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CLINICAL STUDY

Effects of complete water fasting and regeneration diet on kidney function, oxidative stress and antioxidants

Mojto V[1], Gvozdjakova A[2], Kucharska J[2], Rausova Z[2], Vancova O[2], Valuch J[3]

3rd Department of Internal Medicine, Faculty of Medicine, Comenius University and University Hospital Bratislava, Slovakia. **viliam.mojto@gmail.com**

ABSTRACT

OBJECTIVE: The aim of the study was to observe the influence of 11-days complete water fasting (WF) and regeneration diet (RD) on renal function, body weight, blood pressure and oxidative stress.

BACKGROUND: Therapeutic WF is considered a healing method.

METHODS: Ten volunteers drank only water for 11 days, followed by RD for the next 11 days. Data on body weight, blood pressure, kidney functions, antioxidants, lipid peroxidation, cholesterols, triacylglycerols and selected biochemical parameters were obtained.

RESULTS: WF increased uric acid and creatinine and decreased glomerular filtration rate. After RD, the parameters were comparable to baseline values. Urea was not affected. Lipid peroxidation (TBARS) decreased and maintained stable after RD. Fasting decreased α-tocopherol and increased γ-tocopherol, no significant changes were found after RD. Coenzyme Q_{10} decreased after RD. HDL-cholesterol decreased in WF. Total- and LDL-cholesterol decreased after RD. Other biochemical parameters were within the range of reference values.

CONCLUSIONS: The effect of the complete fasting on kidney function was manifested by hyperuricemia. Renal function was slightly decreased, however maintained within the reference values. After RD, it returned to baseline values. The positive effect of the complete water fasting was in the reduction of oxidative stress, body weight and blood pressure *(Tab. 3, Ref. 25)*. Text in PDF *www.elis.sk.*

KEY WORDS: antioxidants, body weight, complete water fasting, kidney function, oxidative stress, regeneration diet.

Introduction

Therapeutic water fasting (WF) ranges from several days to a few weeks of a complete abstinence from food intake and drinking only water. The onset of organism regeneration begins after the end of fasting and lasts at least as long as the fasting time. Fasting for medical purposes has been used since ancient times, but the concept of ”fasting dietary therapy“ was introduced in Russia by Dr. Yuri S. Nikolayev. Since the early 1950ies, it has been used in specialised hospitals (1). Longo and Mattson recommended therapeutic WF regarding human life extension (2). Therapeutic WF is considered to be a healing process, when the human body is adapted to endogenous nutrition, living at the expense of own reserves, mobilizing the body defences. It is responsible for removing fat, salt, old and diseased cells, body cleansing, regenerating body organs and systems. Therapeutic WF is used for mental health and mental disorders, in cardiovascular diseases, asthma, indigestion, intestinal infections, rheumatology, endocrinology, toxicology (alcoholism, smoking, and drugs), and obesity (3, 4). However, nutrition experts have different opinions on WF in the healthy and sick organism.

During the complete WF, the liver enzymes for the storage of glycogen are reducing, while the synthesis of enzymes providing gluconeogenesis is increasing. Over the next days, the body is activating defence and adaptation mechanisms, protecting proteins and minimizing the loss of essential trace elements. Induction of autolytic enzyme-utilization and ketone bodies instead of glucose occurs in the brain (5).

Side effects of complete WF, such as headaches, nausea, and feeling of weakness can occur during acidosis due to lowering the alkaline reserves in the body. The phagocytic activity of leukocytes gradually increases, removing worn-out and diseased cells and the body is regenerated. During the first days of WF, acidosis is increased and the so-called acidic crisis culminates. After this crisis, between days 7–14, acidosis and weakness slightly decrease, the concentration of glucose in urine increases and a decrease in concentrations of acetone and ammonia occurs (6). Once the acidotic crisis is over, pH decreases, and the blood glucose level increases, glucose being produced by the body from its supplies

[1]3rd Department of Internal Medicine, Faculty of Medicine, Comenius University and University Hospital Bratislava, Slovakia, [2]Pharmacobiochemical Laboratory of 3rd Department of Internal Medicine, Faculty of Medicine, Comenius University Bratislava, Slovakia, and [3]Medico-Legal Workplace, Health Care Surveillance Authority, Bratislava, Slovakia

Address for correspondence: V. Mojto, MD, PhD, MHA, 3rd Department of Internal Medicine, Faculty of Medicine, Comenius University and University Hospital Bratislava, Limbova 5, SK-833 05 Bratislava, Slovakia. Phone: +421.2.59542349

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of fat and protein. The metabolism improves and ketones in the blood decrease. Acidosis is then maintained at the same level, with only small fluctuations.

Contraindications of WF may include malignant tumours, leukaemia, liver cirrhosis, renal impairment, diseases of the central nervous system, acute appendicitis, colitis, various cysts, gangrene, and a severe form of tuberculosis, states of exhaustion, cachexia in older adults, pregnancy, breastfeeding, and immobility in any disease (7).

The aim of the study

The aim of this study was to obtain the effects of the complete 11 days WF and 11 days regeneration diet (RD) on the kidney function, body weight, blood pressure, glucose, oxidative stress, selected antioxidants, lipid fractions, and metabolic parameters in human subjects.

Subjects and methods

Ten human subjects staying in a spa for 15 days were included in the complete WF (drinking only water) for 11 days followed by the regeneration diet (1) for 4 days. The rest of the days of regeneration diet continued at home under supervision. The group included five men, the mean age 46.4 years (range 31–58 years) and five women, the mean age 53.6 years (range 44–63 years). All medication was discontinued (antihypertensives, statins, drugs for coxarthrosis and hypothyreosis). Subjects were instructed to walk 6–10 km daily, swim and get massages. Body weight, blood pressure, glucose, kidney functions (creatinine, uric acid, urea and glomerular filtration), antioxidants (coenzyme $Q_{10\text{-TOTAL}}$ ($CoQ_{10\text{-TOTAL}}$), γ-tocopherol, α-tocopherol), lipid peroxidation (TBARS – oxidative stress parameter) and lipid fractions were monitored three times (before and after WF and after regeneration) during the study.

All human subjects involved in the complete WF signed the informed consent.

Metabolic parameters

Kidney functions (urea and uric acid) were measured spectrophotometrically with Roche kinetic test. Creatinine was measured by the kinetic – colorimetric methods, Jaffe reaction. Antioxidants ($CoQ_{10\text{-TOTAL}}$, α-tocopherol and γ-tocopherol) were measured by HPLC method (8, 9, 10), with UV detection at 275 nm and 295 nm, lipid peroxidation spectrophotometrically (11), total cholesterol, LDL-cholesterol, HDL-cholesterol and triacylglycerols by enzymatic colorimetric methods. Na, K, Cl were measured with ISE (Ion selective electrode) by indirect potentiometry, AST, ALT, GMT, ALP by the spectrophotometric method.

Statistical analysis

Multiple one-way analysis of variance (ANOVA) with Bonferroni correction was used. Statistical significance: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ were evaluated; WF vs baseline values (a), regeneration diet vs baseline values (b) and regeneration diet vs WF (c).

Results

The effects of 11-days complete WF and RD on selected parameters (body weight, systolic and diastolic blood pressure, glucose, total proteins, total bilirubin, CRP (C-reactive protein), CK (creatine kinase), sodium, potassium, chlorides, AST, ALT, GMT and ALP) are shown in the Table 1.

The complete WF decreased glucose ($p < 0.0019$), systolic blood pressure ($p < 0.001$) (Tab. 1) and TBARS ($p < 0.015$) (Tab. 2). In the last case, the values maintained stable also after RD. The complete WF increased serum creatinine from the baseline values 45.49 ± 2.87 to 73.82 ± 3.83 μmol/l ($p < 0.0002$), after regeneration they returned to the baseline values, however, they maintained within the reference values. Uric acid was increased from the baseline values 295.48 ± 29.69 μmol/l to 821.78 ± 41.82 μmol/l after the complete WF ($p < 0.0001$) and returned to the baseline values after the regeneration diet (Tab. 2). The concen-

Tab. 1. Effect of 11-days complete water fasting and regeneration diet on selected parameters.

	Reference values	Baseline	Complete water fasting	Regeneration diet
Body weight (kg)		76.6±4.83^{b***}	69.5±4.52^{a***}	70.3±4.39
SBP (mmHg)	90–120	125±3	111±2^{a**}	117±4
DBP (mmHg)	80–60	80±2^{b*}	74±2^{a**}	75±3
Glucose (mmol/l)	3.30–5.59	3.45±0.16	2.69±0.12^{a**}	3.71±0.15^{c***}
Total proteins (g/l)	57–83	75.20±0.98^{b***}	73.30±1.05	66.80±1.14^{c***}
Total bilirubin (μmol/l)	4–22	18.50±2.69^{b**}	21.20±2.53	7.86±0.96^{c***}
CRP (mg/l)	0–5	2.77±0.80^{b*}	2.48±1.07	0.58±0.17
CK (μkat/l)	0.42–3.25	2.67±0.45	4.05±0.95	3.46±0.97
Sodium (mmol/l)	135–145	138.40±0.32	134.0±0.90^{a**}	139.6±0.33^{c***}
Potassium (mmol/l)	3.60–5.30	5.24±0.09	3.92±0.08^{a***}	5.05±0.18^{c***}
Chlorides (mmol/l)	97–111	100.4±0.59^{b*}	94.0±0.91^{a***}	104.1±0.86^{c***}
AST (μkat/l)	0.20–0.71	0.455±0.06	0.706±0.15	0.434±0.05
ALT (μkat/l)	0.13–0.95	0.516±0.10	0.780±0.24	0.506±0.09
GMT (μkat/l)	0–1.13	0.518±0.09^{b*}	0.412±0.06	0.295±0.05
ALP (μkat/l)	0.67–2.15	1.203±0.12	1.478±0.32	0.931±0.08

SBP – systolic blood pressure, DBP – diastolic blood pressure, CRP – C-reactive protein, CK – creatine kinase, AST – aspartate transferase, ALT – alanine aminotransferase, ALP – alkaline phosphatase, GMT – gamma-glutamyltransferase; Statistics: paired Student´s t-test; a = water fasting vs baseline; b = regeneration vs baseline; c = regeneration vs water fasting; * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

Tab. 2. Effect of 11-days complete water fasting and regeneration diet on kidney function, oxidative stress, antioxidants and lipid fractions.

	Reference values	Baseline	Water fasting	Regeneration diet
Kidney function				
Creatinine (μmol/l)	42–100	45.49±3.02	73.82±3.83[a***]	46.24±5.63[c***]
Uric acid (μmol/l)	135–420	295.48±29.69	821.78±41.82[a***]	221.31±24.7[c***]
Urea (mmol/l)	2.0–7.8	3.539±0.74	3.499±1.11	3.481±0.97
GFR (ml/s)	1.15–2	1.868±0.19	1.324±0.03[a***]	1.814±0.09
Oxidative stress				
TBARS (μmol/l)	<4.5	5.14±0.22[b*]	4.53±0.20[a*]	4.77±0.14
Antioxidants				
Coenzyme Q_{10} – total (μmol/l)	0.4–1.0	0.655±0.06[b**]	0.623±0.05	0.420±0.04[c**]
α-tocopherol (μmol/l)	15–40	36.0±1.37[b**]	28.3±1.25[a***]	27.6±1.73
γ-tocopherol (μmol/l)	2.0–7.0	3.74±0.27[b*]	6.30±1.04[a*]	5.50±0.66
Lipid fractions				
Cholesterol (mmol/l)	3.2–5.0	5.892±0.39[b*]	6.159±0.46	4.739±0.38[c*]
HDL (mmol/l)	1.0–2.20	1.468±0.09[b*]	1.164±0.08[a*]	1.205±0.08
LDL (mmol/l)	1.0–3.0	4.437±0.41[b*]	4.925±0.48	3.314±0.34[c***]
TAG (mmol/l)	0.4–1.82	1.086±0.17	1.095±0.09	1.030±0.13

GFR – Glomerular filtration rate, TBARS – thiobarbituric acid reactive substances; HDL – high-density lipoprotein, LDL – low-density lipoprotein, TAG – triacylglycerols, Statistics: paired Student´s t-test; a = water fasting vs baseline; b = regeneration vs baseline; c = regeneration vs water fasting; * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

tration of urea was not affected. GFR was decreased ($p < 0.001$) after the complete WF, which may be related to the reduction in muscle mass and returned to the baseline values after regeneration. Alpha-tocopherol decreased after the complete WF ($p < 0.001$) and maintained reduced also after RD ($p < 0.002$). Conversely, γ-tocopherol increased after WF ($p < 0.005$) and maintained elevated after RD. Coenzyme $Q_{10\text{-TOTAL}}$ concentration was reduced after WF and after RD ($p < 0.01$) (Tab. 2).

The concentration of HDL-cholesterol was decreased after WF and diet. Total cholesterol and LDL-cholesterol were increased after WF and decreased after RD, and triacylglycerols were not affected (Tab. 2).

Discussion

The complete WF as a healing method has had its supporters and opponents over the whole human history. It was considered a panacea, but at the same time, many people denied it and some still deny its effects. Almost all the ancient nations considered abstention from food as the best way of cleansing the body and spirit. Hippocrates (460–370 B.C.) pointed out the diet therapy as one of the main ways of treating patients. He argued that food should be considered our medicine. He paid close attention to lifestyle. In the 20th century, with increasing technical achievements, scientists and physicians studied medicinal effects of complete WF in more detail. The interest in this method increased. The method of therapeutic WF involves a period of complete WF and also RD, which lasts at least as long as the complete WF. The right foods supply is essential in the regeneration diet after the complete WF. Suggested kinds of food are shown in the Table 3. The therapeutic WF also includes suitable physical activities, exercising, walking and hiking.

Numerous scientific experiments on the effect of complete WF on the body have been carried out (3). Longo with colleagues recommended the therapeutic WF for extending human life and as a prevention of cancer (3, 2). Rizza connects the restriction of caloric intake with longevity (12), though some studies suggest that obesity is connected with life expectancy (13). According to

Tab. 3. Regeneration diet after complete water fasting (1).

Food (g)/Days	Regeneration diet						
	1	2–3	4–5	6–7	8–10	11–15	16–30
Juices: carrot, apple, grape	500	1000	500	600	–	–	–
Grated fruits	–	–	500	600	450	375	500
Grated carrots	–	–	250	600	300	200	–
Kefir, buttermilk	–	–	–	–	300	400	600
Vegetable soup with rice	–	–	200	400	700	700	700
Honey	–	–	–	40	60	60	75
Nuts	–	–	–	–	70	100	100
Brown bread	–	–	–	–	100	300	400
Vinegret salad: (beetroot, onion, potatoes, carrots, pickles)	–	–	–	300	400	400	500
Vegetable fat, oil	–	–	–	–	15	15	30
Custard	–	–	–	150	200	200	200
Raw vegetable salad	–	–	–	–	400	400	400
Fresh butter	–	–	–	–	20	20	20

Speakman, restriction of caloric intake reduces oxidative stress and enhances autophagy (14).

Some participants of our study reported subjective symptoms, such as hunger, headache and nausea occurring on days 2–4 of the complete WF. These subjective difficulties were sought to be avoided by walking in the fresh air, breathing exercises to intensify lung ventilation, enhance breathing out ketones more intensively and alleviate symptoms of acidosis. For these purposes, also enemas were applied, as well as baths in the thermal water. In some subjects, food excitation appeared on days 2–3 of WF, activation of the memories of the meals, after soundscapes, such as those of clashing cutlery.

The complete WF leads to two characteristic changes in kidney function: a reduction in glomerular filtration rate and a decrease in renal uric acid clearance by the impairment of tubular uric acid secretion with a consequent hyperuricemia. Formed ketone bodies compete with uric acid for a common tubular secretion site. Acetoacetic acid benzyl ester, beta-hydroxybutyric acid and acetone are known as ketone bodies. An increased urinary excretion of ketone bodies points to an increased lipolysis and increased production of acetyl-CoA, which, due to under-utilization of glucose in the absence of insulin, is normally metabolized in the Krebs cycle. This process results in the accumulation of acetyl-CoA, which condenses the acetoacetic acid. A greater part of acetoacetic acid in the liver is reduced to β-hydroxybutyric acid. The smaller part is spontaneously decarboxylated to acetone. The development of these renal complications was also described by Kirch and Gicycki (15). It is essential for the prophylaxis of renal complications during the complete WF to ensure that a sufficient fluid intake is maintained and the urinary output is controlled. Before the therapeutic WF is commenced, parameters of renal function (urinalysis, blood urea, serum creatinine, serum uric acid) must be determined and then monitored at regular intervals. After the complete WF has commenced, the administration of uricosuric agents must be avoided and intravenous pyelography is contraindicated (15). Zürcher et al. reported two cases of acute urate nephropathy during WF for body weight reduction. Under these conditions, ketoacidosis causes an impaired renal uric acid excretion and hyperuricemia (16).

Relatively few studies have focused on the effect of the complete WF and RD in volunteers. There is no information available in literature on the impact of the complete WF on renal function, selected antioxidants as $CoQ_{10\text{-TOTAL}}$, α- and γ-tocopherol and lipid peroxidation in volunteers. The results of our study were partially presented at the 52nd ERA-EDTA Congress (17).

Reduced kidney function was confirmed in the ten member group after 11-days complete WF by the decrease in estimated glomerular filtration rate (eGFR). Parameter eGFR returned to the baseline values after RD.

There was almost a threefold increase in uric acid after the complete WF – from 295.48 ± 28.2 μmol/l to 821.88 ± 39.7 μmol/l.

The complete WF caused a decrease in the concentration of α-tocopherol level. Conversely, γ-tocopherol concentration in plasma increased probably as the result of cytochrome P450 inhibition by ketone bodies in the liver during WF and remained elevated also after RD, but within the reference values.

Antioxidants such as tocopherols protect cells from free radicals that are linked with diabetes type 2, cardiovascular and other diseases (18). Coenzyme Q_{10} is the key component of the mitochondrial respiratory chain and it is essential for ATP production and protection of cells from free radical damage and premature ageing (19). Drop in the concentration below the reference level is manifested by a decreased energy, fatigue and reduced ability to regenerate (20). After RD, the concentrations of $CoQ_{10\text{-TOTAL}}$ were within the reference values. The complete WF significantly reduced the oxidative stress similarly to Speakman (16).

Lee et al. (21) suggested that multiple cycles of fasting promote differential stress sensitization in a wide range of tumours and could potentially replace or augment the efficacy of certain chemotherapy drugs in the treatment of various cancers.

The experimental work shows that 40 % calorie restriction for one month in aged rats stimulates the production of coenzyme Q in the mitochondria of liver, heart and kidneys and reduces the concentration of α-tocopherol (22). In another study, the concentration of α-tocopherol was reduced in the tissue, but the concentration of coenzyme Q was not affected by fasting. The authors suggested that an increased oxidative damage to mitochondria in older adults might be related to the lack of coenzyme Q and α-tocopherol (23).

It is known that coenzyme Q_9 is dominant in rats, whereas CoQ_{10} is dominant in humans. Daily calorie restriction by 40 % for one month stimulated the production of coenzyme Q_9 and Q_{10} in rat skeletal muscle. In the heart, the level of coenzyme Q_9 was reduced, whereas the level of CoQ_{10} was not affected. The authors suggested that coenzyme Q and COQ genes in tissues were the targets of calorie restriction, as reflected in the changes in the biosynthesis of coenzyme Q (24).

Further studies are needed to understand the effects and level of calorie restriction, the frequency of consumption of food as related to slowing down the ageing process and the prevention of diseases associated with an advanced age (25). Restriction of calorie intake lowers steady-state levels of oxidative stress and damage, retards age-associated changes and extends the maximum life span in mammals.

Conclusions

The complete WF enabled the volunteers to lose their body weight. Although the greater part of the body weight loss after WF was regained, their body weight did not return to the baseline before fasting. The complete 11-days WF lowered blood pressure, increased levels of uric acid. Increased creatinine, however, maintained within the reference values and parameter GFR was decreased, which may be related to the reduction in muscle mass.

The positive effect of the complete WF was reflected in the reduction of oxidative stress, body weight and blood pressure. The negative effect of complete WF results in the reduction of $CoQ_{10\text{-TOTAL}}$, α-tocopherol concentration and hyperuricemia. It remains questionable whether the positive effect that appeared directly during WF and after WF and RD can have a positive effect on the body, the function of various organs, especially the kidneys and the genetic potential of the organism in the long-term duration.

Since there are relatively few subjects involved in this study, further studies with more volunteers are needed to be carried out, focused on the examination of a number of metabolic parameters, particularly on the function of the brain, heart, liver, pancreas, kidneys, skeletal muscle and immunology.

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