DH and extremely low RP values, as does reduced water, but it has no SOD-like activity.

These results suggest that the **SOD-like activity of reduced water is not due to the dissolved molecular hydrogen but due to the dissolved atomic hydrogen (active hydrogen).** Although SOD accumulated H2O2 when added to the HX-XOD system, reduced water decreased the amount of H2O2 produced by XOD. Reduced water, as well as catalase and ascorbic acid, could directly scavenge H2O2. Reduce water suppresses single-strand breakage of DNA by active oxygen species produced by the Cu(II)-catalyzed oxidation of ascorbic acid in a dose-dependent manner, suggesting that **reduced water can scavenge not only O2.- and H2O2, but also 1O2 and .OH.**
PMID:
9169001

Água rica em hidrogênio protege contra lesões da isquemia-reperfusão intestinal: diminui diamino-oxidase , TNF-alfa, IL-1beta e IL-6 no soro, MDA, proteínas carbonil e mieloperoxidase tissular

12/06/11

O Hidrogênio possui 1 elétron na camada de valência e assim possui ação redutora (antioxidante), principalmente contra o grande vilão da história oxidativa , o radical hidroxila e também contra o radical peroxinitrito, fato esquecido por muito médicos incluindo eu. Acresce que o hidrogênio por ser molécula muito pequena chega facilmente nas mitocôndrias e no núcleo. Jose de Felippe Junior

Hydrogen-rich saline protects against intestinal ischemia/reperfusion injury in rats.

Zheng X, Mao Y, Cai J, Li Y, Liu W, Sun P, Zhang JH, Sun X, Yuan H.

Free Radic Res. 2009 May;43(5):478-84.

Source

Chinese PLA Institute of Burn Surgery & Department of Burn Surgery, Changhai Hospital, Second Military Medical University, Shanghai, PR China.

Abstract

Hydrogen gas was reported to reduce reactive oxygen species and alleviate cerebral, myocardial and hepatic ischemia/reperfusion (I/R) injuries. This paper studied the effect of hydrogen-rich saline, which was easier for clinical application, on the intestinal I/R injury. Model of intestinal I/R injury was induced in male Sprague-Dawley rats. Physiological saline, hydrogen-rich saline or nitrogen-rich saline (5 ml/kg) was administered **via intravenous infusion at 10 min before reperfusion**, respectively. The intestine damage was detected microscopically and was assessed by Chiu score system after I/R injury. In addition, **serum diamino oxidase (DAO) activity, TNF-alpha, IL-1beta and IL-6 levels, tissue MDA, protein carbonyl and MPO activity were all increased significantly by I/R injury. Hydrogen-rich saline reduced these markers and relieved morphological intestinal injury,** while no significant reduction was observed in the nitrogen-rich saline-treated animals. In conclusion, hydrogen-rich saline protected the small intestine against I/R injury, possibly by reduction of inflammation and oxidative stress.

PMID: 19353364

Água rica em hidrogênio protege o cérebro da lesão por isquemia-reperfusão: aumenta neurônios sobreviventes, diminui NF-kappaB, TNF-alfa e IL-6 (diminui inflamação), diminui MDA (diminui estresse oxidativo) e diminui caspase-3 (diminui apoptose).

12/06/11

The effect of hydrogen-rich saline on the brain of rats with transient ischemia.

Ji Q, Hui K, Zhang L, Sun X, Li W, Duan M.

J Surg Res. 2011 Jun 1;168(1):e95-e101.

Source

Department of Anesthesiology, Jinling Hospital, School of Medicine, Nanjing University, Nanjing, P. R. China.

Abstract

BACKGROUND:

Due to its antioxidant and anti-inflammatory properties, hydrogen gas (H(2)) has protective effects on a variety of organs from damage induced by ischemia/reperfusion (I/R). In this study, we tested the protective effect of hydrogen-rich saline on the brain in a global cerebral I/R model.

MATERIALS AND METHODS:

We used a four-vessel occlusion model of global cerebral ischemia (15 min) and reperfusion with rats. The rats were divided into four groups (n = 96): sham, I/R plus physiologic saline injected intraperitoneally, I/R plus hydrogen-rich saline injected intraperitoneally at the beginning of reperfusion, and I/R plus hydrogen-rich saline injected intraperitoneally 6 h after reperfusion began. One group of rats was sacrificed after 24 h of reperfusion. Malondialdehyde (MDA) was measured to quantify the oxidative stress. Caspase-3 was measured to indicate the status of apoptosis. Tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), and nuclear factor-κB (NF-κB) were measured to monitor the inflammation. Another group of rats was sacrificed after 72 h of reperfusion to measure the histologic damages in hippocampus by hematoxylin and eosin staining and Nissl staining.

RESULTS:

Compared with rats with I/R only, hydrogen-rich saline treatment significantly improved the amount of surviving cells. NF-κB, TNF-α, IL-6, MDA, and caspase-3 were all increased significantly by I/R injury. Hydrogen-rich saline reduced all these markers.

CONCLUSIONS:

Our data demonstrate that intraperitoneal injection of hydrogen-rich saline has strong protective effect on the transient global cerebral ischemia-reperfusion rats.

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PMID:
21435662

Água rica em hidrogênio protege o coração dos efeitos da radiação ionizante: diminui MDA e 8-OHdG (8-hidroxideoxiguanosina) e aumenta antioxidantes endógenos no miocárdio

12/06/11

O Hidrogênio possui 1 elétron na camada de valência e assim possui ação redutora(antioxidante),principalmente contra o grande vilão da história oxidativa , o radical hidroxila, e contra o radical peroxi-nitrito, fato esquecido por muito médicos incluindo eu. Jose de Felippe Junior

The potential cardioprotective effects of hydrogen in irradiated mice.
Qian L, Cao F, Cui J, Wang Y, Huang Y, Chuai Y, Zaho L, Jiang H, Cai J.
J Radiat Res (Tokyo). 2010;51(6):741-7.

Source
Department of Radiation Medicine, Faculty of Naval Medicine, Second Military Medical University, Shanghai, PR China. qlr2007@126.com

Abstract
Most ionizing radiation-induced damage is caused by hydroxyl radicals, and the selective reduction of hydroxyl by hydrogen in vitro has been demonstrated previously. Irradiation of the heart can cause chronic cardiac disease. This study was designed to test the hypothesis that hydrogen-rich water (pure water saturated with molecular hydrogen), which is easy to use, induces cardioprotection against ionizing irradiation injury in mice. In this paper, we demonstrate that hydrogen can protect myocardium degeneration from radiation-induced injury, decrease myocardium malondialdehyde (MDA), 8-hydroxydeoxyguanosine (8-OHdG) levels, and increase myocardium endogenous antioxidants in vivo. We suggest that hydrogen has a cardioprotective effect against radiation induced injury.
PMID: 21116102

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Água rica em hidrogênio reduz estresse oxidativo e inflamação em modelo murino de substância amilóide-beta induzindo doença de Alzheimer por inibir JNK e NF-kappaB e IL-1beta no cérebro

12/06/11

O Hidrogênio possui 1 elétron na camada de valência e assim possui ação redutora (antioxidante), principalmente contra o grande vilão da história oxidativa , o radical hidroxila e também contra o radical peroxinitrito, fato esquecido por muito médicos incluindo eu. Acresce que o hidrogênio por ser molécula muito pequena chega facilmente nas mitocôndrias e no núcleo. Jose de Felippe Junior

Hydrogen-rich saline reduces oxidative stress and inflammation by inhibit of JNK and NF-κB activation in a rat model of amyloid-beta-induced Alzheimer's disease.

Wang C, Li J, Liu Q, Yang R, Zhang JH, Cao YP, Sun XJ.

Neurosci Lett. 2011 Mar 17;491(2):127-32.

Source

Department of Neurology, the First Affiliated Hospital of China Medical University, Shenyang 110001, PR China.

Abstract

This study is to examine if hydrogen-rich saline reduced amyloid-beta (Aβ) induced neural inflammation and oxidative stress in a rat model by attenuation of activation of JNK and NF-κB. Sprague-Dawley male rats (n=18, 280-330 g) were divided into three groups, sham operated, Aβ1-42 injected and Aβ1-42 plus hydrogen-rich saline treated animals. Hydrogen-rich saline (5 ml/kg, i.p., daily) was injected for 10 days after intraventricular injection of Aβ1-42. The levels of IL-1β were assessed by ELISA analysis, 8-OH-dG by immunohistochemistry in the brain slides, and JNK and NF-κB by immunohistochemistry and western blotting. After Aβ1-42 injection, the level of IL-1β, 8-OH-dG, JNK and NF-κB all increased in brain tissues, while hydrogen-rich saline treatment decreased the level of IL-1β, 8-OH-dG and the activation of JNK and NF-κB. In conclusion, hydrogen-rich saline prevented Aβ-induced neuroinflammation and oxidative stress, possibly by attenuation of activation of c-Jun NH_2-terminal kinase (JNK) and nuclear factor-κB (NF-κB) in this rat model.

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Água rica em hidrogênio. Inalação de hidrogênio molecular suprime colite induzida por sulfato de sódio

27/06/11

Hydrogen mediates suppression of colon inflammation induced by dextran sodium sulfate.

Kajiya M, Silva MJ, Sato K, Ouhara K, Kawai T.

Biochem Biophys Res Commun. 2009 Aug 14;386(1):11-5.

Source

Department of Immunology, The Forsyth Institute, Boston, MA 02115, USA.

Abstract

By its antioxidant effect, molecular hydrogen gas (H2) was reported to protect organs from tissue damage induced by ischemia reperfusion. To evaluate its anti-inflammatory effects, we established a mouse model of human inflammatory bowel disease (IBD) by supplying mice with water containing (1) dextran sodium sulfate (DSS) (5%), (2) DSS (5%) and H2, or (3) H2 only ad libitum up to 7 days. At day-7, DSS-induced pathogenic outcomes including, loss of body weight, increase of colitis score, pathogenic shortening of colon length, elevated level of IL-12, TNF-alpha and IL-1beta in colon lesion, were significantly suppressed by the addition of H2 to DSS solution. Histological analysis also revealed that the DSS-mediated colonic tissue destruction accompanied by macrophage infiltration was remarkably suppressed by H2. Therefore, the present study indicated that H2 can prevent the development of DSS-induced colitis in mice.

PMID:
19486890

Água rica em hidrogênio protege contra lesão da isquemia-reperfusão miocárdica: diminui MDA no plasma e miocárdio, diminui apoptose das miofibrilas , diminui 8-hidroxiguanosina na área peri-infarto e diminui tamanho do infarto

27/06/11

O Hidrogênio possui 1 elétron na camada de valência e assim possui ação redutora(antioxidante),principalmente contra o grande vilão da história oxidativa , o radical hidroxila, e contra o radical peroxi-nitrito, fato esquecido por muito médicos incluindo eu. Jose de Felippe Junior

Hydrogen-rich saline protects myocardium against ischemia/reperfusion injury in rats.

Sun Q, Kang Z, Cai J, Liu W, Liu Y, Zhang JH, Denoble PJ, Tao H, Sun X.

Exp Biol Med (Maywood). 2009 Oct;234(10):1212-9.

Source

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Abstract

Protective effect of hydrogen (H(2)) gas on cardiac ischemia-reperfusion (I/R) injury has been demonstrated previously. This study was designed to test the hypothesis that hydrogen-rich saline (saline saturated with molecular hydrogen), which is easy to use, induces cardioprotection against ischemia (30 min) and reperfusion (24 h) injury in rats. Adult male Sprague-Dawley rats underwent 30-min occlusion of the left anterior descending (LAD) coronary artery and 24-h reperfusion. Intraperitoneal injection of hydrogen-rich saline before reperfusion significantly decreased plasma and myocardium malondialdehyde (MDA) concentration, decreased cardiac cell apoptosis, and myocardial 8-hydroxydeoxyguanosine (8-OHdG) in area at risk zones (AAR), suppressed the activity of caspase-3, and reduced infarct size. The heart function parameters including left ventricular systolic pressure (LVSP), left ventricular diastolic pressure (LVDP), +(dP/dt)(max) and -(dP/dt)(max) were also significantly improved 24 h after reperfusion. It is concluded that hydrogen-rich saline is a novel, simple, safe, and effective method to attenuate myocardial I/R injury.

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19596825

Hydrogen-Rich Saline Protects Myocardium Against Ischemia/Reperfusion Injury in Rats

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Abstract

Protective effect of hydrogen (H2) gas on cardiac ischemia-reperfusion (I/R) injury has been demonstrated previously. This study was designed to test the hypothesis that hydrogen-rich saline (saline saturated with molecular hydrogen), which is easy to use, induces cardioprotection against ischemia (30 min) and reperfusion (24 h) injury in rats. Adult male Sprague-Dawley rats underwent 30-min occlusion of the left anterior descending (LAD) coronary artery and 24-h reperfusion. Intraperitoneal injection of hydrogen-rich saline before reperfusion significantly decreased plasma and myocardium malondialdehyde (MDA) concentration, decreased cardiac cell apoptosis, and myocardial 8-hydroxydeoxyguanosine (8-OHdG) in area at risk zones (AAR), suppressed the activity of caspase-3, and reduced infarct size. The heart function parameters including left ventricular systolic pressure (LVSP), left ventricular diastolic pressure (LVDP), +(dP/dt)max and −(dP/dt)max were also significantly improved 24 h after reperfusion. It is concluded that hydrogen-rich saline is a novel, simple, safe, and effective method to attenuate myocardial I/R injury.

Keywords: reperfusion, oxidative stress, hydrogen-rich saline, apoptosis

Introduction

Currently, restoring blood flow in an acutely occluded vessel represents the most effective, long-term clinical therapy for acute myocardial infarction (AMI) (1). Although restoration of blood flow is critical, the reintroduction of molecular oxygen triggers a cytotoxic cascade during which reactive oxygen species (ROS) are generated by the mitochondria. This burst of reactive oxygen species irrevocably drives downstream signaling networks that lead to cellular necrosis and apoptosis, which is named lethal reperfusion injury (2). Reperfusion injury accounts for up to 50% of the final size of the infarct (3), providing an important potential target for protection of the heart.

The central role of ROS in reperfusion injury has been well demonstrated in recent studies showing that inhibitors of mitochondrial respiratory complexes I and III prevent reperfusion ROS generation and improve cellular viability (4–6). However, therapy to reduce free radicals during early reperfusion failed to relieve this pathological cascade of oxidative damage after reperfusion injury (7, 8). A recent article demonstrated that molecular hydrogen (H2) is a novel antioxidant agent which confers protection in focal brain ischemia reperfusion injury (9). This observation was echoed by others in different organs such as in I/R injury in intestine (10), liver (11), and heart (12) through the inhibition of oxidant stress. In a neonatal hypoxia–ischemia rat model, we have demonstrated that inhalation of hydrogen reduced apoptosis of brain cells (13).

In the current study, we tested whether hydrogen-rich saline, which is easy to use, safe, and economical, confers cardioprotection

against myocardial ischemia reperfusion injury in rats. We evaluated specifically the reduction of infarction, the oxidative stress, and improvement of functions at 24 h after intraperitoneal injection of hydrogen-rich saline.

Materials and Methods

All the protocols were approved by the Second Military Medical University, China, in accordance with the Guide for Care and Use of Laboratory Animals published by the US NIH (publication No. 96–01). Adult male Sprague-Dawley rats weighing 250–280 g were used in all experiments. The animals were housed in individual cages in a temperature-controlled room with a 12-h light/dark cycle and free access to food and distilled water.

Hydrogen-Rich Saline Production.

Hydrogen was dissolved in physiological saline for 6 h under high pressure (0.4 MPa) to a supersaturated level using hydrogen-rich saline-producing apparatus produced by our department. The saturated hydrogen saline was stored under atmospheric pressure at 4°C in an aluminum bag with no dead volume. Hydrogen-rich saline was sterilized by gamma radiation and freshly prepared every week, which ensured that a concentration of 0.6 mmol/L was maintained. Gas chromatography was used to confirm the content of hydrogen in saline by the method described by Ohsawa et al. (9).

In Vivo Coronary Artery Occlusion.

Rats were intraperitoneally anesthetized with chloral hydrate (300mg/ kg). The rats were intubated and ventilated with a small-animal ventilator. Briefly, the hearts were exposed through a left thoracotomy in the fourth intercostal space. The pericardium was opened, and a 5.0-prolene suture was tightened around the proximal left anterior descending (LAD) coronary artery (before the first branch of diagonal artery); after 30 min of ischemia, the tube for the myocardial reperfusion was removed. Then, the muscle layer and the skin were closed separately and the animals were allowed to recover.

Experimental Protocol.

Animals were randomly assigned to four groups: Sham, Sham+H2, Control, and H2. There were 18 animals in Sham, Control, and H2 group: 6 for the measurement of infarct size, 6 for histological and immunohistochemical studies, and 6 for the measurement of the caspase-3 activity and MDA concentration. The Sham+H2 group (n = 6) was just for the measurement of hemodynamic parameters. In the Sham group, the ligature was placed under the LCA without occlusion for 30 min. In the Sham+H2 group, the ligature was placed under the LCA without occlusion for 30 min and hydrogen-rich saline (5ml/ Kg) was intraperitoneally injected into rats 25 min after placing the ligature. In the Control group, the LAD was reversibly occluded for 30 min and saline water (5ml/Kg) was intraperitoneally injected at 5 min before the reperfusion. In the H2 group, the LAD was reversibly occluded for 30 min. Hydrogen-rich saline (5ml/Kg) was intraperitoneally injected into rats 5 min before the reperfusion. The reperfusion was continued for 24 h in all experiments.

Hemodynamic Measurements.

Hemodynamic measurements were adapted from our previous study (14). Rats were intraperitoneally anesthetized with chloral hydrate (300mg/Kg) 24 h after ischemia reperfusion. A small incision was made to the right of the midline in the neck. The right carotid artery was identified and a PE 50 catheter was introduced into the artery. The proximal end of the catheter was connected to a low pressure transducer. The inserted tip of this catheter was advanced down until it reached the left ventricular lumen and the left ventricular pressure (LVP) signal was obtained. The pressure signals were monitored, analyzed, and recorded in real time. Heart rate (HR), LVSP, LVDP, and ±(dP/dt)max were all calculated from the continuously obtained LVP signal.

Since we used fluid-filled catheters to get the signal, end-diastolic pressure was difficult to measure accurately; LVDP represents minimum diastolic pressure here.

Infarct Size Determination.

The suture around the coronary artery was retied 24 h after reperfusion and 2% Evans blue dye was infused into the heart through the apex to mark the AAR as unstained (not blue) tissue. The hearts were excised and placed in a −20°C freezer for 30 min. Frozen hearts were then cut into 2-mm thick slices parallel to the atrioventricular groove. Sections were thawed and incubated in a 1% tetrazolium chloride (TTC) phosphate-buffered solution (pH 7.4) at 37°C for 15 min and fixed in 10% formalin to increase the contrast of the Evan's blue and TTC staining. Tissue sections were compressed to a uniform 2-mm thickness by placing them between two glass plates separated by a 2-mm space. The viable tissue was stained red with TTC, while the dead tissue (infarcted tissue) was unstained. The infarct size was calculated as a percentage volume of the infarct area (white area) versus the AAR (non-blue area).

Determination of MDA Concentration in Plasma and Myocardium.

Plasma MDA concentration, a presumptive marker of oxidant-mediated lipid peroxidation, was quantified to estimate the extent of lipid peroxidation in the AAR myocardium (15). Arterial blood samples (0.6ml) were collected after 24 h of reperfusion. MDA product has a long half-life in plasma, and its levels are therefore cumulative. These samples were immediately centrifuged at 2500 rpm and 4°C for 10 min, and the plasma was stored at −80°C until analyzed. To measure the MDA concentration in AAR, 2 ml of 1% Evan's blue dye was infused into the heart through the apex to mark the AAR as unstained (not blue) tissue. Then, the AAR was saved for analysis, and the samples were stored at −80°C until assayed. In brief, transmural tissue from AAR was homogenized in buffer and centrifuged. After determining protein concentration, the MDA concentration was measured using a commercial kit (Jianchen Biological Institute, China) and expressed as μmol/g protein.

Caspase-3 Activity.

Caspase-3 activity was determined using a Fluorometric Assay Kit (BIOVISION Research Products, 980 Linda Vista Avenue, Mountain View, CA), according to the manufacturer's instructions. In brief, 20–200μg cell lysates of AAR were incubated in a 96-well plate with 2xReaction Buffer (50μl). The reaction was started by adding 1mM DEVD–APC substrate (5μl). After incubation in the dark at 37°C, the plate was read in a fluorometer equipped with a 400-nm excitation filter and a 505-nm emission filter. Fold-increase in caspase-3 activity was determined by comparing these results with the level of the uninduced control.

Histological and Immunohistochemical Studies.

The hearts were harvested, sectioned, and immersion-fixed in 4% buffered paraformaldehyde. The paraffin was cut into 4-μm thick serial sections. The standard deparaffinization protocol was used.

Hematoxylin–Eosin (H&E) Staining.

Tissues were stained with hematoxylin–eosin. Slides were then assessed in a blinded fashion by a pathologist and scored for the following: myodegeneration, cardiomyocyte hydropic changes, neutrophilic infiltrate, hemorrhage, lymphohistio-cytic infiltrate, and acute myocardial necrosis.

In Situ Apoptosis Assay.

TUNEL staining was performed on paraffin-embedded sections by using the in situ cell death detection kit (Roche). According to standard protocols, the sections were dewaxed and rehydrated by heating the slides at 60°C. Then, these sections were incubated in a 20-μg/ml proteinase K working solution for 15 min at room temperature. The slides were rinsed three times with PBS before they were incubated in TUNEL reaction mixture for 1 h at 37°C. Dried area around sample by filter paper and added Converter-AP on samples for 1 h at 37°C. After rinsing with PBS (5 min, three times), sections were coloured in dark with nitroblue tetrazolium (NBT) and 5-bromo-4-chloro-3-indolylphosphate (BCIP). Four slide fields were randomly examined using a defined rectangular field area with magnification (x40). One hundred cells were counted in each field. The data were represented as the percentage of TUNEL-positive cells of total cell nuclei per field.

Immunohistochemistry for Myocardial 8-OHdG.

The paraffin sections were deparaffinized in xylene, rehydrated using various grades of ethanol, and pretreated with 10 μg/ml proteinase K (to permeabilize the nucleus) for 30 min at 37°C. Nonspecific binding of immunoglobulins was blocked by incubating the

sections in 10% BSA for 20 min. Then, the sections were incubated with primary goat polyclonal anti-8-OHdG antibody (Alpha Diagnostics) (1:200, overnight at room temperature), and secondary rabbit anti-goat IgG-HRP conjugated Cat #30220. Four slide fields were randomly examined using a defined rectangular field area with magnification (x40). 8-OHdG positive cells were counted in each field. The data were represented as the number of 8-OHdG positive cells per field.

Statistical Analysis.

All results were expressed as means ± SEM. For comparison of changes in hemodynamic parameters between groups, two-way ANOVA followed by Student-Newman-Keuls tests were utilized. For comparison of infarct size, MDA concentration, caspase-3 activity, apoptosis, and 8-OHdG, differences between groups were determined with a one-way ANOVA followed by Student-Newman-Keuls tests. A value of $P < 0.05$ was considered to denote statistical significance.

Results

Hemodynamic Measurements.

The result of AN-OVA revealed significant interactions between hydrogen-rich saline and myocardial ischemia reperfusion on all the hemodynamic parameters ($P < 0.05$). As displayed in Figure 1, the hemodynamic parameters remained unchanged with hydrogen-rich saline alone (Sham+H2 group). The intraperitoneal injection of hydrogen-rich saline, however, decreased the I/R-induced degrading of hemodynamic parameters including LVSP, LVDP, +(dP/dt)max, and − (dP/dt)max. All of the hemodynamic parameters, except LVDP, in both the Control and H2 groups were significantly lower than those in the Sham or Sham+H2 groups. There were no significant differences in LVDP between the H2 group and Sham group ($P > 0.05$). No statistical difference was found for heart rate after 24 h of ischemia reperfusion (data not shown).

Measurement of Infarct Size.

The infarct size in the H2 group was significantly smaller than in the Control group (9.8 ± 3.6% vs. 32.1 ± 3.4%, * $P < 0.01$), as shown in Figure 2 and Figure 3. There was no significant difference in AAR/LV between the Control group and H2 group (62 ± 4.7% vs. 58 ± 3.9%).

Plasma and Myocardium MDA Concentration after Reperfusion.

The plasma MDA concentration was measured at 24 h of reperfusion (Fig. 4A). Plasma MDA concentration at 24 h of reperfusion in the H2 group was significantly lower than that of the Control group. The myocardium MDA concentration was also measured at 24 h of reperfusion (Fig. 4B). Myocardium MDA concentration at 24 h of reperfusion in the H2 group was significantly lower than that of the Control group.

Caspase-3 Activity.

The caspase-3 activity is shown in Figure 4C. I/R significantly increased caspase-3 activity relative to the nonischemic myocardium. H2 comparably reduced caspase-3 activity relative to the Control group.

Histopathological Examination by H&E Staining.

Blinded histological analysis of heart sections stained with H&E was scored 24 h after reperfusion (Fig. 5). Rats in the H2 group displayed a reduced degree of myocardial neutrophilic infiltrate, necrosis, hemorrhage, and spindle-shaped interstitial cells as compared with rats in the Control group.

Detection of Apoptotic Cell Death.

As shown in Figure 6, the number of TUNEL-positive cells was increased in the AAR myocardium in the Control group. H2 comparably decreased the frequency of TUNEL-positive cells relative to the Control group (15 ± 1% vs. 24 ± 1%, * $P < 0.05$ vs. Control group).

Detection of 8-OHdG Positive Cell Death.

As shown in Figure 7, the numbers of 8-OHdG positive cells were increased in the AAR myocardium in the Control group. H2 comparably decreased the number of 8-OHdG positive cells relative to the Control group (49 ± 7 vs.103 ± 8, * $P < 0.01$ vs. Control group).

Discussion

As we are aware, this is the first study demonstrating that hydrogen-rich saline significantly improved post-ischemic functional recovery of rat hearts. The improvement in post-ischemic functional recovery was paralleled by a significant reduction in infarct size, decreased plasma and myocardium MDA concentration, attenuation of cardiac cell apoptosis and DNA oxidative stress in AAR. Histological analysis revealed a substantial decrease in hemorrhage and necrosis as well as a decrease in the number of leukocytes within the ischemic zone. This cardiac improvement may result from radical oxygen species (ROS) scavenging effect of molecular H2, as previously reported in a brain injury model (9).

ROS are produced on reperfusion of ischemic myocardium, and are considered a major cause of lethal reperfusion injury (17–19). Radical oxygen species O2− and H2O2 are detoxified by antioxidant defense enzymes, unlike ·OH and ONOO−, which so far no enzyme could detoxify. Recently it was demonstrated that hydrogen gas selectively reduces these two detrimental ROS (9). Since the hydrogen molecule is electrically neutral and much smaller than the oxygen molecule, it easily penetrates membranes and enters cells and organelles such as the nucleus and mitochondria. This is particularly important, as the latter is the primary site of generation of reactive oxygen species after reperfusion and is notoriously difficult to target (20). Since the heart is one of the most highly perfused tissues, it is possible that the intramyocardial H2 concentration increases immediately following intraperitoneal injection of hydrogen-rich saline. 8-OHdG is formed from deoxyguanosine in DNA by hydroxyl free radicals and might serve as a sensitive biomarker of intracellular oxidative stress in vivo (21). Our findings show that hydrogen-rich saline reduced the level of 8-OHdG positive cells in AAR. Meanwhile, we found reduced MDA concentration in both the plasma and myocardium in the H2 group. In the current study, one may speculate that at the onset of reperfusion, H2 reduces ROS generation and preserves mitochondrial membrane potential, maintains ATP synthesis, prevents DNA damage, and decreases lipid peroxidation, and thus protects the heart. One of the intensive mechanisms underlining the protective effect may be the inhibition of the opening of the permeability-transition pore. At the time of reperfusion after prolonged ischemia, abrupt high accumulation of calcium and overproduction of reactive oxygen species trigger the opening of the pore (22, 23). The resulting collapse of the membrane potential, uncoupling of the respiratory chain, efflux of pro-apoptotic factors, and hydrolysis of ATP may ultimately cause irreversible damage. Although it has been reported that necrosis, as a major form of pathological cell death, leads to a destruction of a large portion of cardiomyocytes after myocardial ischemia and reperfusion, an attenuation of myocardial apoptosis has been associated with an inhibition in extension of infarct size at late phase of reperfusion (24). Consistent with previous reports, in the present study we find treatment with hydrogen-rich saline inhibited activation of down-stream caspase-3 and reduces apoptosis cardio-myocytes, providing evidence that limitation in reperfusion injury can be achieved by hydrogen-rich saline when it is only applied at 5 min before reperfusion.

Recently, supplementation with hydrogen-rich pure water via gastric intestine has shown beneficial effects on lipid and glucose metabolism in humans by providing protection against oxidative stress (25). Hydrogen-rich water decreases superoxide formation caused by ischemia–reperfusion in the brain slices of mice (26). Our laboratory proved neuroprotective effects of hydrogen saline in a neonatal hypoxia-ischemia rat model (27). In this study, intraperitoneal injection of hydrogen-rich saline 5 min before reperfusion had a similar effect compared to inhalation of H2. The improved heart function and reduced infarct size demonstrated the preserved state of

heart after ischemic insult, along with a reduction of oxidative stress and less cell death. Therefore, the current study supports other observations and for the first time indicates that hydrogen-rich saline is an effective alternative pharmacological strategy in myocardial ischemia reperfusion management. Our results indicate hydrogen-rich saline may induce protective effects through the anti-oxidative stress and apoptotic pathways.

Use of flammable hydrogen gas is associated with hazards due to violent reactions of hydrogen with oxidizing elements such as chlorine and fluorine. Hydrogen is a highly diffusible gas and reacts with hydroxyl radical to produce water (16), and thus is an ROS scavenger. Hydrogen gas cannot be produced by the human body since mammalian cells lack the hydrogenase activity (28). However, it is continuously produced by colonic bacteria in the body and normally circulates in the blood (29), so it is physiologically safe for humans to inhale hydrogen at a relatively low concentration. Medical use of hydrogen in the past was limited to test the effects of antibiotic therapy (30). Previously, other therapeutic strategies for scavenging reactive oxygen species seemed promising in animal models, but most of them failed in human clinical trials (31). Hydrogen-rich saline may, on the basis of our observation, offer a simple, easy to use, safe, and economic novel approach for future cardiac protection.

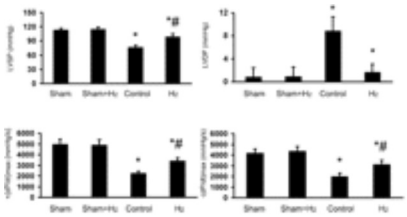

Figure 1. The changes of LVDP, LVSP, +(dP/dt)max and – (dP/dt)max after 24 h of ischemia reperfusion. Results are expressed as means ± SEM (n = 6, * P < 0.01 relative to Sham group, # P < 0.05 relative to Control group).

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Figure 2. Representative photographs of serial heart sections obtained from rats subjected to myocardial ischemia–reperfusion injury in the presence or absence of hydrogen-rich saline injection. A color version of this figure is available in the online journal.

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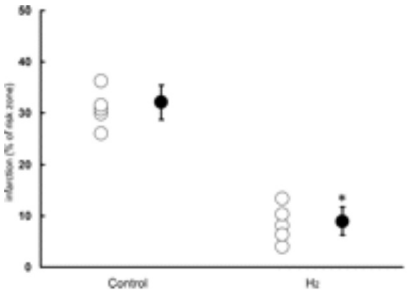

Figure 3. Infarct size as a % of AAR. Individual points are represented by open circles and group means by filled-in circles. H2-dependent reduction in infarct size is expressed as a percentage volume of the infarct area versus the AAR (n = 6 for each group, * P < 0.01 compared to Control group).

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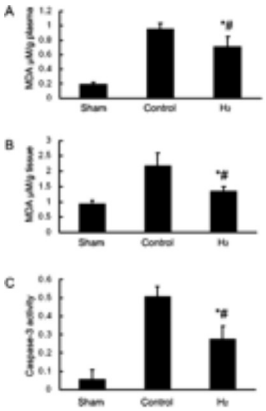

Figure 4. (A) Plasma MDA concentration at the end of 24 h of reperfusion. H2 significantly reduced MDA concentration (n = 6, * P < 0.05 compared to Control group; # P < 0.01 relative to Sham group). (B) Myocardium MDA concentration at the end of 24 h of reperfusion. H2 significantly reduced MDA concentration (n = 6, * P < 0.05 compared to Control group; # P < 0.05 relative to Sham group). (C) Caspase-3 activity in the Sham, Control, and H2 groups at the end of 24 h of reperfusion (n=6, * P < 0.05 compared to Control group; # P < 0.01 relative to Sham group).

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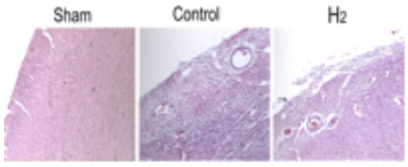

Figure 5. Representative H&E-stained histological images after 30 min of LCA ischemia and 24 h of reperfusion. Rats in the Control group displayed a high degree of hemorrhage and infiltrating leukocytes within the ischemic zone. Histopathology was attenuated in the myocardial sections of rats treated with hydrogen-rich saline. A color version of this figure is available in the online journal.

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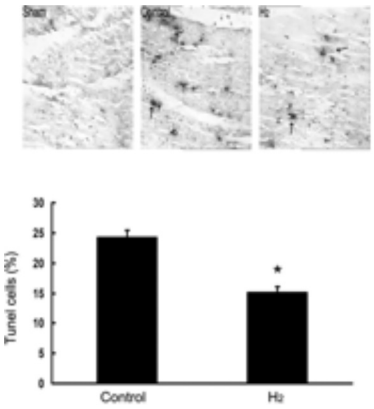

Figure 6. Detection of apoptotic cell death by TUNEL staining in the Sham, Control, and H2 groups at the end of 24 h of reperfusion. Relative to the Control group, H2 significantly reduced the number of TUNEL-positive cells (blue staining). Values are mean ± SEM; * P < 0.01 compared to Control group, n = 6 for each group.

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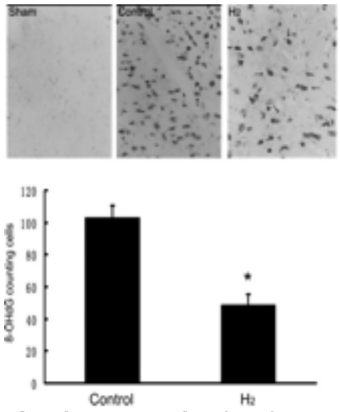
Figure 7. Oxidative DNA damage assessed by 8-OHdG immunoreactivity. Staining was localized to nuclei of myocardium in AAR. Shown are, at the end of 24 h of reperfusion, 8-OHdG positive cells in the Sham, Control, and H2 groups. Relative to the Control group, H2 significantly reduced the number of 8-OHdG positive cells (brown staining) per field. Values are mean ± SEM; * P < 0.01 compared to Control group, n =6 for each group.



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Footnotes

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Água rica em hidrogênio. Síndrome metabólica melhora com a ingestão de água alcalina rica em hidrogênio feita com magnésio metálico sem a necessidade de mudança no estilo de vida: aumenta a geração da enzima superóxido dismutase , diminui metabolitos dos radicais livres no sangue, aumenta HDL e diminui o colesterol total/HDL

27/06/11

N=20 pts com síndrome metabólica
Ingestão de 1,5 – 2,0 l/dia de água rica em hidrogênio por 8 semanas
Resultados:
- aumenta 39% a geração da enzima SOD
- diminui 43% o MDA no sangue (metabolitos dos radicais livres)
- aumenta 8% o HDL-colesterol
- diminui 13% a razão colesterol total/HDL

Jose de Felippe Junior

Effectiveness of hydrogen rich water on antioxidant status of subjects with potential metabolic syndrome-an open label pilot study.
Nakao A, Toyoda Y, Sharma P, Evans M, Guthrie N.
J Clin Biochem Nutr. 2010 Mar;46(2):140-9.

Heart, Lung and Esophageal
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Abstract
Metabolic syndrome is characterized by cardiometabolic risk factors that include obesity, insulin resistance, hypertension and dyslipidemia. Oxidative stress is known to play a major role in the pathogenesis of metabolic syndrome. The objective of this study was to examine the effectiveness of hydrogen rich water (1.5-2 L/day) in an open label, 8-week study on 20 subjects with potential metabolic syndrome. Hydrogen rich water was produced, by placing a metallic magnesium stick into drinking water (hydrogen concentration; 0.55-0.65 mM), by the following chemical reaction; Mg + 2H(2)O --> Mg (OH)(2) + H(2). The consumption of hydrogen rich water for 8 weeks resulted in a 39% increase ($p<0.05$) in antioxidant enzyme superoxide dismutase (SOD) and a 43% decrease ($p<0.05$) in thiobarbituric acid reactive substances (TBARS) in urine. Further, subjects demonstrated an 8% increase in high density lipoprotein (HDL)-cholesterol and a 13% decrease in total cholesterol/HDL-cholesterol from baseline to week 4. There was no change in fasting glucose levels during the 8 week study. In conclusion, drinking hydrogen rich water represents a potentially novel therapeutic and preventive strategy for metabolic syndrome. The portable magnesium stick was a safe, easy and effective method of delivering hydrogen rich water for daily consumption by participants in the study.
PMID: 20216947

Effectiveness of Hydrogen Rich Water on Antioxidant Status of Subjects with Potential Metabolic Syndrome—An Open Label Pilot Study

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Abstract
Metabolic syndrome is characterized by cardiometabolic risk factors that include obesity, insulin resistance, hypertension and dyslipidemia. Oxidative stress is known to play a major role in the pathogenesis of metabolic syndrome. The objective of this study was to examine the effectiveness of hydrogen rich water (1.5–2 L/day) in an open label, 8-week study on 20 subjects with potential metabolic syndrome. Hydrogen rich water was produced, by placing a metallic magnesium stick into drinking water (hydrogen concentration; 0.55–0.65 mM), by the following chemical reaction; Mg + 2H2O → Mg (OH)2 + H2. The consumption of hydrogen rich water for 8 weeks resulted in a 39% increase ($p<0.05$) in antioxidant enzyme superoxide dismutase (SOD) and a 43% decrease ($p<0.05$) in thiobarbituric acid reactive substances (TBARS) in urine. Further, subjects demonstrated an 8% increase in high density lipoprotein (HDL)-cholesterol and a 13% decrease in total cholesterol/HDL-cholesterol from baseline to week 4. There was no change in fasting glucose levels during the 8 week study. In conclusion, drinking hydrogen rich water represents a potentially novel therapeutic and preventive strategy for metabolic syndrome. The portable magnesium stick was a safe, easy and effective method of delivering hydrogen rich water for daily consumption by participants in the study.
Keywords: hydrogen, drinking water, magnesium, oxidative stress, metabolic syndrome

Metabolic syndrome is characterized by a constellation of metabolic and anthropometric abnormalities, which include excess weight, hyperglycemia, hypertension, low concentration of high density lipoprotein (HDL) cholesterol and hypertriglyceridemia [1–3]. Metabolic disease remains a serious concerns in the United States and people with metabolic syndrome are at increased risk of developing cardiovascular disease and type II diabetes [3, 4].
Free radicals and other reactive oxygen species (ROS) are derived either from normal essential metabolic processes in the human body or from external sources such as exposure to X-rays, ozone, cigarette smoking, air pollutants and industrial chemicals [5]. Disturbance of the balance between production of oxygen free radicals (or some other radical species) and activity of the antioxidant system of protection causes oxidative stress [6]. Recent evidence implicated oxidative stress in the pathogenesis of metabolic syndrome [1, 2,

7]. Oxidative stress and nutritional changes also contribute to the aging process and to many age-related diseases and may affect cardiovascular function by either involving the long-term development of atherosclerosis or causing immediate damage during a heart attack or stroke [8]. Typically, ROS reacts with lipids causing lipid peroxidation leading to oxidative destruction of unsaturated fatty acids and damage of cell membranes with indirect damage to other cell constituents [9]. Therefore mitigating oxidative stress may have a significant impact for people in pre-metabolic syndrome status.

Hydrogen has been identified as having therapeutic antioxidant properties by selectively reducing cytotoxic ROS in tissues [10, 11]. As hydrogen is a gaseous molecule, inhaled hydrogen might be an easy delivery strategy. Although it is safe at a concentration lower than its threshold of 4.6% in air, the translational applicability of inhaled hydrogen gas is limited to medical care facilities as it is an inflammable gas and cannot be realistically and safely administered [12]. Oral intake of liquid containing hydrogen represents a novel and easily translatable method of delivery of hydrogen gas. Previous animal studies have linked daily consumption of hydrogen rich water, generated by bubbling or direct contact with hydrogen gas, with reduced atherosclerosis in apolipoprotein E knockout mice [13], alleviated cisplatin-induced nephrotoxicity [14], improved vitamin C deficiency-induced brain injury [15] and prevented chronic allograft nephropathy after renal transplantation [16]. In addition, the beneficial effects of consuming hydrogen rich water in the prevention of adult onset diabetes and insulin resistance has been reported in a human study [17].

We hypothesized that oral intake of hydrogen rich water generated via a magnesium stick may reduce oxidative stress in human subjects with potential metabolic syndrome. As metabolic syndrome is a disease closely associated with lifestyle-related habits, oral intake of hydrogen on a daily basis via drinking water may be ideal, for people without complicating or changing their life style. The administration of hydrogen rich water via a portable magnesium stick was considered to be a safe and feasible method of delivery and was investigated in an open label study, on subjects with potential metabolic syndrome.

Materials and Methods

Subjects and Design

This study was an open label pilot study conducted at a single site with an 8 week treatment period. Twenty subjects ≥40 years, males (n = 10) and females (n = 10) were enrolled from existing patient databases or by advertisement. In order to qualify, subjects were required to have one or more of the following conditions: body mass index (BMI) between 25.0 and 34.9 kg/m2, waist circumference of ≥100 cm for males and ≥88 cm for females, pre-hypertension (diastolic blood pressure of 80–89 mmHg and systolic blood pressure of 139 mmHg or lower), pre-diabetes (fasting plasma glucose from 5.2 to 6.9 mmol/L), total cholesterol >5.18 mmol/L and/or low density lipoprotein (LDL) >2.59 mmol/L. At screening, subjects provided written informed consent and, inclusion and exclusion criteria, medical history and prior use of concomitant medications were reviewed.

Subjects were required to be weight stable (for 3 months prior to study) and those subjects that were smokers were encouraged not to change their smoking habits. Subjects were required to discontinue other natural health products three weeks prior to randomization and during the study and to maintain their current level of physical activity and dietary habits during the course of the study. Subjects were excluded from participating if they were pregnant, breastfeeding, or planning to become pregnant, had uncontrolled hypertension, or history of diagnosed disease or condition including diabetes (Type I or II), cardiovascular disease, cancer, renal and/or liver disease, history of psychiatric disorder or drug/alcohol abuse, used prescription or over the counter products for vasodilation, erectile dysfunction, weight loss, and/or hypercholesterolemia, use of anticoagulants or had participated in a clinical research trial within 30 days prior to randomization.

This study was conducted at KGK Synergize, Inc., London ON, Canada. The study was conducted in accordance with Good Clinical Practice Guidelines and the ethical principles of the Declaration of Helsinki (2000). The study protocol and materials were approved by the Institutional Review Board Services (Aurora, Ontario), and all subjects gave written informed consent prior to participation.

Investigational products (Production of hydrogen water)

A plastic shelled product consisting of metallic magnesium (99.9% pure) and natural stones in the polypropylene containers combined with ceramics (Doctor SUISOSUI®, Friendear, Tokyo, Japan) was used to produce hydrogen. The product was capable of generating hydrogen when placed in drinking water by the following chemical reaction; $Mg + 2H2O \rightarrow Mg(OH)2 + H2$ (Fig. 1). Hydrogen water sticks were dispensed at baseline and week 4 and used sticks were collected at week 4 and week 8 and compliance calculated.

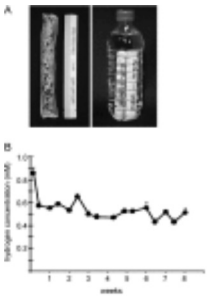

Fig. 1
A. Magnesium stick and the methods to generate hydrogen water in 500 ml bottles of drinking water. A plastic shelled product consisting of metallic magnesium (99.9% pure) and natural stones in the polypropylene containers combined with ceramics (more ...)

In a retrospective study conducted at the University of Pittsburgh, in a setting similar to the study procedures followed in the current study, the hydrogen concentration in a water bottle was sequentially monitored using a hydrogen needle sensor (DHS-001, ABLE, Tokyo, Japan). It was determined that the hydrogen concentration was maintained between 0.55 and 0.65 mM and pH between 7.9 and 8.1 over a 12 to 36 h period. When monitored twice a day at weekly intervals for 4 weeks, it was further documented, that the magnesium stick maintained the hydrogen concentration in the water bottles for the desired length of the study. The concentration of magnesium and calcium in the water were also measured using a standard test method (ASTM D511-09, ASTM International, West Conshohocken, PA, conducted at University of Pittsburgh) and found to be <1.0 mg/L and <1.0 mg/L, respectively.

Study protocols (dose and mode of administration)

Subjects were provided with 500 ml bottles of drinking water and instructed to place two magnesium sticks in each of five bottles of water at the end of each day in preparation for consumption the following day. Participants were asked to drink 300–400 ml from bottle one, each morning, one hour before breakfast; 300–400 ml from bottle two, one hour before lunch; 300–400 ml from bottle three, two hours after lunch; 300–400 ml from bottle four, one hour before supper; and 300–400 ml from bottle five, one-half hour before bedtime as per instructions provided in the informed consent form. Subjects were instructed to reuse the magnesium sticks by transferring the sticks to a new bottle of water after use. In summary, subjects were expected to consume 300–400 ml of hydrogen rich water 5 times/day for a total minimum consumption of 1500 ml (1.5 L) to a maximum consumption of 2000 ml (2.0 L).

Assessment of health and physiological parameters

The study included 4 clinic visits, which occurred at screening, baseline, week 4 and week 8. At baseline, week 4 and week 8, blood pressure, heart rate, waist circumference and concomitant therapies were assessed, weight measurements were recorded and fasting peripheral blood was collected to determine glucose and lipid profile. Serum chemistry and hematology were repeated at week 4 and week 8 and first morning void urine samples from two consecutive days were pooled for urinalysis at baseline, week 4 and week 8. A treatment diary was dispensed at baseline and week 4 and included forms to record daily product use, changes in concomitant therapies and adverse events and was returned and reviewed at week 4 and week 8. Adverse events were reviewed at week 4 and week 8.

Analysis of oxidative stress markers

Laboratory tests for routine health markers such as complete blood count (CBC), creatinine, aspartate aminotransferase (AST), alanine

transaminase (ALT), gamma glutamyl transferase (GGT), bilirubin, total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides and fasting glucose were conducted using standardized procedures at Life Labs Medical Laboratory Services in London, ON. Concentration of 8-hydroxy-2'-deoxyguanosine (8-OHdG) was analyzed by enzyme immunoassay (EIA) (Caymen Chemical, Ann Arbor, MI, Cat. #589320), 8-isoprostane by EIA (Caymen Chemical, Cat. #516351.1), superoxide dismutase (SOD) by enzyme colorimetric assay (Caymen Chemical, Cat. #706002) and thiobarbituric acid reactive substances (TBARS) was analyzed spectrophotometrically using TBARS ASSAY (Caymen Chemical, Cat. #10009055).

Statistical analysis

As this was a pilot study, no formal sample size calculation was performed. Repeated measures analysis of variance (ANOVA) was used to compare pre- and post-treatment measurements of effectiveness and general health markers. Probability values less than 0.05 were considered to be statistically significant. The change from baseline to week 4, and week 8 were compared using Tukey's multiple comparisons test for 8-OHdG, 8-isoprostane, TBARS, and SOD, total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides and fasting glucose. Adverse events were summarized descriptively using frequencies, and categorizing by intensity and body system. A post hoc sub analysis was also conducted on female and male subjects to determine any differences in response according to gender and on subjects who were current smokers for effectiveness. SAS version 9.1 was used to perform the statistical analysis.

Subject characteristics

All subjects completed treatment with mean compliance of 98.7 ± 3.3 and were included in the analysis. The baseline demographics of subjects are presented in Table 1. Subjects enrolled in the study included those who were pre-hypertensive (n = 3), pre-diabetic (n = 7), and had total cholesterol >5.18 mmol/L (n = 12), LDL-c >2.59 mmol/L (n = 17), BMI 25–34.9 (n = 10), and/or smokers (n = 4). All subjects showed mean normal clinical levels of baseline biometric parameters, clinical chemistry and hematology.

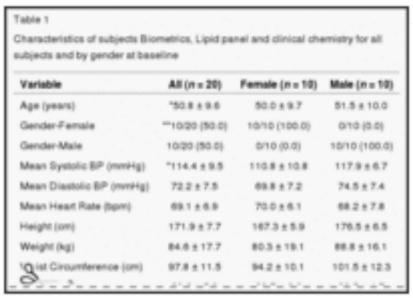

Table 1

Characteristics of subjects Biometrics, Lipid panel and clinical chemistry for all subjects and by gender at baseline

Variable	All (n = 20)	Female (n = 10)	Male (n = 10)
Age (years)	*50.8 ± 9.6	50.0 ± 9.7	51.5 ± 10.0
Gender-Female	**10/20 (50.0)	10/10 (100.0)	0/10 (0.0)
Gender-Male	10/20 (50.0)	0/10 (0.0)	10/10 (100.0)
Mean Systolic BP (mmHg)	**114.4 ± 9.5	110.8 ± 10.8	117.9 ± 6.7
Mean Diastolic BP (mmHg)	72.2 ± 7.5	69.8 ± 7.2	74.5 ± 7.4
Mean Heart Rate (bpm)	69.1 ± 6.9	70.0 ± 6.1	68.2 ± 7.8
Height (cm)	171.9 ± 7.7	167.3 ± 5.9	176.5 ± 6.5
Weight (kg)	84.6 ± 17.7	80.3 ± 19.1	88.8 ± 16.1
Waist Circumference (cm)	97.8 ± 11.5	94.2 ± 10.1	101.5 ± 12.3

The proportion of male smokers was greater (n = 3) than that of the female smokers (n = 1) however all subjects were occasional smokers. The compliance with respect to reporting the number of cigarettes smoked in all the visits was 100%. In two subjects the number of cigarettes smoked remained the same throughout the visits (10 and 20).

Oxidative stress biomarkers

Oxidative stress is a well-recognized mechanism playing an important role in pathological conditions seen in metabolic syndrome [1]. The effect of hydrogen rich water on markers of oxidative stress is presented in Table 2. TBARS are a marker of lipid peroxidation which is indicative of malondialdehyde formation and lipid damage and is a well-established method for screening and monitoring lipid peroxidation [18]. The concentration of urinary TBARS decreased significantly ($p<0.05$) from baseline to week 4 and week 8. Subjects demonstrated a significant increase ($p<0.05$) in SOD from baseline to week 8. Subjects demonstrated increasing trends in 8-isoprostane from baseline to week 4 and week 8. When a post hoc sub analysis by gender was conducted, male subjects demonstrated a significant decrease in urinary TBARS from baseline to week 8 and a significant increase ($p<0.05$) in SOD from baseline to week 8. During oxidative damage to DNA, damaged products are usually eliminated by repair enzymes and detected as nucleoside derivatives. Urinary 8-OHdG is one adduct of this reaction and has been proposed as a sensitive biomarker of oxidative DNA damage and repair [19]. In subjects who were current smokers, there was a trend toward a decrease in urinary 8-OHdG and TBARS levels from baseline to week 4 and week 8. Subjects demonstrated increasing trends in SOD from baseline to week 8 and 8-isoprostane from baseline to week 4 and week 8. Urinary 8-OHdG, 8-isoprostane, TBARS and SOD were higher in subjects who were current smokers (data not shown).

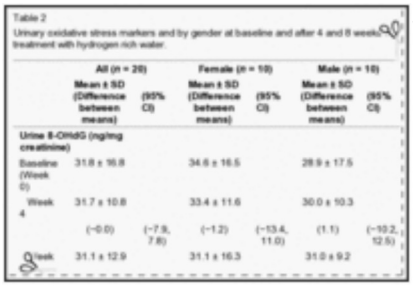

Table 2

Urinary oxidative stress markers and by gender at baseline and after 4 and 8 weeks of treatment with hydrogen rich water.

	All (n = 20)		Female (n = 10)		Male (n = 10)	
	Mean ± SD (Difference between means)	(95% CI)	Mean ± SD (Difference between means)	(95% CI)	Mean ± SD (Difference between means)	(95% CI)
Urine 8-OHdG (ng/mg creatinine)						
Baseline (Week 0)	31.8 ± 16.8		34.6 ± 16.5		28.9 ± 17.5	
Week 4	31.7 ± 10.8		33.4 ± 11.6		30.0 ± 10.3	
	(−0.0)	(−7.9, 7.8)	(−1.2)	(−13.4, 11.0)	(1.1)	(−10.2, 12.5)
Week 8	31.1 ± 12.9		31.1 ± 16.3		31.0 ± 9.2	

Lipid profile and fasting glucose

Subjects demonstrated a significant increase in HDL-cholesterol from baseline to week 4 and week 8 and a decrease in total cholesterol/HDL ratio from baseline to week 4 (Table 3). Post hoc sub analysis by gender demonstrated that female subjects had a significant increase ($p<0.05$) in HDL-cholesterol from baseline to week 4, and a significant decrease ($p<0.05$) in LDL-cholesterol and total cholesterol/HDL-cholesterol ratio from baseline to week 4. There were no changes in HDL cholesterol, cholesterol/HDL ratio and triglycerides from baseline to week 8. Male subjects demonstrated a significant increase in HDL-cholesterol from baseline to week 4 and week 8 and significant decrease in total cholesterol/HDL ratio from baseline to week 4 ($p<0.05$) (Table 3).

Table 3

Blood lipid profile of all subjects and by gender at baseline and after 4 and 8 weeks of treatment with hydrogen rich water.

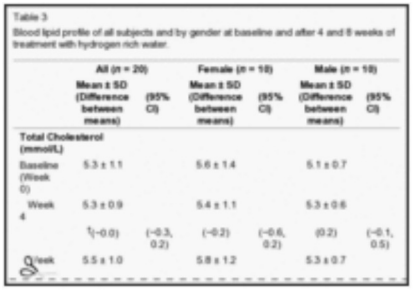

Table 3
Blood lipid profile of all subjects and by gender at baseline and after 4 and 8 weeks of treatment with hydrogen rich water.

	All (n = 20)		Female (n = 10)		Male (n = 10)	
	Mean ± SD (Difference between means)	(95% CI)	Mean ± SD (Difference between means)	(95% CI)	Mean ± SD (Difference between means)	(95% CI)
Total Cholesterol (mmol/L)						
Baseline (Week 0)	5.3 ± 1.1		5.6 ± 1.4		5.1 ± 0.7	
Week 4	5.3 ± 0.9		5.4 ± 1.1		5.3 ± 0.6	
	[1](-0.0)	(−0.3, 0.2)	(−0.2)	(−0.6, 0.2)	(0.2)	(−0.1, 0.5)
Week 8	5.5 ± 1.0		5.8 ± 1.2		5.3 ± 0.7	

The effects of hydrogen rich water on the lipid profile in subjects who were current smokers demonstrated that there was a significant decrease in the total cholesterol/HDL ratio from baseline to week 4 (data not shown) and a significant increase in HDL from baseline to week 4 ($p<0.05$).
Results showed that there were no statistical differences from baseline to week 8 for fasting glucose in participants after consumption of hydrogen rich water (data not shown).
Biometric parameters, clinical chemistry and hematology
There were no significant differences in blood pressure, heart rate, weight and BMI assessed at any time point (data not shown). Analysis of clinical chemistry parameters demonstrated that ALT and creatinine were significantly decreased ($p<0.05$) from baseline to week 4 and week 8 in all subjects (Table 4). Further analysis demonstrated that 80% of subjects (9 females and 7 males) had a decrease in ALT from baseline to week 8 and 95% of subjects (10 females and 9 males) had a decrease in creatinine from baseline to week 8.

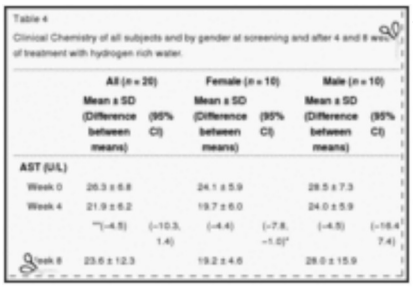

Table 4
Clinical Chemistry of all subjects and by gender at screening and after 4 and 8 weeks of treatment with hydrogen rich water.

	All (n = 20)		Female (n = 10)		Male (n = 10)	
	Mean ± SD (Difference between means)	(95% CI)	Mean ± SD (Difference between means)	(95% CI)	Mean ± SD (Difference between means)	(95% CI)
AST (U/L)						
Week 0	26.3 ± 6.8		24.1 ± 5.9		28.5 ± 7.3	
Week 4	21.9 ± 5.2		19.7 ± 6.0		24.0 ± 5.9	
	[1](−4.5)	(−10.3, 1.4)	(−4.4)	(−7.8, −1.0)*	(−4.5)	(−16.4, 7.4)
Week 8	23.6 ± 12.3		19.2 ± 4.6		28.0 ± 15.9	

The decrease in ALT was significant ($p<0.05$) from baseline to week 4 and week 8 in female subjects but not male subjects. Creatinine was significantly decreased ($p<0.05$) in both genders from baseline to week 4 and week 8. Significant increases were demonstrated from baseline to week 4 and week 8 for bilirubin in subjects on hydrogen rich water. Eight females and seven males demonstrated an increase in bilirubin from baseline to week 8. This increase was significant in female subjects, but not in male subjects. GGT was significantly increased ($p<0.05$) from baseline to week 8 with 85% of all subjects demonstrating an increase during this period (8 females and 9 males). Ninety percent of all subjects demonstrated a decrease in AST from baseline to week 8 (9 females and 9 males). This decrease was significant from baseline to weeks 4 and week 8 in female subjects but not in male subjects. The mean values for these parameters were within the normal acceptable reference range for male and female subjects. In subjects who were current smokers, significant increases were demonstrated from baseline to week 8 for bilirubin and this increase was within normal acceptable reference ranges (data not shown).
Adverse events
A total of 28 adverse events were experienced by 13 of the 20 subjects (65.0%) enrolled in the study. Overall, 6 adverse events, experienced by 4 subjects (20.0%) were assessed by the investigator as having a possible relationship to the test article. These adverse events included loose stools (3 subjects), increase in frequency of bowel movement (1 subject) heartburn (1 subject), and headache (1 subject). These adverse events having "possible" relationship to the test article were classified as mild in intensity. There were no serious adverse events which occurred during the study.
Discussion
In this study, we demonstrated that drinking hydrogen rich water increased urinary anti-oxidant enzyme SOD, an endogenous defensive system against ROS-induced cellular injury, associated with reduction of oxidative stress markers, in subjects with metabolic syndrome [7]. SOD plays an important role in the antioxidant defense system against superoxide anion (O2−) generated in vivo and is involved in defense against many diseases [20–22]. Our data demonstrated that subjects consuming hydrogen rich water for 8 weeks showed significantly increased SOD levels from baseline to week 8, suggesting that hydrogen rich water is capable of inducing SOD activity. Although the detailed mechanisms are undefined an increase in SOD levels correlated with decreasing trends in 8-OHdG levels, and thus supported our hypothesis that oxidative stress is reduced by consuming hydrogen rich water.
Oxidative modification of LDL in the arterial wall plays a key role in the pathogenesis of atherosclerosis [2]. A high level of HDL-cholesterol is reported to protect against cardiovascular disease, and low HDL-cholesterol levels (less than 40 mg/dL) increase the risk of heart disease [23]. Results of the current study demonstrated a significant increase in HDL-cholesterol leading to a significant decrease in total cholesterol/HDL ratio by week 4. Decreasing trends were also seen for LDL-cholesterol from baseline to week 4, and triglycerides from baseline to week 8. Though there was an increase in total cholesterol and LDL-cholesterol in subjects consuming hydrogen rich water from baseline until week 8, these values were not clinically significant and were still within a normal acceptable range. The increasing trends may possibly be associated with higher saturated fat consumption, individual food habits and physical activity of subjects. It is possible that the hypolipidemic effect of hydrogen rich water may be due to its ability to prevent lipid peroxidation, as demonstrated by the significant decrease in TBARS, resulting in lower total cholesterol/ HDL ratio, triglycerides and an increase in HDL-cholesterol. Although an improvement of lipid and glucose metabolism after supplementation with hydrogen rich water have been observed in patients with type II diabetes [17], our results showed that there were no statistical differences in fasting glucose in pre-diabetic participants from baseline to week 8. These results are supported by a previous study where hydrogen water was found to lower the blood glucose level of participants with abnormally high blood glucose levels and did not induce a reduction of a normal blood glucose level [17].
GGT is an enzyme widely distributed in the human body, especially in the kidney and liver [24]. The results of the present study demonstrated that there was a significant increase in GGT ($p<0.05$) within group from baseline to week 8. However this increase was still within the normal acceptable clinical range for these values for both females and males.
Previous studies have showed that there is a positive association between dietary factors and GGT levels [25]. Alcohol and meat consumption are reported to increase GGT levels in a dose dependant manner. However as food records were not maintained in this study we were unable to confirm that the increases in the GGT levels were related to these factors. As the other liver markers such as AST and ALT were not impacted it is possible to suggest that hydrogen water did not have a negative effect on liver function. In this study we found that AST decreased from baseline to week 4 and week 8 in both female and male subjects and these decreases

attained significance in the female subjects. The levels of ALT decreased significantly from week 4 to week 8 and in the subgroup analysis this significance was also seen in the female subjects.

Taken together it is possible to suggest that the increases in GGT may reflect changes associated with food intake and alcohol consumption of the participants. The values for GGT remained within an acceptable clinical range for this parameter.

Interestingly, subjects demonstrated a significant increase in total bilirubin from baseline to week 4 and week 8. These increases remained within normal clinically acceptable range. Serum ALT and AST decreased with hydrogen rich water consumption and the elevation of bilirubin levels seen in this study may be a specific effect afforded by hydrogen. Schwertner et al. previously reported that there was a significant inverse correlation between bilirubin concentration and the prevalence of cardiovascular disease and lower serum bilirubin concentrations were correlated with the presence of ischemic heart disease [26]. Madhavan et al. showed that plasma bilirubin concentration is positively correlated with HDL-cholesterol and confirms the results demonstrated in our study [27]. Thus, the elevations of serum bilirubin levels, below toxic levels, are likely to be protective for cardiovascular disease.

The exact mechanisms involved in bilirubin elevation in the subjects treated with hydrogen rich water are not fully understood, however, the antioxidant effects of hydrogen may not be the sole explanation for this increase and other as yet undefined mechanisms may be involved, such as a role in signaling pathways or perhaps other physiological functions. There is a possibility that the higher bilirubin levels are associated with the degradation of heme by heme oxygenase into equimolar quantities of biliverdin (bilirubin) and carbon monoxide (CO), while the central iron is released [28]. The induction of heme oxygenase (HO-1), which is the rate-limiting enzyme, catalyzes the degradation of heme [29]. Further studies are required to determine if hydrogen can induce HO-1. As our hematological data was not altered by hydrogen water consumption and as the elevations in serum bilirubin remained within the normal acceptable range, it is not likely that hemolysis contributed to the increase of serum bilirubin levels.

Mean values of all hematological parameters were within normal clinically acceptable ranges. Biometric parameters assessed as a measure of safety remained unchanged during the 8 week period of the study. Results also showed that there were no changes in blood pressure, BMI and weight in subjects after consuming hydrogen rich water for 8 weeks.

A sub analysis was conducted on subjects who were smokers as previous documentation has established that smokers are likely to have more oxidative stress [30] and thus may show a greater benefit from an antioxidant intervention. Subjects who smoked demonstrated a decrease in urinary creatinine, urinary 8-OHdG and TBARS with hydrogen rich water. Further subjects who smoked demonstrated increasing trends in SOD from baseline to week 8 and 8-isoprostane from baseline to week 4 and week 8, and higher urinary 8-OHdG, 8-isoprostane, TBARS and SOD. There was a statistically significant and a clinically important decrease in total cholesterol/HDL ratio from baseline to week 4 and a statistically significant increase in HDL from baseline to week 4. These results demonstrated that oxidative stress was perhaps impacted more significantly in subjects who smoked.

In conclusion, consumption of hydrogen rich water generated via a magnesium stick demonstrated improvement in the levels of oxidative stress markers associated with metabolic syndrome and boosted the body's antioxidant activity. Hydrogen rich water represents a potentially novel therapeutic and preventive strategy for the treatment of metabolic syndrome. This method of delivery was advantageous as magnesium sticks are portable and proved to be an easy and safe administration of hydrogen rich water for daily consumption.

Acknowledgments

We would like to thank the volunteers of this study for their willingness and diligence in complying with the protocol. This study was managed by KGK Synergize Inc. London, ON, Canada, under the supervision of the medical directors, David Crowley, MD and Dale Wilson, MD. Statistical guidance and analysis was provided by Larry Stitt, Assistant Director of the Biostatistical Support Unit, University of Western Ontario, London, ON, Canada. We acknowledge the technical contribution of Joshua Baisley and thank Sonya Barss for overseeing the conduct of the study. This study was supported by Friendear Inc. (Decoupage Minami Aoyama 4F, 5-10-13 Minami Aoyama, Minato-ku, Tokyo 107-0062, Japan).

Abbreviations

8-isoprostane	15-F2t-15-isoprostane (8-isoprostane F2α)
8-OHdG	8-hydroxy-2'-deoxyguanosine
ALT	alanine transaminase
ANOVA	analysis of variance
AST	aspartate aminotransferase
BMI	body mass índex

DNA	deoxyribonucleic acid
GCP	Good Clinical Practices
GGT	gamma glutamyl transferase
HDL	high density lipoproteins
LDL	low density lipoprotein
IRB	institutional review board
MCH	mean corpuscular hemoglobin
Mg	Magnesium metal
Mg (OH)2	Magnesium hydroxide
ROS	reactive oxygen species
SD	standard deviation
SOD	superoxide dismutase
TBARS	Thiobarbituric Acid Reactive Substances
eGFR	estimated glomerular filtration rate

HO-1 heme oxygenase

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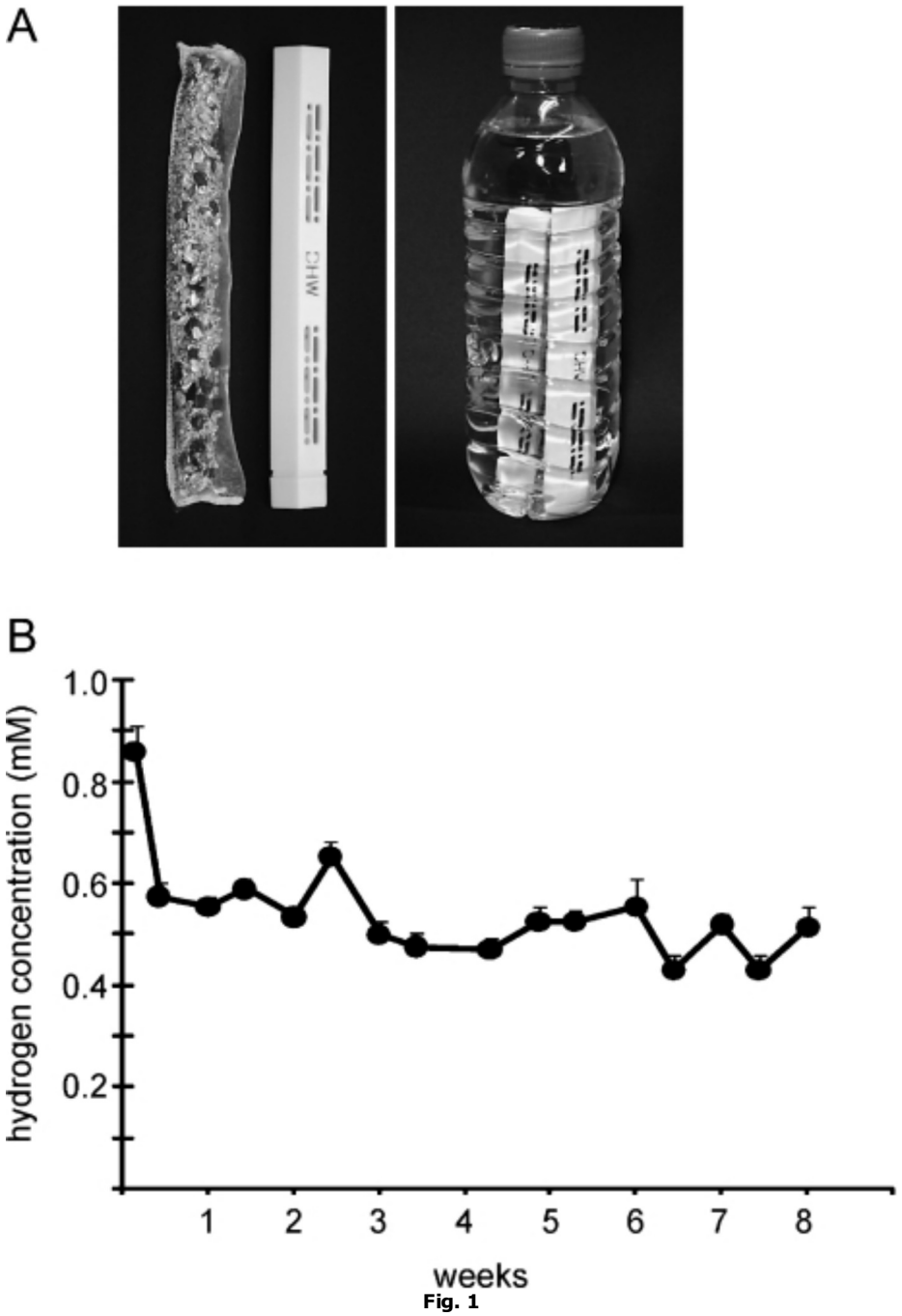

Fig. 1

A. Magnesium stick and the methods to generate hydrogen water in 500 ml bottles of drinking water. A plastic shelled product consisting of metallic magnesium (99.9% pure) and natural stones in the polypropylene containers combined with ceramics (Doctor SUISOSUI®, Friendear, Tokyo, Japan) was used to produce hydrogen. The product was capable of generating hydrogen when placed in drinking water by the following chemical reaction; $Mg + 2H_2O \rightarrow Mg(OH)_2 + H_2$. B. Hydrogen concentrations in the water bottle (n = 3). The hydrogen concentration in a water bottle was maintained between 0.55 and 0.65 mM over an 8 week period.

Table 1

Characteristics of subjects Biometrics, Lipid panel and clinical chemistry for all subjects and by gender at baseline

Variable	**All (*n* = 20)**	**Female (*n* = 10)**	**Male (*n* = 10)**
Age (years)	*50.8 ± 9.6	50.0 ± 9.7	51.5 ± 10.0
Gender-Female	**10/20 (50.0)	10/10 (100.0)	0/10 (0.0)
Gender-Male	10/20 (50.0)	0/10 (0.0)	10/10 (100.0)
Mean Systolic BP (mmHg)	*114.4 ± 9.5	110.8 ± 10.8	117.9 ± 6.7

Mean Diastolic BP (mmHg)	72.2 ± 7.5	69.8 ± 7.2	74.5 ± 7.4
Mean Heart Rate (bpm)	69.1 ± 6.9	70.0 ± 6.1	68.2 ± 7.8
Height (cm)	171.9 ± 7.7	167.3 ± 5.9	176.5 ± 6.5
Weight (kg)	84.6 ± 17.7	80.3 ± 19.1	88.8 ± 16.1
Waist Circumference (cm)	97.8 ± 11.5	94.2 ± 10.1	101.5 ± 12.3
BMI (kg/m2)	28.6 ± 5.8	28.7 ± 6.9	28.5 ± 4.7
Fasting Glucose (mmol/L)	4.9 ± 0.5	4.6 ± 0.6	4.9 ± 0.4
Alcohol Use			
Daily	**2/20 (10.0)	0/10 (0.0)	2/20 (10.0)
Occasional	14/20 (70.0)	6/10 (60.0)	8/10 (30.0)
Weekly	4/20 (20.0)	4/10 (40.0)	0/10 (0.0)
Tobacco Use			
Current	4/20 (20.0)	1/10 (10.0)	3/10 (30)
Former	7/20 (35.0)	3/10 (30.0)	4/10 (40.0)
None	9/20 (45.0)	6/10 (60.0)	3/10 (30.0)

* Mean ± SD, **f/n (%) = Number of subjects/Total Number of subjects (percent). BP, indicates blood pressure; BMI, body mass index.

Table 2
Urinary oxidative stress markers and by gender at baseline and after 4 and 8 weeks of treatment with hydrogen rich water.

	All (*n* = 20)		**Female (*n* = 10)**		**Male (*n* = 10)**	
	Mean ± SD (Difference between means)	**(95% CI)**	**Mean ± SD (Difference between means)**	**(95% CI)**	**Mean ± SD (Difference between means)**	**(95% CI)**
Urine 8-OHdG (ng/mg creatinine)						
Baseline (Week 0)	31.8 ± 16.8		34.6 ± 16.5		28.9 ± 17.5	
Week 4	31.7 ± 10.8		33.4 ± 11.6		30.0 ± 10.3	
	(−0.0)	(−7.9, 7.8)	(−1.2)	(−13.4, 11.0)	(1.1)	(−10.2, 12.5)
Week 8	31.1 ± 12.9		31.1 ± 16.3		31.0 ± 9.2	
	(−0.7)	(−8.5, 7.1)	(−3.6)	(−15.8, 8.7)	(2.2)	(−9.2, 13.5)
8-Isoprostane (ng/mmol creatinine)						

Baseline (Week 0)	122.9 ± 33.9		125.9 ± 29.5		120.0 ± 39.2	
Week 4	130.0 ± 43.1		122.8 ± 38.4		137.2 ± 48.2	
	(7.1)	(−17.7, 31.8)	(−3.1)	(−34.6, 28.5)	(17.2)	(−24.8, 59.2)
Week 8	140.3 ± 32.8		138.2 ± 20.8		142.4 ± 42.8	
	(17.4)	(−7.4, 42.2)	(12.3)	(−19.2, 43.8)	(22.5)	(−19.5, 64.5)
TBARS (µmol/g creatinine)						
Baseline (Week 0)	7.7 ± 5.2		8.4 ± 5.9		7.1 ± 4.5	
Week 4	5.0 ± 3.8		5.7 ± 4.6		4.3 ± 2.9	
	(−2.7)	(−4.9, −0.6)*	(−2.6)	(−5.7, 0.4)	(−2.8)	(−6.2, 0.6)
Week 8	4.5 ± 2.9		5.4 ± 3.4		3.6 ± 2.0	
	(−3.3)	(−5.4, −1.1)*	(−3.0)	(−6.1, 0.1)	(−3.5)	(−6.9, −0.2)*
SOD (U/mmol creatinine)						
Baseline (Week 0)	122.1 ± 106.4		155.9 ± 122.3		88.3 ± 80.2	
Week 4	129.8 ± 62.3		153.6 ± 61.3		106.1 ± 56.3	
	(7.8)	(−25.3, 40.8)	(−2.3)	(−59.6, 55.0)	(17.8)	(−22.4, 58.0)
Week 8	169.7 ± 94.1		208.2 ± 106.2		131.3 ± 64.3	
	(47.7)	(14.6, 80.7)*	(52.3)	(−5.0, 109.6)	(43.0)	(2.8, 83.2)*

* denotes statistically significant differences ($p<0.05$), 95% confidence intervals about the mean difference between baseline and week 4 and baseline and week 8 were obtained via Tukey's multiple comparisons test. ** Change in urinary oxidative stress markers from baseline to week 4. † Change in urinary oxidative stress markers from baseline to week 8 of treatment. 8-OHdG, indicates 8-hydroxy-2'-deoxyguanosine; TBARS, thiobarbituric acid; SOD, superoxide dismutase.

Água rica em hidrogênio protege contra lesão hepática em ratos com icterícia obstrutiva

11/06/11

O Hidrogênio possui 1 elétron na camada de valência e assim possui ação redutora (antioxidante), principalmente contra o grande vilão da história oxidativa , o radical hidroxila e também contra o radical peroxinitrito, fato esquecido por muito médicos incluindo eu. Acresce que o hidrogênio por ser molécula muito pequena chega facilmente nas mitocôndrias e no núcleo. Jose de Felippe Junior

Hydrogen-rich saline protects against liver injury in rats with obstructive jaundice.

Liu Q, Shen WF, Sun HY, Fan DF, Nakao A, Cai JM, Yan G, Zhou WP, Shen RX, Yang JM, Sun XJ.

Liver Int. 2010 Aug;30(7):958-68.

Source

Department of Special Treatment, Eastern Hepatobiliary Surgery Hospital, Second Military Medical University, Shanghai, China.

Abstract

BACKGROUND:
Hydrogen selectively reduces levels of hydroxyl radicals and alleviates acute oxidative stress in many models. Hydrogen-rich saline provides a high concentration of hydrogen that can be easily and safely applied.
AIMS:
In this study, we investigated the effects of hydrogen-rich saline on the prevention of liver injury induced by obstructive jaundice in rats.
METHODS:
Male Sprague-Dawley rats (n=56) were divided randomly into four experimental groups: sham operated, bile duct ligation (BDL) plus saline treatment [5 ml/kg, intraperitoneal (i.p.)], BDL plus low-dose hydrogen-rich saline treatment (5 ml/kg, i.p.) and BDL plus high-dose hydrogen-rich saline treatment (10 ml/kg, i.p.).
RESULTS:
The liver damage was evaluated microscopically 10 days after BDL. Serum alanine aminotransferase and aspartate aminotransferase levels, tissue malondialdehyde content, myeloperoxidase activity, tumour necrosis factor-alpha, interleukin (IL)-1beta, IL-6 and high-mobility group box 1 levels were all increased significantly by BDL. Hydrogen-rich saline reduced levels of these markers and relieved morphological liver injury. Additionally, hydrogen-rich saline markedly increased the activities of anti-oxidant enzymes superoxide dismutase and catalase and downregulated extracellular signal-regulated protein kinase (ERK)1/2 activation.
CONCLUSIONS:
Hydrogen-rich saline attenuates BDL-induced liver damage, possibly by the reduction of inflammation and oxidative stress and the inhibition of the ERK1/2 pathway.

PMID:
20492513

Água rica em hidrogênio. Água reduzida por eletrólise protege DNA,RNA e proteínas da lesão oxidativa

11/06/11

O Hidrogênio possui 1 elétron na camada de valência e assim possui ação redutora (antioxidante), principalmente contra o grande vilão da história oxidativa , o radical hidroxila e também contra o radical peroxinitrito, fato esquecido por muito médicos incluindo eu. Acresce que o hidrogênio por ser molécula muito pequena chega facilmente nas mitocôndrias e no núcleo. Jose de Felippe Junior

Electrolyzed-reduced water protects against oxidative damage to DNA, RNA, and protein.

Lee MY, Kim YK, Ryoo KK, Lee YB, Park EJ.

Appl Biochem Biotechnol. 2006 Nov;135(2):133-44.

Source

Department of Genetic Engineering, Soonchunhyang University, Asan, Chungnam 336-600, Korea. miyoung@sch.ac.kr

Abstract

The generation of reactive oxygen species is thought to cause extensive oxidative damage to various biomolecules such as DNA, RNA, and protein. In this study, the preventive, suppressive, and protective effects of in vitro supplementation with electrolyzed-reduced water on H2O2-induced DNA damage in human lymphocytes were examined using a comet assay. Pretreatment, cotreatment, and posttreatment with electrolyzed-reduced water enhanced human lymphocyte resistance to the DNA strand breaks induced by H2O2 in vitro. Moreover, electrolyzed-reduced water was much more effective than diethylpyrocarbonate-treated water in preventing total RNA degradation at 4 and 25 degrees C. In addition, electrolyzed-reduced water completely prevented the oxidative cleavage of horseradish peroxidase, as determined using sodium dodecyl sulfate-polyacrylamide gels. Enhancement of the antioxidant activity of ascorbic acid dissolved in electrolyzed-reduced water was about threefold that of ascorbic acid dissolved in nonelectrolyzed deionized water, as measured by a xanthine-xanthine oxidase superoxide scavenging assay system, suggesting an inhibitory effect of electrolyzedreduced water on the oxidation of ascorbic acid.

PMID:
17159237

Água rica em hidrogênio atenua lesão pulmonar provocada por isquemia intestinal

11/06/11

A água rica em hidrogênio diminui a infiltração de neutrófilos, a peroxidação lipídica, a ativação do NF-kappaB e as interleucinas pró-inflamatórias: IL-1beta e TNF-alfa no tecido pulmonar . Jose de Felippe junior

Hydrogen-rich saline reduces lung injury induced by intestinal ischemia/reperfusion in rats.

Mao YF, Zheng XF, Cai JM, You XM, Deng XM, Zhang JH, Jiang L, Sun XJ.

Biochem Biophys Res Commun. 2009 Apr 17;381(4):602-5. .

Source

Department of Surgical Intensive Care Unit, Xinhua Hospital, Shanghai Jiaotong University School of Medicine, PR China.

Abstract

OBJECTIVE:

Hydrogen has been reported to selectively reduce the hydroxyl radical, the most cytotoxic of reactive oxygen species. In this study we investigated the effects of hydrogen-rich saline on the prevention of lung injury induced by intestinal ischemia/reperfusion (I/R) in rats.

METHODS:

Male Sprague-Dawley rats (n=30, 200-220g) were divided randomly into three experimental groups: sham operated, intestinal I/R plus saline treatment (5ml/kg, i.v.), and intestinal I/R plus hydrogen-rich saline treatment (5ml/kg, i.v.) groups. Intestinal I/R was produced by 90min of intestinal ischemia followed by a 4h of reperfusion.

RESULTS:

Hydrogen-rich saline treatment decreased the neutrophil infiltration, the lipid membrane peroxidation, NF-kappaB activation and the pro-inflammatory cytokine interleukin IL-1beta and TNF-alpha in the lung tissues compared with those in saline-treated rat.

CONCLUSION:

Hydrogen-rich saline attenuates lung injury induced by intestinal I/R.

PMID:
19249288

Água rica em hidrogênio. Inalação do gás hidrogênio (2%) melhora a sobrevida de inflamação generalizada provocada por zimosan : Seria eficaz na falência de múltiplos órgãos em pacientes de UTI?:

Hydrogen gas improves survival rate and organ damage in zymosan-induced generalized inflammation model.

Xie K, Yu Y, Zhang Z, Liu W, Pei Y, Xiong L, Hou L, Wang G.

Shock. 2010 Nov;34(5):495-501.

Source

Department of Anesthesiology, General Hospital of Tianjin Medical University, Tianjin, People's Republic of China.

Abstract

Sepsis/multiple organ dysfunction syndrome is the leading cause of death in critically ill patients. Recently, it has been suggested that hydrogen gas (H2) exerts a therapeutic antioxidant activity by selectively reducing hydroxyl radical (•OH, the most cytotoxic reactive oxygen species). We have found that H2 inhalation significantly improved the survival rate and organ damage of septic mice with moderate or severe cecal ligation and puncture. In the present study, we investigated the effects of 2% H2 treatment on survival rate and organ damage in zymosan (ZY)-induced generalized inflammation model. Here, we found that 2% H2 inhalation for 60 min starting at 1 and 6 h after ZY injection, respectively, significantly improved the 14-day survival rate of ZY-challenged mice from 10% to 70%. Furthermore, ZY-challenged mice showed significant multiple organ damage characterized by the increase in serum biochemical parameters (aspartate aminotransferase, alanine aminotransferase, blood urea nitrogen, and creatinine), as well as lung, liver, and kidney histopathological scores at 24 h after ZY injection, which was significantly attenuated by 2% H2 treatment. In addition, we found that **the beneficial effects of H2 treatment on ZY-induced organ damage were associated with the decreased levels of oxidative product, increased activities of antioxidant enzyme, and reduced levels of early and late proinflammatory cytokines in serum and tissues**. In conclusion, this study provides evidence that H2 treatment protects against multiple organ damages in ZY-induced generalized inflammation model, suggesting the potential use of H2 as a therapeutic agent in the therapy of conditions associated with inflammation-related multiple organ dysfunction syndrome.PMID: 20351628

Água rica em hidrogênio. Hidrogênio molecular atenua a nefrotoxicidade provocada pela cisplatina sem comprometer a atividade anti-tumoral

11/06/11

O Hidrogênio possui 1 elétron na camada de valência e assim possui ação redutora (antioxidante), principalmente contra o grande vilão da história oxidativa , o radical hidroxila e também contra o radical peroxinitrito, fato esquecido por muito médicos incluindo eu. Acresce que o hidrogênio por ser molécula muito pequena chega facilmente nas mitocôndrias e no núcleo. Jose de Felippe Junior

Molecular hydrogen alleviates nephrotoxicity induced by an anti-cancer drug cisplatin without compromising anti-tumor activity in mice.

Nakashima-Kamimura N, Mori T, Ohsawa I, Asoh S, Ohta S.

Cancer Chemother Pharmacol. 2009 Sep;64(4):753-61.

Source

Department of Biochemistry and Cell Biology, Institute of Development and Aging Sciences, Nippon Medical School, Kawasaki, Kanagawa, Japan.

Abstract

PURPOSE:

Cisplatin is a widely used anti-cancer drug in the treatment of a wide range of tumors; however, its application is limited by nephrotoxicity, which is affected by oxidative stress. We have reported that molecular hydrogen (H(2)) acts as an efficient antioxidant (Ohsawa et al. in Nat Med 13:688-694, 2007). Here we show that hydrogen efficiently mitigates the side effects of cisplatin by reducing oxidative stress.

METHODS:

Mice were administered cisplatin followed by inhaling hydrogen gas (1% H(2) in air). Furthermore, instead of inhaling hydrogen gas, we examined whether drinking water containing hydrogen (hydrogen water; 0.8 mM H(2) in water) is applicable by examining oxidative stress, mortality, and body-weight loss. Nephrotoxicity was assessed by morphological changes, serum creatinine and blood urea nitrogen (BUN) levels.

RESULTS:

Inhalation of hydrogen gas improved mortality and body-weight loss caused by cisplatin, and alleviated nephrotoxicity. Hydrogen was detected in blood when hydrogen water was placed in the stomach of a rat. Consuming hydrogen water ad libitum also reduced oxidative stress, mortality, and body-weight loss induced by cisplatin in mice. Hydrogen water improved metamorphosis accompanying decreased apoptosis in the kidney, and nephrotoxicity as assessed by serum creatinine and BUN levels. Despite its protective effects against cisplatin-induced toxicity, hydrogen did not impair anti-tumor activity of cisplatin against cancer cell lines in vitro and tumor-bearing mice in vivo.

CONCLUSION:

Hydrogen has potential for improving the quality of life of patients during chemotherapy by efficiently mitigating the side effects of cisplatin.

PMID:
19148645

Água rica em hidrogênio. Inalação de água rica em hidrogênio previne o aparecimento de pneumonite provocada pela radioterapia

11/06/11

O Hidrogênio possui 1 elétron na camada de valência e assim possui ação redutora (antioxidante), principalmente contra o grande vilão da história oxidativa , o radical hidroxila e também contra o radical peroxinitrito, fato esquecido por muito médicos incluindo eu. Acresce que o hidrogênio por ser molécula muito pequena chega facilmente nas mitocôndrias e no núcleo. Jose de Felippe Junior

A possible prevention strategy of radiation pneumonitis: combine radiotherapy with aerosol inhalation of hydrogen-rich solution.

Chuai Y, Zhao L, Ni J, Sun D, Cui J, Li B, Qian L, Gao F, Cai J.

Med Sci Monit. 2011 Apr 1;17(4):HY1-4.

Source

Department of Radiation Medicine, Faculty of Naval Medicine, 2nd Military Medical University, Shanghai, PR China.

Abstract

Radiotherapy is an important modality of cancer treatment. Radiation pneumonitis is a major obstacle to increasing the radiation dose in radiotherapy, and it is important to prevent this radiation-induced complication. Recent studies show that hydrogen has a potential as an effective and safe radioprotective agent by selectively reducing hydroxyl and peroxynitrite radicals. Since most of the ionizing radiation-induced cellular damage is caused by hydroxyl radicals, we hypothesize that a treatment combining radiotherapy with aerosol inhalation of a hydrogen-rich solution may be an effective and novel prevention strategy for radiation pneumonitis (hydrogen is explosive, while a hydrogen-rich solution such as physiological saline saturated with molecular hydrogen is safer).

PMID:
21455114

Água rica em hidrogênio . Hidrogênio molecular um potente agente antioxidante com efeitos antiinflamatório, anti-apoptótico e anti-alérgico

11/06/11

O Hidrogênio possui 1 elétron na camada de valência e assim possui ação redutora (antioxidante), principalmente contra o grande vilão da história oxidativa , o radical hidroxila e também contra o radical peroxinitrito, fato esquecido por muito médicos incluindo eu. Acresce que o hidrogênio por ser molécula muito pequena chega facilmente nas mitocôndrias e no núcleo. Jose de Felippe Junior

Hydrogen as a selective antioxidant: a review of clinical and experimental studies.

Hong Y, Chen S, Zhang JM.

J Int Med Res. 2010;38(6):1893-903.

Source

Department of Neurosurgery, Second Affiliated Hospital, School of Medicine and Institute of Brain Medicine, Zhejiang University, Hangzhou, Zhejiang Province, China.

Abstract

Oxidative stress is implicated in the pathogenesis of many diseases; however, currently used antioxidants have a high toxicity that constrains administration to a narrow window of therapeutic dosage. There is a clear need for more effective and safer antioxidants. Diatomic hydrogen (H(2)) was proposed as a novel antioxidant that selectively reduces levels of toxic reactive-oxygen species. Recently, many studies have reported that H(2) (inhaled or orally ingested, typically as approximately 0.8 mM H(2)-saturated water), can exert beneficial effects in diverse animal models of ischaemia-reperfusion injury, and inflammatory and neurological disease. In the clinic, oral administration of H(2)-saturated water is reported to improve lipid and glucose metabolism in subjects with diabetes or impaired glucose tolerance; promising results have also been obtained in reducing inflammation in haemodialysis patients and treating metabolic syndrome. These studies suggest H(2) has selective antioxidant properties, and can exert antiapoptotic, antiinflammatory and antiallergy effects. This review summarizes recent research findings and mechanisms concerning the therapeutic potential of H(2).

PMID: 21226992