

MOLECULAR HYDROGEN IMPROVES OBESITY AND DIABETES BY INDUCING HEPATIC FGF21 AND STIMULATING ENERGY METABOLISM IN DB/DB MICE

Obesity (Silver Spring). 2011 Jul;19(7):1396-403. doi: 10.1038/oby.2011.6. Epub 2011 Feb 3.
Kamimura N, Nishimaki K, Ohsawa I, Ohta S.

Source

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Abstract

Recent extensive studies have revealed that molecular hydrogen (H₂) has great potential for improving oxidative stress-related diseases by inhaling H₂ gas, injecting saline with dissolved H₂, or drinking water with dissolved H₂ (H₂-water); however, little is known about the dynamic movement of H₂ in a body. First, we show that hepatic glycogen accumulates H₂ after oral administration of H₂-water, explaining why consumption of even a small amount of H₂ over a short span time efficiently improves various disease models. This finding was supported by an in vitro experiment in which glycogen solution maintained H₂.

Next, we examined the benefit of ad libitum drinking H₂-water to type 2 diabetes using db/db obesity model mice lacking the functional leptin receptor. Drinking H₂-water reduced hepatic oxidative stress, and significantly alleviated fatty liver in db/db mice as well as high fat-diet-induced fatty liver in wild-type mice. Long-term drinking H₂-water significantly controlled fat and body weights, despite no increase in consumption of diet and water. Moreover, drinking H₂-water decreased levels of plasma glucose, insulin, and triglyceride, the effect of which on hyperglycemia was similar to diet restriction.

To examine how drinking H₂-water improves obesity and metabolic parameters at the molecular level, we examined gene-expression profiles, and found enhanced expression of a hepatic hormone, fibroblast growth factor 21 (FGF21), which functions to enhance fatty acid and glucose expenditure. Indeed, H₂ stimulated energy metabolism as measured by oxygen consumption. The present results suggest the potential benefit of H₂ in improving obesity, diabetes, and metabolic syndrome.

PMID:21293445 [PubMed - indexed for MEDLINE]

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ANTI-OBESITY EFFECT OF ALKALINE REDUCED WATER IN HIGH FAT-FED OBESE MICE

Biol Pharm Bull. 2013;36(7):1052-9.

Ignacio RM, Kang TY, Kim CS, Kim SK, Yang YC, Sohn JH, Lee KJ.

Source

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Abstract

Whether or not alkaline reduced water (ARW) has a positive effect on obesity is unclear. This study aims to prove the positive effect of ARW in high-fat (HF) diet-induced obesity (DIO) in C57BL/6 mice model. Toward this, obesity was induced by feeding the C57BL/6 male mice with high-fat diet (w/w 45% fat) for 12 weeks. Thereafter, the animals were administered with either ARW or tap water. Next, the degree of adiposity and DIO-associated parameters were assessed: clinico-pathological parameters, biochemical measurements, histopathological analysis of liver, the expression of cholesterol metabolism-related genes in the liver, and serum levels of adipokine and cytokine. We found that ARW-fed mice significantly ameliorated adiposity: controlled body weight gain, reduced the accumulation of epididymal fats and decreased liver fats as compared to control mice. Accordingly, ARW coordinated the level of adiponectin and leptin. Further, mRNA expression of cytochrome P450 (CYP)7A1 was upregulated. In summary, our data shows that ARW intake inhibits the progression of HF-DIO in mice. This is the first note on anti-obesity effect of ARW, clinically implying the safer fluid remedy for obesity control.

PMID: 23811554 [PubMed - indexed for MEDLINE]

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ANTI-DIABETIC EFFECT OF ALKALINE-REDUCED WATER ON OLETF RATS

Biosci Biotechnol Biochem. 2006 Jan;70(1):31-7.

Jin D, Ryu SH, Kim HW, Yang EJ, Lim SJ, Ryang YS, Chung CH, Park SK, Lee KJ.

Source

Department of Microbiology, Wonju College of Medicine, Yonsei University, South Korea.

Abstract

Alkaline-reduced water (ARW) is known to exert several anti-cancer effects, as well as to scavenge reactive oxygen species (ROS) and reduce blood-glucose levels. This study was performed in order to determine the effects of ARW on the control of spontaneous diabetes in Otsuka Long-Evans Tokushima Fatty (OLETF) rats. We assigned 16 male OLETF rats (4 wk) to two groups: an experimental group, which was given ARW, and a control group, which received laboratory tap water. From week 6 to 32, the body weight, lipid composition, and glucose levels in the blood of the rats were measured. The glucose levels of both groups tended to increase. However, the ARW group's glucose levels were significantly lower than those of the control group after 12 weeks ($p < 0.05$). The total cholesterol and triglyceride levels in the ARW group were found to be significantly lower than those of the control group during the experimental period. These results suggest that ARW spurred the growth of OLETF rats during the growth stage, and that long-term ingestion of ARW resulted in a reduction in the levels of glucose, triglycerides, and total cholesterol in the blood.

PMID:16428818 [PubMed - indexed for MEDLINE]

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SUPPRESSIVE EFFECTS OF ELECTROLYZED REDUCED WATER ON ALLOXAN-INDUCED APOPTOSIS AND TYPE 1 DIABETES MELLITUS

Cytotechnology. 2011 Mar;63(2):119-31. doi: 10.1007/s10616-010-9317-6. Epub 2010 Nov 10.

Li Y, Hamasaki T, Nakamichi N, Kashiwagi T, Komatsu T, Ye J, Teruya K, Abe M, Yan H, Kinjo T, Kabayama S, Kawamura M, Shirahata S.

Source

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Abstract

Electrolyzed reduced water, which is capable of scavenging reactive oxygen species, is attracting recent attention because it has shown improved efficacy against several types of diseases including diabetes mellitus. Alloxan produces reactive oxygen species and causes type 1 diabetes mellitus in experimental animals by irreversible oxidative damage to insulin-producing β -cells. Here, we showed that electrolyzed reduced water prevented alloxan-induced DNA fragmentation and the production of cells in sub-G1 phase in HIT-T15 pancreatic β -cells. Blood glucose levels in alloxan-induced type 1 diabetes model mice were also significantly suppressed by feeding the mice with electrolyzed reduced water. These results suggest that electrolyzed reduced water can prevent apoptosis of pancreatic β -cells and the development of symptoms in type 1 diabetes model mice by alleviating the alloxan-derived generation of reactive oxygen species.

Introduction.

Diabetes mellitus (DM) is classified into two major types, type 1 (T1DM) and type 2 (T2DM) (Kuzuya et al. 2002). DM is a metabolic disease characterized by chronic hyperglycemia, and is recognized as one of the major health problems in today's society. Thirty thousand people are reported to be diagnosed with T1DM every year and several million people are affected worldwide (Bresson and von Herrath 2007). Apoptosis is believed to cause pancreatic β -cell loss in T1DM, while apoptosis or necrosis is implicated in T2DM (Cnop et al. 2005). In the case of T1DM, β -cell loss by apoptosis causes insulin deficiency leading to hyperglycemia, which often results in life threatening complications (Cnop et al. 2005).

It has been reported that, under hyperglycemic conditions, oxidative stress by free radicals is markedly increased in tissues (Valko et al. 2007). In particular, pancreatic β -cells are highly sensitive to reactive oxygen species (ROS) attack because of their low expression of antioxidant enzyme genes which results in low levels of catalase, glutathione peroxidase and superoxide dismutase (SOD) activities (Lenzen et al. 1996; Sigfrid et al. 2004). In addition, several studies have suggested that ROS plays an important role in contributing to β -cell dysfunction and disease progression through direct free radical-mediated oxidative damage to bio-molecules including DNA, which leads to apoptosis, and causes various forms of tissue damage (Takasu et al. 1991; Kaneto et al. 1996; Pennathur and Heinecke 2007). These results indicate that ROS are the major triggering molecules to induce apoptosis in pancreatic β -cells.

Therefore, the control of ROS levels could be the first step in preventing or reversing DM. In support of this idea, many reports suggest that ROS toxicity may be circumvented by overexpression of mitochondrial catalase and/or SOD in insulin-producing cells (Lortz and Tiedge 2003; Gurgul et al. 2004; Lortz et al. 2005).

In recent years electrolyzed reduced water (ERW) has attracted increasing attention because it has been shown to possess antioxidative effects by functioning as a free-radical scavenger. ERW scavenged ROS in vitro and protected DNA from oxidative damage (Shirahata et al. 1997), stimulating glucose uptake by muscle cells and adipocytes (Oda et al. 1999). It was demonstrated that ERW scavenged intracellular ROS, inhibited the decrease of pancreatic β -cell viability and enhanced glucose-stimulated insulin secretion in pancreatic β -cells damaged by alloxan (ALX) (Li et al. 2002). In addition, it was reported that ERW prepared from tap water could elevate blood insulin level as well as other indexes in genetically diabetic db/db mice, a model of human T2DM (Kim and Kim 2006). Thus ERW as a new ROS scavenger may be expected to show therapeutic efficacy against diabetes mellitus in general.

Discussion

Recently, hydrogen molecules have been reported to prevent various oxidative stress-related diseases (Ohsawa et al. 2006; Fukuda et al. 2007; Hayashida et al. 2007), suggesting that hydrogen molecules may participate in the anti-diabetes effect of ERW. The present study suggests that ERW can scavenge ROS and enhance anti-oxidant status in cells and animals, which then prevents ALX-induced apoptotic β -cell death and the development of diabetes in experimental animals.

PMID: 21063772 [PubMed] PMCID: PMC3080478

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SUPPLEMENTATION OF HYDROGEN-RICH WATER IMPROVES LIPID AND GLUCOSE METABOLISM IN PATIENTS WITH TYPE 2 DIABETES OR IMPAIRED GLUCOSE TOLERANCE

Nutr Res. 2008 Mar;28(3):137-43. doi: 10.1016/j.nutres.2008.01.008.

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.

Source

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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 [PubMed - indexed for MEDLINE]

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REDUCED HEMODIALYSIS-INDUCED OXIDATIVE STRESS IN END-STAGE RENAL DISEASE PATIENTS BY ELECTROLYZED REDUCED WATER

Kidney Int. 2003 Aug;64(2):704-14.
Huang KC, Yang CC, Lee KT, Chien CT.

Source:

Department of Family Medicine, National Taiwan University College of Medicine and National Taiwan University Hospital, Taipei, Taiwan.

Abstract

BACKGROUND: Increased oxidative stress in end-stage renal disease (ESRD) patients may oxidize macromolecules and consequently lead to cardiovascular events during chronic hemodialysis. Electrolyzed reduced water (ERW) with reactive oxygen species (ROS) scavenging ability may have a potential effect on reduction of hemodialysis-induced oxidative stress in ESRD patients.

METHODS: We developed a chemiluminescence emission spectrum and high-performance liquid chromatography analysis to assess the effect of ERW replacement on plasma ROS (H₂O₂ and HOCl) scavenging activity and oxidized lipid or protein production in ESRD patients undergoing hemodialysis. Oxidized markers, dityrosine, methylguanidine, and phosphatidylcholine hydroperoxide, and inflammatory markers, interleukin 6 (IL-6), and C-reactive protein (CRP) were determined.

RESULTS: Although hemodialysis efficiently removes dityrosine and creatinine, hemodialysis increased oxidative stress, including phosphatidylcholine hydroperoxide, and methylguanidine. Hemodialysis reduced the plasma ROS scavenging activity, as shown by the augmented reference H₂O₂ and HOCl counts (Rh₂o₂ and Rhocl, respectively) and decreased antioxidative activity (expressed as total antioxidant status in this study). ERW administration diminished hemodialysis-enhanced Rh₂o₂ and Rhocl, minimized oxidized and inflammatory markers (CRP and IL-6), and partly restored total antioxidant status during 1-month treatment.

CONCLUSION: This study demonstrates that hemodialysis with ERW administration may efficiently increase the H₂O₂- and HOCl-dependent antioxidant defense and reduce H₂O₂- and HOCl-induced oxidative stress.

PMID:12846769 [PubMed - indexed for MEDLINE]

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ELECTROLYZED-REDUCED WATER REDUCED HEMODIALYSIS-INDUCED ERYTHROCYTE IMPAIRMENT IN END-STAGE RENAL DISEASE PATIENTS

Kidney Int. 2006 Jul;70(2):391-8. Epub 2006 Jun 7.

Huang KC, Yang CC, Hsu SP, Lee KT, Liu HW, Morisawa S, Otsubo K, Chien CT.

Source:

Department of Family Medicine, National Taiwan University College of Medicine and National Taiwan University Hospital, Taipei, Taiwan.

Abstract

Chronic hemodialysis (HD) patients increase erythrocyte susceptibility to hemolysis and impair cell survival. We explored whether electrolyte-reduced water (ERW) could palliate HD-evoked erythrocyte impairment and anemia. Forty-three patients undergoing chronic HD were enrolled and received ERW administration for 6 month. We evaluated oxidative stress in blood and plasma, erythrocyte methemoglobin (metHb)/ferricyanide reductase activity, plasma metHb, and proinflammatory cytokines in the chronic HD patients without treatment (n=15) or with vitamin C (VC)- (n=15), vitamin E (VE)-coated dialyzer (n=15), or ERW treatment (n=15) during an HD course. The patients showed marked increases (15-fold) in blood reactive oxygen species, mostly H₂O₂, after HD without any treatment. HD resulted in decreased plasma VC, total antioxidant status, and erythrocyte metHb/ferricyanide reductase activity and increased erythrocyte levels of phosphatidylcholine hydroperoxide (PCOOH) and plasma metHb. Antioxidants treatment significantly palliated single HD course-induced oxidative stress, plasma and RBC PCOOH, and plasma metHb levels, and preserved erythrocyte metHb /ferricyanide reductase activity in an order VC>ERW>VE-coated dialyzer. However, ERW had no side effects of oxalate accumulation easily induced by VC. Six-month ERW treatment increased hematocrit and attenuated proinflammatory cytokines profile in the HD patients. In conclusion, ERW treatment administration is effective in palliating HD-evoked oxidative stress, as indicated by lipid peroxidation, hemolysis, and overexpression of proinflammatory cytokines in HD patients.

PMID:16760903 [PubMed - indexed for MEDLINE]

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INTAKE OF WATER WITH HIGH LEVELS OF DISSOLVED HYDROGEN (H₂) SUPPRESSES ISCHEMIA-INDUCED CARDIO-RENAL INJURY IN DAHL SALT-SENSITIVE RATS

Nephrol Dial Transplant. 2011 Jul;26(7):2112-8. doi: 10.1093/ndt/gfq727. Epub 2010 Dec 30
Zhu WJ, Nakayama M, Mori T, Nakayama K, Katoh J, Murata Y, Sato T, Kabayama S, Ito S.

Source:

Division of Nephrology, Endocrinology and Vascular Medicine, Graduate School of Medicine, Tohoku University, Sendai, Japan.

Abstract

BACKGROUND: Hydrogen (H₂) reportedly produces an antioxidative effect by quenching cytotoxic oxygen radicals. We studied the biological effects of water with dissolved H₂ on ischemia-induced cardio-renal injury in a rat model of chronic kidney disease (CKD).

METHODS: Dahl salt-sensitive rats (7 weeks old) were allowed ad libitum drinking of filtered water (FW: dissolved H₂, 0.00 ± 0.00 mg/L) or water with dissolved H₂ produced by electrolysis (EW: dissolved H₂, 0.35 ± 0.03 mg/L) for up to 6 weeks on a 0.5% salt diet. The rats then underwent ischemic reperfusion (I/R) of one kidney and were killed a week later for investigation of the contralateral kidney and the heart.

RESULTS: In the rats given FW, unilateral kidney I/R induced significant increases in plasma monocyte chemoattractant protein-1, methylglyoxal and blood urea nitrogen. Histologically, significant increases were found in glomerular adhesion, cardiac fibrosis, number of ED-1 (CD68)-positive cells and nitrotyrosine staining in the contralateral kidney and the heart. In rats given EW, those findings were significantly ameliorated and there were significant histological differences between rats given FW and those given EW.

CONCLUSION: Consumption of EW by ad libitum drinking has the potential to ameliorate ischemia-induced cardio-renal injury in CKD model rats. This indicates a novel strategy of applying H₂ produced by water electrolysis technology for the prevention of CKD cardio-renal syndrome.

PMID: 21193644 [PubMed - indexed for MEDLINE]

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ELECTROLYZED-REDUCED WATER DIALYSATE IMPROVES T-CELL DAMAGE IN END-STAGE RENAL DISEASE PATIENTS WITH CHRONIC HAEMODIALYSIS

Nephrol Dial Transplant. 2010 Aug;25(8):2730-7. doi: 10.1093/ndt/gfq082. Epub 2010 Feb 26.
Huang KC(1), Hsu SP, Yang CC, Ou-Yang P, Lee KT, Morisawa S, Otsubo K, Chien CT.

Source

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Abstract

BACKGROUND: T-cell damage by increased oxidative stress in end-stage renal disease (ESRD) patients undergoing chronic haemodialysis (HD) led to the increased T-cell apoptosis and the alteration of surface markers and Th1/Th2 ratio in CD4(+) T lymphocytes. Antioxidant electrolyzed-reduced water (ERW) was used as the dialysate in ESRD patients undergoing chronic HD to test for improved oxidative stress-related T-cell apoptosis, alterations of surface markers and intracellular cytokine profile.

METHODS: We evaluated apoptosis formation by annexin V, CD25-related surface markers, and cytokine ratio of Th1/Th2 in CD4(+) T lymphocytes and Tc1/Tc2 in CD8(+) T lymphocytes of 42 ESRD patients haemodialysed with ERW for 1 year.

RESULTS: In comparison to 12 healthy individuals, the ESRD patients had more T-cell apoptosis and less CD3(+), CD4(+) and CD8(+) T cells and CD25/CD69/CD94/CD3(+) phenotypes at baseline. Lower intracellular IL-2 and IFN-gamma levels in the Th1/CD4(+) and Tc1/CD8(+) cells and higher intracellular IL-4, IL-6 and IL-10 levels in the Th2/CD4(+) and Tc2/CD8(+) cells were also noted in the ESRD patients.

After a 1-year ERW treatment, the patients had a decrease in T-cell apoptosis and increases in CD3(+), CD4(+) and CD8(+) cell numbers and CD25/CD69/CD94/CD3(+) phenotypes in the T cells. The intracellular IL-2 and IFN-gamma levels in the Th1/Tc1 cells significantly ($P < 0.05$) increased and the intracellular IL-4, IL-6 and IL-10 levels in the Th2/Tc2 cells decreased. Furthermore, the Th1/Th2 and Tc1/Tc2 cytokine ratios were improved toward a normal status.

CONCLUSION: One-year ERW treatment effectively ameliorated T-cell apoptosis, altered CD25-related surface markers and intracellular cytokine profile in the HD patients.

PMID: 20190245 [PubMed - indexed for MEDLINE]

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