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A Clinical Trial of Orally Administered Alkaline Reduced Water

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Effects of alkaline reduced water (ARW) on the scavenging of reactive oxygen species (ROS) and diabetes were recently reported. However, no studies have yet been investigated on general drinking effects. In this study, we examined 100 patients hospitalized for senile disease treatment and recuperation. All examinees received the ARW for 2 months. WBC level was decreased from 6.34±1.9 ($\times 10^9$/L) to 5.66±1.7 ($\times 10^9$/L). SGPT level was decreased from 27.47±14 U/L to 23.95±8.8 U/L. Cholesterol level was increased from 167.9±32 mg/dl to 176.21±42 mg/dl within normal range. However, the levels of potassium, adiponectin, SGOT and blood pressure showed no significant difference. The levels of growth hormone and homocysteine and mini-mental state examination also showed no significant difference. We suppose that the slight blood parameter trends indicate an improved physical condition induced by the ARW. Furthermore, we could found no harmful effect of the ARW in this study.

Key Words: Alkaline reduced water, Blood parameter, Clinical investigation, Human

INTRODUCTION

In general, alkaline reduced water (ARW) generated at the negative cathode plate in a water electrolyzer pool, has a high alkalinity and low oxidation-reduction potential (ORP). Before ionization, the water is purified by charcoal, membrane and UV filters to remove impurities such as chloride, microorganisms, and harmful chemicals. During ionization, the alkaline water generated at the cathode has a high molecular hydrogen saturation. The acidic water generated at the anode has a high molecular oxygen saturation. Four OH^- ions and two H_2 molecules are generated from four H_2O molecules and our electrons reacting at the cathode. The alkaline water generated from the electrolyzer has a high density of positive ion minerals and a high deoxidization potential, due to the low ORP. ARW has a pH of 7.5~10 and an ORP-50 of ~-500 mV. Tap water is H 6~7 and ORP-100~300 mV.

Shirahata et al (1997) reported that reactive oxygen species (ROS) are removed from ARW and proposed the active hydrogen theory. His theory proposes that the active hydrogen in ARW functions similar to superoxide dismutase (SOD) in preventing DNA breakage caused by ROS, and is the initiative for experimental ARW trials. Hanaoka (2001) reported that ARW's effects don't originate from its anti-oxidative effects, but rather, its support of other antioxidants (Hanaoka, 2001). Prior to this, ARW's antioxidative effects were thought to be its most effective characteristic (Chen, et al., 2003; Feig et al., 1994; Reid and Loeb, 1992). ROS oxidative stress can aggravate several diseases, such as: cancer, diabetes, atopic dermatitis, hypertension, cardiovascular disease, liver disease, senile disease and dementias (Cai and Harrison, 2000; Eid et al., 2002; Kagawa et al., 1997; Kim et al., 2002; Rho and Kim, 2002; Saller et al., 2001; Sedeek et al., 2003; Zekry et al., 2003). The atomic hydrogen, ORP, H_2O cluster and alkalinity are all known to be important ARW functional elements. Among these, low degree ORP and hydrogen are presumed to be the biggest contributors to the antioxidative effect (Shirahata et al., 1997).

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Table 1. Age and sex distribution of the 100 patients

Sex \ Age	31~40	41~50	51~60	61~70	71~80	81~90	91~	Total
Female	0	1	4	11	19	23	4	62
Male	1	4	5	15	9	4	0	38
Total	1	5	9	16	28	27	4	100

Recent research has shown that ARW has diverse beneficial effects on diabetes, hyperlipidemia and abnormal intestinal fermentation (Lee et al., 2004; Park et al., 2004). Based on these and other ARW effects, its usage has spread into the food and agriculture industries. On the other hand, there have been continuous skeptical problems regarding the safety of oral ARW administration. AWR might enhance gastric secretion, thereby negatively affecting the stomach. Watanabe (1997) reported a pathologic change in rat cardiac muscle following oral ARW administration, and it seems that hyperkalemia might have been involved.

Until now, very few experiments have confirmed the clinical effects and safety of ARW. This experiment was performed to study several parameters related to oral ARW administration.

MATERIALS AND METHODS

1. Experimental group and oral ARW administration

In this study, we examined 100 patients (Table 1) hospitalized for senile disease treatment and recuperation in Gyeongbuk Geriatric Provincial Hospital, Andongshi, Korea. All examinees received 1.5 liters of ARW (pH 9.5, ORP -100 mV) a day for 2 months. The ARW was generated in an electrolyzer (BTM 500. Biontech Co. LTD).

2. Examination of blood parameters

Blood pressure was used as an evaluation of the patients' general condition. Each examinee had several blood parameters measure before and after ARW treatment. Electrolytes (kalium and potassium), liver enzymes [serum glutamic oxaloacetic transaminase (SGOT) and serum glutamic pyruvic transaminase (SGPT)], cholesterol, adiponectin and human growth hormone (HGH) were measured after blood centrifugation.

White blood cells (WBC) were measured by an automatic granular counter (XE-2100 Sysmex Co. Korea). Electrolytes were indirectly measured by ion selective electrodes (Hitachi ISE, Toshiba ISE, Japan). Liver enzymes were measured by a kinetic UV method, and cholesterol levels were measure by the cholesterol reagent enzyme method (Toshiba-200FR, Japan). Adiponectin was detected by a cobra II counter (Packard, USA) after radioimmunoassay with the RIA kit (Linco Research. Inc., USA). Human Growth Hormone (HGH) was also detected on a cobra II counter after immunoradiometric assay (IRMA) with the Daiich GH Kit (TFB, Japan). Homocysteine was detected by Axsym (Abbott, USA) with a fluorescence polarization immunoassay (FPIA) and the appropriate homocysteine reagents (Abbot, USA).

3. The mental state evaluation

The Korean mini-mental state examination (K-MMSE) score was used to evaluate the mental recognition in aged dementia patients. The K-MMSE is designed to evaluate memory, verbal, counting and concentration abilities (Lee, 2001). A perfect K-MMSE score is 30, and a score less than 24 is reason to infer dementia.

4. Statistical analysis

The data was analyzed by Sigma Plot 7.0 using the Student's t-test.

RESULTS

1. Blood parameter changes after oral ARW administration

The white blood cell (WBC) count had a decreasing trend [6.34±1.9 ($\times 10^9$/L) to 5.66±1.7 ($\times 10^9$/L)] following two months of ARW treatment (Fig. 1). Potassium levels were no different (3.98±0.3 mmol/L before and 3.95±0.3 mmol/L after) (Fig. 2). SGOT (a liver enzyme) levels were not significantly different, going from 21.26±5.2 U/L before to 21.37±5.8 U/L after treatment. SGPT levels decreased slightly from 27.47±14 U/L to 23.95±8.8 U/L (Fig. 3). Adiponectin was 14.87±8.23 μg/ml before and 15.11± 8.49 μg/ml after ARW treatment (Fig. 4). Cholesterol levels

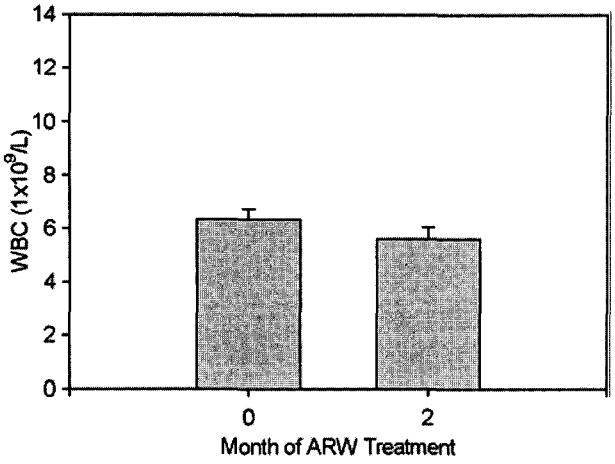

Fig. 1. Peripheral blood mean WBC after ARW treatment. Bar indicates mean ± standard deviation (n=19).

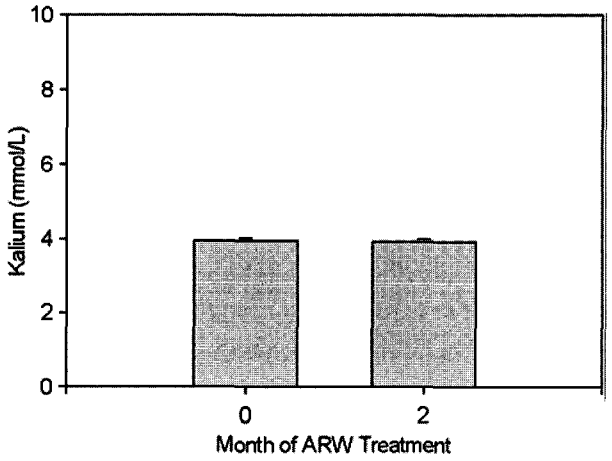

Fig. 2. Serum kalium levels after ARW treatment. Bar indicates mean ± standard deviation (n=19).

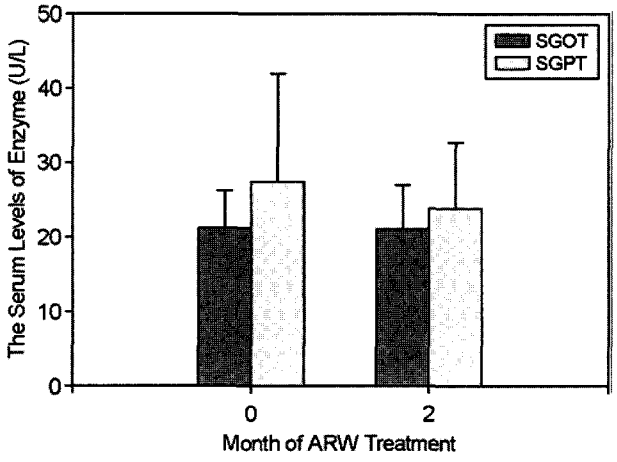

Fig. 3. Serum SGOT and SGPT changes after ARW treatment. Bar indicates mean ± standard deviation (n=19).

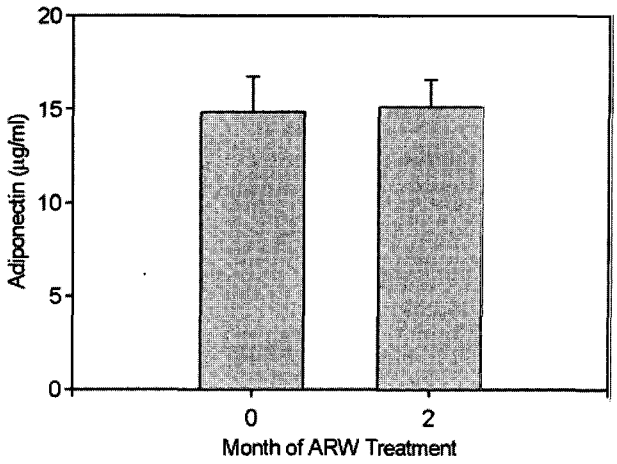

Fig. 4. Serum adiponectin concentrations after ARW treatment. Bar indicates mean ± standard deviation (n=19).

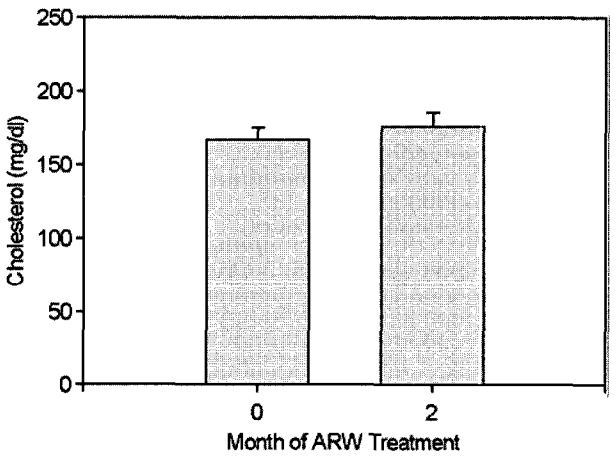

Fig. 5. Serum cholesterol levels after ARW treatment. Bar indicates mean ± standard deviation (n=19).

appeared to increase slightly from 167.9±32 mg/dl to 176.21±42 mg/dl, though this is within the normal range (Fig. 5). Human growth hormone (HGH) was found to be 1.55±1.83 mg/ml before and 1.75±2.71 mg/ml after, again showing no significant difference (Fig. 6). Both systolic and diastolic blood pressure remained stable. The systolic blood pressure was 126.84±12.0 mmHg before and 124.74±9.05 mmHg after treatment. Diastolic was 73.16±8.2 mmHg before and 71.58±6.02 mmHg after treatment (Fig. 7). Homocysteine was 15.94±7.20 μmol/L before and 16.96± 7.73 μmol/L after treatment (Fig. 8).

2. The K-MMSE score

The K-MMSE score was 17.68±7.34 before ARW treatment. After two months of ARW treatment the K-MMSE

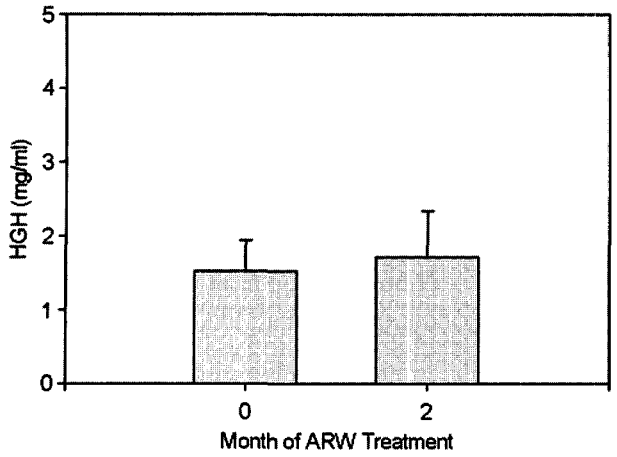

Fig. 6. Serum human growth hormone levels after ARW treatment. Bar indicates mean ± standard deviation (n=20).

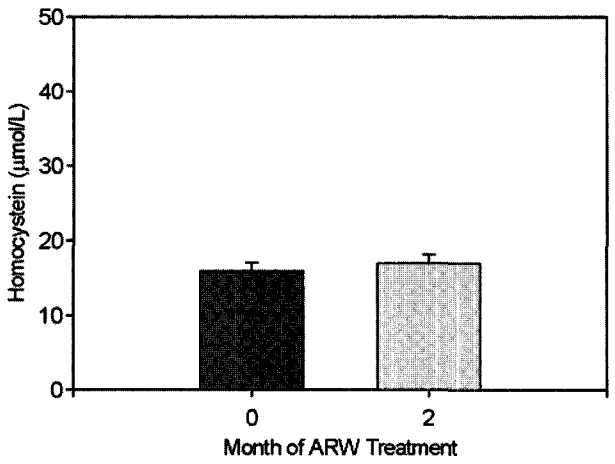

Fig. 8. Serum homocysteine concentrations after ARW treatment. Bar indicates mean ± standard deviation (n=45).

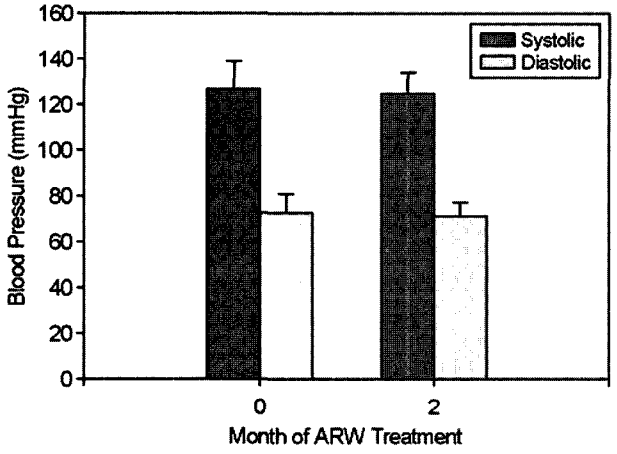

Fig. 7. Systolic and diastolic blood pressure change after ARW treatment. Bar indicates mean ± standard deviation (n=19).

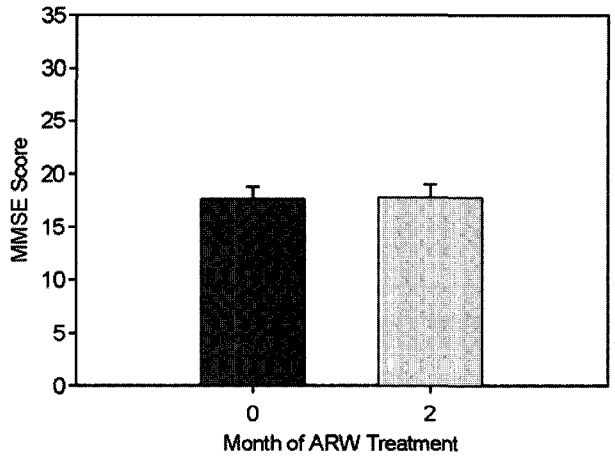

Fig. 9. Mini-mental state examination (MMSE) scores after ARW treatment. Bar indicates mean ± standard deviation (n=38).

scores were not significantly different (17.79±7.63) (Fig. 9).

DISCUSSION

Leading a healthy life is of common interest in modern society. Oral ARW administration began in Japan and has been used for medical materials both in Japan and Korea for decades. Drinking ARW is increasing in popularity as new information on its positive biological effects is elucidated. ARW's primary beneficial mechanism is as an antioxidant (Chen et al., 2003; Feig et al., 1994; Hanaoka, 2001; Reid and Loeb, 1992; Shirahata et al., 1997). In general, ROS are essential to life and disappear when they react. A ROS overdose can damage the human body and induce the development of several diseases (Cai and Harrison, 2000; Eid et al., 2002; Kagawa et al., 1997; Kim et al., 2002; Rho and Kim, 2002; Saller et al., 2001; Sedeek et al., 2003; Zekry et al., 2003). Although a conjecture has been made relating ARW to beneficial effects on several diseases, no clinical trial on the safety and general effects of ARW has been done. This research followed several basic wellness parameters after oral ARW administration. Though most of the data didn't change significantly, we were able to estimate the general effects by comparison to prior research and reports.

ARW has several features that make it distinct from general purified drinking water, such as small H_2O cluster size and high H_2 density. Given the nature of the ARW H_2O cluster, ARW could pass through the smallest spaces at high speed, thus eliminating bodily waste. Recently, it has been

seen that ARW modulates intestinal immune function in an infected trematode (unpublished data). Because there are no added mineral or drug components in ARW, the water will at least not damage the human body and could have beneficial effects.

The serum WBC count showed a decreasing trend after ARW treatment in old-age hospitalized patients. WBC, including mast cells, plasma cells, monocytes and macrophages, is part of the immune response and can move to a reaction site. An increased WBC count, within the normal range, indicates inflammation. A decreased WBC count, within the normal range, shows an alleviation of symptoms and is a sign of a healthy condition. Potassium, a serum electrolyte, did not change with ARW treatment. Watanabe (1997) reported that oral ARW administration caused hyperkalemia and pathologic changes, such as WBC infiltration and heart muscle fibrosis in rats. Hyperkalemia is serious sign of risk in the aged, because it can cause ventricular fibrillation and atrioventricular blockage due to increasing intracellular potassium. This study showed normal potassium levels after ARW treatment for 2 months. Watanabe presumed that an increased metabolism due to oral ARW administration and organic substances in the ARW might cause hyperkalemia. In a mouse model, inflammation or histological differences were observed when compared to the control group after ARW oral administration (Yang et al., 2006). Our research suggests that the intake of different foods might adjust any electrolyte disequilibrium.

SGOT is found in the liver, heart, kidney, brain and muscle while SGPT is mainly found in the liver (Little, 1970). Both of these intracellular enzymes increase in response to liver inflammation and liver cell necrosis (Little, 1970; Yoon et al., 1981). There was no change in SGOT though SGPT showed a decreasing trend within the normal range. Thus drinking ARW does not influence liver function.

Adiponectin and cholesterol both tended to increase after ARW treatment. Adiponectin is a cytokine released from adipose tissue that oxidizes lipids in muscle. Low blood adiponectin levels are related to obesity, atherosclerosis and hyperlipidemia (Lee et al., 2005). Cholesterol is involved in hormone synthesis, cellular maintenance, glucose metabolism, electrolyte balance, and sexual function. At high blood levels, however, it can cause atherosclerosis and cardiovascular disorder (Connor et al., 1994; Hayek et al., 1995). Cholesterol is supplied extrinsically (food intake) and intrinsically (synthesis in the liver, adrenal gland, and other organs). The amount of cholesterol synthesis in liver depends on extrinsic cholesterol. Insufficient extrinsic cholesterol results in enhanced liver cholesterol formation, HMG-CoA reductase elevation and increased LDL receptor production (Kienle et al., 1973; Watkinson et al., 1971). The slightly increasing cholesterol levels, within normal range, are conjectured to be a compensation for the decreased cholesterol from adiponectin lipid oxidation. We saw reduced serum cholesterol in OLETF rats after 8 months of ARW treatment (Jin et al., 2006). We also saw similar liver lipid metabolism results in broiler chickens after a one-month ARW treatment. RT-PCR for HMG-CoA reductase, (a cholesterol synthesis enzyme) and CYP7A1 (a cholesterol digestion enzyme) were liver lipid metabolism markers. While serum cholesterol decreased, HMG-CoA reductase mRNA increased and CYP7A1 mRNA did not change (Unpublished data). ARW might reduce serum cholesterol and compensate for a lack of cholesterol synthesis due to an HMG-CoA reductase increase.

HGH is involved in protein synthesis, energy production and organ development, thus, it is a concern in aging and lipid degradation (Rogol, 1989). After ARW treatment, a slight increase in serum HGH was found, suggesting an increase in lipid degradation. Both systolic and diastolic blood pressure decreased within the normal range after 2 months of ARW treatment. Dementia results in chronic cognitive function failure. The MMSE (mini-mental state examination) is carried out to understand the degree of dementia (Garcia and Zanibbi, 2004; Lee, 2001). Homocysteine, a methionine metabolite related to brain atrophy, atherosclerosis and Alzheimer's disease, increases in progressive dementia (Ellinson et al., 2004; Garcia and Zanibbi, 2004; Welch and Loscalzo, 1998). Neither a positive nor negative effect on dementia as measured by K-MMSE and homocysteine was observed.

We found that there were neither distinct beneficial nor harmful effects in aged patients due to ARW. All blood parameters measured in this study were within the normal range and differences were not statistically significant. Based on these results, ARW does not induce any bad effects and might lead to a favorable body condition. Until now, only limited data on the clinical effects of ARW oral administration has been available. Further clinical trials are therefore needed.

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